



ctos[®]

2021 *Virtual* Annual Meeting

November 10 - 13, 2021

2021 CTOS President

Rick Haas, MD, PhD

2021 CTOS Program Chairs

Winan J. van Houdt, MD, PhD, MSc

Elizabeth G. Demicco, MD, PhD

Yen-Lin Chen, MD

Emanuela Palmerini, MD, PhD

Striving to unleash the potential of mTOR inhibition using precision medicine and nanoparticle albumin-bound technology.



Please attend these scientific oral sessions of accepted abstracts for the latest data on investigational *nab-sirolimus* in malignant PEComa

Friday, Nov 12
1:15 to 2:30 PM ET
(Session 8)

Final analysis from AMPECT, an open-label Phase 2 registration trial of *nab-sirolimus* for patients with advanced malignant perivascular epithelioid cell tumors (PEComa)

Abstract ID: 1080747

Saturday, Nov 13
1:15 to 2:30 PM ET
(Session 12)

Nab-sirolimus in patients with malignant PEComa previously treated with mTOR inhibitors: emerging experience from an expanded access program

Abstract ID: 1080984



Visit Aadi Bioscience Sponsor Profile Page



www.aadibio.com

Thank You

The Connective Tissue Oncology Society

greatly appreciates your support of the 2021 Annual Meeting. Your funding is vital and will advance the medical science and care of patients with bone and soft tissue tumors.

Platinum Sponsor



Gold Sponsors



Silver Sponsors



Bronze Sponsors



Special Thanks to:



Advenchen



Welcome to the 2021 CTOS Virtual Annual Meeting!

The summer of 2021 has passed and unfortunately, the COVID pandemic is still not completely over yet. While we all hoped we would be able to meet each other in Vancouver, we are very excited to present another informative and lively virtual meeting, November 10-13.

This year, we have tried our best to adapt the virtual meeting format by taking into account the different time zones, the experiences from last year as well as the hot topics in the multi-disciplinary sarcoma science and clinical practice. The meeting will include relatively short sessions that include pre-recorded presentations but longer live discussions with all the presenters. We hope that this format will encourage audience participation and interesting discussions while preventing screen time exhaustion after a couple of years of virtual meetings!

All the session topics and selected oral abstracts were carefully chosen to have a truly multi-disciplinary angle throughout the meeting in order to stimulate our collaboration and appreciate our sarcoma colleagues in other specialties.

This year, we would like to encourage more togetherness by organizing CTOS watch parties in your institution, region or country. Sharing photos and short videos of these parties are highly appreciated, and we hope this will give us a true appetite for the live meeting next year in Vancouver.

Thank you for your participation and expertise, we trust together we will have a truly inspirational meeting of high quality.

Sincerely,

2021 Program Chairs

Winan van Houdt MD, PhD, MS, Program Chair

Elizabeth Demicco, MD, PhD, Program Chair

Yen-Lin Chen, MD, Program Co-Chair

Emanuela Palmerini, MD, PhD, Program Co-Chair





ctos[®]



2021 *Board of Directors*

Rick Haas, MD, *President*
r.haas@nki.nl

William Tap, MD, *Vice President*
tapw@mskcc.org

Carol Swallow, MD, *Secretary*
Carol.Swallow@sinaihealthsystem.ca

Damon Reed, MD, *Treasurer*
Damon.Reed@moffitt.org

Kirsten Sundby Hall, MD, PhD, *Immediate Past President*
ksh@ous-hf.no

Elizabeth Demicco, MD, PhD (2019-2021)
elizabeth.demicco@gmail.com

Kevin Jones, MD (2019-2021)
kevin.jones@hci.utah.edu

Eugenie Kleinerman, MD (2019-2021)
ekleiner@mdanderson.org

Silvia Stacchiotti, MD (2019-2021)
silvia.stacchiotti@istitutotumori.mi.it

Maureen O'Sullivan, MD (2020-2022)
OSULLM10@tcd.ie

Dirk Strauss, MD (2020-2022)
Dirk.Strauss@rmh.nhs.uk

Robin Jones, MD (2020-2022)
robin.jones@doctors.org.uk

Winette van der Graaf, MD (2020-2022)
w.vd.graaf@nki.nl

Margaret von Mehren, MD (2021-2023)
margaret.vonmehren@fccc.edu

Bernd Kasper, MD, PhD (2021-2023)
bernd.kasper@medma.uni-heidelberg.de

E. Alejandro Sweet-Cordero, MD (2021-2023)
alejandro.sweet-cordero@ucsf.edu

Barbara Rapp, *Executive Director*
ctos@ctos.org



ctos[®]



2021 *Virtual* Annual Meeting

November 10 - 13, 2021

Schedule at a Glance

ALL TIMES ARE EASTERN STANDARD TIME (EST)

Tuesday, 9 November, 2021

10:00 AM - 12:00 PM **JOINT CTOS & SPAEN VIRTUAL KICK-OFF MEETING
"GLOBAL PATIENT INVOLVEMENT IN SARCOMA CARE"**

Wednesday, 10 November, 2021

8:00 AM - 12:00 PM **TARPSWG Meeting**

12:00 PM - 2:00 PM **Ultra Rare Sarcoma Meeting**

2:30 PM - 4:30 PM **SELNET Meeting: State of the Art of Management for Localized STS in Limbs
and Retroperitoneum**

Thursday, 11 November, 2021

9:00 AM - 9:15 AM **OPENING SESSION
INTRODUCTION TO CTOS 2021**
President: **Rick Haas, MD, PhD**
Program Chairs: **Winan van Houdt, MD PhD MSc, Elizabeth Demicco, MD, PhD,
Yen-Lin Chen, MD, Emanuela Palmerini, MD, PhD**

9:15 AM - 10:30 AM – Session 1 –
BIG DATA AND BIG SCIENCE
Chair: **Rebecca A. Gladdy, MD, PhD, FRCSC FACS**

10:30 AM - 11:00 AM – Session 2 –
COVID-19 AND SARCOMA
Chair: **Samuel J. Ford, PhD**

11:00 AM - 12:00 PM – Session 3 –
GIST
Chair: **Jason K. Sicklick, MD, FACS**

12:00 PM - 12:30 PM Break

12:30 PM - 1:15 PM **NINA AXELRAD LECTURE –
THE MARRIAGE BETWEEN SURGERY AND ONCOLOGY**
Allessandro Gronchi

Thursday, 11 November, 2021

1:15 PM - 2:30 PM	– Session 4 – BONE TUMORS Chair: Sandra Strauss, BA, MBBS, MRCP (UK), PhD
2:30 PM - 3:15 PM	POSTER SESSION 1 – (POSTERS 001-136)
3:15 PM - 3:30 PM	Break
3:30 PM - 5:30 PM	SARC Meeting
5:30 PM - 6:30 PM	Deciphera Symposium (Invite Only)
5:30 PM - 7:30 PM	Adaptimmune Symposium SPOTLIGHT ON SYNOVIAL SARCOMA: WHERE ARE WE NOW? WHAT NEXT?

Friday, 12 November, 2021

8:00 AM - 9:00 AM	CTOS Executive Committee
9:00 AM - 10:00 AM	– Session 5 – DIAGNOSTIC AND SURGICAL TECHNIQUES Chair: Peter Hohenberger, MS, PhD
10:00 AM - 11:00 AM	– Session 6 – IMMUNOTHERAPY & IMMUNE MICROENVIRONMENT Chair: Breelyn A. Wilky, MD
11:00 AM - 12:00 PM	– Session 7 – LOW GRADE AND INDOLENT TUMORS Chair: Bernd Kasper, MD
12:00 PM - 12:40 PM	Break
12:40 PM - 1:15 PM	– Young Investigator Awards –
1:15 PM - 2:30 PM	– Session 8 – ONCOLOGY AND CLINICAL TRIALS Chair: Herbert Loong, MBBS, PDipMDPath, MRCP, FRCP
2:30 PM - 3:15 PM	POSTER SESSION 2 – (POSTERS 138-261)
3:30 PM - 4:30 PM	Aadi Symposium THE CHALLENGES IN STUDYING RARE DISEASES: EMERGING THERAPIES FOR RARE SARCOMAS

Saturday, 13 November, 2021

8:00 AM - 9:00 AM	CTOS Board of Directors
9:00 AM - 10:15 AM	– Session 9 – MULTIDISCIPLINARY MANAGEMENT, NEOADJUVANT THERAPY & TREATMENT OF OLIGOMETASTATIC DISEASE Chair: Christina L. Roland, MD
10:15 AM - 11:00 AM	– Session 10 – QUALITY OF LIFE AND PATIENTS PERSPECTIVE Chair: Winette van der Graaf, MD, PhD

Saturday, 13 November, 2021

11:00 AM - 12:00 PM	– Session 11 – RETROPERITONEAL SARCOMA Chair: Elizabeth H. Baldini, MD, MPH
12:00 PM - 12:30 PM	Break
12:30 PM - 1:15 PM	HERMAN SUIT LECTURE – SARCOMA MODELING TOWARDS PATIENT SPECIFIC TREATMENT Judith V.M.G. Bovée, MD, PhD
1:15 PM - 2:30 PM	– Session 12 – ULTRA-RARE AND TRANSLOCATION SARCOMAS Chair: Thierry Alcindor, MD, MSc, FRCPC
2:30 PM - 2:45 PM	CTOS 2031; LOOKING BACK 10 YEARS Presenter: Rick L. Haas, MD, PhD, 2021 CTOS President
2:45 PM - 3:30 PM	CTOS Business Meeting

For US healthcare professionals.


Turalio[®]
pexidartinib ^{200 mg}
capsules

SEE WHAT'S
MOVING AT
CTOS | 2021

Learn more about **TURALIO**

Please see [Important Safety Information](#)
and full [Prescribing Information](#), including
Boxed WARNING, and Medication Guide
at TURALIOhcp.com

TURALIO[®] is a registered trademark of Daiichi Sankyo Company, Limited.
© 2021 Daiichi Sankyo, Inc. PP-US-TU-0738 09/21

 **Daiichi-Sankyo**



ctos[®]



2021 *Virtual* Annual Meeting

November 10 - 13, 2021

ALL TIMES ARE EASTERN STANDARD TIME (EST)

Tuesday, 9 November, 2021

10:00 AM - 12:00 PM **JOINT CTOS & SPAEN VIRTUAL KICK-OFF MEETING
"GLOBAL PATIENT INVOLVEMENT IN SARCOMA CARE"**

Wednesday, 10 November, 2021

8:00 AM - 12:00 PM **TARPSWG Meeting**
12:00 PM - 2:00 PM **Ultra Rare Sarcoma Meeting**
2:30 PM - 4:30 PM **SELNET Meeting: State of the Art of Management for Localized STS in Limbs
and Retroperitoneum**

Thursday, 11 November, 2021

9:00 AM - 9:15 AM **OPENING SESSION**
INTRODUCTION TO CTOS 2021
President: **Rick Haas, MD, PhD**
Program Chairs: **Winan van Houdt, MD PhD MSc, Elizabeth Demicco, MD, PhD,
Yen-Lin Chen, MD, Emanuela Palmerini, MD, PhD**

9:15 AM - 10:30 AM **– Session 1 –**
BIG DATA AND BIG SCIENCE
Chair: **Rebecca A. Gladdy, MD PhD FRCSC FACS**

9:15 AM - 9:22 AM
Paper #01 #1818715
3D GENOME STRUCTURAL ALTERATIONS AND ONCOGENE EXPRESSION IN CHORDOMA GENOMES
Kadir Akdemir; Khalida Wani; David R. Ingram; Wei-Lien Wang; Shaan M. Raza; Andrew J. Bishop; Christopher Alvarez-Breckenridge; Claudio Tatsui; Anthony P. Conley; Laurence D. Rhines; Andrew Futreal; Alexander Lazar
The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES

Thursday, 11 November, 2021

9:22 AM - 9:29 AM

Paper #02 #1818739

COMPARATIVE REVIEW OF HUMAN AND CANINE PERIPHERAL NERVE SHEATH TUMORS

Keila E. Torres¹; **Jace Landry**¹; Veena Kochat¹; Sharon M. Landers¹; Angela D. Bhalla¹; Rossana Lazcano¹; Lindsay Parker²; Tasha Miller²; David R. Ingram¹; Dominique Wiener²; Brian Davis²; Beth Boudreau²; Wei-Lien Wang¹; Emily Z. Keung¹; Christopher P. Scally¹; Christina L. Roland¹; Kelly K. Hunt¹; Barry W. Feig¹; John M. Slopis¹; Heather Wilson-Robles²; Alexander Lazar¹

¹The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES; ²Texas A&M University, College Station, Texas, UNITED STATES

9:29 AM - 9:36 AM

Paper #03 #1818745

CATEGORIZING SYNOVIAL SARCOMAS BASED ON EPIGENOMIC LANDSCAPE

Alvin Qiu; Edmund Su; Qi Cao; Marcus Wong; Michelle Moksa; Martin Hirst; Torsten Nielsen
University of British Columbia, Vancouver, British Columbia, CANADA

9:36 AM - 9:43 AM

Paper #04 #1818749

ATRX DELETION IMPAIRS CGAS-STING SIGNALING AND INCREASES RESPONSE TO RADIATION AND ONCOLYTIC HERPESVIRUS IN SOFT TISSUE SARCOMA

Warren Floyd; Matthew Pierpoint; Chang Su; Lixia Luo; Amy J. Wisdom; Yan Ma; Suzanne Bartholf DeWitt; Nerissa T Williams; Jason A. Somarelli; David L Corcoran; William C. Eward; Dianna M. Cardona; David G. Kirsch
Duke University, Durham, Carolina, UNITED STATES

9:43 AM - 9:50 AM

Paper #05 #1818718

CHALLENGES AND PATTERNS OF REGISTRY RESEARCH IN SARCOMA

Joshua M. Lawrenz; Andrew Chi; Gabriel Bendfeldt; Jennifer L. Halpern; Ginger E. Holt; Herbert S. Schwartz
Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES

9:50 AM - 9:58 AM

Paper #06 #1818728

SINGLE-CELL OMICS REVEALS DIVERSE EPIGENETIC AND TRANSCRIPTOMIC REPROGRAMMING OF NF1-DEFICIENT CELLS THROUGH THE LOSS OF POLYCOMB REPRESSIVE COMPLEX 2 IN MALIGNANT PERIPHERAL NERVE SHEATH TUMORS

Xiyuan Zhang¹; Hannah Lou²; Vishaka Gopalan¹; Zhihui Liu¹; Haiyan Lei¹; C. Paige Jones¹; Carly M. Sayers¹; Marielle Yohe¹; Prashant Chittiboina³; Brigitte C. Widemann¹; Carol J. Thiele¹; Michael Kelly⁴; Sridhar Hannenhalli¹; Jack F. Shern¹

¹NCI, Bethesda, Maryland, UNITED STATES; ²NCI, Indianapolis, Indiana, UNITED STATES;

³NINDS, Bethesda, Maryland, UNITED STATES; ⁴Frederick National Laboratory, Bethesda, Maryland, UNITED STATES

9:58 AM - 10:04 AM

Paper #07 #1818764

PROTEOMIC LANDSCAPE OF 205 BONE AND SOFT TISSUE SARCOMAS FROM THE INTERNATIONAL SARCOMA KINDRED STUDY REVEALS DISTINCT PROTEOMIC SIGNATURE OF LEIOMYOSARCOMAS

Elizabeth Connolly¹; Zainab Noor¹; Asim Anees¹; Daniel Bucio-Noble¹; Peter Hains¹; Phillip J. Robinson¹; Mandy Ballinger²; Qing Zhong³; Jia Liu³; David Thomas⁴; Roger Reddel³

¹ProCan®, Children's Medical Research Institute, Faculty of Medicine and Health, The University of Sydney, Sydney, New South Wales, AUSTRALIA; ²Garvan Institute, Faculty of Medicine, Western Sydney University, Darlinghurst, New South Wales, AUSTRALIA; ³ProCan®, Children's Medical Research Institute, Faculty of Medicine and Health, The University of Sydney, Westmead, New South Wales, AUSTRALIA; ⁴Garvan Institute of Medical Research, Sydney, New South Wales, AUSTRALIA

10:04 AM - 10:11 AM

Paper #08 #1818786

REMARKABLY STABLE COPY-NUMBER PROFILES IN OSTEOSARCOMA CONTEST UNSTABLE GENOME HYPOTHESIS

Ryan D. Roberts¹; Sanjana Rajan¹; Simone Zaccaria PhD², Matthew V. Cannon¹; Maren Cam¹; Amy Gross³; Benjamin J. Raphael⁴

¹Nationwide Children's Hospital, Columbus, Ohio, UNITED STATES; ²University College London, London, England, UNITED KINGDOM; ³Center for Childhood Cancer, Nationwide Children's Hospital, The Ohio State University James Comprehensive Cancer Center, Columbus, Ohio, UNITED STATES; ⁴Princeton University, Princeton, New Jersey, UNITED STATES

10:11 AM - 10:30 AM Q&A

10:30 AM - 11:00 AM

– Session 2 –

COVID-19 AND SARCOMA

Chair: **Samuel J. Ford, PhD**

Panelists: **James Glasbey – COVIDSurg; Rebecca Gladdy – GIST Care during COVID; Krisha Howell – Mednet; Giuseppe Curigliano – ESMO; Nadia Hindi – SELNET**

10:35 AM - 10:42 AM

Paper #09 #1818706

DEMOGRAPHICS, PROGNOSIS FACTORS, AND OUTCOMES FOR PATIENTS (PTS) WITH SARCOMA AND COVID-19: A CCC19-REGISTRY BASED RETROSPECTIVE COHORT ANALYSIS

Michael J. Wagner¹; Matthew Ingham²; Corrie Painter³; Rashmi Chugh⁴; Emily Jonczak⁵; Vivek Subbiah⁶; Nam Bui⁷; Lisa Tachiki¹; Elizabeth S. Nakasone¹; Elizabeth T. Loggers¹; Chris Labaki⁸; Rana R. McKay⁹; Elizabeth A. Griffiths¹⁰; Katherine A. Thornton¹¹; Clara Hwang¹²; James L. Chen¹³; Thorvardur R. Halfdanarson¹⁴; Anup Kasi¹⁵; Daniel Y. Reuben¹⁶; Cathleen Park¹⁷

¹University of Washington/Fred Hutch/Seattle Cancer Care Alliance, Seattle; Washington; UNITED STATES; ²New York Presbyterian Hospital/Columbia University Medical Center, New York, New York, UNITED STATES; ³The Broad Institute of MIT and Harvard, Cambridge, Massachusetts, UNITED STATES; ⁴University of Michigan, Ann Arbor, Michigan, UNITED STATES; ⁵Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES; ⁶The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES; ⁷Stanford University Department of Oncology, Stanford, California, UNITED STATES; ⁸Dana-Farber Cancer Institute, Boston, Massachusetts, UNITED STATES; ⁹Moore's Cancer Center at the University of California, San Diego, San Diego, California, UNITED STATES; ¹⁰Roswell Park Comprehensive Cancer Center, Buffalo, New York, UNITED STATES; ¹¹Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES; ¹²Henry Ford Cancer Institute, Detroit, Michigan, UNITED STATES; ¹³Ohio State University, Columbus, UNITED STATES; ¹⁴Mayo Clinic, Rochester, Minnesota, UNITED STATES; ¹⁵The University of Kansas Cancer Center, Kansas City, Kansas, UNITED STATES; ¹⁶Hollings Cancer Center at the Medical University of South Carolina, Charleston, South Carolina, UNITED STATES; ¹⁷University of Cincinnati Cancer Center, Cincinnati, Ohio, UNITED STATES

10:42 AM - 11:00 AM

Q&A

11:00 AM - 12:00 PM

– Session 3 –

GIST

Chair: **Jason K. Sicklick, MD, FACS**

11:00 AM - 11:07 AM

Paper #10 #1818708

RIPRETINIB AS ≥4TH-LINE TREATMENT IN PATIENTS WITH ADVANCED GASTROINTESTINAL STROMAL TUMOR: LONG-TERM UPDATE FROM THE PHASE 3 INVICTUS STUDY

Robin L. Jones¹; Michael C. Heinrich²; Suzanne George³; John Zalcborg⁴; Sebastian Bauer⁵; Hans Gelderblom⁶; Patrick Schöffski⁷; César Serrano⁸; Steven Attia⁹; Gina D'Amato¹⁰; Ping Chi¹¹; Peter Reichardt¹²; Julie Meade¹³; Vienna Reichert¹³; Kelvin Shi¹³; Rodrigo Ruiz-Soto¹³; Jean-Yves Blay¹⁴; Margaret von Mehren¹⁵;

¹The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, England, UNITED KINGDOM;

²Hematology/Medical Oncology, OHSU Knight Cancer Institute, Portland, UNITED STATES; ³Sarcoma Center, Medical Oncology, Dana Farber Cancer Institute, Boston, Massachusetts, UNITED STATES; ⁴OAM, School of Public Health, Faculty of Medicine, Monash University, Melbourne, Victoria, AUSTRALIA; ⁵University Hospital Essen Westdeutsches Tumorzentrum, Essen, Nordrhein-Westfalen, GERMANY; ⁶Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS; ⁷General Medical Oncology, University Hospitals Leuven – Campus Gasthuisberg, Leuven, Brabant Wallon, BELGIUM; ⁸Sarcoma Translational Research Program, Department of Medical Oncology, Sarcoma Translational Research, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Catalonia, SPAIN; ⁹The Mayo Clinic, Jacksonville, Florida, UNITED STATES; ¹⁰Sylvester Comprehensive Cancer Center/University of Miami, Miami, Florida, UNITED STATES; ¹¹Human Oncology and Pathogenesis Program/Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES; ¹²Oncology and Palliative Care, Sarcoma Center, Helios Klinikum Berlin-Buch, Berlin, Berlin, GERMANY; ¹³Deciphera Pharmaceuticals, LLC, Waltham, Massachusetts, UNITED STATES; ¹⁴Centre Léon Bérard, Lyon, Auvergne, FRANCE; ¹⁵Sarcoma Oncology, Hematology/Oncology, Fox Chase Cancer Center, Philadelphia, Pennsylvania, UNITED STATES

11:07 AM - 11:14 AM

Paper #11 #1818776

REGISTRI: REGORAFENIB IN FIRST-LINE OF KIT/PDGF R WILD TYPE METASTATIC GIST: A COLLABORATIVE SPANISH (GEIS), ITALIAN (ISG) AND FRENCH SARCOMA GROUP (FSG) PHASE II TRIAL

Javier Martin-Broto¹; Claudia M. Valverde²; Nadia Hindi³; Bruno Vincenzi⁴; Javier Martinez-Trufero⁵; Giovanni Grignani⁶; Antonine Italiano⁷; Javier Lavernia⁸; Ricardo Gonzalez-Campora⁹; Ana Vallejo¹⁰; Diana Hernandez-Jover¹¹; Antonio Gutierrez¹²; Cesar Serrano¹³; David Moura¹⁴; Jose Antonio Lopez-Guerrero⁸; Julia Cruz⁸; Antonio Fernández-Serra⁸; Jean-Yves Blay¹⁵; Elena Fumagalli¹⁶; Virginia Martínez-Marín¹⁷

¹Fundacion Jimenez Diaz University Hospital, Madrid, Madrid, SPAIN; ²Genitourinary, Sarcoma, CNS, CUP Unit, Hospital Universitario Vall d'Hebron, Barcelona, Catalonia, SPAIN; ³Fundacion Jimenez Diaz University Hospital, Madrid, Madrid, SPAIN; ⁴Department of Medical Oncology, Università Campus Bio-Medico di Roma, Rome, ITALY; ⁵Miguel Servet University Hospital, Zaragoza, Aragon, SPAIN; ⁶Department of Medical Oncology-Sarcoma Unit, Candiolo Cancer Institute FPO-IRCCS, Candiolo, Piemonte, ITALY; ⁷Institute Bergonié, Bordeaux, Aquitaine, FRANCE; ⁸Fundacion Instituto Valenciano de Oncologia, Valencia, Comunidad Valenciana, SPAIN; ⁹Hospital Quironsalud Cordoba, Cordoba, Andalucia, SPAIN; ¹⁰Virgen Macarena University Hospital, Seville, Andalucia, SPAIN; ¹¹Hospital Sant Pau, Barcelona, Catalonia, SPAIN; ¹²Son Espases University Hospital, Palma de Mallorca, Islas Baleares, SPAIN; ¹³Vall d'Hebron University Hospital Barcelona, Catalonia, SPAIN; ¹⁴CITIUS III, Seville, Andalucia, SPAIN; ¹⁵Centre Léon Bérard, Lyon, Auvergne, FRANCE; ¹⁶Fondazione IRCCS Istituto Nazionale Dei Tumori Di Milano, Milan, Lombardia, ITALY; ¹⁷H. U. La Paz, Madrid, Madrid, SPAIN

11:14 AM - 11:21 AM

Paper #12 #1818782

TRANSPERINEAL RESECTION OF RECTAL GASTROINTESTINAL STROMAL TUMOR: ANALYSIS OF SURGICAL AND ONCOLOGICAL OUTCOMES AT A SINGLE REFERRAL CENTER

Valentina Messina MD; Francesco Barretta; Marco Fiore; Stefano Radaelli; Chiara Colombo; Marta Barisella; Carlo Morosi; Elena Rosa Fumagalli; Rosalba Miceli; Alessandro Gronchi; Dario Callegaro
Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY

11:21 AM - 11:28 AM

Paper #13 #1818778

THE USE OF LOCAL TREATMENT IN METASTASIZED GIST PATIENTS

Pien Brink¹; Gijsbert M. Kalisvaart¹; Dirk J. Grünhagen²; Cornelis Verhoef²; Hans Gelderblom¹; Henk H. Hartgrink¹; Winan J. van Houdc³; Winette T. A. van der Graaf³; Neeltje Steeghs³; Lukas Been⁴; An Reyners⁴; Robert Van Ginkel⁴; Yvonne M. Schrage¹; Marta Fiocco¹; Jos A. van der Hage¹;

¹Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS; ²Erasmus MC Cancer Institute, Rotterdam, Zuid-Holland, NETHERLANDS; ³The Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS;

⁴University Medical Center Groningen (UMCG), Groningen, Groningen, NETHERLANDS

11:28 AM - 11:35 AM

Paper #14 #1818751

EFFICACY AND SAFETY OF RIPRETINIB IN PATIENTS WITH ADVANCED GASTROINTESTINAL STROMAL TUMOR: ANALYSES OF A SINGLE-ARM, PHASE 2 TRIAL

Jian Li¹; Shirong Cai²; Yongjian Zhou³; Jun Zhang⁴; Ye Zhou⁵; Hui Cao⁶; Xin Wu⁷; Yanhong Deng⁸; Biao Zhang⁹; Juan Dong⁹; Lin Shen¹;

¹Peking University Cancer Hospital & Institute, Beijing, Beijing, CHINA (PEOPLE'S REPUBLIC); ²The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, Guangdong, CHINA (PEOPLE'S REPUBLIC); ³Fujian Medical University Union Hospital, Fuzhou, Fujian, CHINA (PEOPLE'S REPUBLIC); ⁴The First Affiliated Hospital of Chongqing Medical University, Chongqing, Chongqing, CHINA (PEOPLE'S REPUBLIC); ⁵Fudan University Shanghai Cancer Center, Shanghai, Shanghai, CHINA (PEOPLE'S REPUBLIC); ⁶Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, Shanghai, CHINA (PEOPLE'S REPUBLIC); ⁷Chinese PLA General Hospital, Beijing, Beijing, CHINA (PEOPLE'S REPUBLIC); ⁸The Sixth Affiliated Hospital, Sun Yat-sen University, Guangzhou, Guangdong, CHINA (PEOPLE'S REPUBLIC); ⁹Zai Lab (Shanghai) Co., Ltd, Shanghai, Shanghai, CHINA (PEOPLE'S REPUBLIC)

11:35 AM - 11:42 AM

Paper #15 #1818725

PATIENT-REPORTED SYMPTOMS AND HEALTH-RELATED QUALITY OF LIFE IN GASTROINTESTINAL STROMAL TUMOUR PATIENTS TREATED WITH TYROSINE KINASE INHIBITORS

Dide den Hollander¹; Ingrid Desar²; Hans Gelderblom³; Astrid Oosten⁴; An Reyners⁵; Neeltje Steeghs⁶; Winette T. A. van der Graaf⁶; Olga Husson⁶;

¹Netherlands Cancer Institute/ Radboud University Medical Center Nijmegen, Amsterdam, Noord-Holland, NETHERLANDS;

²Radboud University Medical Center, Nijmegen, Gelderland, NETHERLANDS; ³Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS; ⁴Erasmus Medical Center Rotterdam, Rotterdam, Zuid-Holland, NETHERLANDS;

⁵University Medical Center Groningen, Groningen, Groningen, NETHERLANDS; ⁶Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS

11:42 AM - 12:00 PM Q&A

12:00 PM - 12:30 PM Break

Thursday, 11 November, 2021

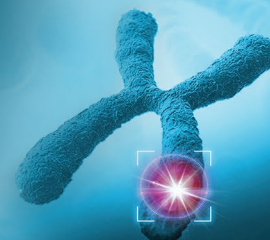
12:30 PM - 1:15 PM

**NINA AXELRAD LECTURE –
THE MARRIAGE BETWEEN SURGERY AND ONCOLOGY**

Allessandro Gronchi

NEW DATA PRESENTED AT CTOS 2021

**EXPLORE THE UPDATED EFFICACY AND SAFETY OF A
TRK INHIBITOR IN ADULT AND PEDIATRIC SARCOMAS**



Friday, November 12 - 2:30-3:15 PM

Poster Session 2*

P 240: Comparative Effectiveness

Abstract ID: 1818861

P 241: Pediatric

Abstract ID: 1818904

P 244: Histology

Abstract ID: 1818905

P 252: Adult

Abstract ID: 1818903

Saturday, November 13 - 1:15-2:30 PM

Oral Session 12*

**Paper 70: Ultra-Rare and
Translocation Sarcomas**

***Click on any title to access the session.**

CTOS, Connective Tissue Oncology Society; TRK, tropomyosin receptor kinase.

©2021 Bayer HealthCare Pharmaceuticals, Inc. All rights reserved.
PP-PF-ONC-US-2227-1 10/21



1:15 PM - 2:30 PM

– Session 4 –

BONE TUMORS

Chair: **Sandra Strauss, BA, MBBS, MRCP (UK), PhD**

1:15 PM - 1:22 PM

Paper #16 #1818705

THE PROPHYLACTIC ANTIBIOTIC REGIMENS IN TUMOR SURGERY (PARITY) INTERNATIONAL RANDOMIZED CONTROLLED TRIAL

Michelle Ghert; The PARITY Investigators

McMaster University, Oakville, Ontario, CANADA

1:22 PM - 1:29 PM

Paper #17 #1818784

OSTEOSARCOMA EXPLORER: A DATA COMMONS WITH CLINICAL, GENOMIC, PROTEIN AND TISSUE IMAGE DATA FOR OSTEOSARCOMA RESEARCH

Donghan Yang¹; Qinbo Zhou¹; Lauren Furman¹; Xian Cheng¹; Lin Xu¹; Bo Yao¹; Danni Luo¹; Hongyin Lai¹; Patrick Leavey¹; Tammy Lo²; David S. Shulman³; Donald A. Barkauskas⁴; Katherine A. Janeway³; Chand Khanna⁵; Richard Gorlick⁶; Stephen Skapek¹; Laura Klesse¹; Brian D. Crompton³; Yang Xie¹

¹UT Southwestern Medical Center, Dallas, Texas, UNITED STATES; ²Children's Oncology Group, Monrovia, California, UNITED STATES; ³Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, Massachusetts, UNITED STATES; ⁴Keck School of Medicine of the University of Southern California, Los Angeles, California, UNITED STATES; ⁵Ethos Discovery, Washington, District of Columbia, UNITED STATES; ⁶MD Anderson Cancer Center, Houston, Texas, UNITED STATES

1:29 PM - 1:36 PM

Paper #18 #1818756

SAFETY AND EFFICACY OF THE TETRAVALENT DEATH RECEPTOR 5 AGONIST INBRX-109 IN PATIENTS WITH CONVENTIONAL CHONDROSARCOMA: UPDATE FROM THE PHASE 1 EXPANSION COHORT

Vivek Subbiah¹; Anthony P. Conley¹; Christopher Lieu²; Breelyn A. Wilky²; Nehal Lakhani³; Anthony Tolcher⁴; Joseph Chao⁵; Warren Chow⁵; Klaus Wagner⁶; Vasily Andrianov⁶; Analeah Heidt⁶; Emily Rowell⁶; Brendan Eckelman⁶; Quinn Deveraux⁶; James Kalabus⁶; Victoria T. Chua-Alcala⁷;

¹The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES; ²University of Colorado, Aurora, Colorado, UNITED STATES; ³START Midwest, Grand Rapids, Michigan, UNITED STATES; ⁴NEXT Oncology, LLC, San Antonio, Texas, UNITED STATES; ⁵City of Hope Comprehensive Cancer Center, Duarte, California, UNITED STATES; ⁶Inhibrx, Inc., La Jolla, California, UNITED STATES; ⁷Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES

1:36 PM - 1:43 PM

Paper #19 #1818787

NOVEL ANTIBODY DISRUPTS BIOFILM IN MOUSE MODEL OF IMPLANT ASSOCIATED INFECTION

Christopher M. Hart; Zach Burke; Benjamin Kelley; Zeinab Mamouei; Troy Sekimura; Michael Le; Michael Arnold; Alan Li; Amr Turkmani; Christopher Hamad; Nicolas Cevallos; Gideon Blumstein; Kellyn Hori; Sam Clarkson; Sam Uweh; Brian Zukotynski; Alexandra Stavrakis; Nicholas M. Bernthal
UCLA, Santa Monica, California, UNITED STATES

1:43 PM - 1:50 PM

Paper #20 #1818721

METRONOMIC SIROLIMUS AND CYCLOPHOSPHAMIDE IN METASTATIC OR UNRESECTABLE CHONDROSARCOMA; RESULTS OF THE COSYMO PHASE II TRIAL

Astrid Lipplaa¹; Javier Martin-Broto²; Antonio Lopez-Pousa³; Roberto Diaz Diaz-Beveridge⁴; Claudia M. Valverde⁵; Antonio Casado⁶; Jacco de Haan⁷; Jesus Rodriguez Pascual⁸; Linda Verhoeff¹; Elma Meershoek - Klein Kranenbarg¹; Pancras Hogendoorn MD PhD¹; Jean-Yves Blay⁹; Judith V.M.G. Bovée¹; Hans Gelderblom¹

¹Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS; ²Hospital Universitario Virgen del Rocío, Sevilla, Andalucia, SPAIN; ³Hospital de la Santa Creu i Sant Pau, Barcelona, Catalonia, SPAIN; ⁴H. U. La Fe, Valencia, Comunidad Valenciana, SPAIN; ⁵Genitourinary, Sarcoma, CNS, CUP unit, Hospital Universitario Vall d'Hebron, Barcelona, Catalonia, SPAIN; ⁶Hospital Clínico Universitario San Carlos, Madrid, Madrid, SPAIN; ⁷University Medical Center Groningen, Groningen, Groningen, NETHERLANDS; ⁸HM-CIOCC Madrid, Madrid, Madrid, SPAIN; ⁹Centre Léon Bérard, Lyon, Auvergne, FRANCE

1:50 PM - 1:57 PM

Paper #21 #1818717

TARGETING VULNERABILITIES CAUSED BY THE IDH MUTATION IN CHONDROSARCOMA: THE MODEL MATTERS

Sanne Venneker; Alwine B. Kruisselbrink; Tessa A.H. Wilpshaar; Ieva Palubeckaite; Pauline M. Wijers-Koster; Hans J. Baelde; René J.M. van Zeijl; Bram Heijss; Karoly Szuhai; Judith V.M.G. Bovée
Leiden University Medical Center, Leiden, Zuid-Holland, Netherlands

Thursday, 11 November, 2021

1:57 PM - 2:04 PM

Paper #22 #1818704

TERT PROMOTER MUTATION IS AN OBJECTIVE CLINICAL MARKER FOR DISEASE PROGRESSION IN CHONDROSARCOMA

Yifan Zhang¹; Yi Chen²; Nelly Seger²; Asle Hesla²; Panagiotis Tsagkozis²; Olle Larsson²; Yingbo Lin²; Felix Haglund¹

¹Department of Pathology and Cancer Diagnostics, Karolinska University Hospital, Stockholm, Sweden and Department of Oncology-Pathology, Karolinska Institute, Solna, Stockholm, SWEDEN;

²Karolinska Institute, Stockholm, Lan, SWEDEN

2:04 PM - 2:11 PM

Paper #23 #1818723

ROTATED MASSIVE AUTOGRAFT RECONSTRUCTION FOR BONE TUMORS: SAFE AND REPRODUCIBLE TECHNIQUE

Ana C. Belzarena¹; **Pablo Stoppello**²; Leticia Gaiero²; Gottardo Bianchi²; Nicolas Casales²; Claudio Silveri²;

¹Miami Cancer Institute, Miami, Florida, UNITED STATES; ²Unidad de Patología Oncológica Musculo Esquelética, Instituto Nacional de Ortopedia y Traumatología, Montevideo, Montevideo, URUGUAY

2:11 PM - 2:30 PM Q&A

2:30 PM - 3:15 PM **POSTER SESSION 1**
(POSTERS 001-136)

3:15 PM - 3:30 PM Break

3:30 PM - 5:30 PM **SARC Meeting**

5:30 PM - 6:30 PM **Deciphera Symposium (Invite Only)**

5:30 PM - 7:30 PM **Adaptimmune Symposium**

SPOTLIGHT ON SYNOVIAL SARCOMA: WHERE ARE WE NOW? WHAT NEXT?

Presenter: **Shreyaskumar Patel, MD**

University of Texas MD Anderson Cancer Center

Presenter: **Luis G. Hidalgo**

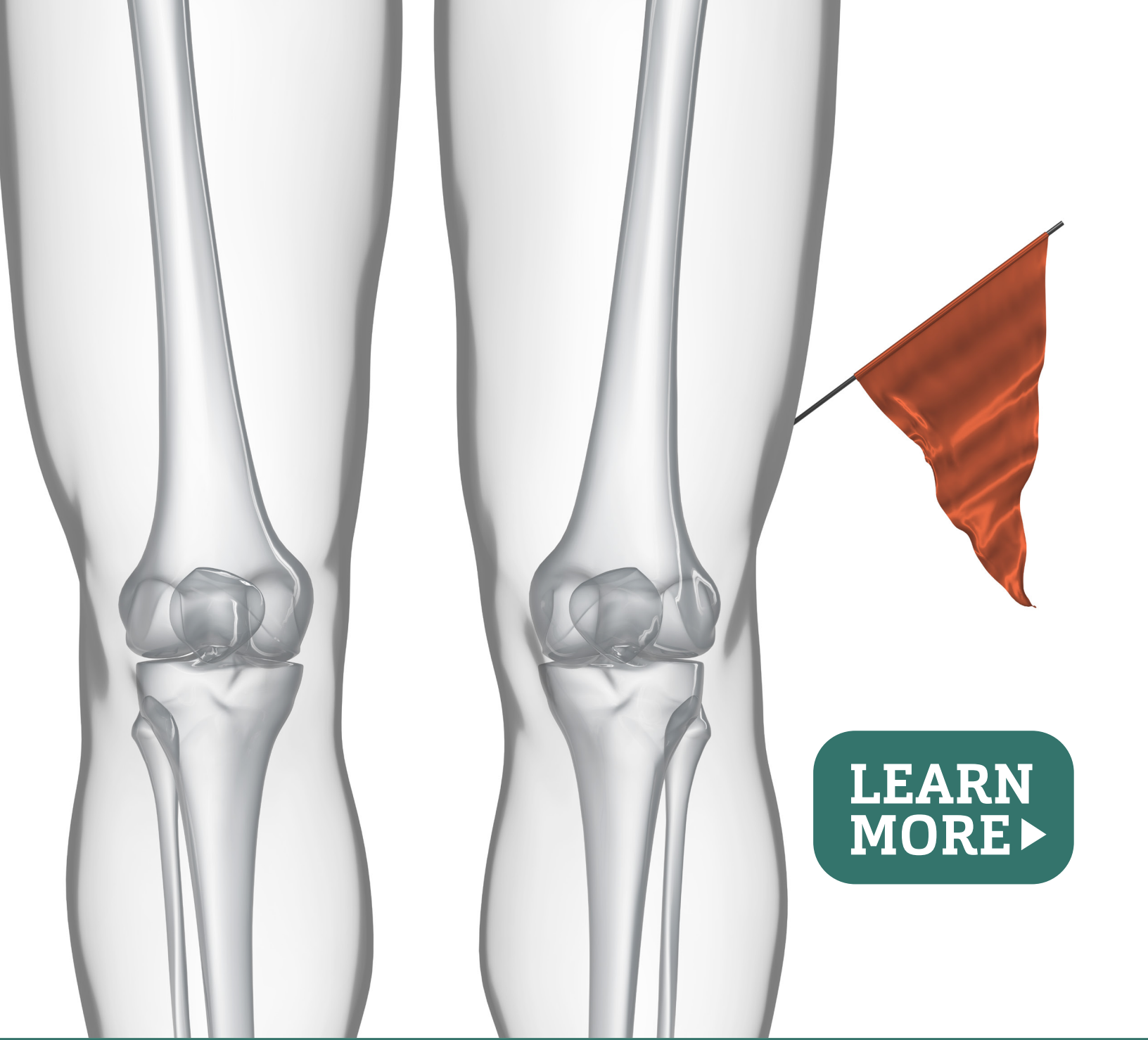
University of Wisconsin

Presenter: **Krishna Komanduri, MD**

Sylvester Comprehensive Cancer Center, University of Miami

Moderator: **Sandra McGuigan, MD, MBA**

Adaptimmune Favorite



**LEARN
MORE ▶**

DON'T MISS THE SIGNALS

Spotting the red flags of **SYNOVIAL SARCOMA**
can make all the difference.

8:00 AM - 9:00 AM CTOS Executive Committee

9:00 AM - 10:00 AM

– Session 5 –

DIAGNOSTIC AND SURGICAL TECHNIQUES

Chair: **Peter Hohenberger, MS, PhD**

9:00 AM - 9:07 AM

Paper #24 ID#1818750

DIFFUSION-WEIGHTED IMAGING FOR DIFFERENTIATION OF SACRAL CHORDOMA AND CHONDROSARCOMA

Raul Valenzuela; Liu Chenglei; William Green; William Murphy; Behrang Amini

MD Anderson Cancer Center, Houston, Texas, UNITED STATES

9:07 AM - 9:14 AM

Paper #25 #1818757

DUAL-ENERGY CT VITAL IODINE TUMOR BURDEN AS A QUANTITATIVE RESPONSE PARAMETER IN PATIENTS WITH GIST UNDERGOING TARGETED THERAPY - PROSPECTIVE MULTI-CENTER TRIAL

Peter Hohenberger¹; Mathias Meyer¹; Christina Messiou²; Charlotte Benson²; Hideki Ota³; Stefan Schönberg¹

¹Mannheim University Medical Center, Mannheim, Baden-Wurttemberg, GERMANY; ²The Royal Marsden NHS

Foundation Trust, London, England, UNITED KINGDOM; ³Yamagata Prefecture Shinjo Hospital, Shinjo, Yamagata, JAPAN

9:14 AM - 9:21 AM

Paper #26 ID#1818771

FLUORESCENCE GUIDED SURGERY WITH INDOCYANINE GREEN FOR SARCOMA RESECTION- A 39 PATIENT CASE SERIES

Kenneth S. Rankin¹; Corey D. Chan²; Marcus J. Brookes²; Riya Tanwani²; Toni Pringle²; James Knight²;

Thomas Beckingsale¹; Timothy Crowley¹; Kanishka M. Ghosh¹; Claire Jones³; Thomas Ness³; Sanjay Gupta⁴;

Maniram Ragbir²;

¹North of England Bone and Soft Tissue Tumour Service, Newcastle upon Tyne, England, UNITED KINGDOM;

²Newcastle University, Newcastle upon Tyne, England, UNITED KINGDOM; ³Newcastle Novopath MRC Pathology Node,

Newcastle upon Tyne, England, UNITED KINGDOM; ⁴Glasgow Royal Infirmary, Glasgow, Scotland, UNITED KINGDOM

9:21 AM - 9:28 AM

Paper #27 ID#1818760

SENTINEL LYMPH NODE BIOPSY AND FORMAL LYMPHADENECTOMY FOR SOFT TISSUE SARCOMA: A SINGLE CENTER EXPERIENCE OF 86 CONSECUTIVE CASE

Russell G. Witt; Yi-Ju Chiang; Derek Erstad MD; Christopher P. Scally; Keila E. Torres; Kelly K. Hunt; Barry W. Feig;

Christina L. Roland; Emily Z. Keung

University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES

9:28 AM - 9:35 AM

Paper #28 #1818699

DOES SYNOVIAL SARCOMA GRADE PREDICT ONCOLOGIC OUTCOMES, AND DOES A LOW-GRADE VARIANT EXIST?

Michael P. Fice; Abdullah Almajnooni; Charles A. Gusho; Reagan Chapman; Subramanya Mallikarjunappa; Marta Batus;

Steven Gitelis; Matthew W. Colman; Ira Miller; Alan T. Blank

Rush University Medical Center, Chicago, Illinois, UNITED STATES

9:35 AM - 9:42 AM

Paper #29 #1818785

DISTRIBUTION AND RATE OF MYXOID LIPOSARCOMA SPINAL METASTASES: IMPACT ON SURVEILLANCE IMAGING

Benjamin M. Vierra¹; Jake Awtry²; Lily V. Saadat²; Jason L. Hornick²; Jyothi P. Jagannathan³; Marco L. Ferrone²; Andrew J. Wagner³; Jiping Wang²; Chandrajit P. Raut³; Mark Fairweather²

¹Harvard Medical School, Boston, Massachusetts, UNITED STATES; ²Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES; ³Harvard Medical School, Dana Farber Cancer Institute, Boston, Massachusetts, UNITED STATES

9:42 AM - 10:00 AM Q&A

10:00 AM - 11:00 AM

– Session 6 –

IMMUNOTHERAPY & IMMUNE MICROENVIRONMENT

Chair: **Breelyn A. Wilky, MD**

10:00 AM - 10:07 AM

Paper #30 #1818753

SPEARHEAD-1: A PHASE 2 TRIAL OF AFAMITRESGENE AUTOLEUCEL (FORMERLY ADP-A2M4) IN PATIENTS WITH ADVANCED SYNOVIAL SARCOMA OR MYXOID/ROUND CELL LIPOSARCOMA

Brian Andrew A. Van Tine¹; Sandra P. D'Angelo²; Steven Attia³; Jean-Yves Blay⁴; Sandra Strauss⁵; Claudia Maria Valverde Morales⁶; Albiruni Ryan Abdul Razak⁷; Kristen N. Ganjoo⁸; Michael J. Wagner⁹; Axel Le Cesne¹⁰; Erin Van Winkle¹¹; Trupti Trivedi¹¹; Swethajit Biswas¹²; Dennis Williams¹¹; Elliot Norry¹¹; Dejka M. Araujo¹³

¹Washington University School of Medicine, St. Louis, Missouri, UNITED STATES; ²Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES; ³The Mayo Clinic, Jacksonville, Florida, UNITED STATES; ⁴Centre Léon Bérard, Lyon, Auvergne, FRANCE; ⁵University College London Hospital, London, England, UNITED KINGDOM; ⁶Vall D'Hebron University Hospital, Barcelona, Catalonia, SPAIN; ⁷Solid Tumor Program and Medical Oncology Lead, Sarcoma Program, Division of Medical Oncology, Princess Margaret Cancer Centre, University Health Network, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, CANADA; ⁸Stanford Cancer Center, Stanford, California, UNITED STATES; ⁹University of Washington/Fred Hutch/Seattle Cancer Care Alliance, Seattle, Washington, UNITED STATES; ¹⁰Institut Gustave Roussy-Gustave Roussy Cancer Center-DITEP, Villejuif, Ile-de-France, FRANCE; ¹¹Adaptimmune, Philadelphia, Pennsylvania, UNITED STATES; ¹²Adaptimmune, Abingdon, England, UNITED KINGDOM; ¹³The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES

10:07 AM - 10:14 AM

Paper #31 #1818726

SAFETY AND EFFICACY OF LETETRESGENE AUTOLEUCEL (LETE-CEL; GSK3377794) IN ADVANCED MYXOID/ROUND CELL LIPOSARCOMA (MRCLS) FOLLOWING HIGH LYMPHODEPLETION (COHORT 2): INTERIM ANALYSIS

Sandra P. D'Angelo¹; Mihaela Druta²; Brian Andrew A. Van Tine³; David Liebner⁴; Scott Schuetze⁵; Aisha N. Hasan⁶; Andrew P. Holmes⁶; Anne Huff⁶; Gurpreet Kapoor⁶; Stefan Zajic⁶; Neeta Somaiah⁷

¹Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES; ²H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida, UNITED STATES; ³Washington University School of Medicine, St. Louis, Missouri, UNITED STATES; ⁴The Ohio State University, Columbus, Ohio, UNITED STATES; ⁵University of Michigan, Ann Arbor, Michigan, UNITED STATES; ⁶GlaxoSmithKline, Collegeville, Pennsylvania, UNITED STATES; ⁷The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES

10:14 AM - 10:21 AM

Paper #32 #1818746

PHASE II STUDY OF ERIBULIN AND PEMBROLIZUMAB IN PATIENTS WITH METASTATIC SOFT TISSUE SARCOMA

Suzanne George¹; Michael Nathenson¹; Edwin Choy²; Emanuele Mazzola¹; Jeffrey Morgan¹; Gregory M. Cote²; Melissa Hohos¹; Susan Carrozza¹; Sora Limor¹; Kristen Finn²; Julia Digiovanni²; Nicola Bothwick¹; Priscilla Merriam¹; Andrew J. Wagner¹

¹Sarcoma Center, Dana Farber Cancer Institute, Boston, Massachusetts, UNITED STATES;

²Massachusetts General Hospital, Boston, Massachusetts, UNITED STATES

10:21 AM - 10:28 AM

Paper #33 #1818738

SAFETY AND EFFICACY FROM A PHASE 1/2 STUDY OF INTRATUMORAL INT230-6 ALONE OR IN COMBINATION WITH IPILIMUMAB [INTENSITY# IT-01; BMS# CA184-592] IN ADULT SUBJECTS WITH METASTATIC SARCOMAS (NCT 03058289)

Ian B. Walters¹; Matthew Ingham²; James S. Hu³; Giles Whalen⁴; Jacob Thomas⁵; Anthony B. El-Khoueiry⁶; Diana Hanna⁶; Anthony Olszanski⁷; Christian F. Meyer⁸; Nilofer S. Azad⁸; Syed Mahmood⁹; Lewis Bender⁹; Lillian L. Siu¹⁰; Albiruni Ryan Abdul Abdul Razak¹⁰

¹Intensity Therapeutics, Inc, Westport, Connecticut, UNITED STATES; ²New York Presbyterian Hospital/Columbia University Medical Center, New York, New York, UNITED STATES; ³USC, Los Angeles, California, UNITED STATES;

⁴UMass Memorial Medical Center, Worcester, Massachusetts, UNITED STATES; ⁵USC Norris Cancer Hospital,

Los Angeles, California, UNITED STATES; ⁶Keck School of Medicine of USC, Los Angeles, California, UNITED STATES;

⁷Fox Chase Cancer Center, Philadelphia, Pennsylvania, UNITED STATES; ⁸Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, Maryland, UNITED STATES; ⁹Intensity Therapeutics, Inc., Westport, Connecticut, UNITED STATES; ¹⁰Princess Margaret Cancer Centre, Toronto, Ontario, CANADA

10:28 AM - 10:35 AM

Paper #34 #1818766

IMMUNOLOGICAL PROFILING OF PATIENTS WITH SPORADIC DESMOID FIBROMATOSIS UNDER ACTIVE SURVEILLANCE TO IDENTIFY PROGNOSTIC MARKERS

Chiara Colombo; Viviana Vallacchi; Laura Bergamaschi; Federica Perrone; Francesca Rini; Elena Palassini; Sandro Pasquali; Stefano Radaelli; Dario Callegaro; Marco Fiore; Chiara Castell; Alessandro Gronchi
Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY

10:35 AM - 10:42 AM

Paper #35 #1818731

IMMUNE CHECKPOINT INHIBITORS PROVIDE FAVORABLE RESPONSES IN PATIENTS WITH RECURRENT CHORDOMA

Andrew J. Bishop; Behrang Amini; Heather Lin; Shaan M. Raza; Jason T. Smith; Shreyaskumar Patel; David Grosshans; Ahsan Farooqi; B. Ashleigh Guadagnolo; Devarati Mitra; Kadir Akdemir; Alexander Lazar; Wei-Lien Wang; Justin E. Bird; Laurence D. Rhines; Anthony P. Conley

The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES

10:42 AM - 11:00 AM Q&A

11:00 AM - 12:00 PM

– Session 7 –

LOW GRADE AND INDOLENT TUMORS

Chair: **Bernd Kasper, MD**

11:00 AM - 11:07 AM

Paper #36 #1818777

A NATIONWIDE PROSPECTIVE CLINICAL TRIAL ON ACTIVE SURVEILLANCE IN PATIENTS WITH NON-INTRA-ABDOMINAL DESMOID-TYPE FIBROMATOSIS; THE GRAFITI TRIAL

Anne-Rose W. Schut¹; Milea Timbergen¹; Danique van Broekhoven¹; Thijs van Dalen²; Winan J. van Houdt³; Han Bonekamp⁴; Stefan Sleijfer¹; Dirk J. Grünhagen¹; Cornelis Verhoef¹; Frits van Coevorden³; Lukas Been⁵; Robert Van Ginkel⁵; Marc Bemelmans⁶; Jos A. van der Hage⁷; Sander Dijkstra⁷

¹Erasmus Medical Center, Rotterdam, Zuid-Holland, NETHERLANDS; ²UMC Utrecht, Utrecht, Utrecht, NETHERLANDS; ³The Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS; ⁴Radboud University Medical Center, Nijmegen, Gelderland, NETHERLANDS; ⁵University Medical Center Groningen, Groningen, Groningen, NETHERLANDS; ⁶Maastricht University Medical Center, Maastricht, Limburg, NETHERLANDS; ⁷Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS

11:07 AM - 11:14 AM

Paper #37 #1818736

SAFETY AND PRELIMINARY EFFICACY OF VIMSELTINIB IN TENOSYNOVIAL GIANT CELL TUMOR (TGCT)

Andrew J. Wagner¹; Albiruni Ryan Abdul Razak²; Hans Gelderblom³; Amparo Sánchez-Gastaldo⁴; Piotr Rutkowski⁵; Breelyn A. Wilky⁶; Michiel van de Sande³; Mary Michenzie⁷; Marc Vallee⁷; Maitreyi Sharma⁷; Matthew L. Sherman⁷; Rodrigo Ruiz-Soto⁷; William D. Tap⁸

¹Harvard Medical School, Dana-Farber Cancer Institute, Boston, Massachusetts, UNITED STATES; ²Princess Margaret Cancer Centre, University Health Network, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, CANADA; ³Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS; ⁴Hospital Universitario Virgen del Rocío, Sevilla, Andalucia, SPAIN; ⁵Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Mazowieckie, POLAND; ⁶University of Colorado Cancer Center, Aurora, Colorado, UNITED STATES; ⁷Deciphera Pharmaceuticals, LLC, Waltham, Massachusetts, UNITED STATES; ⁸Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES

11:14 AM - 11:21 AM

Paper #38 #1818780

ACTIVITY OF HORMONAL TREATMENT IN STUMP/LOW GRADE UTERINE LEIOMYOSARCOMA: A MULTICENTRE RESTROSPECTIVE STUDY FROM THE LEIOMYOSARCOMA FOUNDATION ROUND TABLE

Roberta Sanfilippo¹; Chiara Fabbroni¹; Isabelle Ray-Coquard²; Fatma Guermazi²; Felix Blanc-Durand³; Robin L Jones⁴; Angelo Paolo Dei Tos⁵; Marisa Nucci⁶; Annie Achee⁷; Bernd Kasper⁸; Paul Huang⁹; Hemming Matthew¹⁰; Rebecca A. Gladdy¹¹; Jonathan C. Trent¹²; Salvatore Provenzano¹; Francesco Raspagliesi¹; Scott Okuno¹³; Paolo G. Casali¹

¹Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY; ²Centre Leon Bérard, Lyon, Centre, FRANCE; ³Gustave Roussy, Paris, Centre, FRANCE; ⁴Royal Marsden NHS Foundation Trust, London, England, UNITED KINGDOM; ⁵Università di Padova (UniPD), Padova, Veneto, ITALY; ⁶Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES; ⁷National Leiomyosarcoma Foundation (NLMSF), Denver, Colorado, UNITED STATES; ⁸Mannheim University Medical Center, Mannheim, Hessen, GERMANY; ⁹The Institute of Cancer Research, London, England, UNITED KINGDOM; ¹⁰Department of Medicine, Columbia University School of Medicine, New York, New York, UNITED STATES; ¹¹Princess Margaret Hospital, University Health Network and Mount Sinai Hospital, Toronto; Lunenfeld Tanenbaum Research Institute, Sinai Health System, Toronto, Toronto, Ontario, CANADA; ¹²Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES; ¹³Mayo Clinic, Rochester, Minnesota, UNITED STATES

11:21 AM - 11:28 AM

Paper #39 #1818719

ADMINISTRATION OF PATIENT REPORTED OUTCOMES QUESTIONNAIRES IN TENOSYNOVIAL GIANT CELL TUMOR MANAGEMENT: EXPERIENCE FROM TENOSYNOVIAL GIANT CELL TUMOR OBSERVATIONAL PLATFORM PROJECT

Xin Ye PhD¹; Nicholas M. Bernthal²; Florence Mercier³; Petra Laeis³; Michiel van de Sande⁴

¹Daiichi Sankyo, Inc., Basking Ridge, New Jersey, UNITED STATES; ²David Geffen School of Medicine at UCLA, Santa Monica, California, UNITED STATES; ³Daiichi Sankyo Europe GmbH, Munich, Bayern, GERMANY;

⁴Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS

11:28 AM - 11:35 AM

Paper #40 #1818744

THE NATURAL HISTORY OF GANGLIONEUROMA: AN INTERNATIONAL STUDY BY THE TRANSATLANTIC AUSTRALASIAN RETROPERITONEAL SARCOMA WORKING GROUP

Sangkyu Noh¹; Carolyn Nessim²; Emily Z. Keung³; Dirk Strauss⁴; Ferdinando Cananzi⁵; Jun Chen⁶; Rebecca Gladdy⁷; Samuel J. Ford⁸; Piotr Rutkowski⁹; Elisabetta Pennacchioli¹⁰; Kenneth Cardona¹¹; Daphne Hompes¹²; Attila Kollár¹³; Nikolaos Vassos¹⁴; Chandrajit P. Raut¹⁵; Dagmar Adamkova Krakorova¹⁶; Sergio Quildrian¹⁷; Andraz Perhavec¹⁸; Eran Nizri¹⁹; Jeffrey Farma²⁰

¹Western University of Health Sciences, College of Osteopathic Medicine of the Pacific, Del Mar, California, UNITED STATES; ²The Ottawa Hospital, Ottawa, Ontario, CANADA; ³The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES; ⁴The Royal Marsden Hospital NHS Foundation Trust, London, England, UNITED KINGDOM; ⁵Humanitas Clinical and Research Center, Humanitas University; Milan, Lombardia, ITALY; ⁶Peking University International Hospital, Beijing, Beijing, CHINA (PEOPLE'S REPUBLIC); ⁷Mount Sinai Hospital, University Health Network, Toronto, Ontario, CANADA; ⁸University Hospital Birmingham NHS Foundation Trust, Birmingham, England, UNITED KINGDOM; ⁹Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Mazowieckie, POLAND; ¹⁰IEO European Institute of Oncology, Milan, Lombardia, ITALY; ¹¹Winship Cancer Institute, Emory University, Atlanta, Georgia, UNITED STATES; ¹²Department of Surgical Oncology, University Hospitals Leuven, Leuven, Belgium, Leuven, Vlaams-Brabant, BELGIUM; ¹³Inselspital, Universitätsspital Bern, Bern, Bern, SWITZERLAND; ¹⁴Division of Surgical Oncology, Mannheim University Medical Center, University of Heidelberg, Mannheim, Baden-Württemberg, GERMANY; ¹⁵Harvard Medical School, Dana-Farber Cancer Institute, Harvard University, Boston, Massachusetts, UNITED STATES; ¹⁶Masaryk Memorial Cancer Institute, Brno, Jihomoravsky Kraj, CZECH REPUBLIC; ¹⁷Buenos Aires British Hospital; Angel Roffo Institute of Oncology, University of Buenos Aires, Buenos Aires, Buenos Aires, ARGENTINA; ¹⁸Institute of Oncology Ljubljana, Ljubljana, Ljubljana, SLOVENIA; ¹⁹Tel Aviv Sourasky Medical Center, Tel Aviv, Tel Aviv, ISRAEL; ²⁰Fox Chase Cancer Center, Philadelphia, Pennsylvania, UNITED STATES

11:35 AM - 11:42 AM

Paper #41 #1818779

DOXORUBICIN-ELUTING BEAD TRANSARTERIAL CHEMOEMBOLIZATION (DEB-TACE) IN EXTRA-ABDOMINAL DESMOID TUMORS: INITIAL EXPERIENCE

DaeHee Kim¹; Mary Lou Keohan²; Mrinal M. Gounder²; Aimee M. Crago²; Joseph P. Erinjeri²

¹The Warren Alpert Medical School of Brown University, Providence, Rhode Island, UNITED STATES;

²Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES

11:42 AM - 12:00 PM Q&A

12:00 PM - 12:40 PM Break

12:40 PM - 1:15 PM	– Young Investigator Awards –
12:40 PM - 12:48 PM	#1862531 SARCOMA CELLULAR ECOSYSTEMS ARE ASSOCIATED WITH PROGNOSIS AND PREDICT IMMUNOTHERAPY RESPONSE Everett J. Moding ; Timothy J. Sears; Neda Nemat-Gorgani; Bogdan A. Luca; Chloe B. Steen; Maggie Y. Zhou; David G. Mohler; Matt van de Rijn; Kristen N. Ganjoo; Greg W. Charville; Nam Bui; Aaron M. Newman Stanford University School of Medicine, Stanford, California, UNITED STATES
12:48 PM - 12:56 PM	#1862532 ADJUVANT IMATINIB IN GIST PATIENTS HARBORING EXON 9 KIT MUTATIONS: RESULTS FROM A MULTI-INSTITUTIONAL EUROPEAN RETROSPECTIVE STUDY Andrea Napolitano ¹ ; Bruno Vincenzi ¹ ; Marta Fiocco ² ; Olivier Mir ³ ; Piotr Rutkowski ⁴ ; Jean-Yves Blay ⁵ ; Peter Reichardt ⁶ ; Heikki Joensuu ⁷ ; Elena Fumagalli ⁸ ; Margherita Nannini ⁹ ; Antonine Italiano ¹⁰ ; Giovanni Grignani ¹¹ ; Antonella Brunello ¹² ; Silvia Gasperoni ¹³ ; Tommaso Martino De Pas ¹⁴ ; Giuseppe Badalamenti ¹⁵ ; Maria A. A. Pantaleo ¹⁶ ; Winan J. van Houdt ¹⁷ ; Nikki S. IJzerman ¹⁷ ; Neeltje Steeghs ¹⁷ ¹ Università Campus Bio-Medico di Roma, Roma, Lazio, ITALY; ² The Leiden University Medical Center, Zuid-Holland, NETHERLANDS; ³ Gustave Roussy, Villejuif, Ile-de-France, FRANCE; ⁴ Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Mazowieckie, POLAND; ⁵ Centre Léon Bérard, Lyon, Auvergne, FRANCE; ⁶ Helios Klinikum Berlin-Buch, Berlin, Berlin, GERMANY; ⁷ Helsinki University Hospital and University of Helsinki, Helsinki, Uusimaa, FINLAND; ⁸ Fondazione IRCCS Istituto Nazionale Dei Tumori Di Milano, Milan, Lombardia, ITALY; ⁹ IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Emilia-Romagna, ITALY; ¹⁰ Institute Bergonié, Bordeaux, Aquitaine, FRANCE; ¹¹ Candiolo Cancer Institute FPO-IRCCS, Candiolo, Piemonte, ITALY; ¹² Istituto Oncologico Veneto IOV – IRCCS, Padova, Veneto, ITALY; ¹³ University Hospital Careggi, Florence, Toscana, ITALY; ¹⁴ IEO - European Institute of Oncology IRCCS, Milan, Lombardia, ITALY; ¹⁵ Policlinico “Paolo Giaccone”, University of Palermo, Palermo, Sicilia, ITALY; ¹⁶ IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Emilia-Romagna, ITALY; ¹⁷ The Netherlands Cancer Institute; Amsterdam, Noord-Holland, NETHERLAND
12:56 PM - 1:10 PM	Young Investigator Live Q&A
1:10 PM - 1:15 PM	NATIONAL LEIOMYOSARCOMA FOUNDATION RESEARCH GRANT Seth M. Pollack, MD Northwestern University, Chicago, Illinois, UNITED STATES

Friday, 12 November, 2021

1:15 PM - 2:30 PM

– Session 8 –

ONCOLOGY AND CLINICAL TRIALS

Chair: **Herbert Loong, MBBS, PDipMDPath, MRCP, FRCP**

1:15 PM - 1:22 PM

Paper #42 #1818712

LONG-TERM EVALUATION OF NBTXR3, A NOVEL RADIOENHANCER, PLUS RADIOTHERAPY IN PATIENTS WITH LOCALLY ADVANCED SOFT TISSUE CARCINOMA TREATED IN THE PHASE II/III ACT.IN.SARC TRIAL

Sylvie Bonvalot¹; Piotr L. Rutkowski²; Juliette Thariat³; Sébastien Carrère⁴; Anne Ducassou⁵; Marie-Pierre Sunyach⁶; Peter Agoston⁷; Angela Hong⁸; Augustin Mervoyer⁹; Marco Rastrelli¹⁰; Cécile Le Péchoux¹¹; Victor Moreno¹²; Rubi K. Li¹³; Béatrice Tiangco¹⁴; Zsusanna Papai¹⁵

¹Institut Curie, PSL Research University, Paris, Ile-de-France, FRANCE; ²Maria Sklodowska-Curie Institute -Oncology Center, Institute of Oncology, Warsaw, Mazowieckie, POLAND; ³Centre François Baclesse, Caen, France; Department of Radiation Oncology, Centre Lacassagne, Nice, Provence-Alpes-Cote d'Azur, FRANCE; ⁴Centre Regional De Lutte Contre Le Cancer Paul Lamarque, Montpellier, Languedoc-Roussillon, FRANCE; ⁵Institut Claudius Regaud (ICR), Institut Universitaire du Cancer de Toulouse-Oncopole (IUCT-O), Toulouse, Languedoc-Roussillon, FRANCE;

⁶Léon Bérard Cancer Center, Lyon, Rhone-Alpes, FRANCE; ⁷Országos Onkologiai Intézet, Budapest, Budapest, HUNGARY;

⁸Chris O'Brien Lifecare and The University of Sydney, Camperdown, Victoria, AUSTRALIA; ⁹Institut de Cancerologie de l'Ouest- Rene Gauducheau, Saint-Herblain, Pays de la Loire, FRANCE; ¹⁰Istituto Oncologico Veneto IRCCS, Padova, Veneto, ITALY; ¹¹Gustave Roussy, Villejuif, Ile-de-France, FRANCE; ¹²Hospital Fundación Jimenez Diaz, Madrid, Madrid, SPAIN; ¹³St. Luke's Medical Center, Quezon City, Quezon, PHILIPPINES; ¹⁴The Medical City APS Cancer Institute, Pasig City, Rizal, PHILIPPINES; ¹⁵Medical Centre, Hungarian Defence Forces, Budapest, Budapest, HUNGARY

INHIBRX

PHASE 1 STUDY



PHASE 2 STUDY



INBRX-109: Advancing Care for Sarcoma Patients.

Inhibrx has leveraged its protein engineering expertise to develop [INBRX-109](#), a tetravalent Death Receptor 5 (DR5) agonist precisely designed to achieve optimal therapeutic activity where many others have failed. Join the fight against Sarcoma and enroll your patients in ChonDRAGON — the phase 2 study in Chondrosarcoma.

For more information, check out our [Chondro Presentation](#) and be sure to view our [Ewing Sarcoma Poster](#).



ChonDRAGON

Chondrosarcoma Study with Death Receptor Agonist

For partnering inquiries, please contact colleen@inhibrx.com.

1:22 PM - 1:29 PM

Paper #43 #1818754

PROSPECTIVE SINGLE-ARM CONTROLLED TRIAL OF 3-WEEK-COURSE HYPOFRACTIONATED PREOPERATIVE RADIOTHERAPY FOR SOFT TISSUE SARCOMA OF THE EXTREMITY OR TRUNK

B. Ashleigh Guadagnolo; Devarati Mitra; Ahsan Farooqi; Caroline Hempel; Courtney Dorber; Rony Mathai; Wei-Lien Wang; Ravin Ratan; Keila E. Torres; Neeta Somaiah; Kelly K. Hunt; Christopher P. Scally; Emily Z. Keung; Robert Satcher; Justin E. Bird; Patrick Lin; Bryan Moon; Valerae Lewis; Christina L. Roland; Andrew J. Bishop MD
The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES

1:29 PM - 1:36 PM

Paper #44 #1818730

A PHASE IA/IB DOSE-ESCALATION/EXPANSION STUDY OF THE MDM2-P53 ANTAGONIST BI 907828 IN PATIENTS WITH ADVANCED/METASTATIC SARCOMA

Mrinal M. Gounder¹; Manish R. Patel²; Noboru Yamamoto³; Todd M. Bauer⁴; Scott Laurie⁵; Alejandro Perez-Pitarch⁶; Junxian Geng⁷; Jan Cheng⁷; Mehdi Lahmar⁶; Patricia LoRusso⁸
¹Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES; ²Sarah Cannon Research Institute, Florida Cancer Specialists & Research Institute, Sarasota, Florida, UNITED STATES; ³National Cancer Center Hospital, Tokyo, Tokyo, JAPAN; ⁴Sarah Cannon Research Institute Tennessee Oncology, Nashville, Tennessee, UNITED STATES; ⁵The Ottawa Hospital Cancer Centre, Ottawa, Ontario, CANADA; ⁶Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Rheinland-Pfalz, GERMANY; ⁷Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, Connecticut, UNITED STATES; ⁸Yale University School of Medicine, Yale Cancer Center, New Haven, Connecticut, UNITED STATES

1:36 PM - 1:43 PM

Paper #45 #1818752

FINAL ANALYSIS FROM AMPECT, AN OPEN-LABEL PHASE 2 REGISTRATION TRIAL OF NAB-SIROLIMUS FOR PATIENTS WITH ADVANCED MALIGNANT PERIVASCULAR EPITHELIOID CELL TUMORS (PECOMA)

Andrew J. Wagner¹; Vinod Ravi²; Richard F. Riedel³; Kristen N. Ganjoo⁴; Brian Andrew A. Van Tine⁵; Rashmi Chugh⁶; Lee D. Cranmer⁷; Erlinda M. Gordon⁸; Jason L. Hornick⁹; Heng Du⁹; Berta Grigorian¹⁰; Anita N. Schmid¹⁰; Shihe Hou¹⁰; Katherine Harris¹⁰; David J. Kwiatkowski⁹; Neil P. Desai¹⁰; Mark A. Dickson¹¹
¹Harvard Medical School, Dana-Farber Cancer Institute, Boston, Massachusetts, UNITED STATES; ²The University of Texas MD Anderson Cancer Center, Houston, UNITED STATES; ³Duke Cancer Institute, Duke University Medical Center, Durham, North Carolina, UNITED STATES; ⁴Stanford Cancer Center, Stanford, California, UNITED STATES; ⁵Washington University School of Medicine, St. Louis, Missouri, UNITED STATES; ⁶University of Michigan, Ann Arbor, Michigan, UNITED STATES; ⁷Univ Washington/Fred Hutchinson Cancer Res Ctr, Seattle, Washington, UNITED STATES; ⁸Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES; ⁹Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES; ¹⁰Aadi Bioscience, Pacific Palisades, California, UNITED STATES; ¹¹Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES

1:43 PM - 1:50 PM

Paper #46 #1818788

A PHASE 2 STUDY OF TALIMOGENE LAHERPAREPVEC, NIVOLUMAB AND TRABECTEDIN (TNT) IN ADVANCED SARCOMA

Sant P. Chawla; Simranjit Sekhon; Ted Kim; Noufil Adnan; Ania Moradkhani; Victoria T. Chua-Alcala; Ishrat Bhuiyan; Kitty Zheng; Erlinda M. Gordon
Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES

1:50 PM - 1:57 PM

Paper #47 #1818707

SCOPES, AN INNOVATIVE RANDOMIZED TRIAL FOR EXTREMITY SOFT TISSUE SARCOMA PATIENTS: A MODIFIED PICK-THE-WINNER DESIGN

Lisette Wiltink¹; Astrid Scholten²; Augustinus Krol¹; Winan J. van Houdt²; Yvonne M. Schrage¹; Michiel van de Sande¹; Jos A. van der Hage¹; Judith V.M.G. Bovée¹; Marta Fiocco¹; Rick L. Haas²
¹The Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS; ²The Netherlands Cancer Institute, Amstetdam, Noord-Holland, NETHERLANDS

1:57 PM - 2:04 PM

Paper #48 #1818765

SAKK 57/16 NNAB-PACLITAXEL AND GEMCITABINE IN SOFT TISSUE SARCOMA (NAPAGE): RESULTS FROM PHASE IB/II TRIAL

Antonia Digkila¹; Attila Kollár²; Marie-Noelle Kronig²; Christian Britschgi³; Tamara Rordorf³; Markus Joerger⁴; Fatime Krasniqo⁵; Yannis Metaxas⁶; Ilaria Colombo⁷; Daniel Dietrich⁸; Karin Rothgiesser⁹; Karin Ribi¹⁰; Christian Rothermundt⁴

¹CHUV, Lausanne, Vaud, SWITZERLAND; ²Inselspital, Bern University Hospital, University of Bern, Bern, SWITZERLAND;

³University Hospital Zurich, Zurich, SWITZERLAND; ⁴Kantonsspital St. Gallen, St Gallen, Sankt Gallen, SWITZERLAND;

⁵University Hospital of Basel, Bale, Basel-Stadt, SWITZERLAND; ⁶Cantonal Hospital Grison, Chur, Graubunden, SWITZERLAND; ⁷Oncology Institute of Southern Switzerland, Ente Ospedaliero Cantonale, Bellinzona, Ticino, SWITZERLAND;

⁸Swiss Group for Clinical Cancer Research (SAKK) Coordinating Center, Bern, SWITZERLAND; ⁹Swiss Group for Clinical Cancer Research (SAKK) Coordinating Center, Bern, SWITZERLAND; ¹⁰International Breast Cancer Study Group IBCSG (IBCSG), Bern, SWITZERLAND

2:04 PM - 2:11 PM

Paper #49 #1818775

PHASE I TRIAL OF OLARATUMAB PLUS TRABECTEDIN IN ADVANCED SOFT-TISSUE SARCOMA PATIENTS: OLATRASTS, A SPANISH GROUP FOR RESEARCH ON SARCOMA (GEIS) STUDY

Javier Martin-Broto¹; Claudia M. Valverde²; Rosa Alvarez³; Roberto Diaz⁴; Daniel Bernabeu⁵; Rafael Ramos⁶; César Serrano⁷; Antonio Gutierrez⁶; David Moura⁸; **Nadia Hindi**¹

¹Fundacion Jimenez Diaz University Hospital, Madrid, Madrid, SPAIN; ²Hospital Universitario Vall d'Hebron, Barcelona, Catalonia, SPAIN; ³Gregorio Marañon University Hospital, Madrid, Madrid, SPAIN; ⁴La Fe University Hospital, Valencia, Comunidad Valenciana, SPAIN; ⁵La Paz University Hospital, Madrid, Madrid, SPAIN; ⁶Son Espases University Hospital, Palma de Mallorca, Islas Baleares, SPAIN; ⁷Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Catalonia, SPAIN;

⁸CITIUS III, Seville, Andalucia, SPAIN

2:11 PM - 2:30 PM Q&A

2:30 PM - 3:15 PM **POSTER SESSION 2**
(POSTERS 138-261)

3:30 PM - 4:30 PM **Aadi Symposium**
THE CHALLENGES IN STUDYING RARE DISEASES:
EMERGING THERAPIES FOR RARE SARCOMAS

Moderator: **Andrew J. Wagner, MD, PhD**
Dana-Farber Cancer Institute

Presenter: **Jason L. Hornick, MD, PhD**
Brigham and Women's Hospital, Harvard Medical School

Presenter: **Javier Martin-Broto, MD PhD**
University Hospital Fundacion Jimenez Diaz and Research Group ATBsarc

Presenter: **Silvia Stacchiotti**
Fondazione IRCCS Istituto Nazionale Tumori

8:00 AM - 9:00 AM

CTOS Board of Directors

9:00 AM - 10:15 AM

– Session 9 –

**MULTIDISCIPLINARY MANAGEMENT, NEOADJUVANT THERAPY
& TREATMENT OF OLIGOMETASTATIC DISEASE**

Chair: **Christina L. Roland, MD**

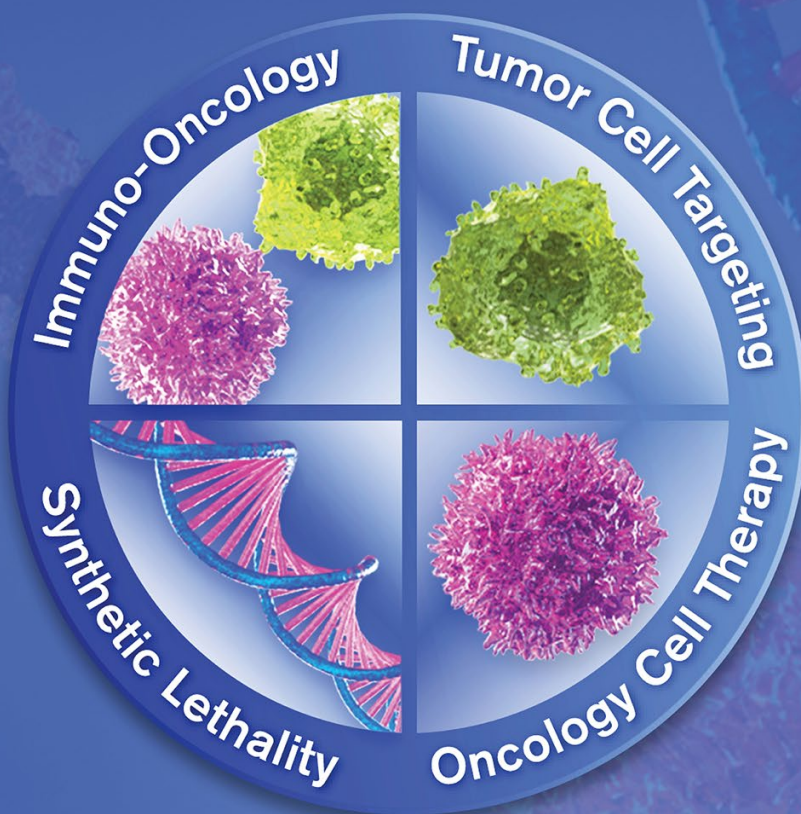
9:00 AM - 9:07 AM

Paper #50 #1818769

QUALITY INDICATORS OF SARCOMA WORK-UP

Bruno Fuchs¹; Philip Heesen¹; Gabriela Studer²; Beata Bode¹; Stefan Breitenstein¹; Javier Martin-Broto³; Alessandro Gronchi⁴; Jean-Yves Blay⁵; Axel LeCesne⁶

¹Swiss Sarcoma Network, Zurich, SWITZERLAND; ²University Hospital, Luzern; Swiss Sarcoma Network, Luzern, SWITZERLAND; ³University of Sevilla, SELNET; Swiss Sarcoma Network, Sevilla, Galicia, SPAIN; ⁴Istituto Tumori, Milano; Swiss Sarcoma Network, Milano, Lombardia, ITALY; ⁵Centre Leon-Berard; Swiss Sarcoma Network, Lyon, Rhone-Alpes, FRANCE; ⁶Gustave Roussy, Paris; Swiss Sarcoma Network, Paris, Centre, FRANCE



Explore our science

Visit the GSK virtual booth to learn more

41 GSK oncology pipeline **clinical trials** currently underway*

*Includes a trial in collaboration with 23andMe, a trial in collaboration and license alliance with iTeos Therapeutics, and trials on assets in-license or from other partnership with third parties.

9:07 AM - 9:14 AM

Paper #51 #1818695

NEOADJUVANT AND ADJUVANT RADIOTHERAPY DECREASES THE RISK OF LOCAL RECURRENCE AND IMPROVES OVERALL SURVIVAL IN A MULTICENTRE COHORT OF 2162 EXTREMITY SOFT TISSUE SARCOMA PATIENTS

Joanna Szkandera¹; Maria Anna Smolle¹; Judith Woelfel¹; Ibtissam Acem²; Michiel van de Sande²; Lee Jays³; Han Bonekamp⁴; Rob Pollock⁵; Johnny Keller⁶; Per-Ulf Tunn⁷; Rick Haas²; Robert Van Ginkel⁸; Cornelis Verhoef⁹; Florian Posch¹; Bernadette Liegl-Atzwanger¹; Dalia Moustafa-Hubmer¹; Philipp Jost¹; Andreas Leithner¹

¹Medical University of Graz, Graz, Steiermark, AUSTRIA; ²Leiden University Medical Centre, Leiden, Zuid-Holland, NETHERLANDS; ³The Royal Orthopaedic Hospital, Birmingham, England, UNITED KINGDOM; ⁴Radboud University Medical Center, Nijmegen, Gelderland, NETHERLANDS; ⁵Royal National Orthopaedic Hospital, London, England, UNITED KINGDOM; ⁶Aarhus University Hospital, Aarhus, Midtjylland, DENMARK; ⁷HELIOS Klinikum Berlin-Buch, Berlin, Berlin, GERMANY; ⁸University Medical Center Groningen (UMCG), Groningen, Groningen, NETHERLANDS; ⁹Erasmus MC Cancer Institute, Rotterdam, Zuid-Holland, NETHERLANDS

9:14 AM - 9:21 AM

Paper #52 #1818772

THE ROLE OF PERIOPERATIVE CHEMOTHERAPY IN PRIMARY HIGH-GRADE EXTREMITY SOFT TISSUE SARCOMA: A RISK-STRATIFIED ANALYSIS USING PERSARC

Ibtissam Acem¹; Anja Rueten-Budde²; Dirk J. Grünhagen¹; Hans Gelderblom²; Winan J. van Houdt³; Cornelis Verhoef¹; Michiel van de Sande²

¹Erasmus MC Cancer Institute, Rotterdam, Zuid-Holland, NETHERLANDS; ²Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS; ³The Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS

9:21 AM - 9:28 AM

Paper #53 #1818773

IMMUNE INFILTRATE IN PRIMARY HIGH-RISK SOFT TISSUE SARCOMAS TREATED WITH NEOADJUVANT CHEMOTHERAPY AND SURGERY IN THE ISG-ST5-1001 RANDOMISED TRIAL: A PROGNOSTIC STUDY

Sandro Pasquali¹; Chiara Castelli¹; Paola Collini¹; Cleofe Romagosa²; Silvia Bague³; Jean-Michel Coindre⁴; Angelo Paolo Dei Tos⁵; Marta Barisella¹; Salvatore Lorenzo Renne⁶; Luca Lalli¹; Biagio Eugenio Leone⁷; Viviana Vallacchi¹; Emanuela Palmerini⁸; Vittorio Lorenzo Quagliuolo⁶; Javier Martin-Broto⁹; Antonio Lopez-Pousa³; Giovanni Grignani MD¹⁰; Jean-Yves Blay¹¹; Robert Diaz Beveridge¹²; Franco Domenico Merlo¹³

¹Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY; ²Hospital Universitari Vall d'Hebron, and Universitat Autònoma de Barcelona, Barcelona, Catalonia, SPAIN; ³Hospital de la Santa Creu i Sant Pau, Barcelona, Catalonia, SPAIN; ⁴Institut Bergonié, Bordeaux, Aquitaine, FRANCE; ⁵Università di Padova (UniPD), Padova, Veneto, ITALY; ⁶Humanitas Clinical and Research Center, Milano, Lombardia, ITALY; ⁷Università di Milano Bicocca, Milano, Lombardia, ITALY; ⁸IRCCS Istituto Ortopedico Rizzoli, Bologna, Emilia-Romagna, ITALY; ⁹Hospital Universitario Virgen del Rocío, Sevilla, Andalucía, SPAIN; ¹⁰Candiolo Cancer Institute FPO-IRCCS, Candiolo, Piemonte, ITALY; ¹¹Centre Léon Bérard, Lyon, Auvergne, FRANCE; ¹²Hospital Universitario y Politécnico La Fe, Valencia, Comunidad Valenciana, SPAIN; ¹³AUSL Reggio Emilia, Reggio Emilia, Emilia-Romagna, ITALY

9:28 AM - 9:35 AM

Paper #54 #1818694

A MODERATE DOSE OF PREOPERATIVE RADIOTHERAPY MAY IMPROVE RESECTABILITY IN MYXOID LIPOSARCOMA

Jules Lansu¹; Kirsten van Langevelde²; Pètra Braam³; Erik van Werkhoven¹; Astrid Scholten¹; Yvonne M. Schrage²; Winan J. van Houdt¹; Rick L. Haas¹

¹Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS; ²Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS; ³Radboud University Medical Center, Nijmegen, Overijssel, NETHERLANDS

9:35 AM - 9:42 AM

Paper #55 #1818748

PRELIMINARY RESULTS OF PHASE II SINGLE-ARM STUDY ON PREOPERATIVE INTENSITY-MODULATED RADIOTHERAPY WITH CONCURRENT ANLOTINIB FOR PATIENTS WITH NON-METASTATIC EXTREMITY AND TRUNK SOFT TISSUE SARCOMA

Ning-Ning Lu¹; Li-Bin Xu²; Hong-Tu Zhang²; Zhen-Guo²; Zhao-Yang²; Ting Liu²; Xin-Xin Zhang²; Meng Li²; Lei Miao Master²; Hao Jing²; Qing Chang²; YiHeBaLi Chi²; Jia-Yu Wang²; Shu-Lian Wang²; Sheng-Ji Yu²

¹Chinese Academy of Medical Sciences, Beijing, Beijing, CHINA (PEOPLE'S REPUBLIC);

²Cancer Hospital, Cancer Institute, Beijing, Beijing, CHINA (PEOPLE'S REPUBLIC)

9:42 AM - 9:49 AM

Paper #56 #1818789

SAFE MARGIN SURGERY USING PLASTIC RECONSTRUCTION IN EXTREMITIES OR PARIETAL TRUNK SOFT TISSUE SARCOMA: A TERTIARY SINGLE CENTER EXPERIENCE

Laura Samà¹; Jean Philippe Binder²; Lauren Darrigues²; Benoit Couturaud Couturaud²; Benoit Boura²; Sylvie Helfre²; Laurent Chiche²; Nayla Nicolas²; Dimitri Tzanis²; Toufik Bouhadiba²; Julie Perlberg-Samson²; Sylvie Bonvalot

¹Humanitas Clinical and Research Hospital/Humanitas University, Milan, Lombardia, ITALY; ²Institute Curie, Paris, Ile-de-France, FRANCE

9:49 AM - 9:56 AM

Paper #57 #1818729

RESTAGING AFTER NEOADJUVANT RADIOTHERAPY FOR SOFT TISSUE SARCOMA OF THE EXTREMITIES AND TRUNK

Bob Schultze; Ibtissam Acem; Dirk J. Grünhagen; Cornelis Verhoef
Erasmus MC Cancer Institute, Rotterdam, Zuid-Holland, NETHERLANDS

9:56 AM - 10:15 AM Q&A

10:15 AM - 11:00 AM

– Session 10 –

QUALITY OF LIFE AND PATIENTS PERSPECTIVE

Chair: **Winette van der Graaf, MD, PhD**

10:15 AM - 10:22 AM

Paper #58 #1818703

SETTING THE INTERNATIONAL RESEARCH AGENDA FOR SARCOMA TOGETHER WITH PATIENTS AND CARERS: FIRST RESULTS OF THE SARCOMA PATIENT EURONET (SPAEN) PATIENT INVOLVEMENT AND PRIORITY PROJECT

Olga Husson¹; Kathrin Schuster²; Paul van Kampen³; Carlos Kooops³; Olga Husson¹; Marije Weidema⁴; Richard Davidson⁵; Markus Wartenberg²; Estelle Artzner²; Ornella Gonzato⁶; Natalia Fernandez²; Phil Green²; Bernd Kasper⁷; Kai Pilgermann²; Sami Sandakly²; Lotta Våde²; Roger Wilson⁵; Winette T. A. van der Graaf¹; Gerard van Oortmerssen³

¹Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS; ²Sarcoma Patients EuroNet (SPAEN), Riemerling, Bayern, GERMANY; ³Dutch Sarcoma Patient Platform, Utrecht, Utrecht, NETHERLANDS; ⁴Radboud University Medical Center, Nijmegen, Gelderland, NETHERLANDS; ⁵Sarcoma UK, London, England, UNITED KINGDOM; ⁶Trust Paola Gonzato-Rete Sarcoma, Milan, Lombardia, ITALY; ⁷Mannheim Cancer Center (MCC), University of Heidelberg, Mannheim University Medical Center, Mannheim, Baden-Wurttemberg, GERMANY

10:22 AM - 10:29 AM

Paper #59 #1818735

SARCOMA UK SUPPORT LINE - 5 YEARS ON

Helen Stradling; Sam Hackett; Carly McDonald BSc
Sarcoma UK, London, England, UNITED KINGDOM

10:29 AM - 10:36 AM

Paper #60 #1818762

DEFINING DEPRESSION AND ANXIETY IN ORTHOPAEDIC SARCOMA PATIENTS

Elizabeth Polfer; Yesne Alici; Ray Baser; John H. Healey; Meredith Bartelstein
Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES

10:36 AM - 10:43 AM

Paper #61 #1818759

HEALTH-RELATED QUALITY OF LIFE PREDICTS 1-YEAR-SURVIVAL IN SARCOMA PATIENTS - RESULTS OF A GERMAN OBSERVATIONAL STUDY

Martin Eichler¹; Susanne Singer²; Leopold Hentschel¹; Stephan Richter¹; Peter Hohenberger³; Bernd Kasper³; Dimosthenis Andreou⁴; Daniel Pink⁴; Jens Jakob⁵; Martin Bornhäuser¹; Jochen Schmitt⁶; Markus K. Schuler¹;
¹University Hospital Carl Gustav Carus, Dresden, Sachsen, GERMANY; ²University Hospital Mainz, Mainz, Rheinland-Pfalz, GERMANY; ³Mannheim University Medical Center, University of Heidelberg, Mannheim, Baden-Württemberg, GERMANY; ⁴Helios Klinikum Bad Saarow, Bad Saarow, Brandenburg, GERMANY; ⁵University Hospital Goettingen, Goettingen, Niedersachsen, GERMANY; ⁶National Center for Tumor Diseases (NCT/UCC), Dresden, Sachsen, GERMANY

10:43 AM - 11:00 AM Q&A

11:00 AM - 12:00 PM

– Session 11 –

RETROPERITONEAL SARCOMA

Chair: **Elizabeth H. Baldini, MD, MPH**

11:00 AM - 11:07 AM

Paper #63 #1818702

ASSOCIATION BETWEEN AGEING AND SHORT-TERM SURVIVAL OUTCOMES IN PATIENTS UNDERGOING SURGERY FOR PRIMARY RETROPERITONEAL SARCOMA

Fabio Tirota¹; Michael Fadel¹; Helene Wilkerson¹; Alessandro Parente²; James Hodson²; Marco Baia²; Jonathan Hannay³; Max Almond²; Myles Smith³; Samuel J. Ford²; Andrew J. Hayes³; Anant Desai²; Dirk Strauss³

¹The Royal Marsden Hospital NHS Foundation Trust, London, England, UNITED KINGDOM; ²University Hospital Birmingham NHS Foundation Trust, Birmingham, England, UNITED KINGDOM; ³The Royal Marsden Hospital NHS Foundation Trust, London, England, UNITED KINGDOM

11:07 AM - 11:14 AM

Paper #64 #1818767

PROGNOSIS PREDICTION IN PATIENTS WITH RETROPERITONEAL SARCOMA: UPDATE OF CURRENT NOMOGRAMS

Dario Callegaro¹; Francesco Barretta¹; Chandrajit P. Raut²; Sally Burtenshaw³; Dirk Strauss⁴; Charles Honoré⁵; Sylvie Bonvalot⁶; Mark Fairweather⁷; Piotr L. Rutkowski⁸; Winan J. van Houdt⁹; Rebecca A. Gladdy¹⁰; Fabio Tirota⁴; Dimitri Tzanis⁶; Jacek Skoczylas⁸; Rick L. Haas⁹; Rosalba Miceli¹; Carol J. Swallow¹⁰; Alessandro Gronchi¹

¹Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY; ²Harvard Medical School, Dana-Farber Cancer Institute, Harvard University, Boston, Massachusetts, UNITED STATES; ³Mount Sinai Hospital, Toronto, Ontario, CANADA; ⁴The Royal Marsden Hospital NHS Foundation Trust, London, England, UNITED KINGDOM; ⁵Institut Gustave Roussy, Villejuif, Ile-de-France, FRANCE; ⁶Institut Curie, Paris, Ile-de-France, FRANCE; ⁷Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES; ⁸Maria Sklodowska-Curie Institute -Oncology Center, Institute of Oncology, Warsaw, Mazowieckie, POLAND; ⁹The Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS; ¹⁰Princess Margaret Hospital, University Health Network and Mount Sinai Hospital, Toronto; Lunenfeld Tanenbaum Research Institute, Sinai Health System, Toronto, Ontario, CANADA

11:14 AM - 11:21 AM

Paper #65 #1818737

A COMPARISON OF SURVIVAL OUTCOMES AT SPECIALIST VS. NON-SPECIALIST SARCOMA CENTRES, FOR PATIENTS WITH PRIMARY RETROPERITONEAL SARCOMA: AN ENGLISH POPULATION-BASED COHORT ANALYSIS

Fabio Tirotta¹; Shane Collins²; Andrew Bacon³; Anant Desai⁴; Lizz Paley⁵; Dirk Strauss¹; Sandra J. Strauss²

¹The Royal Marsden Hospital NHS Foundation Trust, London, England, UNITED KINGDOM; ²University College London Cancer Institute, London, England, UNITED KINGDOM; ³National Cancer Registration and Analysis Service, Public Health England, London, England, UNITED KINGDOM; ⁴University Hospital Birmingham NHS Foundation Trust, Birmingham, England, UNITED KINGDOM; ⁵National Cancer Registration and Analysis Service, Public Health England, London, England, UNITED KINGDOM

11:21 AM - 11:28 AM

Paper #66 #1818758

RECLASSIFYING ABDOMINAL NON-UTERINE LEIOMYOSARCOMA: USING A RADIOLOGICAL ANATOMIC APPROACH WITH IMPLICATIONS FOR PATIENT OUTCOMES

Korosh Khalili¹; David Cyr²; Usman Tarique²; Carlo Morosi³; Giorgio Greco³; Rebecca A. Gladdy⁴; Brendan C. Dickson⁵; Dario Callegaro³; Carol J. Swallow⁴

¹University of Toronto, Toronto, Ontario, CANADA; ²Sinai Health System, Toronto, Ontario, CANADA; ³Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY; ⁴Princess Margaret Hospital, University Health Network and Mount Sinai Hospital, Toronto; Lunenfeld Tanenbaum Research Institute, Sinai Health System, Toronto, Ontario, CANADA; ⁵Mount Sinai Hospital, Toronto, Ontario, CANADA



RAFAEL PHARMACEUTICALS

To Save A Life Is To Save A Universe

Developing innovative therapies that will transform the way we treat patients with rare, hard-to-treat cancers. Paving the path in cancer metabolism-based therapeutics for hard-to-treat cancers, Rafael's first-in-class clinical lead compound, CPI-613[®] (devimistat), targets enzymes that are involved in cancer cell energy metabolism and are located in the mitochondria of cancer cells.

Visit rafaelpharma.com to learn more.

11:28 AM - 11:35 AM

Paper #67 #1818761

WHAT IS THE SIGNIFICANCE OF MICROSCOPIC MARGIN STATUS IN RESECTED PRIMARY RETROPERITONEAL SARCOMA?

Deanna Ng¹; Dario Callegaro²; Brendan C. Dickson³; Dirk Strauss⁴; Sylvie Bonvalot⁵; Chandrajit P. Raut⁶; Charles Honoré⁷; Eberhard Stoeckle⁸; Winan J. van Houdt⁹; Eisar Al-Sukhni³; Shawn Khan³; Rebecca A. Gladdy¹⁰; Marco Fiore²; Mark Fairweather¹¹; Raza Sayyed⁴; Dimitri Tzanis⁵; Yvonne M. Schrage¹²; Alessandro Gronchi²; Carol J. Swallow¹⁰

¹University of Toronto, Toronto, Ontario, CANADA; ²Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY; ³Mount Sinai Hospital, Toronto, Ontario, CANADA; ⁴The Royal Marsden Hospital NHS Foundation Trust, London, England, UNITED KINGDOM; ⁵Institut Curie, PSL Research University, Paris, Ile-de-France, FRANCE; ⁶Harvard Medical School, Dana-Farber Cancer Institute, Harvard University, Boston, Massachusetts, UNITED STATES; ⁷Institut Gustave Roussy, Villejuif, Ile-de-France, FRANCE; ⁸Institut Bergonie, Bordeaux, Aquitaine, FRANCE; ⁹The Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS; ¹⁰Princess Margaret Hospital, University Health Network and Mount Sinai Hospital, Toronto; Lunenfeld Tanenbaum Research Institute, Sinai Health System, Toronto, Ontario, CANADA; ¹¹Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES; ¹²Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS

11:35 AM - 11:42 AM

Paper #68 #1818716

RETROPERITONEAL SOFT TISSUE SARCOMA: RECENT OUTCOME IMPROVEMENT AT A SINGLE INSTITUTION

Marco Fiore¹; Max Almond²; Francesco Barretta¹; Stefano Cioffi¹; Dario Callegaro¹; Chiara Colombo¹; Stefano Radaelli¹; Sandro Pasquali¹; Marta Barisella¹; Carlo Morosi¹; Roberta Sanfilippo¹; Claudia Sangalli¹; Rosalba Miceli¹; Paolo G. Casali¹; Alessandro Gronchi¹

¹Fondazione IRCCS Istituto Nazionale dei Tumori; Milan, Lombardia, ITALY; ²University Hospital Birmingham NHS Foundation Trust, Birmingham, England, UNITED KINGDOM

11:42 AM - 12:00 PM Q&A

12:00 PM - 12:30 PM Break

12:30 PM - 1:15 PM

**HERMAN SUIT LECTURE –
SARCOMA MODELING TOWARDS PATIENT SPECIFIC TREATMENT**

Judith V.M.G. Bovée, MD, PhD

1:15 PM - 2:30 PM

– Session 12 –

ULTRA-RARE AND TRANSLOCATION SARCOMAS

Chair: **Thierry Alcindor, MD, MSc, FRCPC**

1:15 PM - 1:22 PM

Paper #69 #1818698

A ROLE FOR SMARCB1 IN SYNOVIAL SARCOMAGENESIS REVEALS THAT THE SS18-SSX FUSION ONCOPROTEIN INDUCES CANONICAL BAF COMPLEX DESTRUCTION

Jinxu Li¹; Timothy S. Mulvihill¹; Li Li PhD¹; Jared J. Barrott²; Mary Nelson¹; Lena Wagner³; Ian Lock¹; Amir Pozner¹; Sydney L. Lambert¹; Benjamin B. Ozenberger¹; Michael B. Ward¹; Allie H. Grossmann¹; Ting Liu¹; Ana Banito³; Bradley R. Cairns¹; Kevin B. Jones¹

¹Huntsman Cancer Institute, University of Utah, Salt Lake City, Utah, UNITED STATES; ²Idaho State University, Pocatello, Idaho, UNITED STATES; ³Hopp Children's Cancer Center, German Cancer Research Center, Heidelberg, Baden-Wurttemberg, GERMANY

1:22 PM - 1:29 PM

Paper #70 #1818722

DISCONTINUATION OF LAROTRECTINIB PRIOR TO DISEASE PROGRESSION IN PEDIATRIC SARCOMA: ANALYSIS FROM SCOUT TRIAL

Steven G. DuBois¹; Daniel Orbach²; Catherine M. Albert³; Noah C. Federman⁴; Ramamoorthy Nagasubramanian⁵; Neerav Shukla⁶; Daniel A. Morgenstern⁷; Christian Michel Zwaan⁸; Ricarda Norenberg⁹; Marc Fellous¹⁰; Esther De La Cuesta¹¹; Cornelis M. van Tilburg¹²; Theodore W. W. Laetsch¹³; Leo Mascarenhas¹⁴

¹Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, Massachusetts, UNITED STATES; ²SIREDO Oncology Center (Care, Innovation and Research for Children, Adolescents and Young Adults with Cancer), Institut Curie, PSL University, Paris, Ile-de-France, FRANCE; ³Seattle Children's Hospital, University of Washington, Fred Hutchinson Cancer Research Center, Seattle, Washington, UNITED STATES; ⁴Health Sciences Clinical Professor, Pediatrics and Orthopaedic Surgery, UCLA Medical Center, Los Angeles, California, UNITED STATES; ⁵Nemours Children's Hospital, Orlando, Florida, UNITED STATES; ⁶Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES; ⁷Hospital for Sick Children, Toronto, Ontario, CANADA; ⁸Prinses Maxima Centrum, Utrecht, Utrecht, NETHERLANDS; ⁹Chrestos Concept GmbH & Co. KG, Essen, Nordrhein-Westfalen, GERMANY; ¹⁰Bayer HealthCare Pharmaceuticals, Basel, Basel-Stadt, SWITZERLAND; ¹¹Bayer HealthCare Pharmaceuticals, Inc., Whippany, New Jersey, UNITED STATES; ¹²Hopp Children's Cancer Center Heidelberg (KITZ), Heidelberg University Hospital and German Cancer Research Center (DKFZ), Heidelberg, Baden-Wurttemberg, GERMANY; ¹³University of Texas Southwestern Medical Center/Children's Health, Dallas, Texas, UNITED STATES; ¹⁴Children's Hospital Los Angeles, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES

1:29 PM - 1:36 PM

Paper #71 #1818755

NAB-SIROLIMUS IN PATIENTS WITH MALIGNANT PECOMA PREVIOUSLY TREATED WITH MTOR INHIBITORS: EMERGING EXPERIENCE FROM AN EXPANDED ACCESS PROGRAM

Mark A. Dickson MD¹; Vinod Ravi MD²; James L. Chen³; Martina C. Murphy⁴; Christopher Y. Thomas⁵; Anita N. Schmid⁶; Andrew J. Wagner⁷

¹Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES; ²The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES; ³Ohio State University, Columbus, Ohio, UNITED STATES; ⁴University of Florida, Department of Medicine, Gainesville, Florida, UNITED STATES; ⁵Wake Forest Baptist Health, Winston-Salem, North Carolina, UNITED STATES; ⁶Aadi Bioscience, Pacific Palisades, California, UNITED STATES; ⁷Harvard Medical School, Dana-Farber Cancer Institute, Boston, Massachusetts, UNITED STATES

1:36 PM - 1:43 PM

Paper #72 #1818734

INTERIM RESULTS OF AN INTERNATIONAL PHASE 2 STUDY OF THE MICROTUBULE INHIBITOR ERIBULIN, IN PROGRESSIVE METASTATIC ANGIOSARCOMA (AS) AND EPITHELIOID HEMANGIOENDOTHELIOMA (EHE)

Gregory M. Cote¹; Lucille Sebastian²; Edwin Choy¹; Peter Grimison³; Priscilla Merriam⁴; Mandy Ballinger⁵; Alec Colon¹; Subo Thavaneswaran²; Michael Nathenson⁴; Frank Lin⁵; Katherine A. Thornton⁶; Corrie Painter⁷; Esha Jain⁷; John Grady⁵; Michael Millward⁸; Michael Brown⁹; Rosemary Harrup¹⁰; David Espinoza²; George D. Demetri⁴; Suzanne George⁴

¹Massachusetts General Hospital, Boston, Massachusetts, UNITED STATES; ²National Health and Medical Research Council Centre for Clinical Trials, Sydney, New South Wales, AUSTRALIA; ³Chris O'Brien Lifecare, Sydney, New South Wales, AUSTRALIA; ⁴Dana Farber Cancer Institute, Boston, Massachusetts, UNITED STATES; ⁵Garvan Institute, Western Sydney University, Campbelltown, New South Wales, AUSTRALIA; ⁶Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES; ⁷The Broad Institute of MIT and Harvard, Cambridge, Massachusetts, UNITED STATES; ⁸Sir Charles Gairdner Hospital, Perth, Western Australia, AUSTRALIA; ⁹Royal Adelaide Hospital, Adelaide, South Australia, AUSTRALIA; ¹⁰Royal Hobart Hospital, Hobart, Tasmania, AUSTRALIA

1:43 PM - 1:50 PM

Paper #73 #1818711

EXAMINING STRIPES ON A HERD OF ZEBRAS: IMPACT OF GENOMIC MATCHING FOR ULTRARARE SARCOMAS IN PHASE 1 CLINICAL TRIALS

Justin T. Moyers¹; Jason Roszik¹; Roberto Carmagnani Pestana²; J Andrew Livingston¹; Alejandra Zarzour¹; Vinod Ravi¹; Ravin Ratan¹; Neeta Somaiah¹; Anthony P. Conley¹; Vivek Subbiah¹

¹The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES; ²Hospital Israelita Albert Einstein, São Paulo, Sao Paulo, BRAZIL

1:50 PM - 1:57 PM

Paper #74 #1818732

TK216 FOR EWING SARCOMA- INTERIM PHASE 1/2 RESULTS

Ravin Ratan¹; Joseph A. Ludwig¹; Noah C. Federman²; Peter M. Anderson³; Margaret E. Macy⁴; Richard F. Riedel⁵; Lara E. Davis⁶; Najat C. Daw¹; Jade E. Wulff⁷; Aerang Kim⁸; Jeffrey A. Toretsky⁹; Edwina Baskin-Bey¹⁰; James B. Breitmeyer¹⁰; Paul Meyers¹¹

¹University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES; ²UCLA Medical Center, Los Angeles, California, UNITED STATES; ³Cleveland Clinic Foundation, Cleveland, Ohio, UNITED STATES; ⁴University of Colorado and Children's Hospital of Colorado, Aurora, Colorado, UNITED STATES; ⁵Duke Cancer Institute, Duke University Medical Center, Durham, North Carolina, UNITED STATES; ⁶Knight Cancer Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES; ⁷Pediatrics, Texas Children's Hospital, Houston, Texas, UNITED STATES; ⁸Children's National Medical Center, Washington, District of Columbia, UNITED STATES; ⁹Georgetown University, Washington, District of Columbia, UNITED STATES; ¹⁰Oncotherapeutics Inc., San Diego, California, UNITED STATES; ¹¹Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES

1:57 PM - 2:04 PM

Paper #75 #1818713

COMPREHENSIVE ANALYSIS OF INFANTILE SOFT-TISSUE SARCOMAS WITH BCOR ALTERATIONS

Nawal Merjaneh¹; Hee Kim¹; Heather Escoto²; Jonathan Metts³; Anish Ray⁴; Andrew Bukowinski⁵; Zachary LeBlanc⁶; Douglas Fair⁷; Masayo Watanabe⁸; Elizabeth Alva⁹; Kevin Todd¹; Jessica D. Daley⁵; Duncan Hartt⁷; Sara Szabo¹; Joseph Pressey¹

¹Cancer and Blood Diseases Institute/ Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, UNITED STATES; ²Peyton Manning Children's Hospital, Indianapolis, Indiana, UNITED STATES; ³Cancer and Blood Disorders Institute/ Jones Hopkins All Children's Hospital, St Petersburg, Florida, UNITED STATES; ⁴Cook Children's Hospital, Fort Worth, Texas, UNITED STATES; ⁵UPMC Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES; ⁶LSU Health Sciences Center New Orleans, New Orleans, Louisiana, UNITED STATES; ⁷University of Utah, Salt Lake City, Utah, UNITED STATES; ⁸Phoenix Children's Hospital, Phoenix, Arizona, UNITED STATES; ⁹University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES

Saturday, 13 November, 2021

2:04 PM - 2:11 PM

Paper #76 #1818714

A MULTICENTER RETROSPECTIVE ANALYSIS ON THE EFFECT MUTATIONAL STATUS ON OUTCOMES FOR PATIENTS WITH PECOMA

Lawrence W. Liu¹; Carina Dehner¹; Dana C. Borcharding¹; John S. Chrisinger¹; Jingqin Luo¹; Amanda Parkes²; Nam Bui³; Elizabeth J. Davis⁴; Varun Monga⁵; Mohammed Milhem⁵; Ryan Jones⁶; Angela Hirbe⁷

¹Washington University in St. Louis, St. Louis, Missouri, UNITED STATES; ²University of Wisconsin Carbone Cancer Center, Madison, Wisconsin, UNITED STATES; ³Stanford University Department of Oncology, Stanford, California, UNITED STATES; ⁴Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES; ⁵University of Iowa Health Care, Iowa City, Iowa, UNITED STATES; ⁶Tempus, Chicago, Illinois, UNITED STATES; ⁷Siteman Cancer Center, St. Louis, Missouri, UNITED STATES

2:11 PM - 2:30 PM

Q&A

2:30 PM - 2:45 PM

CTOS 2031; LOOKING BACK 10 YEARS

Presenter: **Rick L. Haas, MD, PhD, 2021 CTOS President**

2:45 PM - 3:30 PM

CTOS Business Meeting

We are *inspired* by the sea, *driven* by science, and *motivated* by patients with serious diseases to improve their lives. We intend to continue to be the *world leader* in marine medicinal discovery, development and innovation.

pharmamar.com



QINLOCK[®]
(riporetinib) 50 mg tablets



**NCCN
PREFERRED
CATEGORY 1**

Riporetinib (QINLOCK[®]) is **THE ONLY** therapy recommended for 4th-line advanced GIST by the National Comprehensive Cancer Network[®] (NCCN[®])

FOR ADVANCED **GIST** PATIENTS
TREATED WITH ≥ 3 PRIOR TKIs

BREAK THROUGH RESISTANCE

Choose QINLOCK, the first and only
switch-control kinase inhibitor for
advanced GIST¹

Approved for patients regardless of
mutation, including¹:

✓ **KIT** ✓ **PDGFR α** ✓ **WILD TYPE**

The most common adverse reactions (>35%) include alopecia, fatigue, nausea, and abdominal pain.

The safety and effectiveness of QINLOCK in pediatric patients have not been established.

Administer strong CYP3A inhibitors with caution. Avoid concomitant use with strong and moderate CYP3A inducers. If a moderate CYP3A inducer cannot be avoided, increase QINLOCK dosing frequency from the recommended dose of 150 mg once daily to 150 mg twice daily during the co-administration period.

Please see Brief Summary of Prescribing Information following. Please see additional complete Safety Information and full Prescribing Information including Patient Information, at QINLOCKHCP.com.

To report SUSPECTED ADVERSE REACTIONS, contact Deciphera Pharmaceuticals, LLC, at 1-888-724-3274 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

References: 1. Qinlock [package insert]. Waltham, MA: Deciphera Pharmaceuticals, Inc; 2021. 2. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) for Gastrointestinal Stromal Tumors (GISTs) V.1.2021. ©National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Published October 30, 2020. Accessed October 30, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

INDICATION

QINLOCK is a kinase inhibitor indicated for the treatment of adult patients with advanced gastrointestinal stromal tumor (GIST) who have received prior treatment with 3 or more kinase inhibitors, including imatinib.

SELECT SAFETY INFORMATION

Serious adverse reactions occurred in 31% of patients who received QINLOCK. Serious adverse reactions that occurred in >2% of patients were abdominal pain (4.7%), anemia (3.5%), nausea (2.4%), and vomiting (2.4%).

Palmar-plantar erythrodysesthesia syndrome (PPES), new primary cutaneous malignancies, hypertension, and cardiac dysfunction were reported in patients receiving QINLOCK in the INVICTUS trial.

QINLOCK has the potential to adversely affect wound healing. Withhold QINLOCK for at least 1 week prior to elective surgery. Do not administer for at least 2 weeks following major surgery and until adequate wound healing. The safety of resumption of QINLOCK after resolution of wound healing complications has not been established.

QINLOCK can cause fetal harm. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment and for at least 1 week after the final dose.

QINLOCK[®]

(ripretinib) 50 mg tablets

BRIEF SUMMARY of Prescribing Information

INDICATION: QINLOCK is a kinase inhibitor indicated for the treatment of adult patients with advanced gastrointestinal stromal tumor (GIST) who have received prior treatment with 3 or more kinase inhibitors, including imatinib.

DOSAGE AND ADMINISTRATION: Recommended dosage: 150 mg orally once daily with or without food. Advise patients to swallow tablets whole. Inform patients about what to do in the event they miss a dose or vomit after taking a dose of QINLOCK. If a moderate CYP3A inducer cannot be avoided, increase QINLOCK dosing frequency from the recommended dose of 150 mg once daily to 150 mg twice daily during the co-administration period. If the concomitant moderate CYP3A inducer is discontinued, resume QINLOCK dosage back to 150 mg once daily 14 days after the discontinuation of the moderate CYP3A inducer.

CONTRAINDICATIONS: None

WARNINGS AND PRECAUTIONS

Palmar-Plantar Erythrodysesthesia Syndrome (PPES) - In INVICTUS, Grade 1-2 palmar-plantar erythrodysesthesia syndrome (PPES) occurred in 21% of the 85 patients who received QINLOCK. PPES led to dose discontinuation in 1.2% of patients, dose interruption in 2.4% of patients, and dose reduction in 1.2% of patients. Based on severity, withhold QINLOCK and then resume at same or reduced dose.

New Primary Cutaneous Malignancies - In INVICTUS, cutaneous squamous cell carcinoma (cuSCC) occurred in 4.7% of the 85 patients who received QINLOCK, with a median time to event of 4.6 months (range: 3.8 to 6 months). In the pooled safety population, cuSCC and keratoacanthoma occurred in 7% and 1.9% of 351 patients, respectively.

In INVICTUS, melanoma occurred in 2.4% of the 85 patients who received QINLOCK. In the pooled safety population, melanoma occurred in 0.9% of 351 patients.

Perform dermatologic evaluations when initiating QINLOCK and routinely during treatment. Manage suspicious skin lesions with excision and dermatopathologic evaluation. Continue QINLOCK at the same dose.

Hypertension - In INVICTUS, Grade 1-3 hypertension occurred in 14% of the 85 patients who received QINLOCK, including Grade 3 hypertension in 7%.

Do not initiate QINLOCK in patients with uncontrolled hypertension. Adequately control blood pressure prior to initiating QINLOCK. Monitor blood pressure as clinically indicated during treatment with QINLOCK and initiate or adjust antihypertensive therapy as appropriate. Based on severity, withhold QINLOCK and then resume at same or reduced dose or permanently.

Cardiac Dysfunction - In INVICTUS, cardiac failure occurred in 1.2% of the 85 patients who received QINLOCK. In the pooled safety population, cardiac dysfunction (including cardiac failure, acute left ventricular failure, diastolic dysfunction, and ventricular hypertrophy) occurred in 1.7% of 351 patients, including Grade 3 adverse reactions in 1.1%.

In INVICTUS, Grade 3 decreased ejection fraction occurred in 2.6% of the 77 patients who received QINLOCK and who had a baseline and at least one post-baseline echocardiogram. In the pooled safety population, Grade 3 decreased ejection fraction occurred in 3.4% of the 263 patients who received QINLOCK and who had a baseline and at least one post-baseline echocardiogram.

In INVICTUS, cardiac dysfunction led to dose discontinuation in 1.2% of the 85 patients who received QINLOCK. The safety of QINLOCK has not been assessed in patients with a baseline ejection fraction below 50%.

Assess ejection fraction by echocardiogram or MUGA scan prior to initiating QINLOCK and during treatment, as clinically indicated. Permanently discontinue QINLOCK for Grade 3 or 4 left ventricular systolic dysfunction.

Risk of Impaired Wound Healing - Impaired wound healing complications can occur in patients who receive drugs that inhibit the vascular endothelial growth factor (VEGF) signaling pathway. Therefore, QINLOCK has the potential to adversely affect wound healing.

Withhold QINLOCK for at least 1 week prior to elective surgery. Do not administer for at least 2 weeks following major surgery and until adequate wound healing. The safety of resumption of QINLOCK after resolution of wound healing complications has not been established.

Embryo-Fetal Toxicity - Based on findings from animal studies and its mechanism of action, QINLOCK can cause fetal harm when administered to a pregnant woman.

Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with QINLOCK and for at least 1 week after the final dose.

Advise males with female partners of reproductive potential to use effective contraception during treatment with QINLOCK and for at least 1 week after the final dose.

ADVERSE REACTIONS

Serious adverse reactions occurred in 31% of patients who received QINLOCK. Serious adverse reactions that occurred in >2% of patients were abdominal pain (4.7%), anemia (3.5%), nausea (2.4%), and vomiting (2.4%).

The most common adverse reactions ($\geq 20\%$), were alopecia, fatigue, nausea, abdominal pain, constipation, myalgia, diarrhea, decreased appetite, PPES, and vomiting. The most common Grade 3 or 4 laboratory abnormalities ($\geq 4\%$) were increased lipase and decreased phosphate. Clinically relevant adverse reactions

that occurred in <10% of patients in the pooled safety population included cardiac ischemic events (cardiac arrest, acute coronary syndrome, and myocardial infarction), which occurred in 1.1% of patients. Of these, cardiac arrest and myocardial infarction were reported as fatal adverse reactions.

Permanent discontinuation due to an adverse reaction occurred in 8% of patients who received QINLOCK. Adverse reactions resulting in permanent discontinuation in

$\geq 1\%$ of patients included general physical health deterioration (2.4%), anemia (1.2%), cardiac failure (1.2%), PPES (1.2%), and vomiting (1.2%).

Dose interruptions due to an adverse reaction occurred in 24% of patients who received QINLOCK. Adverse reactions requiring dosage interruption in >2% of patients included nausea (3.5%), increased blood bilirubin (2.4%), and PPES (2.4%).

Dose reductions due to an adverse reaction occurred in 7% of patients who received QINLOCK. Adverse reactions resulting in a dose reduction in $\geq 1.2\%$ of patients were abdominal pain, agitation, alopecia, arthritis, dermatosis, gastrointestinal disorder, hyperesthesia, myalgia, PPES, and decreased weight.

DRUG INTERACTIONS

Coadministration of QINLOCK with strong CYP3A inhibitors may increase the risk of adverse reactions. Monitor patients more frequently for adverse reactions. Avoid concomitant use of QINLOCK with strong and moderate CYP3A inducers.

USE IN SPECIFIC POPULATIONS

Pregnancy - see Embryo-Fetal Toxicity

Lactation - Because of the potential for serious adverse reactions in the breastfed child, advise women not to breastfeed during treatment with QINLOCK and for at least 1 week after the final dose.

Females and Males of Reproductive Potential - QINLOCK can cause fetal harm when administered to a pregnant woman. Verify pregnancy status of females of reproductive potential prior to the initiation of QINLOCK. Advise females of reproductive potential to use effective contraception during treatment and for at least 1 week after the final dose. Advise males with female partners of reproductive potential to use effective contraception during treatment and for at least 1 week after the final dose. Based on findings from animal studies, QINLOCK may impair fertility in males of reproductive potential.

Pediatric Use - The safety and effectiveness of QINLOCK in pediatric patients have not been established.

Geriatric Use - Clinical studies of QINLOCK did not include sufficient numbers of patients aged 65 and older to determine whether they respond differently from younger patients.

Hepatic Impairment - No dose adjustment is recommended in patients with mild hepatic impairment (total bilirubin \leq ULN and AST > ULN or total bilirubin 1 to 1.5 x ULN and AST any). A recommended dosage of QINLOCK has not been established for patients with moderate or severe hepatic impairment.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility -

Carcinogenicity studies have not been conducted with ripretinib.

To report SUSPECTED ADVERSE REACTIONS, contact Deciphera Pharmaceuticals, LLC, at 1-888-724-3274 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Manufactured for and marketed by:
Deciphera Pharmaceuticals, LLC
200 Smith Street, Waltham, MA 02451

deciphera[™]



ctos®

2021 *Virtual* Annual Meeting

Oral Presentations

Thursday, November 10, 2021



9:15 am - 10:30 am

– Session 1 –

BIG DATA AND BIG SCIENCE

9:15 AM - 9:22 AM

Paper #01 #1818715

3D GENOME STRUCTURAL ALTERATIONS AND ONCOGENE EXPRESSION IN CHORDOMA GENOMES

Kadir Akdemir; Khalida Wani; David R. Ingram; Wei-Lien Wang; Shaan M. Raza; Andrew J. Bishop; Christopher Alvarez-Breckenridge; Claudio Tatsui; Anthony P. Conley; Laurence D. Rhines; Andrew Futreal; Alexander Lazar

The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES

Objective: Complex genomic rearrangements occur in sarcomas and central nervous tumors. The patterns of genomic rearrangements in cancer genomes offer insights into tumor etiology and potential vulnerabilities to be exploited therapeutically. Our understanding of genomic alterations in chordoma cells remains limited, partly because of the rare occurrence of this tumor. Therefore, our ability to determine the drivers of genomic rearrangements and the molecular and clinical implications of the complex rearrangements in chordoma genomes remains unknown. The chromatin organization in the nucleus is non-random. Recent evidence has indicated that a critical feature of chromatin organization is that regions of the genome form self-associated domain structures on a megabase scale. These structures are generally known as topologically associated domains (TADs) and have been demonstrated to play a critical role in facilitating proper gene regulation. Our recent studies revealed that the integration of the chromatin organization with cancer genomic datasets provides unique insights into the mechanisms and functional consequences of genomic alterations observed in human tumors. Therefore, in this study, we performed a comprehensive genomic profiling approach to understand the order and nature of complex rearrangements in chordoma cells.

Methods: We generated matching chromatin organization (Hi-C) and whole-genome sequencing (WGS) datasets from 4 chordoma primary samples and 4 cell lines to understand the effects of genomic alterations on chromatin architecture and oncogene expression. The Hi-C assay is used to reveal physical interaction frequency patterns between genes and distal regulatory elements. Genomic data was aligned to the hg38 reference genome using BWA-MEM algorithm. We detected genomic alterations in Hi-C and in WGS data using BreakFinder and BRASS algorithms, respectively.

Results: Our Hi-C and WGS data revealed the occurrence of complex rearrangements in chordoma cells including multiple translocations involving several breakpoints of deletions, inversions and duplications. As Hi-C is the method of choice for identifying TADs, we investigated whether the sites in the genome with genomic rearrangements affecting TAD boundaries indeed show altered chromatin organization structure. We also observed that genomic alterations dramatically affected chromatin folding patterns and lead to formations of several new chromatin domain organizations in our chordoma samples. Lastly, complex rearrangements lead to oncogene amplification in cancer cells, which can occur in the form of extra-chromosomal DNA (ecDNA, previously referred as double minutes) elements or tandemly duplicated arrays inside a chromosomal body (homogeneously staining regions, HSR). Oncogene amplifications have been implicated in therapy resistance and contribute to tumor heterogeneity. We observed evidence of Brachyury ecDNA amplification in the chordoma cell line, JHC7 but not in other chordoma cell lines. These results suggest that there is evidence of extra-chromosomal oncogene amplification in chordomas and the fact that certain genes are amplified in a cancer-specific manner suggests that there could be a lineage-specific occurrence of oncogene amplification in human sarcomas.

Conclusion: Our preliminary data in this study suggested that integrating chromatin organization with genome sequencing of chordomas can significantly expand our understanding of the effects of genomic alterations on oncogene amplification and gene regulation.



9:22 AM - 9:29 AM

Paper #02 #1818739

COMPARATIVE REVIEW OF HUMAN AND CANINE PERIPHERAL NERVE SHEATH TUMORS

Keila E. Torres¹; **Jace Landry**¹; Veena Kochat¹; Sharon M. Landers¹; Angela D. Bhalla¹; Rossana Lazcano¹; Lindsay Parker²; Tasha Miller²; David R. Ingram¹; Dominique Wiener²; Brian Davis²; Beth Boudreau²; Wei-Lien Wang¹; Emily Z. Keung¹; Christopher P. Scally¹; Christina L. Roland¹; Kelly K. Hunt¹; Barry W. Feig¹; John M. Slopis¹; Heather Wilson-Robles²; Alexander Lazar¹

¹The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES;

²Texas A&M University, College Station, Texas, UNITED STATES

Objective: Malignant peripheral nerve sheath tumors (MPNSTs) are heterogeneous sarcomas with significant local recurrence and metastatic spread. The main obstacle in treating these highly chemo- and radio-resistant tumors is a lack of effective systemic therapies. The rarity of MPNSTs presents challenges to performing informative clinical trials. Further, the inability of laboratory animal models, such as mice, to fully recapitulate the complex genetic, biological, and environmental factors driving complex diseases such as sarcomas has impeded the identification of effective therapeutic targets. To address this problem, we evaluated whether canine peripheral nerve sheath tumors (PNSTs) represent a robust model system for human MPNSTs. Although MPNSTs are rare in humans, canine PNSTs are relatively common, accounting for 27% of nervous system tumors with an estimated annual incidence of 1309 – 11,872 per 100,000 dogs per year in the US. This study represents a multi-institutional collaboration to evaluate the similarities and differences between canine PNST and human MPNST. We compare the clinical characteristics, gross morphology, histopathology, epidemiology, and presence or absence of specific histone marks in canine and human tumors.

Methods: We identified all canine patients diagnosed with PNST from 2003 to 2019 treated with surgical resection at Texas A&M University Veterinary Teaching Hospital. Human patients diagnosed with MPNST and evaluated at The University of Texas MD Anderson Cancer Center between 1990 and 2015 were also identified. Demographic information, histopathological characteristics, treatment modalities, and outcomes were recorded. Immunohistochemical staining of 56 canine PNST FFPE samples and 139 tissue microarray MPNST human samples was performed to evaluate the expression of H3K27me3 and H3K27Ac. Staining intensity and positivity scoring were performed manually. Samples were classified into H3K27me3low, H3K27me3high, and H3K27me3mixed.

Results: 62 canine patients and 289 human patients with MPNST were identified. Primary MPNSTs in the human cohort were most frequently located in the trunk (54%), followed by the extremities (31%). Canine PNSTs were found in the trunk (44%), and 40% in the extremities. Almost all human primary MPNSTs (94%) were below the deep fascia, contrasted to only 24% of canine primary PNSTs. Surgical resection was the primary therapeutic approach for both human and canine patients. A significantly smaller percentage of canine patients received chemotherapy when compared to the human cohort (18% vs. 41%, respectively). Neoadjuvant/adjuvant radiation was less often used in the canine cohort versus the human group (13% vs. 52%, respectively). After primary tumor resection, local recurrence and progression to metastatic disease rates were significantly higher in human patients with MPNST than in the canine group (12% vs. 37.5% and 7% vs. 43.8%, respectively). The median survival in dogs diagnosed with MPNST was 20.8 months (range: 14 and 44 months). The 2-year survival for canines with MPNST was 40%. Human tissue microarray analysis of neurofibroma and MPNST samples showed loss of H3K27me3 in 31% (38/121) of MPNSTs, while the mark was retained in neurofibroma samples. The mean percentage of H3K27Ac expression was significantly higher in MPNST (45%) than in neurofibroma (16%). In contrast, 39% (23/59) of canine PNST samples demonstrated lower expression of H3K27me3 when compared to normal nerve (n = 5). Of the tumors with lower expression of H3K27me3, 74% (17/23) had high expression levels of the H3K27Ac mark. Sixteen (27%) of the canine samples demonstrated a heterogeneous expression of H3K27me3 within the same sample. Increased expression of H3K27Ac was observed in 92% (54/59) of canine PNSTs. In human samples, loss of H3K27me3 was associated with gain in H3K27Ac. In contrast, the negative association between H3K27me3 and H3K27Ac expression was not confirmed in the canine samples.

Conclusion: Contrary to the human tumor samples, high expression of H3K27Ac was observed in most PNSTs, including tumors that presented a heterogeneous loss of H3K27me3. These findings point to differences in tumor heterogeneity and microenvironment in the tumors that arise in both species. Unlike neurofibromas being the precursors to MPNST in

humans, no such intermediate stage has been reported to occur in dogs before PNSTs arise. Hence our findings warrant further studies to evaluate whether similar epigenetic deregulations occur in both species and whether they alter similar gene signatures. The knowledge gained from this work will inform whether the canine PNST model can be helpful in understanding and treating MPNST.



9:29 AM - 9:36 AM

Paper #03 #1818745

CATEGORIZING SYNOVIAL SARCOMAS BASED ON EPIGENOMIC LANDSCAPE

Alvin Qiu; Edmund Su; Qi Cao; Marcus Wong; Michelle Moksa; Martin Hirst; Torsten Nielsen
University of British Columbia, Vancouver, British Columbia, CANADA

Objective: Synovial sarcoma (SS) is an aggressive soft-tissue malignancy characterized by a pathognomonic chromosomal translocation leading to the production of SS18-SSX, a fusion oncoprotein. Previous research shows that SS18-SSX associates with BAF, a chromatin remodelling complex, suggesting epigenetic mechanisms drive this cancer. We hypothesize that SS can be sub-grouped based on epigenomic state and that these subgroups relate to disease severity.

Methods: We profiled 31 cases of primary human SS using chromatin immunoprecipitation sequencing (ChIP-seq) for histone modifications (specifically H3K27ac, H3K4me3, H3K4me1, H3K27me3, H3K36me3, H3K36me2, H3K9me3), RNA-seq for transcriptomes, and whole genome bisulfite sequencing (WGBS) for DNA methylomes. Publicly-available cell line data were obtained for comparison.

Results: Unsupervised hierarchical clustering of genome-wide histone ChIP-seq density for the transcriptionally active marks (H3K27ac, H3K4me1, H3K4me3) reveals two major SS sub-groups. Enhancers (regions marked by H3K27ac) from SS Group 1 tumors show lower levels of BAF binding compared to SS Group 2 enhancers. Using published isogenic cell line models, Group 2 enhancers also show greater overlap with binding sites of non-oncogenic BAF complexes (lacking SS18-SSX) compared to oncogenic BAF complexes (containing SS18-SSX). Genes associated with Group 2 enhancers are expressed at lower levels in SS compared to other soft-tissue sarcomas, suggesting Group 2 tumors express SS signature genes at lower levels than Group 1 tumors. Clinical data show that Group 2 tumors are lower grade tumors. Treating SS cells with quisinostat, a histone deacetylase inhibitor, leads to cell death and increases the expression of Group 2 enhancer genes.

Conclusion: SS can be sub-grouped into two distinct classes based on epigenomic state, associated with differences in BAF activity. Using a histone deacetylase inhibitor pushes cells into a phenotype that resembles the less aggressive sub-group, supporting its value as a therapeutic strategy in SS.



9:36 AM - 9:43 AM

Paper #04 #1818749

ATRX DELETION IMPAIRS CGAS-STING SIGNALING AND INCREASES RESPONSE TO RADIATION AND ONCOLYTIC HERPESVIRUS IN SOFT TISSUE SARCOMA

Warren Floyd; Matthew Pierpoint; Chang Su; Lixia Luo; Amy J. Wisdom; Yan Ma; Suzanne Bartholf DeWitt; Nerissa T Williams; Jason A. Somarelli; David L Corcoran; William C. Eward; Dianna M. Cardona; David G. Kirsch
Duke University, Durham, Carolina, UNITED STATES

Objective: ATRX is one of the most frequently altered genes in human soft tissue sarcomas, but the role of ATRX in tumor development and response to cancer therapies remains poorly understood. Here, we developed a primary mouse model of soft tissue sarcoma and tested whether *Atrx* loss of function mutation increases therapeutic response to established and emerging therapies.

Methods: The TCGA database was used to analyze the effect of ATRX alteration on radiation response in human soft tissue sarcomas. Isogenic primary soft tissue sarcoma cell lines with or without *Atrx* knockout (*Atrx* isogenic cell lines) were derived by CRISPR/Cas9-mediated knockout of ATRX. Next radiation clonogenic assays were performed, as well as qPCR and fluorescence in situ hybridization with immunofluorescence to study the effect of radiation on these cell lines. Using qPCR, the effect of *Atrx* deletion on soft tissue sarcoma response to cGAS-STING signaling and oncolytic herpesvirus response in vitro was studied. Next two different primary genetically engineered mouse models of soft tissue sarcoma with *Atrx* deletion were generated. To generate the first primary mouse model of soft tissue sarcoma, 4-hydroxytamoxifen (4-OHT) was injected into the gastrocnemius muscle. This injection led to activation of the CreERT2 expressed from the endogenous Pax7 promoter in muscle satellite cells. Activation of the CreERT2 then activated expression of *Kras*G12D and deleted floxed p53 and floxed *Atrx* alleles (P7KPA model). The P7KP model is identical, except it retains functional *Atrx* allele(s). A second, carcinogen-induced primary mouse model of soft tissue sarcoma was also generated. Using these models, as well as athymic nude mouse models, the effect of *Atrx* deletion on tumor development, radiation response, and response to the oncolytic herpesvirus was tested.

Results: Using data from a cohort of patients with soft tissue sarcomas, we saw that ATRX alteration was associated with significantly poorer disease specific survival in the absence of radiation. Interestingly, this survival disadvantage was lost in ATRX altered sarcomas treated with radiation. Next, using three different *Atrx* isogenic cell lines, we demonstrated by clonogenic assay that *Atrx* deletion sensitized soft tissue sarcoma to radiation therapy. We then showed that *Atrx* deletion increased persistent double stranded DNA breaks at telomeres and mitotic catastrophe 3 days after 4 Gy of ionizing radiation. We then generated the P7KP and P7KPA primary mouse models of soft tissue sarcoma and found that *Atrx* deletion increased radiosensitivity, necrosis, and TUNEL staining after 20 Gy of ionizing radiation in vivo. Subsequently we found that *Atrx* deletion increased radiosensitivity in a second carcinogen-induced primary mouse model of soft tissue sarcoma. Interestingly, RNA sequencing analysis of our P7KP and P7KPA models showed that deletion of *Atrx* resulted in a downregulation of innate immune response pathways, including the cGAS-STING signaling pathway, after radiation. Using athymic nude mice, we demonstrated that *Atrx* deletion can radiosensitize soft tissue sarcomas in a T cell-autonomous manner. We then used our sarcoma models to demonstrate that *Atrx* deletion suppresses type I interferon signaling in a cGAS-STING dependent manner. Finally, we demonstrated that this loss of cGAS-STING signaling caused by *Atrx* deletion sensitized soft tissue sarcomas to oncolytic herpesvirus. In vivo studies with oncolytic herpesvirus in P7KPA and P7KP mice are currently underway.

Conclusion: Collectively, these results show that loss of ATRX function impairs the cGAS-STING signaling pathway in soft tissue sarcomas and promotes their response to radiation therapy and oncolytic virus therapy. These findings identify ATRX as a biomarker in treatment response and identify novel genomically-informed therapeutic strategies for treatment of soft tissue sarcoma.



9:43 AM - 9:50 AM
 Paper #05 #1818718

CHALLENGES AND PATTERNS OF REGISTRY RESEARCH IN SARCOMA

Joshua M. Lawrenz; Andrew Chi; Gabriel Bendfeldt; Jennifer L. Halpern; Ginger E. Holt; Herbert S. Schwartz
 Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES

Objective: Publications using the Surveillance Epidemiology End Results (SEER) and National Cancer Database (NCDB) are proliferating in sarcoma research. Between 2010 and 2015, annual SEER publications remained unchanged, while the number doubled in the next five. NCDB publications doubled between 2010-2015 and increased by 220% between 2015-2020. We test the hypothesis that big data registry research is increasing and can be misleading for sarcoma. Our objective is two-fold: 1. To provide a descriptive analysis of publication patterns using large administrative databases in sarcoma research; and 2. To perform an internal audit comparing the administrative registry-reported data at our institution to a prospective physician kept log.

Methods: PubMed was searched from 2000 through 2020 for all publications using any large administrative database including SEER or NCDB, and sarcoma. Manuscripts were tabulated for frequency, subject matter, authorship, and outcomes. Particular attention was directed at publications which asked the same question but reported differing results. Furthermore, The Journal of Bone and Joint Surgery (JBJS) was similarly queried with the Editor's permission, seeking additional information regarding acceptance and re-submission rates.

Table 1. Disparate Outcomes between National Registry Studies and Institutional Based Studies in Sarcoma.

Topic	Data Source	Year	Journal	Disparate Outcome
Radiation and Survival in Extremity STS	Multi-institution group vs. NCDB	2018	Journal of Surgical Oncology	Institutional data suggested no value of radiation, and the NCDB demonstrated improved overall survival
Radiation and Survival in Extremity STS	NCDB	2015	Annals of Surgical Oncology	Radiation associated with improved survival
Radiation and Survival in Extremity STS	SEER	2008	Cancer	Blacks worse survival
Radiation and Survival in Extremity STS	SEER + NCDB	2018	Cancer Medicine	Blacks no different survival
EWS Survival	SEER	2019	BMC Cancer	Blacks worse survival
EWS Survival	SEER	2018	Expert Review of Anticancer Therapy	No difference in survival between surgery, XRT and surgery + XRT
EWS Survival	NCDB	2017	Journal of Surgical Oncology	1. Blacks no different survival 2. Surgery > XRT for survival
EWS Survival	SEER	2016	Journal of Medical Imaging and Radiation Oncology	Surgery > XRT for survival in all patients, though no different in localized or appendicular disease
Mesenchymal CSA Survival	SEER	2017	Clinical Orthopaedics and Related Research	51% 5-year overall survival
Mesenchymal CSA Survival	SEER	2020	Journal of Orthopaedic Research	38% 5-year overall survival
Radiation and Survival in RP STS	Consortium	2019	Journal of Surgical Oncology	No association with improved survival
Radiation and Survival in RP STS	NCDB	2021	The American Journal of Surgery	Improved survival in all sized tumors
Pelvic CSA Survival	SEER	2019	Cancer Medicine	70% 5-year overall survival
Pelvic CSA Survival	Consortium	2018	Journal of Bone and Joint Surgery	59% 5-year overall survival

*Color shadings represent six separate topics in sarcoma research. Articles with same color shading demonstrate disparate outcomes regarding the same research topic.

Lastly, an internal coding audit was performed at the host’s institution comparing administrative registry-reported sarcoma data to a prospective physician kept log.

Results: Sarcoma registry publications numbered 159 between the years 2000-2020. Interestingly, 34 publications were authored from non-US countries, as Chinese institutions numbered 30. The same institution often published similar type articles ranging from 3-8 articles per institution; the total was 38. Consortiums, governmental or health system databases contributed 14 publications of the 159. Six examples of disparate results are presented dealing with survival, treatment results and demographics. JBJS accepted only 6 manuscripts, while rejecting 25 between 2002-2020. Nineteen times a JBJS rejection was resubmitted and accepted for publication elsewhere. The internal coding audit yielded registry-reported data errors in adjuvant treatment (19%), margins (38%) and stage (77%) during a three-year sample of 77 patients.

Table 2. Coding Mismatch between Physician-kept Log Data and Registry-Reported Data.

Year	N	DOB	Surgery Date	Margin Status	Tumor Size*	Stage	Adjuvant Treatment
2018	31	0	3	5	6	15	4
2019	26	1	8	15	4	24	6
2020	20	2	7	9	6	20	5
Total	77	3	14	29	16	59	15
% Mismatch		4%	18%	38%	21%	77%	19%

Mismatch defined as when registry-reported data to be “empty or not reported” or “inaccurate” as compared to the Physician-kept Log.

*Size was considered a mismatch if >50% different as compared to the Physician-kept Log.

Conclusion: Registries aggregating information from many hospitals have the advantage of achieving statistical power. However, this comes at a cost when complex variables must be abstracted from the medical record. Demographics, dates, and death are examples of ‘hard’ endpoints abstracted with high efficiency. Many cancers, and especially sarcoma variables, contain ‘soft’ endpoints which are nuanced and abstracted with low efficiency making registry data suspect. Caution should be used when interpreting certain sarcoma outcomes derived from large national and multi-institutional databases.



9:50 AM - 9:58 AM

Paper #06 #1818728

SINGLE-CELL OMICS REVEALS DIVERSE EPIGENETIC AND TRANSCRIPTOMIC REPROGRAMMING OF NF1-DEFICIENT CELLS THROUGH THE LOSS OF POLYCOMB REPRESSIVE COMPLEX 2 IN MALIGNANT PERIPHERAL NERVE SHEATH TUMORS
Xiyuan Zhang¹; Hannah Lou²; Vishaka Gopalan¹; Zhihui Liu¹; Haiyan Lei¹; C. Paige Jones¹; Carly M. Sayers¹; Marielle Yohe¹; Prashant Chittiboina³; Brigitte C. Widemann¹; Carol J. Thiele¹; Michael Kelly⁴; Sridhar Hannenhalli¹; Jack F. Shern¹
¹NCI, Bethesda, Maryland, UNITED STATES; ²NCI, Indianapolis, Indiana, UNITED STATES;

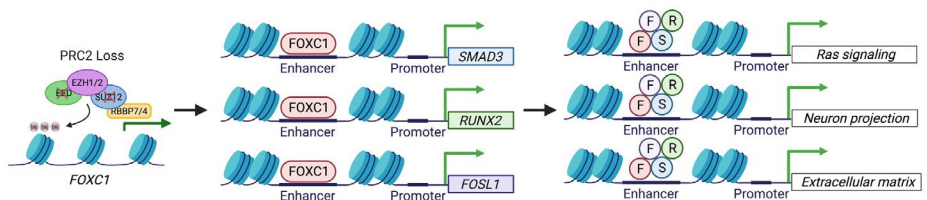
³NINDS, Bethesda, Maryland, UNITED STATES; ⁴Frederick National Laboratory, Bethesda, Maryland, UNITED STATES

Objective: Recurrent loss-of-function mutations in the polycomb repressive complex 2 (PRC2) genes, SUZ12 or EED, occur in malignant peripheral nerve sheath tumors (MPNST), which are aggressive sarcomas that originate from NF1-deficient Schwann cells. In MPNST, the loss of PRC2 results in a diverse set of transcriptomic and phenotypic consequences, including gain of acetylated H3K27 (H3K27ac) accompanying the loss of trimethylated H3K27 (H3K27me3), hyperactivated Ras signaling, and tumor escape from immune surveillance. Mechanistic understanding of how the loss of PRC2 results in these diverse, but specific consequences remain unresolved.

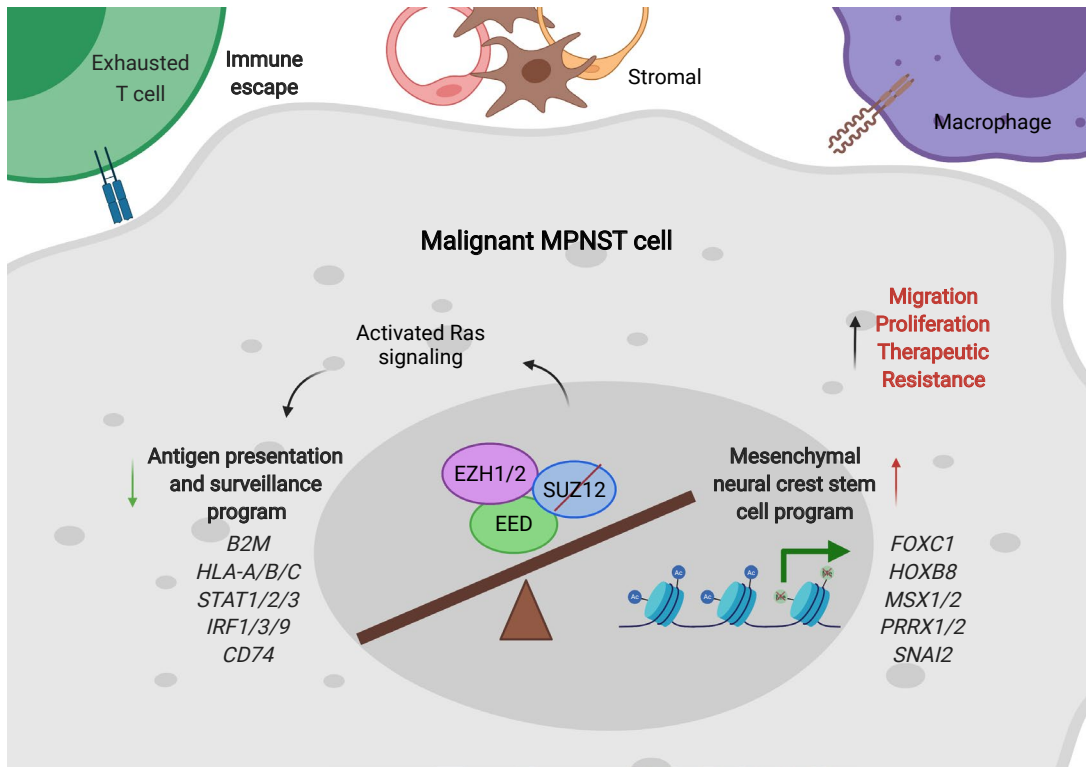
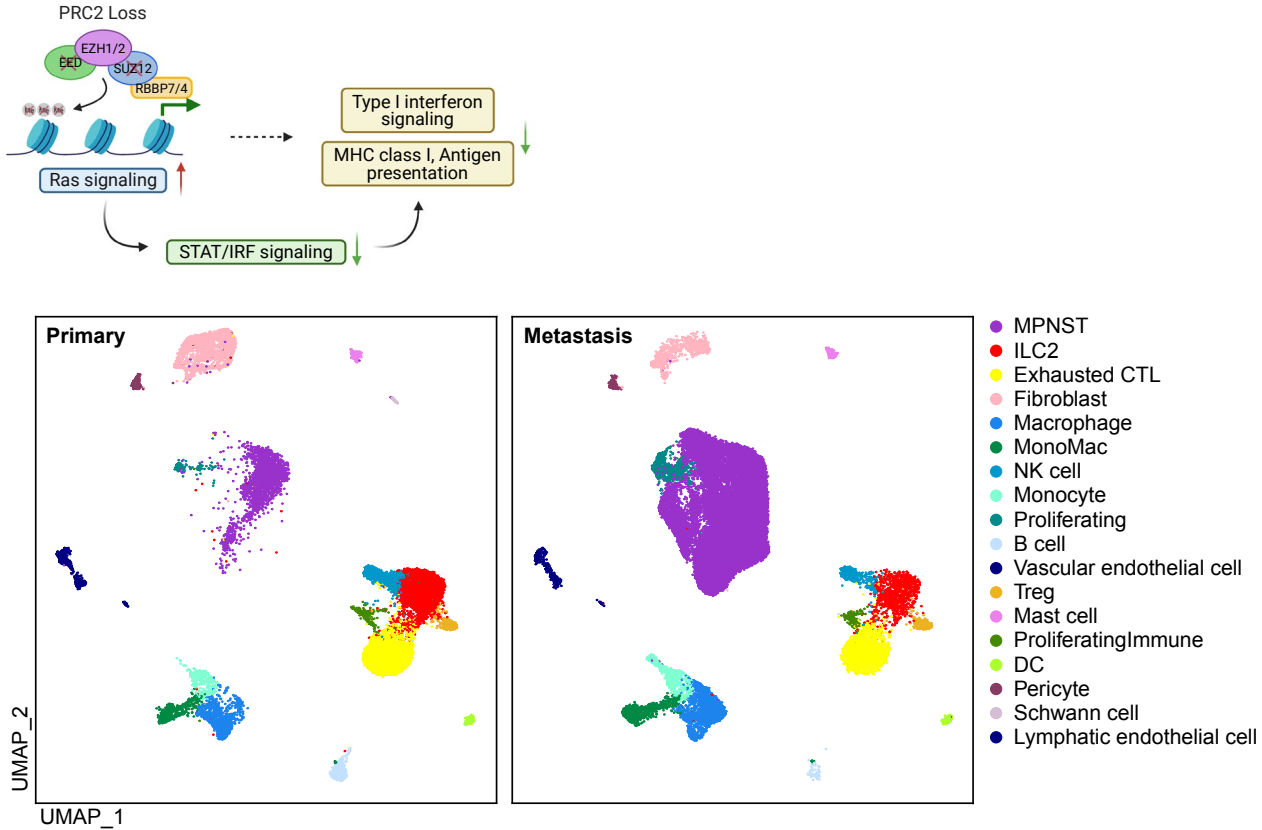
Methods: To delineate the oncogenic mechanisms mediated by PRC2 loss, we engineered MPNST cell lines to dynamically reassemble a functional PRC2 and evaluated the transcriptomic and epigenetic consequences of PRC2 restoration by RNA sequencing (RNAseq) and chromatin immunoprecipitation with massively parallel DNA sequencing (ChIP-seq), respectively. We further extended these findings using single cell sequencing from human MPNST and integrated the analysis with the results from in vitro model systems.

Results: Through integrative analysis of RNAseq and H3K27me3 ChIP-seq in PRC2-deficient MPNST cells, we identified 6134 H3K27me3 peaks (5820 associated genes), which were commonly gained in three cell lines when a functional PRC2 was restored. Interestingly, the majority of these genes (84.9%) were either not expressed or transcriptionally unaltered, regardless of the PRC2 status in the cells. Of the 876 (15.1%) significantly altered genes, 699 (12%) genes were downregulated, and 177 (3.1%) genes were upregulated when a restored PRC2 caused genome-wide redistribution of H3K27me3 peaks. Detailed mechanistic dissection of these PRC2-regulated genes revealed a two-pronged oncogenic process mediated by PRC2 loss which cooperatively contributes to the tumorigenesis of MPNST. First, PRC2 loss leads to the upregulation of a transcriptional circuit that remodels the enhancer landscape of MPNST cells and establishes an enhancer-driven transcription factor, FOXC1, as a master regulator and thus a core vulnerability of the cell (Figure 1). Second, PRC2 loss reduces type I interferon (IFN) signaling and antigen presentation as a downstream consequence of the upregulated Ras signaling (Figure 2). Data from these in vitro experiments was further integrated with single-cell RNAseq (scRNAseq) and single-cell whole genome sequencing (scWGS) of PRC2-deficient primary and metastatic human MPNSTs (Figure 3). Importantly, we discovered that the PRC2-deficient tumor cells have a corrupted transcriptional program characteristic of a mesenchymal precursor cell found during the trajectory of normal Schwann cell development. Interestingly, malignant cells expressing high levels of IFN and antigen presentation genes were absent in metastatic MPNST, potentially allowing the tumor cells to escape immune surveillance. The transcriptional circuit established by PRC2-regulated FOXC1 and its downstream target genes sustains the malignant program in both primary and metastatic MPNST.

Conclusion: In summary, we discovered the activation of a lineage specific oncogenic transcription program in PRC2-deficient MPNST, which is characteristic of a neural crest-derived mesenchymal stem cell. In addition, we found that the transcriptional activation of the Ras signaling caused by PRC2 loss leads to the downregulation of genes involved in type I IFN



signaling and tumor antigen presentation (Figure 4). Our findings provide mechanistic understanding of the metastatic potential, chemotherapy and radiotherapy resistance, and immune escape that are clinically characteristic of these tumors.





9:58 AM - 10:04 AM

Paper #07 #1818764

PROTEOMIC LANDSCAPE OF 205 BONE AND SOFT TISSUE SARCOMAS FROM THE INTERNATIONAL SARCOMA KINDRED STUDY REVEALS DISTINCT PROTEOMIC SIGNATURE OF LEIOMYOSARCOMAS
Elizabeth Connolly¹; Zainab Noor¹; Asim Anees¹; Daniel Bucio-Noble¹; Peter Hains¹; Phillip J. Robinson¹; Mandy Ballinger²; Qing Zhong³; Jia Liu³; David Thomas⁴; Roger Reddel³
¹ProCan®, Children's Medical Research Institute, Faculty of Medicine and Health, The University of Sydney, Sydney, New South Wales, AUSTRALIA; ²Garvan Institute, Faculty of Medicine, Western Sydney University, Darlinghurst, New South Wales, AUSTRALIA; ³ProCan®, Children's Medical Research Institute, Faculty of Medicine and Health, The University of Sydney, Westmead, New South Wales, AUSTRALIA; ⁴Garvan Institute of Medical Research, Sydney, New South Wales, AUSTRALIA

Objective: Sarcomas demonstrate extensive histologic diversity with over 175 subtypes. Several subtypes lack defining histopathological features, with misclassification occurring in up to 20% of cases. Proteomic profiling of bone and soft tissue sarcomas (STS) was undertaken to assess the proteomic landscape of sarcoma, define sarcoma subtype biology in relation to genomic features and perform multi-omic clustering analyses to potentially find new classifications.

Methods: A total of 205 formalin-fixed paraffin-embedded (FFPE) tissue specimens from 180 sarcoma patients from the International Sarcoma Kindred Study (ISKS) were analysed. Samples included bone and soft tissue tumours from over 30 histological subtypes and were grouped into 16 histopathological categories and 'other' (Figure 1). Samples were also analysed based on genomic status.² Histopathological diagnoses were provided by participating sites in ISKS, and have not been centrally reviewed. Proteomic analysis was completed at ProCan® (the Australian Cancer Research Foundation International Centre for the Proteome of Human Cancer) utilizing data-independent acquisition mass spectrometry (DIA-MS).¹ Differential expression analysis of proteins enriched in distinct proteomic subgroups, e.g., leiomyosarcoma (LMS) and genomic categories was completed at 1% false discovery rate.

Results: After removal of four samples from the analysis, we quantified 28,506 peptides corresponding to 3,754 proteins across the remaining 201 cases. Two samples were removed where the diagnosis was not consistent with sarcoma and two samples due to poor sample integrity. The mean age of sarcoma patients was 52 years (range 15-81), 48% were male, and the distribution of genomic subtypes was: genomically unstable (56%), diploid (21%), translocation associated sarcoma (TAS; 17%), and unknown (6%). Several sarcoma subgroups demonstrated distinct proteomic profiles on t-SNE visualization including LMS, SFT and a group of TAS (mLPS, SS, PNET + Ewing sarcoma) (Figure 2). uLMS separated from non-uterine LMS and two distinct clusters of TAS emerged when samples were organised by genomic subtypes. Distinct proteomic profiles did not emerge based on anatomical location or gender. 133 proteins were significantly upregulated in LMS and 29 proteins were downregulated compared with other subtypes. Consistent with previous reports, myogenic pathways were significantly enriched in LMS, including smooth muscle contraction and extracellular matrix interactions, in keeping with their histopathological lineage. Downregulation of apoptotic pathways was seen. ADD3, a protein that is associated with tumour growth and angiogenesis when downregulated in glioblastoma³, was found to be strongly downregulated (fold change -1.19) in LMS relative to all other sarcoma samples. In hierarchical clustering, the majority (65%) of LMS display a unique signature allowing differentiation from other sarcomas (Figure 3). Outliers, however, were noted which necessitate further evaluation.

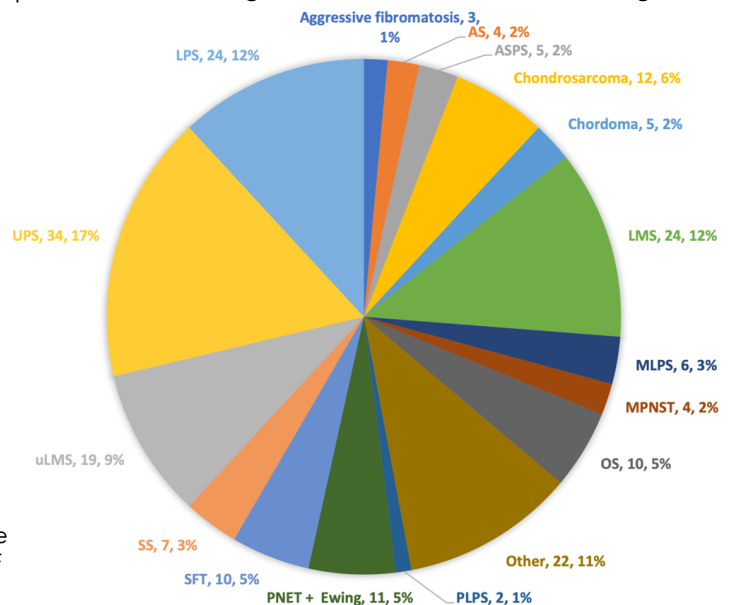


Figure 1. Pie chart showing distribution of sarcoma histotypes in the study. Each slice is annotated with the sarcoma subtype, number of cases, and percentage of total samples.

Conclusion: In this relatively large and diverse sarcoma cohort from the ISKS, proteomic analyses revealed that a number of sarcoma subtypes, in particular LMS, carry unique proteomic profiles associated with biological pathways. These can be used to better understand processes that drive sarcoma progression, and from which novel therapeutic targets may be identified. A validated proteomic signature differentiating LMS from other sarcomas could have clinical utility in differentiating LMS where there is diagnostic uncertainty. Further subtype-specific analyses will be reported at the meeting, including of subpopulations of TAS that cluster separately, and integrated proteogenomic analyses with multi-omic clustering.

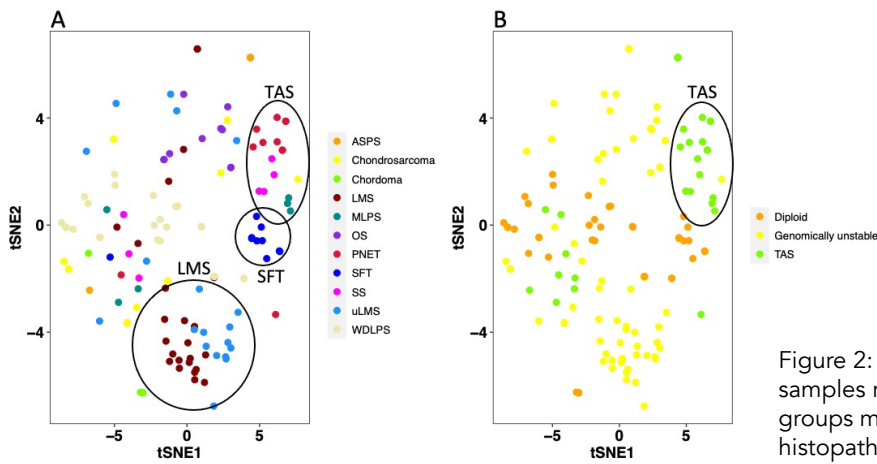


Figure 2: t-SNE plots with UPS and subgroups of less than five samples removed for improved visualization, with distinct subgroups manually highlighted with circular figures. [A] displays histopathological categories and [B] genomic categories.

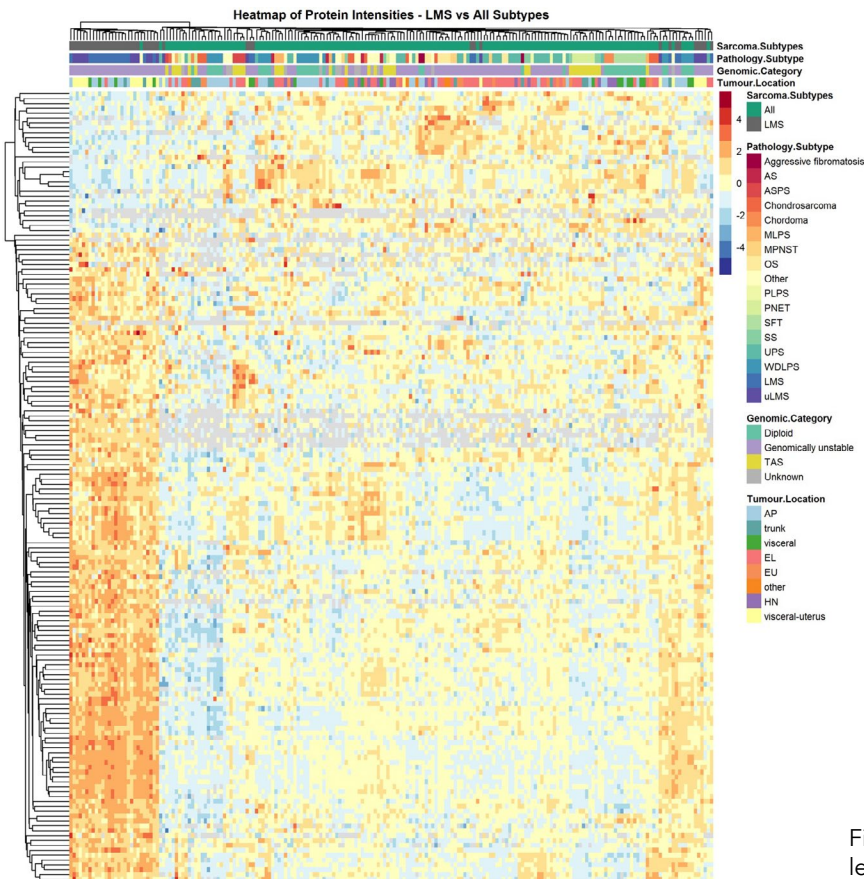


Figure 3. Unsupervised hierarchical clustering reveals leiomyosarcomas carry distinct proteomic signature.

References

1. Poulos et al. Nat Commun 2020;11:3793.
2. Ballinger ML et al. Lancet Oncol. 2016;17(9):1261-71.
3. Kiang KM et al. Cancer Lett. 2020 Apr 1;474:118-126.



10:04 AM - 10:11 AM

Paper #08 #1818786

REMARKABLY STABLE COPY-NUMBER PROFILES IN OSTEOSARCOMA CONTEST UNSTABLE GENOME HYPOTHESIS

Ryan D. Roberts¹; Sanjana Rajan¹; Simone Zaccaria PhD², Matthew V. Cannon¹; Maren Cam¹; Amy Gross³; Benjamin J. Raphael⁴

¹Nationwide Children's Hospital, Columbus, Ohio, UNITED STATES; ²University College London, London, England, UNITED KINGDOM; ³Center for Childhood Cancer, Nationwide Children's Hospital, The Ohio State University James Comprehensive Cancer Center, Columbus, Ohio, UNITED STATES; ⁴Princeton University, Princeton, New Jersey, UNITED STATES

Objective: Osteosarcoma is an aggressive disease that is characterized molecularly by p53 mutations and a very high level of genomic complexity. This complexity, combined with the paucity of recurrent point mutations, has suggested that the widespread somatic copy number aberrations (SCNAs) that occur within most osteosarcoma tumors are the primary drivers of malignancy. The chaotic genome of most osteosarcomas has led many to describe it as a disease exhibiting significant genomic/chromosomal instability. However, such conclusions have been drawn primarily from single-timepoint bulk-tumor analyses. More recent studies have begun to question this assumption of chromosomal instability, hypothesizing that the genomic complexity results from an early catastrophic event followed by the faithful propagation of a highly complex malignancy-promoting genome.

Methods: To determine whether osteosarcoma tumors show evidence of instability (which would promote copy number heterogeneity from within tumors), we performed single-cell whole-genome sequencing of >14,000 osteosarcoma cells obtained from 15 distinct lesions resected from 8 individual patients. Using the CHISEL algorithm, we inferred allele- and haplotype-specific copy numbers from this sequencing data. To evaluate how the SCNA profiles changed during the evolutionary pressures associated with metastatic dissemination and therapy, we compared the single-cell SCNA profiles of paired samples collected from both primary sites and metastases and from pre-treatment and relapsed specimens. We likewise compared profiles of patient tumors propagated orthotopically in mouse tibias to those grown within the lung to evaluate for tissue-dependent emergence of rare subclones.

Results: Despite extensive structural variations that give rise to highly complex patterns of SCNA, the cells within each tumor showed remarkably little heterogeneity. We found similar evidence of chromosomal stability when we reconstructed phylogenetic trees to identify the evolutionary relationships of cells collected from metastatic lesions or at relapse. Despite being evolutionarily distant, the vast majority of variation occurred within the trunk of the phylogenetic tree, with only modest changes occurring in any of the branches. This result suggests that nearly all the SCNAs were acquired during an early event, followed by a period of either intact genome maintenance or sustained selective pressure to preserve a particular pattern of SCNA. Analysis of bulk whole-genome sequencing from serially collected patient samples supports this conclusion of little SCNA variation over time.

Conclusion: This work demonstrates the power of combining single-cell DNA sequencing with an allele- and haplotype-specific CNV inference algorithm. Our approach resolves longstanding questions about the genetics of osteosarcoma initiation and progression, calling into question previous assumptions of genomic instability inferred from single-timepoint bulk sequencing data. Our data show that osteosarcoma exhibits marked intra-tumoral genomic homogeneity and that it maintains its markedly aberrant genome through evolutionary time with little cell-to-cell or lesion-to-lesion variability. These results suggest that an isolated, early catastrophic event, rather than sustained genomic instability, gives rise to the complex genome that characterizes osteosarcoma tumors.



10:30 am - 11:00 am

– Session 2 –

COVID-19 AND SARCOMA

10:35 AM - 10:42 AM

Paper #09 #1818706

DEMOGRAPHICS, PROGNOSIS FACTORS, AND OUTCOMES FOR PATIENTS (PTS) WITH SARCOMA AND COVID-19: A CCC19-REGISTRY BASED RETROSPECTIVE COHORT ANALYSIS

Michael J. Wagner¹; Matthew Ingham²; Corrie Painter³; Rashmi Chugh⁴; Emily Jonczak⁵; Vivek Subbiah⁶; Nam Bui⁷; Lisa Tachiki¹; Elizabeth S. Nakasone¹; Elizabeth T. Loggers¹; Chris Labaki⁸; Rana R. McKay⁹; Elizabeth A. Griffiths¹⁰; Katherine A. Thornton¹¹; Clara Hwang¹²; James L. Chen¹³; Thorvardur R. Halfdanarson¹⁴; Anup Kasi¹⁵; Daniel Y. Reuben¹⁶; Cathleen Park¹⁷

¹University of Washington/Fred Hutch/Seattle Cancer Care Alliance, Seattle; Washington; UNITED STATES; ²New York Presbyterian Hospital/Columbia University Medical Center, New York, New York, UNITED STATES; ³The Broad Institute of MIT and Harvard, Cambridge, Massachusetts, UNITED STATES; ⁴University of Michigan, Ann Arbor, Michigan, UNITED STATES; ⁵Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES; ⁶The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES; ⁷Stanford University Department of Oncology, Stanford, California, UNITED STATES; ⁸Dana-Farber Cancer Institute, Boston, Massachusetts, UNITED STATES; ⁹Moore's Cancer Center at the University of California, San Diego, San Diego, California, UNITED STATES; ¹⁰Roswell Park Comprehensive Cancer Center, Buffalo, New York, UNITED STATES; ¹¹Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES; ¹²Henry Ford Cancer Institute, Detroit, Michigan, UNITED STATES; ¹³Ohio State University, Columbus, UNITED STATES; ¹⁴Mayo Clinic, Rochester, Minnesota, UNITED STATES; ¹⁵The University of Kansas Cancer Center, Kansas City, Kansas, UNITED STATES; ¹⁶Hollings Cancer Center at the Medical University of South Carolina, Charleston, South Carolina, UNITED STATES; ¹⁷University of Cincinnati Cancer Center, Cincinnati, Ohio, UNITED STATES

Objective: Pts with sarcoma may receive aggressive immunosuppressive therapy and be at high risk for severe COVID-19. Demographics, risk factors and outcomes for pts with sarcoma and COVID-19 are unknown. We aimed to describe the course of COVID-19 in pts with sarcoma and to identify factors associated with outcomes.

Methods: The COVID-19 and Cancer Consortium (CCC19) (NCT04354701) is an international registry of pts with cancer and COVID-19. Adult pts with sarcoma and laboratory confirmed SARS-CoV-2 between March 17, 2020 and April 23, 2021 were included. Demographics, sarcoma histologic type, treatments, and course of COVID-19 infection were analyzed. Primary endpoint was the composite rate of hospitalization or death at 30 days from COVID-19 diagnosis. Secondary outcomes were 30-day all-cause mortality, hospitalization rate, O2 need, and ICU admission. Descriptive statistics and univariate Fisher tests are reported.

Results: N=228 pts were included. Median follow up was 42 days. Median age was 57 years (IQR 42-67); 109 (48%) were men. 30 (13%) had ECOG performance status ≥ 2 ; 116 (51%) received cancer treatment, including systemic, surgery, or radiation, within 3 months of COVID-19 diagnosis; 170 (75%) had active cancer, of whom 43 (19%) had lung metastases; 106 (46%) pts met the composite primary endpoint; 102 (45%) were hospitalized and 19 (8%) died within 30 days from COVID-19 diagnosis; 68 (33%) required oxygen, and 20 (9%) required ICU admission. Primary endpoint rates were similar for pts who received recent cytotoxic chemotherapy (39/65, 60%) or targeted therapy (17/30, 57%). Pts with higher rates of the primary endpoint included patients ≥ 60 years old (56% vs 40%, OR 1.86, 95% CI 1.06-3.29, $p=0.023$), pts with ECOG PS ≥ 2 vs 0-1 (90% vs 40%, OR 13.5, 95% CI 3.84-73.0, $p<0.001$), pts receiving any systemic therapy within 3 months of COVID-19 diagnosis (58% vs 39%, OR 2.18, 95% CI 1.23-3.91, $p=0.005$), and pts with lung metastases (60% vs 41%, OR 2.15, 95% CI 1.03-4.58, $p=0.038$). Primary endpoint rates were similar across sarcoma subtypes (Table).

Conclusion: This is the largest cohort study of pts with sarcoma and COVID-19 to date and showed high complication rates from COVID-19. Older age, poor performance status, recent systemic anti-cancer therapy, and lung metastases had worse outcomes. Limitations include retrospective nature, lack of randomization, selection and confounding biases.

Sarcoma Type	Pts⁺, n (%)	Age 60+, n (%)	Recent systemic cancer therapy, n (%)	Composite outcome, n (%)
Bone sarcoma				
Osteosarcoma	21 (9)	*	7 (33)	11 (52)
Ewing sarcoma	13 (6)	0	9 (69)	5 (38)
Chondrosarcoma	8 (4)	*	*	*
Soft tissue sarcoma (STS)				
Leiomyosarcoma (uterine and non-uterine)	21 (9)	12 (57)	14 (67)	14 (67)
Undifferentiated pleomorphic sarcoma/Myxofibrosarcoma	25 (11)	17 (68)	5 (20)	11 (44)
Dedifferentiated Liposarcoma (LPS), MRCLPS, LPS NOS	21 (9)	9 (43)	11 (52)	10 (48)
Well-differentiated LPS	14 (6)	10 (71)	*	*
Synovial sarcoma	8 (4)	*	*	*
Malignant peripheral nerve sheath tumor	5 (2)	0	*	*
Angiosarcoma	6 (3)	*	*	*
Kaposi sarcoma	7 (3)	*	*	*
Spindle cell sarcoma/STS NOS	24 (11)	9 (38)	6 (25)	11 (46)
Other STS	9 (4)	*	*	*
Gastrointestinal stromal tumor	35 (15)	29 (83)	21 (60)	17 (49)
"Indolent" histologies	10 (4)	*	7 (70)	*

+2 pts had 2 different sarcomas, *<5 pts in subgroup

-Other: Epithelioid sarcoma, parotid sarcoma, Alveolar soft part sarcoma, Anaplastic hemangiopericytoma, Phyllodes tumor, Rhabdomyosarcoma, Sclerosing epithelioid fibrosarcoma, SMARCA4 deficient sarcoma

-"Indolent" histologies: Giant cell tumor of bone, Dermatofibrosarcoma protuberans, Desmoid fibromatosis, Tenosynovial giant cell tumor, Smooth muscle tumor of uncertain malignant potential, Solitary fibrous tumor



ctos®

2021 Virtual Annual Meeting

Oral Presentations

Thursday, November 10, 2021



11:00 am - 12:00 pm

– Session 3 –

GIST

11:00 AM - 11:07 AM

Paper #10 #1818708

RIPRETINIB AS ≥4TH-LINE TREATMENT IN PATIENTS WITH ADVANCED GASTROINTESTINAL STROMAL TUMOR: LONG-TERM UPDATE FROM THE PHASE 3 INVICTUS STUDY

Robin L. Jones¹; Michael C. Heinrich²; Suzanne George³; John Zalcborg⁴; Sebastian Bauer⁵; Hans Gelderblom⁶; Patrick Schöffski⁷; César Serrano⁸; Steven Attia⁹; Gina D'Amato¹⁰; Ping Chi¹¹; Peter Reichardt¹²; Julie Meade¹³; Vienna Reichert¹³; Kelvin Shi¹³; Rodrigo Ruiz-Soto¹³; Jean-Yves Blay¹⁴; Margaret von Mehren¹⁵;

¹The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, England, UNITED KINGDOM;

²Hematology/Medical Oncology, OHSU Knight Cancer Institute, Portland, UNITED STATES; ³Sarcoma Center,

Medical Oncology, Dana Farber Cancer Institute, Boston, Massachusetts, UNITED STATES; ⁴OAM, School of Public

Health, Faculty of Medicine, Monash University, Melbourne, Victoria, AUSTRALIA; ⁵University Hospital Essen

Westdeutsches Tumorzentrum, Essen, Nordrhein-Westfalen, GERMANY; ⁶Leiden University Medical Center, Leiden,

Zuid-Holland, NETHERLANDS; ⁷General Medical Oncology, University Hospitals Leuven – Campus Gasthuisberg,

Leuven, Brabant Wallon, BELGIUM; ⁸Sarcoma Translational Research Program, Department of Medical Oncology,

Sarcoma Translational Research, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Catalonia, SPAIN; ⁹The Mayo

Clinic, Jacksonville, Florida, UNITED STATES; ¹⁰Sylvester Comprehensive Cancer Center/University of Miami, Miami,

Florida, UNITED STATES; ¹¹Human Oncology and Pathogenesis Program/Department of Medicine, Memorial Sloan

Kettering Cancer Center, New York, New York, UNITED STATES; ¹²Oncology and Palliative Care, Sarcoma Center,

Helios Klinikum Berlin-Buch, Berlin, Berlin, GERMANY; ¹³Deciphera Pharmaceuticals, LLC, Waltham, Massachusetts,

UNITED STATES; ¹⁴Centre Léon Bérard, Lyon, Auvergne, FRANCE; ¹⁵Sarcoma Oncology, Hematology/Oncology,

Fox Chase Cancer Center, Philadelphia, Pennsylvania, UNITED STATES

Objective: Ripretinib is an approved switch-control tyrosine kinase inhibitor (TKI) that broadly inhibits mutant KIT and PDGFRA kinase signaling. In INVICTUS, a randomized, double-blind, placebo-controlled trial in ≥4th-line advanced GIST, ripretinib compared with placebo (PBO) significantly improved median progression-free survival (mPFS; 6.3 vs 1.0 months), reducing the risk of disease progression or death by 85%, and showed a clinically meaningful improvement in median overall survival (mOS; 15.1 vs 6.6 months); data as of May 31, 2019 (ESMO 2019). Ripretinib is well tolerated. Here, we present a long-term update of mature data, with a data cut-off date 19 months after the data cut-off date of the primary analysis.

Methods: Patients with advanced GIST previously treated with at least imatinib, sunitinib, and regorafenib were randomized (2:1) to ripretinib 150 mg once daily (QD) or PBO. Upon disease progression determined by blinded independent central review, patients on PBO could cross over to ripretinib 150 mg QD. All patients who received 150 mg QD and had radiological progression could receive 150 mg twice daily.

Results: As of January 15, 2021, of 129 patients randomized, 128 received treatment (ripretinib 150 mg QD, n = 85; PBO, n = 43). Patients randomized to ripretinib had a mPFS of 6.3 months (95% CI 4.6–8.1) vs 1.0 (95% CI 0.9–1.7) month for patients on PBO with a hazard ratio (HR) of 0.16. The mOS in the ripretinib arm was 18.2 months (95% CI 13.1–30.7) vs 6.3 (95% CI 4.1–10.0) months in the PBO arm with a HR of 0.41. No new safety concerns were identified with longer exposure to ripretinib.

Conclusion: Evaluation of primary and secondary endpoints in the phase 3 INVICTUS trial, with a cutoff date 19 months after the primary analysis, demonstrate stable mPFS with no change since the primary data release, and improved mOS for patients randomized to ripretinib. These more mature data continue to support the clinically meaningful benefit in PFS and OS for ripretinib with an acceptable safety profile in patients with advanced GIST treated with 3 or more prior TKIs. Previously presented at ESMO 2021, FPN: Pending, von Mehren M, et al. Reused with permission.



11:07 AM - 11:14 AM

Paper #11 #1818776

REGISTRI: REGORAFENIB IN FIRST-LINE OF KIT/PDGFR WILD TYPE METASTATIC GIST: A COLLABORATIVE SPANISH (GEIS), ITALIAN (ISG) AND FRENCH SARCOMA GROUP (FSG) PHASE II TRIAL

Javier Martin-Broto¹; Claudia M. Valverde²; Nadia Hindi³; Bruno Vincenzi⁴; Javier Martinez-Trufero⁵; Giovanni Grignani⁶; Antonine Italiano⁷; Javier Lavernia⁸; Ricardo Gonzalez-Campora⁹; Ana Vallejo¹⁰; Diana Hernandez-Jover¹¹; Antonio Gutierrez¹²; Cesar Serrano¹³; David Moura¹⁴; Jose Antonio Lopez-Guerrero⁸; Julia Cruz⁸; Antonio Fernández-Serra⁸; Jean-Yves Blay¹⁵; Elena Fumagalli¹⁶; Virginia Martínez-Marín¹⁷

¹Fundacion Jimenez Diaz University Hospital, Madrid, Madrid, SPAIN; ²Genitourinary, Sarcoma, CNS, CUP Unit, Hospital Universitario Vall d'Hebron, Barcelona, Catalonia, SPAIN; ³Fundacion Jimenez Diaz University Hospital, Madrid, Madrid, SPAIN; ⁴Department of Medical Oncology, Università Campus Bio-Medico di Roma, Rome, ITALY; ⁵Miguel Servet University Hospital, Zaragoza, Aragon, SPAIN; ⁶Department of Medical Oncology-Sarcoma Unit, Candiolo Cancer Institute FPO-IRCCS, Candiolo, Piemonte, ITALY; ⁷Institute Bergonié, Bordeaux, Aquitaine, FRANCE; ⁸Fundacion Instituto Valenciano de Oncologia, Valencia, Comunidad Valenciana, SPAIN; ⁹Hospital Quironsalud Cordoba, Cordoba, Andalusia, SPAIN; ¹⁰Virgen Macarena University Hospital, Seville, Andalusia, SPAIN; ¹¹Hospital Sant Pau, Barcelona, Catalonia, SPAIN; ¹²Son Espases University Hospital, Palma de Mallorca, Islas Baleares, SPAIN; ¹³Vall d'Hebron University Hospital Barcelona, Catalonia, SPAIN; ¹⁴CITIUS III, Seville, Andalusia, SPAIN; ¹⁵Centre Léon Bérard, Lyon, Auvergne, FRANCE; ¹⁶Fondazione IRCCS Istituto Nazionale Dei Tumori Di Milano, Milan, Lombardia, ITALY; ¹⁷H. U. La Paz, Madrid, Madrid, SPAIN

Objective: Around 15% of adult GIST are wild type for KIT/PDGFR mutations (KPWT) and usually have SDH deficiencies, exhibit a more indolent behavior and are resistant to imatinib (IM). The underlying protumorigenic mechanisms in KPWT GIST include overexpression of HIF1 α in SDH deficient subset, high IGF1R signaling through MAPK, BRAF activating mutation or STAT3 activation. As Regorafenib (RE) inhibits these signaling pathways, it was hypothesized that RE could be more active as upfront therapy in KPWT GIST

Methods: Adult patients with advanced non pretreated KPWT GIST were eligible after central confirmation by next-generation sequencing (NGS). Eligible patients received RE at 160mg/d for 21/28d cycles. Primary end-point was disease control rate (DCR) according to RECIST 1.1 at 12 weeks by central radiological assessment (CRA). Secondary objectives included: Progression-free survival (PFS), Overall Survival (OS), Overall Response Rate (ORR), both by RECIST and Choi, safety and quality of life. The protocol was amended to allow previous IM exposure (adjuvant). Statistical assumptions [H0 73% and H1 90% (α 0.1 and β 0.2)], defined a sample size of 20 patients.

Results: From May 2016 to October 2020, 30 patients with KPWT GIST by Sanger sequencing underwent central molecular screening. Among the 15 non-eligible patients, 8 harbored KIT exon 11 mutations, 3 exon 9 and 3 PDGFRA exon 18 by NGS. The remaining 16 (53.3%) molecularly eligible patients were enrolled (NCT02638766) and started RE except one patient due to COVID-19 pandemic. The trial was prematurely closed due to low recruitment, especially after COVID outbreak. Patients (8F/7M) had median age 57 years (17-72), 2 locally advanced unresectable/13 metastatic. 5/15 (33%) had previously received IM. Patients received a median of 7.8 (0.3-39) cycles of RE. 8/15 (53%) and 14/15 (93%) patients had any reduction or interruption of RE respectively. The most frequent G3-4 toxicities were: GOT/GPT increase (3 pts, 20%), Palmo-plantar erythrodysesthesia (2 patients, 13%), skin disorders (2 patients, 13%), anemia, diarrhea, hypertension and pruritus, (1 patient each, 7%). 14 patients were evaluable for RECIST response: 1 PR (7%), 12 SD (84%) (7/12 experiencing any dimensional reduction), and 1 PD (7%). Based on CRA, 12w-DCR was 86.7%. With a median (m) follow-up of 26 (5-44) months, 10/15 patients have progressed, with a mPFS of 10.8 months (95% CI 6.9-14.8). 6- months, 9-months and 12-months PFS rates were 65%, 50% and 33% respectively. 2 patients were free of PD at 25 and 43 months from start of RE. 6/15 patients have died, with a mOS of 33.5months (95% CI NR). 10/15 patients had SDH complex deficiency, 3 preserved SDH activity and 2 were not evaluable.

Conclusion: The study results approach the prespecified activity threshold. The low rate of recruitment could have affected this attainment. Other analysis of secondary endpoints are ongoing. The high percentage of overlooked mutant GIST by Sanger raises the need of NGS in presumed KPWT GIST.



11:14 AM - 11:21 AM

Paper #12 #1818782

TRANSPERINEAL RESECTION OF RECTAL GASTROINTESTINAL STROMAL TUMOR: ANALYSIS OF SURGICAL AND ONCOLOGICAL OUTCOMES AT A SINGLE REFERRAL CENTER

Valentina Messina MD; Francesco Barretta; Marco Fiore; Stefano Radaelli; Chiara Colombo; Marta Barisella; Carlo Morosi; Elena Rosa Fumagalli; Rosalba Miceli; Alessandro Gronchi; Dario Callegaro
 Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY

Objective: Approximately 5% of gastrointestinal stromal tumors (GIST) originate in the rectum, mainly in the distal third. In the imatinib era, resection of rectal GIST is most of the time doable without sacrificing the anal sphincter complex. To achieve this goal, the most commonly described surgical techniques include local excision via a transanal or a transvaginal approach and low anterior resection. Here, we analyze surgical and oncological outcomes after local excision of rectal GIST via a transperineal access route.

Methods: This is a retrospective single-center study. We included all adult patients who underwent transperineal resection of a rectal GIST between 2010 and 2021 at Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy. Patients with rectal GIST were systematically offered with transperineal resection when the tumor was located mainly outside of the rectal wall and in close proximity to or with direct involvement of the anal sphincter complex. Clinical data were collected from a prospectively-maintained database. Postoperative complications were classified according to Clavien-Dindo. The main study outcomes were 90-day postoperative complications and crude cumulative incidence (CCI) of local recurrence (LR) calculated in a competing-risk framework. As a secondary outcome, we assessed the association between the clinical characteristics of the patients and the development of postoperative rectal fistulas by means of univariable logistic models.

Results: Twenty-one patients were included (Table 1). 19 patients underwent resection of a primary rectal GIST. Two patients underwent resection of a local recurrence, respectively 6 and 11 years after a transanal excision of the primary tumor. Median follow-up was 49 months (IQR 30-100).

A loop colostomy was created at first surgery in 18 patients. At last follow-up 16 patients were alive and without stoma, with a functioning anal-sphincter complex. Two patients were alive with a stoma, awaiting for the stoma reversal procedure. One patient was alive with a permanent stoma after an abdominal perineal resection performed to treat a local recurrence. One patient was alive with a stoma 6 years after the primary surgery due to a chronic rectal fistula. Median time to colostomy closure was 6 months (IQR: 5-8.75).

Ninety-day postoperative complications \geq Clavien-Dindo grade 3 occurred in 4 patients (19%, all grade 3b). We observed three leaks of the rectal suture and 1 postoperative bleeding. Median length of hospital stay was 8 days (IQR 7-9).

Overall, 9 patients suffered from a rectal fistula (any Clavien-Dindo grade, any time after surgery). There were no major differences in terms of sex, age, disease presentation, tumor size, resection technique, stoma creation at primary surgery, Charlson comorbidity index, concomitant resection of the internal anal sphincter between patients who developed a rectal fistula and those who did not (Table 2) The association analysis was not able to detect any significant results due to the low number of observations (all p-values $>$ 0.3).

Only one patient died during follow-up 7.5 years after surgery, without a stoma, for causes unrelated to the disease. Three patients suffered from LR, at a median time of 43 months after surgery (IQR 28.5-59): two after transperineal resection of primary GIST, one after transperineal resection of a recurrent GIST. Five-year crude cumulative incidence of local recurrence was 12.3% (95% CI 3.2, 47.6), Figure 1.

Conclusion: In this study, the transperineal resection of rectal GIST was associated with good long term local control. Despite the high postoperative fistula rate, most of the patients were able to maintain the anal-sphincter complex function and live without a stoma.

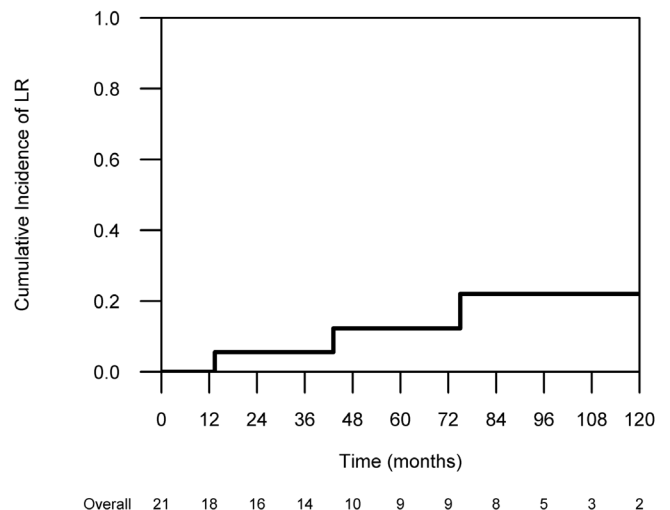
Figure 1


Table 1

	Patient population (n=21)
Age (years) Median (IQR)	62 (58 - 68)
Sex Male Female	13 (61.9) 8 (38.1)
Preoperative imatinib Yes No	21 (100.0) 0 (0.0)
Tumor size before imatinib (mm) Median (IQR)	50 (41.5 - 60)
Tumor size at surgery (mm) Median (IQR)	35 (20 - 40)
Tumor site in the rectum Posterolateral Lateral Anterolateral Anterior	6 (28.6) 4 (19.0) 6 (28.6) 5 (23.8)
Mutation status Kit Ex 11 Kit Ex 9 Other n.a.	14 (66.7) 1 (4.8) 2 (9.5) 4 (19.0)
Concomitant colostomy Yes No	18 (85.7) 3 (14.3)
Colostomy (any time) Yes No	20 (95.2) 1 (4.8)
Type of resection Stapler Manual	9 (42.8) 12 (57.1)
External sphincter partial resection Yes No	2 (9.5) 19 (90.4)
Internal sphincter partial resection Yes No	4 (19.0) 17 (80.9)
Length of hospital stay (days) Median (IQR)	8 (7- 9)
Total number of surgeries Median (IQR)	2 (2 - 2)
Rectal fistula within 90 days Yes No	5 (23.8) 16 (76.2)
Rectal fistula at any time Yes No	9 (42.8) 12 (57.1)
Colostomy closure Yes No	16 (76.2) 4 (19.0)
Margin status R0 R1 n.a.	16 (76.2) 3 (14.2) 2 (9.5)
Operative time Median (IQR)	163 (117- 188)
Presence of colostomy (months) Median (IQR)	6 (5.0 - 8.75)
Conversion to APR (any time)	1 (4.7%)
Disease status at last FU NED AWD DOC DOD	18 (85.7) 2 (9.5) 1 (4.8) 0 (0.0)

Table legend: IQR, interquartile range; APR, abdominal perineal resection; FU, follow-up; NED, no evidence of disease; AWD, alive with disease; DOC, dead of other causes; DOD, dead of disease

Table 2

	Fistula Yes	Fistula No
N	9	12
Sex		
Male	6 (66.7)	7 (58.3)
Female	3 (33.3)	5 (41.7)
Age		
Median (IQR)	63.00 (62.0, 68.0)	60.00 (50.25, 67.50)
Tumor presentation		
Primary	9 (100.0)	9 (75.0)
Recurrent	0 (0.0)	3 (25.0)
Size		
Median (IQR)	35.00 (20.0, 36.0)	34.50 (22.50, 41.25)
Resection technique		
Stapled	5 (55.6)	4 (33.3)
Manual	4 (44.4)	8 (66.7)
Stoma creation at primary surgery		
Yes	7 (77.8)	11 (91.7)
No	2 (22.2)	1 (8.3)
Charlson- Comorbidity Index		
Median (IQR)	4.00 (3.00, 4.00)	4.00 (2.75, 5.00)
Internal sphincter resection		
Yes	2 (22.2)	2 (16.7)
No	7 (77.8)	10 (83.3)

Table legend: IQR, interquartile range



11:21 AM - 11:28 AM

Paper #13 #1818778

THE USE OF LOCAL TREATMENT IN METASTASIZED GIST PATIENTS

Pien Brink¹; Gijsbert M. Kalisvaart¹; Dirk J. Grünhagen²; Cornelis Verhoef²; Hans Gelderblom¹; Henk H. Hartgrink¹; Winan J. van Houdc³; Winette T. A. van der Graaf³; Neeltje Steeghs³; Lukas Been⁴; An Reyners⁴; Robert Van Ginkel⁴; Yvonne M. Schrage¹; Marta Fiocco¹; Jos A. van der Hage¹;

¹Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS; ²Erasmus MC Cancer Institute, Rotterdam, Zuid-Holland, NETHERLANDS; ³The Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS;

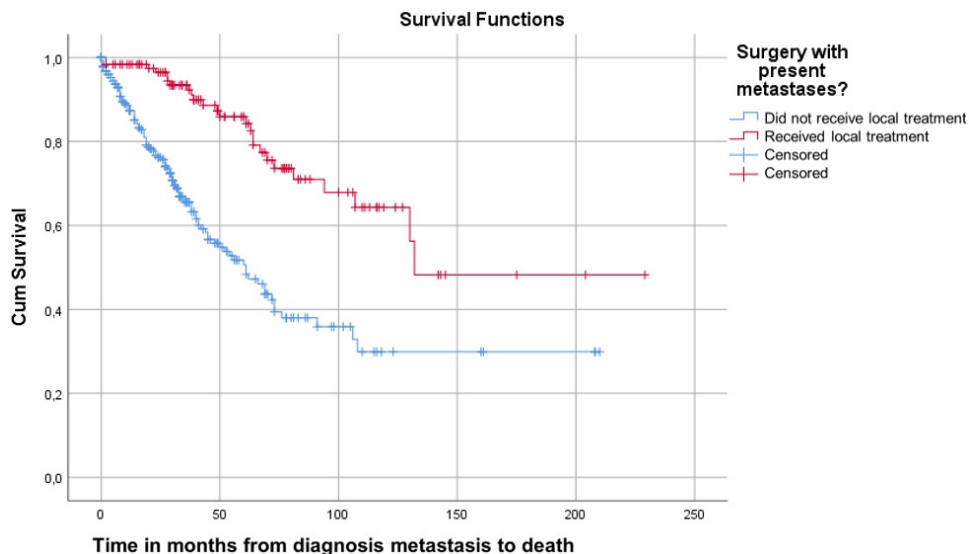
⁴University Medical Center Groningen (UMCG), Groningen, Groningen, NETHERLANDS

Objective: Metastasized GIST patients are typically treated with systemic therapies. Recent studies show that local treatment might improve survival in selected cases. Evidence based guidelines guiding the decision to perform local treatment are missing. This study aims to provide more clarity into considerations on whether or not patients should receive local treatment and what patient and tumor characteristics might contribute to this decision.

Methods: Metastasized GIST patients were selected from the Dutch GIST Registry (DGR), and divided in a group that received local treatment and a group that did not receive local treatment. Kaplan Meier and multivariate Cox-regression analyses were performed, correcting for variables deemed to be of prognostic value by medical specialists in a Delphi study. Furthermore, a multivariate Cox-regression analysis in patients who received local treatment is performed in order to analyze if the variables influence overall survival in this specific group.

Results: A total of 457 metastasized patients were selected, of whom 123 underwent elective locoregional surgery or ablation, for the primary tumor and/or the metastasis. Overall survival time for the locally treated group was estimated 132 months versus 61 months for patients who did not receive locoregional treatment (p < 0.001). The multivariate Cox-regression analysis showed that receiving local treatment (HR = 0.179, p < 0.001) is predictive for overall survival independent of the tested prognostic variables. In the multivariate Cox-regression analysis for the locally treated patients, hepatic metastatic disease showed to be beneficial compared to visceral disease (HR = 0.309, p = 0.040).

Conclusion: This study shows that patients with advanced GIST who received local treatment, have a better overall survival than patients that were not locally treated. Furthermore, the results suggest that especially patients with hepatic metastatic disease have a better outcome after local treatment.





11:28 AM - 11:35 AM

Paper #14 #1818751

EFFICACY AND SAFETY OF RIPRETINIB IN PATIENTS WITH ADVANCED GASTROINTESTINAL STROMAL TUMOR: ANALYSES OF A SINGLE-ARM, PHASE 2 TRIAL

Jian Li¹; Shirong Cai²; Yongjian Zhou³; Jun Zhang⁴; Ye Zhou⁵; Hui Cao⁶; Xin Wu⁷; Yanhong Deng⁸; Biao Zhang⁹; Juan Dong⁹; Lin Shen¹;

¹Peking University Cancer Hospital & Institute, Beijing, Beijing, CHINA (PEOPLE'S REPUBLIC); ²The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, Guangdong, CHINA (PEOPLE'S REPUBLIC); ³Fujian Medical University Union Hospital, Fuzhou, Fujian, CHINA (PEOPLE'S REPUBLIC); ⁴The First Affiliated Hospital of Chongqing Medical University, Chongqing, Chongqing, CHINA (PEOPLE'S REPUBLIC); ⁵Fudan University Shanghai Cancer Center, Shanghai, Shanghai, CHINA (PEOPLE'S REPUBLIC); ⁶Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, Shanghai, CHINA (PEOPLE'S REPUBLIC); ⁷Chinese PLA General Hospital, Beijing, Beijing, CHINA (PEOPLE'S REPUBLIC); ⁸The Sixth Affiliated Hospital, Sun Yat-sen University, Guangzhou, Guangdong, CHINA (PEOPLE'S REPUBLIC); ⁹Zai Lab (Shanghai) Co., Ltd, Shanghai, Shanghai, CHINA (PEOPLE'S REPUBLIC)

Objective: Gastrointestinal stromal tumors (GIST) are common sarcomas of the gastrointestinal (GI) tract, most commonly resulting from KIT or platelet-derived growth factor receptor α (PDGFRA) activating mutations. Ripretinib is a switch-control tyrosine kinase inhibitor (TKI) that broadly inhibits KIT and PDGFRA mutations including the multiple primary and secondary mutations that drive disease progression and drug resistance in GIST. In the INVICTUS phase 3 study (NCT03353753), ripretinib demonstrated a statistically significant improvement in median progression-free survival (mPFS; 6.3 months) compared with placebo (1.0 month) with an acceptable safety profile in patients with ≥ 4 th-line GIST. Ripretinib is approved for ≥ 4 th-line therapy in GIST in the US, Canada, China, Hong Kong, and Australia. We report on the outcome of a phase 2 study (NCT04282980) evaluating the efficacy (based on independent radiologic review [IRR]) and safety of ripretinib in Chinese patients with advanced GIST who had disease progression or were intolerant to ≥ 3 prior anticancer therapies.

Methods: In this multicenter, phase 2, single-arm study, eligible patients were adult patients with advanced GIST who progressed or had documented intolerance despite dose modification to imatinib, sunitinib, and at least one other drug and an Eastern Cooperative Oncology (ECOG) performance status of 0-2. Patients received ripretinib 150 mg once daily for 28-day cycles until disease progression, unacceptable toxicity, or consent withdrawal. The primary endpoint was PFS assessed by IRR. The secondary endpoints included objective response rate (ORR) and disease control rate (DCR) assessed by IRR, overall survival (OS), and safety.

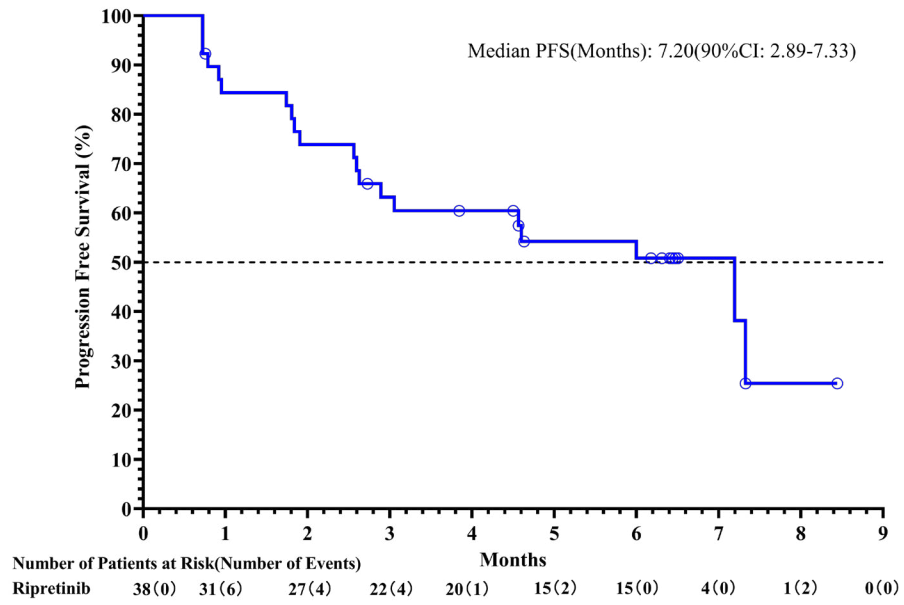
Results: Between Apr 10, 2020, and Aug 06, 2020, 50 patients were assessed, and 39 eligible patients were enrolled and received ≥ 1 dose of study drug and were included in the full analysis set (FAS). Efficacy analysis set (EAS) included 38 patients receiving continuous (≥ 1 dose) drug treatment. In FAS (n=39), the median age was 55 years (range, 37-74) and 7 (17.9%) patients were ≥ 65 years. Thirty-three (84.6%) patients had received 3 prior lines of therapy and 6 (15.4%) patients had received ≥ 4 prior lines of therapy (range, 4-5). The date of data cutoff was Feb 26, 2021. The median PFS assessed by IRR was 7.2 months (90% CI 2.89-7.33) (Figure 1). The ORR assessed by IRR was 18.4% (95% CI 7.7-34.3) and DCR (complete response, partial response, or stable disease lasting ≥ 6 weeks) by IRR was 71.1% (95% CI 54.1-84.6). Seven patients had OS events and the median OS was not reached yet. Among the 7 patients achieving a partial response, the median time to best response (TBR) by IRR was 1.9 months (range, 1.0-3.8). In the FAS, all 39 patients experienced ≥ 1 treatment-emergent adverse event (TEAE). The incidence of TEAEs leading to dose interruption, reduction, and treatment discontinuation was 28.2%, 5.1%, and 10.3%, respectively. No TEAEs leading to death were reported. TEAEs (Any Grade and Grade 3/4) are summarized in Table 1 and 2. Eight (20.5%) patients had serious adverse events (SAEs) including 2 (5.1%) treatment-related SAEs.

Conclusion: Ripretinib demonstrated encouraging antitumor activity with a manageable safety profile in Chinese patients with advanced GIST who have received prior treatment with imatinib, sunitinib, and at least one other drug.

Table 1. TEAEs of Any Grade Occurring in ≥20% of Patients in FAS	
PT	Ripretinib (N=39)
Patients with at least one TEAE	39 (100.0)
Anemia	24 (61.5)
Alopecia	17 (43.6)
Asthenia	13 (33.3)
Blood bilirubin increased	12 (30.8)
Bilirubin conjugated increased	11 (28.2)
Weight decreased	9 (23.1)
Myalgia	9 (23.1)
Diarrhea	8 (20.5)
Hypocalcemia	8 (20.5)
Constipation	8 (20.5)
Palmar-plantar erythrodysesthesia syndrome	8 (20.5)
FAS, full analysis set. TEAE, treatment-emergent adverse event. PT, Preferred Term Data shown as n (%).	

Table 2. Summary of Grade 3/4 TEAEs Occurring in ≥5% of patients in FAS	
PT	Ripretinib (N=39)
Patients with at least one TEAE	20 (51.3)
Anemia	10 (25.6)
Hypokalemia	3 (7.7)
Diarrhea	2 (5.1)
Hypophosphatemia	2 (5.1)
Gastrointestinal Hemorrhage	2 (5.1)
Hypertriglyceridemia	2 (5.1)
FAS, full analysis set. TEAE, treatment-emergent adverse event. PT, Preferred Term Data shown as n (%).	

Figure 1 Kaplan-Meier Plot of Progression-Free Survival Assessed by IRR in EAS



IRR, independent radiologic review; CI, confidence interval; EAS, efficacy analysis set; PFS, progression-free survival.



11:35 AM - 11:42 AM

Paper #15 #1818725

PATIENT-REPORTED SYMPTOMS AND HEALTH-RELATED QUALITY OF LIFE IN GASTROINTESTINAL STROMAL TUMOUR PATIENTS TREATED WITH TYROSINE KINASE INHIBITORS
Dide den Hollander¹; Ingrid Desar²; Hans Gelderblom³; Astrid Oosten⁴; An Reyners⁵; Neeltje Steeghs⁶; Winette T. A. van der Graaf⁶; Olga Husson⁶;

¹Netherlands Cancer Institute/ Radboud University Medical Center Nijmegen, Amsterdam, Noord-Holland, NETHERLANDS;

²Radboud University Medical Center, Nijmegen, Gelderland, NETHERLANDS; ³Leiden University Medical Center, Leiden,

 Zuid-Holland, NETHERLANDS; ⁴Erasmus Medical Center Rotterdam, Rotterdam, Zuid-Holland, NETHERLANDS;

⁵University Medical Center Groningen, Groningen, Groningen, NETHERLANDS; ⁶Netherlands Cancer Institute,

Amsterdam, Noord-Holland, NETHERLANDS

Objective: Treatment with tyrosine kinase inhibitors (TKIs) has dramatically improved survival for metastatic Gastrointestinal Stromal Tumour (GIST) patients. As a consequence, the group of GIST patients living with the disease and long-lasting treatment is increasing. Nevertheless, TKIs are not without adverse events, potentially compromising the experienced benefits of treatment by the patients. This study aimed to examine prevalence of patient-reported symptoms and health-related quality of life (HRQoL) among GIST patients treated with TKIs.

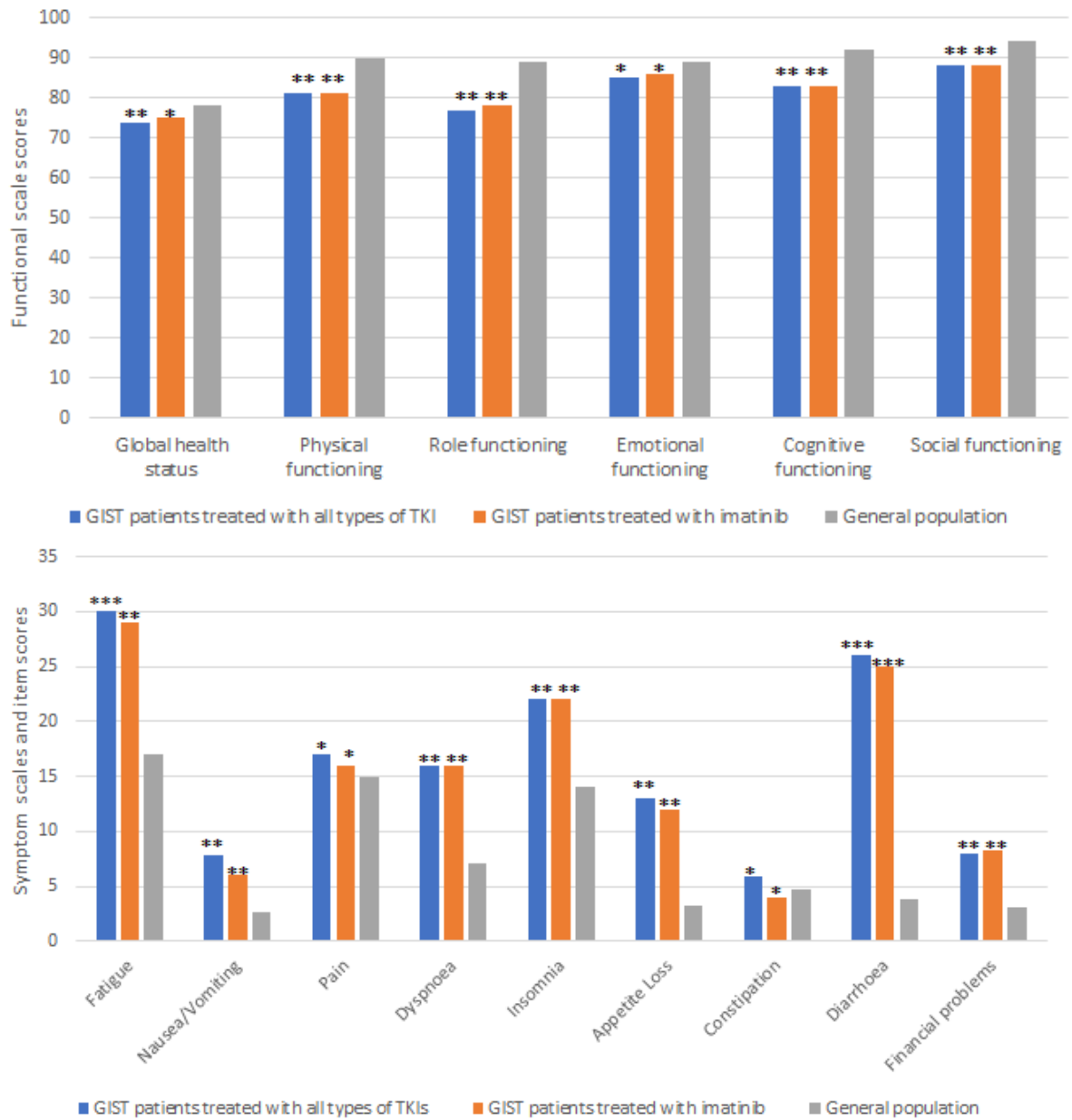
Methods: A cross-sectional study was conducted among Dutch GIST survivors aged ≥ 18 , diagnosed 3-13 years ago in five GIST reference centers. Patients with localized or metastatic GIST on TKI treatment at time of questionnaire completion were selected for analysis. Participants completed items from the EORTC Symptom Based Questionnaire to evaluate symptoms and the EORTC QLQ-C30 as a measure of HRQoL. Sociodemographic and clinical characteristics were collected from the Netherlands Cancer Registry. Prevalence scores for symptoms were determined based on a score of 2 or higher on the 4-point Likert scale being 1- 'not at all', 2- 'a little', 3- 'quite a bit' and 4- 'very much'. HRQoL scores were calculated and compared to normative data derived from a general Dutch population. Clinically relevant differences were determined as large, medium, small or trivial following the EORTC guidelines.

Results: Three hundred thirty-one patients participated in this study (overall response rate 64%), of which 107 were treated with a TKI at time of questionnaire completion and included for analysis. Mean age at diagnosis was 60 years (range 23-83) and GIST patients were treated with imatinib (n= 92), sunitinib (n= 6), regorafenib (n=6), and ripretinib (n=3). The five most prevalent patient-reported symptoms for imatinib were fatigue (73%), muscle pain or cramps (73%), swelling in the face or around the eyes (59%), joint pain (52%), and memory impairment (52%). For sunitinib, fatigue (100%), skin problems (83%), heartburn (83%), mouth pain (83%), change of taste (83%), feeling weak (83%), and nausea (83%) were most frequently reported. Patients using regorafenib reported fatigue (100%), muscle pain or cramps (100%), change of taste (67%), skin problems (67%), feeling weak (67%), and shortness of breath (67%) as most prevalent symptoms (see Table 1). Patients reported lower functional scores and higher symptom scores on the EORTC QLQ-C30 compared to an unmatched Dutch normative population (see Figure 1). When comparing patients treated with all types of TKI, differences were of medium clinical relevance for fatigue and diarrhea. Differences were of small clinical relevance for all functioning scales (except for emotional functioning), nausea/vomiting, dyspnea, insomnia, appetite loss, and financial problems. Trivial differences were found for emotional functioning, pain and constipation. When comparing only patients treated with imatinib to the general population, clinically relevant differences were similar except for a trivial difference in scores on global health status and a small difference for the fatigue scale (see Figure 1).

Conclusion: GIST survivors treated with TKI have reduced HRQoL as a consequence of their disease and/or TKI treatment compared to a normative population, although on many domains differences are small. The course of HRQoL outcomes during long-term TKI-treatment remains unclear. This study shows that patient-reported symptom prevalence is high and the reported symptoms match the known toxicity profiles of the different TKIs. Several symptoms that were frequently reported by GIST patients on TKIs are not part of the currently used cancer-generic HRQoL measure. Therefore it is recommended to capture these symptoms in patient-reported outcome measures to be used in clinical research and care to get a comprehensive overview of treatment effects from a patient perspective.

	Imatinib n=92	Sunitinib n=6	Regorafenib n=6	Ripretinib N=3
Symptoms	Prevalence (%)	Prevalence (%)	Prevalence (%)	Prevalence (%)
Swelling of the face or around the eyes	59*	50	33	0
Swelling in any part of the body	38	18	18	0
Muscles aches, pains, or cramps	73*	67	67*	100*
Aches or pains in joints	52*	67	33	33
Food and drink tasting different from usual	36	83*	67*	0
Pain or soreness in mouth	17	83*	33	0
Indigestion or heartburn	40	83*	18	33
Skin problems (e.g. itchy skin, dry skin, skin discolouration)	50	83*	67*	67*
Hand-foot syndrome	22	50	50	0
Problems because of changed appearance	30	33	0	100*
Feeling confused	16	18	18	0
Trouble speaking	16	33	18	0
Auditory hallucinations	4	0	0	0
Visual hallucinations	8	18	0	0
Shortness of breath	37	18	67*	33
Pain	34	67	50	67*
Feeling weak	41	83*	67*	33
Appetite loss	23	67	33	33
Nausea	23	83*	18	0
Vomiting	5	33	18	0
Constipation	12	50	18	67*
Diarrhoea	50	67	33	33
Fatigue	73*	100*	83*	100*
Problems with concentrating	32	50	18	33
Problems with remembering things	52*	50	33	33

Figure 1: scores of the EORTC QLQ-C30



For functional scales and global health status higher scores indicate higher functioning level/global health

For symptom scale and item scores, higher scores indicate a high level of symptomatology/problems.

* Trivial difference according to EORTC guidelines, compared to the general population

** Small difference according to EORTC guidelines, compared to the general population

*** Medium difference according to EORTC guidelines, compared to the general population



ctos®

2021 Virtual Annual Meeting

Oral Presentations

Thursday, November 10, 2021



1:15 pm - 2:30 pm

– Session 4 –

BONE TUMORS

1:15 PM - 1:22 PM

Paper #16 #1818705

THE PROPHYLACTIC ANTIBIOTIC REGIMENS IN TUMOR SURGERY (PARITY) INTERNATIONAL RANDOMIZED CONTROLLED TRIAL

Michelle Ghert; The PARITY Investigators

McMaster University, Oakville, Ontario, CANADA

Objective: The risk for surgical site infection (SSI) remains high following endoprosthetic reconstruction for tumors of the femur or tibia. The most effective peri-operative antibiotic regimen in preventing post-operative SSIs remains unknown, and the current state of practice varies widely, particularly with respect to antibiotic duration. The Prophylactic Antibiotic Regimens in Tumor Surgery (PARITY) trial aimed to determine whether a long duration (5 days) of post-operative prophylactic antibiotics decreases the risk of SSI when compared to a short duration (1 day).

Methods: The PARITY trial was an international, triple-blinded randomized controlled trial with centralized outcome adjudication. From January 2013 to October 2019, 605 patients across 48 clinical sites in 12 countries were randomized to receive either a long or a short duration of post-operative prophylactic antibiotics following oncologic endoprosthetic reconstruction of the lower extremity. Participants were followed post-operatively at regular intervals for one year. A Cox proportional hazards model was utilized to assess whether a long duration regimen decreases the risk of the primary outcome of SSI.

Results: **PARITY data is embargoed until October 2021 when results will be announced at the MSTs Meeting*** Participants were a mean XX years old and XX% male. Overall, XX SSIs were identified over the one year follow-up period (XX%, 95% CI:YY–YY). A long duration regimen conferred the following risk/protection against developing a SSI: HR:XX, 95% CI:YY–YY, p=X. In comparison to a short duration, a long duration regimen impacted secondary outcomes as follows: antibiotic-related complications (HR:XX, 95% CI:YY–YY, p=X); unplanned re-operations (HR:XX, 95% CI:YY–YY, p=X); and mortality (HR:XX, 95% CI:YY–YY, p=X).

Conclusion: The PARITY trial was the first international collaborative effort in prospective randomized research in orthopaedic oncology. The results of the trial are poised to significantly impact peri-operative clinical practice for lower extremity bone tumor patients.



1:22 PM - 1:29 PM

Paper #17 #1818784

OSTEOSARCOMA EXPLORER: A DATA COMMONS WITH CLINICAL, GENOMIC, PROTEIN AND TISSUE IMAGE DATA FOR OSTEOSARCOMA RESEARCH

Donghan Yang¹; Qinbo Zhou¹; Lauren Furman¹; Xian Cheng¹; Lin Xu¹; Bo Yao¹; Danni Luo¹; Hongyin Lai¹; Patrick Leavey¹; Tammy Lo²; David S. Shulman³; Donald A. Barkauskas⁴; Katherine A. Janeway³; Chand Khanna⁵; Richard Gorlick⁶; Stephen Skapek¹; Laura Klesse¹; Brian D. Crompton³; Yang Xie¹

¹UT Southwestern Medical Center, Dallas, Texas, UNITED STATES; ²Children's Oncology Group, Monrovia, California, UNITED STATES; ³Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, Massachusetts, UNITED STATES; ⁴Keck School of Medicine of the University of Southern California, Los Angeles, California, UNITED STATES; ⁵Ethos Discovery, Washington, District of Columbia, UNITED STATES; ⁶MD Anderson Cancer Center, Houston, Texas, UNITED STATES

Objective: Advances in genomics, digital pathology, and clinical research have led to rich data for osteosarcoma. Utilization of this wealth of data is often limited by institution siloed data generation and collection, lack of standard data structure and representation, lack of expertise in data analytics, and cohort size especially for pediatric patients. The Osteosarcoma Explorer project aims to 1) develop a data commons that integrates and harmonizes osteosarcoma data from multiple institutions and across various data types, and 2) provide this resource together with analytics tools through a user-friendly web interface to the sarcoma research community.

Methods: Clinical and research pediatric osteosarcoma data were collected from various sources, including Therapeutically Applicable Research to Generate Effective Treatments (TARGET), the QuadW-COG High Dimensional Data (HDD) platform, Dana-Farber Cancer Institute (DFCI), and UT Southwestern Medical Center (UTSW). Data included clinical variables, genomic features (gene mutation, copy-number variation, mRNA expression, and ctDNA status), protein expression status, and pathology images. Patients were de-identified and matched through the Unique Specimen Identifier (USI), where applicable. To standardize data representation, a concept map was developed to structure the data according to major clinical episodes when treating osteosarcoma (eg, diagnosis, treatment, and follow-up). Raw clinical, genomic, and imaging data were extracted from the original sources, curated, and processed onto a common data model with a standard terminology. A relational database was constructed to store the curated data, processed omics results, and pathology images. A web portal, Osteosarcoma Explorer (OSE; <https://qbrc.swmed.edu/projects/ose>), was developed for this database to provide end-user functionalities, including cohort discovery, individual patient dashboard, statistical analysis, and image visualization. A local instance of cBioPortal platform was integrated into OSE to provide additional analysis and visualization options.

Results: Four patient cohorts were formed according to the data source (Tab 1): TARGET (n = 306), HDD (n = 164; 7 overlapped with TARGET cohort), DFCI (n = 72; 6 overlapped with TARGET cohort), and UTSW (n = 50). The concept map (Fig 1) captures the typical clinical workflow in osteosarcoma patient care, including initial diagnosis, treatment, biospecimen collection and characterization (imaging, molecular profiling, etc), follow-up and the continuing evaluation of disease status. This concept map further governed the data modeling and curation process, which resulted in a standardized data set with 48 demographic and clinical variables, 5 sets of genomic and protein expression features (gene mutation, copy-number variation, mRNA expression, ctDNA, and HER2 protein expression), and 712 high-resolution H&E images. The OSE portal provides a web-based user interface for viewing and analyzing the data derived from this project. The QUERY PATIENTS module (Figure 2A) allows users to select patients based on demographic, clinical, molecular, and imaging characteristics. Detailed data surrounding each individual patient is accessible in the PATIENT INFO dashboard (Figure 2B). Genomic and protein expression features originally collected from different sources were linked to the matched patient inside this dashboard, providing a comprehensive view of patient-level info. The IMAGE VIEW module (Figure 2C) displays high-resolution H&E images at 40x magnification. The PERFORM ANALYSIS module (Figure 3) offers online statistical analysis based on clinical, genomic, and protein expression status.

Conclusion: OSE was developed as a comprehensive data commons for osteosarcoma research. Clinical, molecular, and imaging data from 4 independent sources were integrated in a standardized manner and provided to investigators through

a friendly, interactive web portal. Future directions include 1) engaging the broader osteosarcoma research community; 2) integrating data from additional sources; and 3) developing additional online data analysis functionalities.

Table 1. Summary of initial data sets included in the OSE.

Source	Number of patients	Clinical data	Genomic data	Protein expression data	Pathology images
TARGET	306	Yes	Yes (mutation, CNV, mRNA expression)	No	No
HDD	164	Yes	No	Yes (HER2)	No
DFCI	72	Yes	Yes (ctDNA)	No	No
UTSW	50	Yes	No	No	Yes

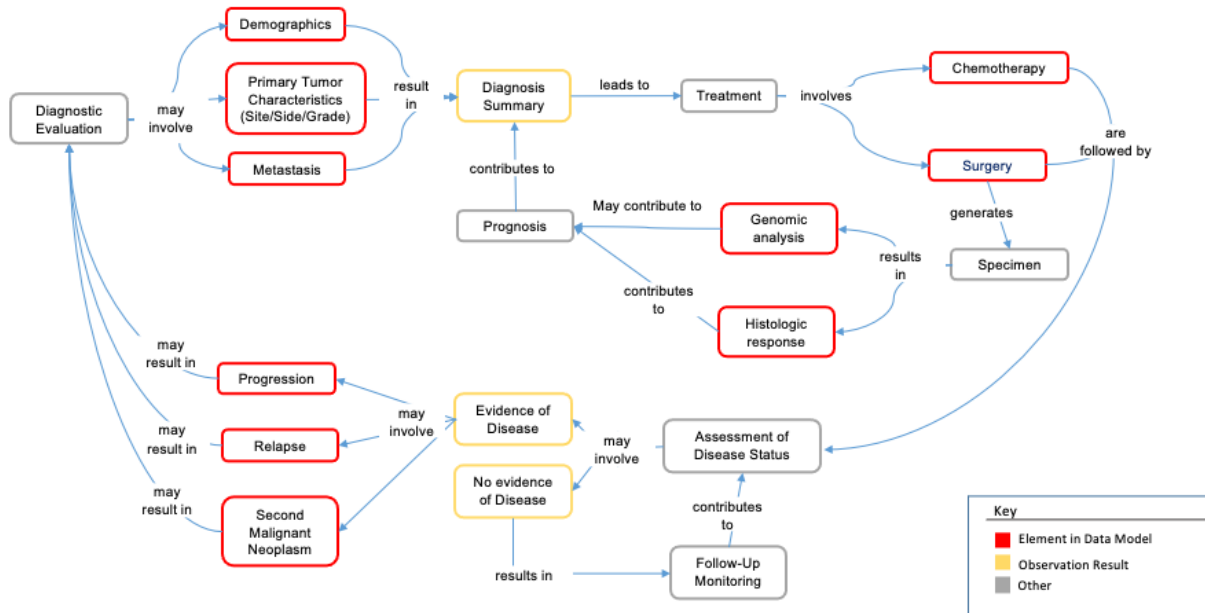


Figure 1. Concept map.



Figure 2. Osteosarcoma Explorer user interface. (A) QUERY PATIENT function for cohort discovery. (B) PATIENT INFO dashboard for individual patient-level information. (C) IMAGE VIEW module for visualizing high-resolution pathology images.

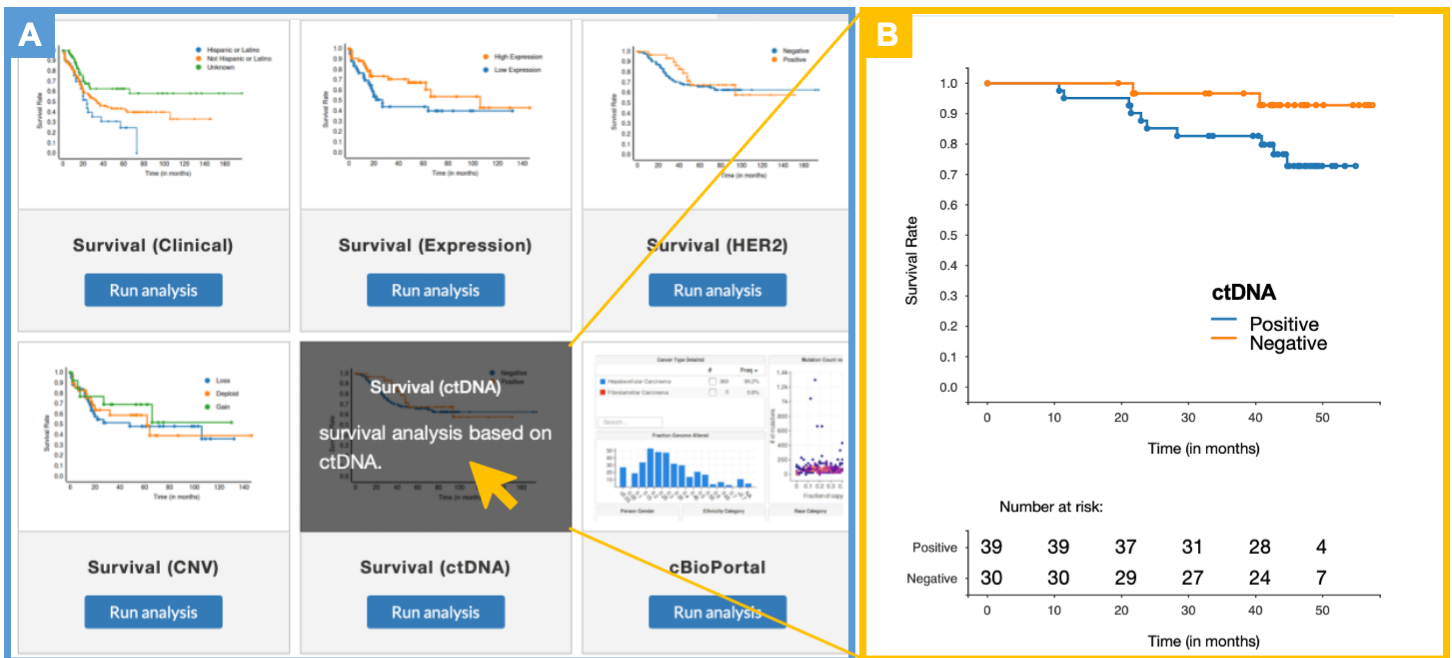


Figure 3. Osteosarcoma Explorer online analysis module. (A) Analysis overview. (B) An example survival analysis result based on ctDNA status. (C) Local instance of cBioPortal.



1:29 PM - 1:36 PM

Paper #18 #1818756

SAFETY AND EFFICACY OF THE TETRAVALENT DEATH RECEPTOR 5 AGONIST INBRX-109 IN PATIENTS WITH CONVENTIONAL CHONDROSARCOMA: UPDATE FROM THE PHASE 1 EXPANSION COHORT

Vivek Subbiah¹; Anthony P. Conley¹; Christopher Lieu²; Breelyn A. Wilky²; Nehal Lakhani³; Anthony Tolcher⁴; Joseph Chao⁵; Warren Chow⁵; Klaus Wagner⁶; Vasily Andrianov⁶; Analeah Heidt⁶; Emily Rowell⁶; Brendan Eckelman⁶; Quinn Deveraux⁶; James Kalabus⁶; Victoria T. Chua-Alcala⁷;

¹The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES; ²University of Colorado, Aurora, Colorado, UNITED STATES; ³START Midwest, Grand Rapids, Michigan, UNITED STATES; ⁴NEXT Oncology, LLC, San Antonio, Texas, UNITED STATES; ⁵City of Hope Comprehensive Cancer Center, Duarte, California, UNITED STATES; ⁶Inhibrx, Inc., La Jolla, California, UNITED STATES; ⁷Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES

Objective: INBRX-109 is a single domain-based agonist antibody targeting death receptor 5 (DR5). Activation of DR5 can induce programmed cell death through the extrinsic apoptosis pathway in a cancer-biased manner. Precisely engineered, the valency of INBRX-109 was empirically selected to include four DR5 binding domains to overcome the limitations of earlier generation agonists that lacked efficacy or ceased development due to hepatotoxicity. In preclinical studies, DR5 receptor clustering by INBRX-109 potently induced cancer cell death, with minimal observed cytotoxicity on human hepatic cells in vitro. This activity translated to potent in vivo anti-tumor activity in patient derived xenograft models derived from numerous cancers, including various sarcomas, and early signs of clinical activity in chondrosarcoma (CS) patients. Herein, we provide an update on the ongoing activity of INBRX-109 in patients with unresectable or metastatic conventional chondrosarcoma.

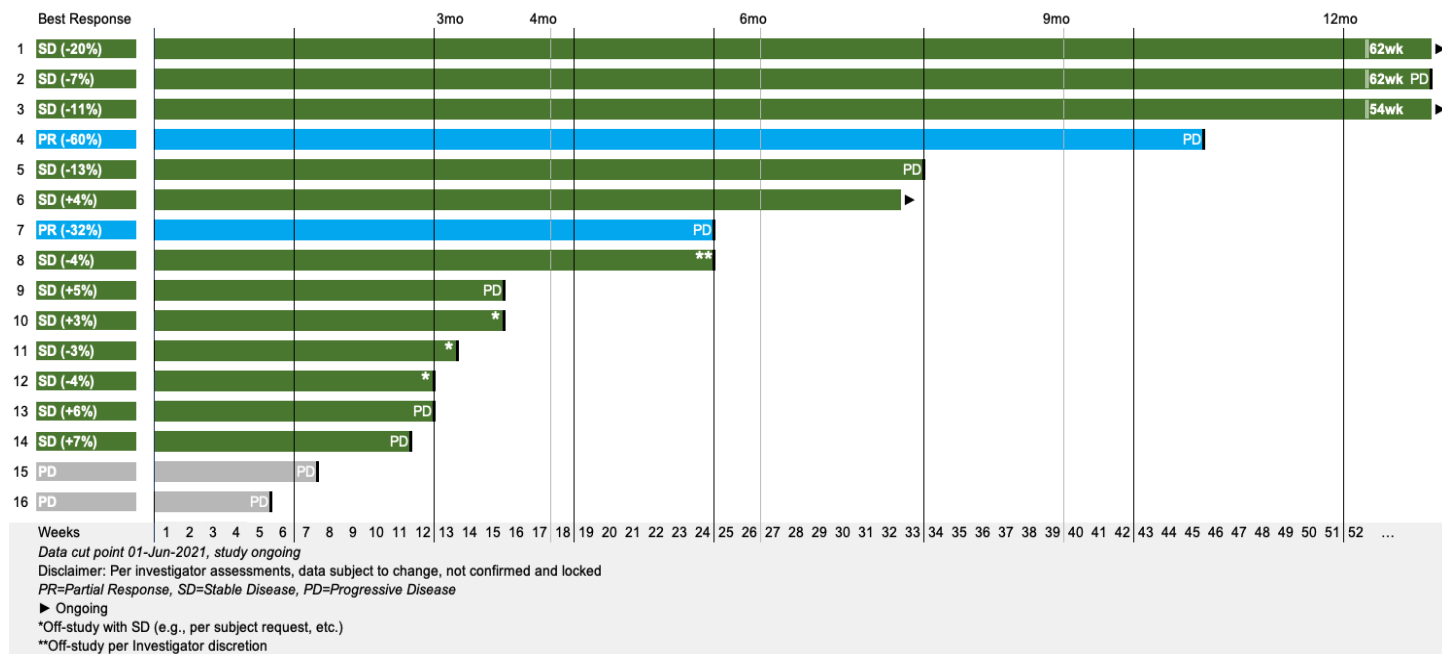
Methods: The INBRX-109 Phase 1 trial (NCT03715933) is an ongoing three-part study. Part 1, a traditional 3+3 dose escalation, was completed in 2019. INBRX-109 was well-tolerated and MTD was not reached. Part 2, single-agent dose expansion and Part 3, combination-dose expansion, are currently enrolling multiple tumor types, including several sarcoma cohorts: CS (n=20 completed enrollment), IDH1/2 mutant conventional CS (n=12 enrollment ongoing), synovial sarcoma (n=10 completed enrollment), Ewing sarcoma (n=20; enrollment ongoing). In these expansion cohorts, the safety, PK, immunogenicity, efficacy and potential predictive biomarkers of INBRX-109 are being evaluated.

Results: As of 01 June 2021, 16 patients with unresectable or metastatic conventional chondrosarcoma were evaluable for efficacy. The median age was 61 (range 25-86) with 14 male and 2 female patients. All patients presented with histological grades of 2 or 3 and the median number of prior therapy lines was one (range 0-4).

Disease Control Rate is 87.5 % (14 of 16 patients). Two of the patients achieved partial responses (12.5%) and 12 of 16 patients had stable disease (75%), as measured by RECISTv1.1. As of the data cutoff date, the median progression-free survival (PFS) is 7.6 months with three patients surpassing 12 months on INBRX-109 treatment, and three patients continue study treatment. The longest duration of stable disease observed thus far is 62 weeks, or approximately 14 months, and is ongoing (Figure 1.). The median overall survival has not been reached (15 of 16 patients are alive). The safety and tolerability profile continues to be favorable, and importantly, approximately 90% of patients experiencing no signs of hepatotoxicity. The trial is ongoing, with an additional cohort of 12 patients with IDH1 or IDH2 mutation positive conventional chondrosarcoma. Updated safety, PK, immunogenicity and efficacy data of single-agent INBRX-109 in conventional chondrosarcoma patients will be presented.

Conclusion: Encouraging early anti-cancer activity supports the continued investigation of INBRX-109 in unresectable or metastatic conventional chondrosarcoma. In January 2021, the U.S. Food and Drug Administration (FDA) granted Fast Track designation to INBRX-109 for the treatment of patients with unresectable or metastatic conventional chondrosarcoma. A randomized, blinded, placebo-controlled, Phase 2 trial of INBRX-109 in this indication is planned to open for enrollment in the 2nd half of 2021 in the U.S. Clinical trial applications in select European countries and the UK are planned to be filed later in 2021.

Figure 1. Time on treatment with INBRX-109 in conventional chondrosarcoma patients, as of 01 June 2021





1:36 PM - 1:43 PM

Paper #19 #1818787

NOVEL ANTIBODY DISRUPTS BIOFILM IN MOUSE MODEL OF IMPLANT ASSOCIATED INFECTION

Christopher M. Hart; Zach Burke; Benjamin Kelley; Zeinab Mamouei; Troy Sekimura; Michael Le; Michael Arnold; Alan Li; Amr Turkmani; Christopher Hamad; Nicolas Cevallos; Gideon Blumstein; Kellyn Hori; Sam Clarkson; Sam Uweh; Brian Zukotynski; Alexandra Stavrakis; Nicholas M. Bernthal
 UCLA, Santa Monica, California, UNITED STATES

Objective: Endoprosthetic and spinal reconstructions following resection of bone and soft tissue sarcomas have an increased risk for developing implant associated infections. Bacterial biofilms on implants are resistant to the host immune response and traditional antibiotic therapy, requiring highly morbid revision surgery to clear the infection. Novel therapies to treat biofilm infections are needed to improve patient outcomes. We hypothesize that a novel human monoclonal antibody against bacterial biofilm matrix will reduce bacterial burden in a mouse model of spinal implant infection.

Methods: TRL1068 is a human monoclonal antibody against a biofilm scaffolding protein that is conserved across both gram positive and gram-negative species. The efficacy of TRL1068 was assessed in a mouse model of spinal implant infection. A stainless-steel pin is implanted in the L4 spinous process and inoculated with a bioluminescent strain of *S. aureus*. Bacterial burden is monitored in vivo. Mice were randomized to treatment on POD 4 and 7 with subcutaneous 15 mg/kg TRL1068, inactive control antibody (CAB), vancomycin alone, or vehicle control. All treatment groups received BID vancomycin 120 mg/kg on POD 7-21. On POD 35 all animals were sacrificed. Implants and peri-implant tissue were harvested separately and sonicated for CFU analysis.

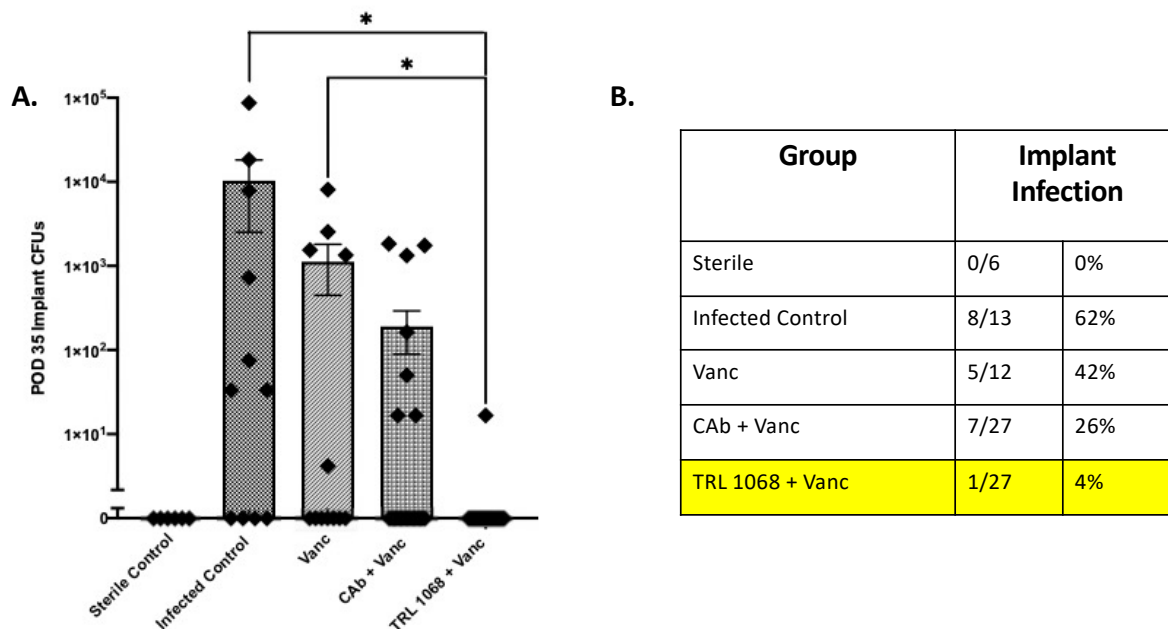


Figure 1. A) POD 35 *ex vivo* mean implant CFUs. There was a 4-log reduction (99.99%) in average implant CFUs in the TRL1068+vancomycin group relative to the infected control group (6.17×10^{-1} vs. 1.03×10^4 , respectively; $p=0.04$), and a 3.3-log reduction (99.9%) in average implant CFUs in the TRL1068+vancomycin group relative to the vancomycin only group (6.17×10^{-1} vs. 1.13×10^4 , respectively; $p=0.02$). B) Binary implant CFUs, 1/27 (4%) of implants from the TRL 1068 group found to have an infection.

Results: Treatment with TRL1068+vancomycin accelerated the decline of the bacterial burden compared to the control-antibody+vancomycin or vancomycin alone. There was a 3.3-log reduction (99.9%) in average implant CFUs in the TRL1068+vancomycin group relative to the vancomycin only group (6.17×10^{-1} vs. 1.03×10^4 , respectively; $p=0.04$). CFUs were enumerated from 42% (5/12) of implants of mice treated with vancomycin alone and 26% (7/27) of implants in mice treated with the control-antibody+vancomycin. In contrast, only 4% (1/27) of the mice treated with TRL1068+vancomycin were found to have an infected implant.

Conclusion: Implant related infections remain a major burden for patients and health systems. The novel human monoclonal antibody TRL1068 may add a valuable therapy to the armamentarium of treatment options as biofilm disruption facilitates the clearance of otherwise recalcitrant bacterial reservoirs.

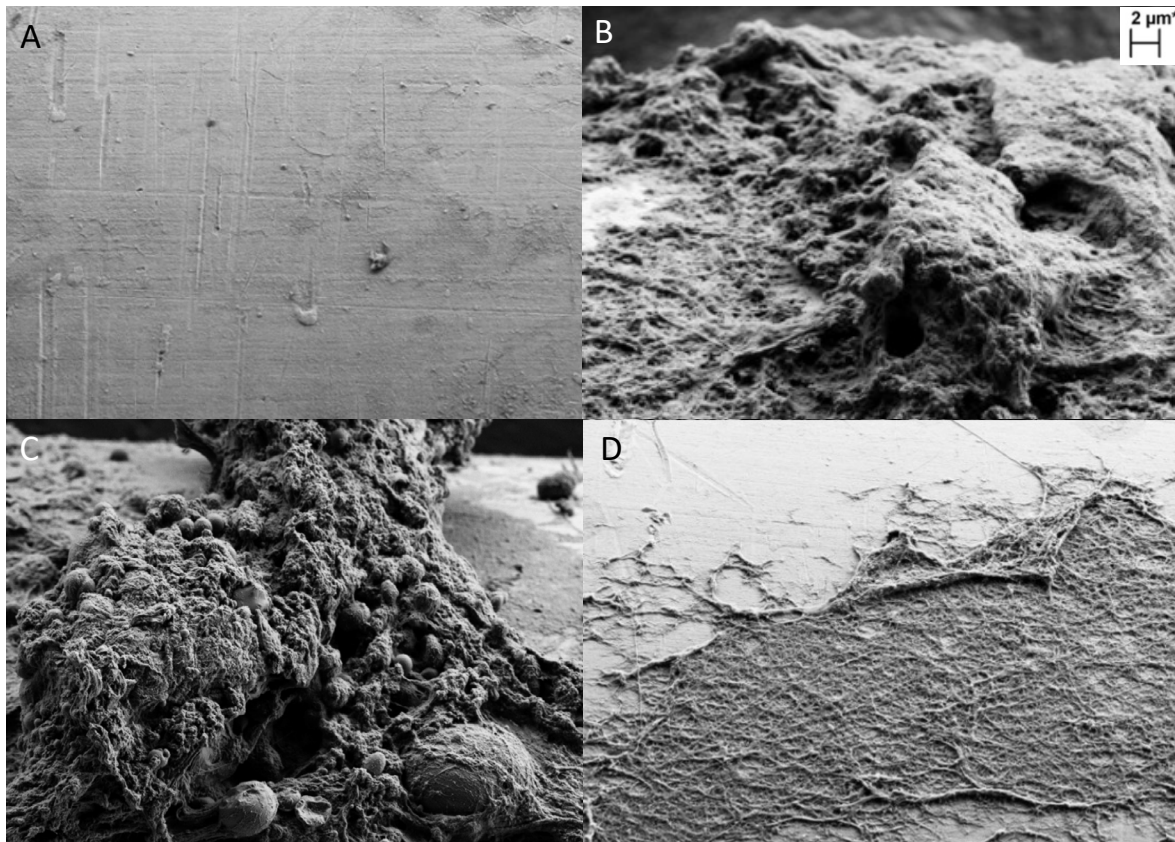


Figure 2. Scanning Electron Microscopy images on post-operative day 8 (after exposure to antibody alone without antibiotics) of *ex vivo* implants from experimental groups A. Sterile Control B. Infected Control C. Control Antibody D. TRL 1068. The image in panel D shows a flattened biofilm remnant as compared to a complex 3-dimensional biofilm with visible cocci in panels B and C.



1:43 PM - 1:50 PM

Paper #20 #1818721

METRONOMIC SIROLIMUS AND CYCLOPHOSPHAMIDE IN METASTATIC OR UNRESECTABLE CHONDROSARCOMA; RESULTS OF THE COSYMO PHASE II TRIAL

Astrid Lipplaa¹; Javier Martin-Broto²; Antonio Lopez-Pousa³; Roberto Diaz Diaz-Beveridge⁴; Claudia M. Valverde⁵; Antonio Casado⁶; Jacco de Haan⁷; Jesus Rodriguez Pascual⁸; Linda Verhoeff⁹; Elma Meershoek - Klein Kranenbarg¹; Pancras Hogendoorn MD PhD¹; Jean-Yves Blay⁹; Judith V.M.G. Bovée¹; Hans Gelderblom¹

¹Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS; ²Hospital Universitario Virgen del Rocío, Sevilla, Andalucia, SPAIN; ³Hospital de la Santa Creu i Sant Pau, Barcelona, Catalonia, SPAIN; ⁴H. U. La Fe, Valencia, Comunidad Valenciana, SPAIN; ⁵Genitourinary, Sarcoma, CNS, CUP unit, Hospital Universitario Vall d'Hebron, Barcelona, Catalonia, SPAIN; ⁶Hospital Clínico Universitario San Carlos, Madrid, Madrid, SPAIN; ⁷University Medical Center Groningen, Groningen, Groningen, NETHERLANDS; ⁸HM-CIOCC Madrid, Madrid, Madrid, SPAIN; ⁹Centre Léon Bérard, Lyon, Auvergne, FRANCE

Objective: COSYMO, a phase II, single-arm, multi-center European trial was designed to evaluate the efficacy of the combination of sirolimus, an mTOR inhibitor, and cyclophosphamide in metastatic or unresectable chondrosarcoma (CS) and myxoid liposarcoma. In pre-clinical studies chondrosarcoma cell-lines were sensitive to mTOR inhibition, and in a case series a median progression free survival (PFS) of 13.4 months was seen on the combination of cyclophosphamide and sirolimus. In this paper we report the results of the CS cohorts of COSYMO study.

Methods: Patients were treated at 8 different sarcoma centers around Europe. Eligible CS patients had conventional, mesenchymal, dedifferentiated or clear cell CS that was unresectable or metastatic, with confirmed measurable and progressive lesions according to Response Evaluation Criteria in Solid Tumors (RECIST) 1.1. Patients with a European Cooperative Oncology Group (ECOG) performance status > 2 or inadequate bone marrow or renal function were excluded. Patients were treated with metronomic sirolimus 4mg orally once daily and cyclophosphamide 200mg orally on day 1-7 and 15-21 in a 4 week cycle until disease progression or patient withdrawal. Radiological assessment of tumor response was performed every 2 cycles. The primary endpoint was time to progression according to RECIST 1.1. Major secondary endpoints were toxicity and objective response according to RECIST 1.1. Patients were enrolled using a Simon's two-stage design, starting with 17 patients in each of the 2 main study cohorts (1. conventional CS and 2. combined mesenchymal or dedifferentiated CS), a minimum of 4 patients per cohort with a time to progression > 16 weeks was required before continuing to a total of 35 patients per cohort. Patients with clear cell CS were enrolled in a third explorative cohort without a pre-specified number of patients.

Results: From December 2014 to December 2020, 63 CS patients were included, 11 were not eligible for efficacy analysis. Of 63 patients enrolled (41 in cohort 1, 20 in cohort 2 and 2 in clear cell CS cohort); 45 (71.4%) were men, median age was 57 (18-83) years, 54 patients (85.7%) underwent prior surgery, 26 (41.3%) radiotherapy and 22 (30.2%) systemic treatment (17 chemotherapy, 5 tyrosine kinase inhibitors, 5 immunotherapy, 1 other). Of 52 efficacy-evaluable patients (33 in cohort 1, 17 in cohort 2 and 2 in clear cell CS cohort); 26 pts (50%; two-sided CI95% = [36-64]) were non-progressive at 16 weeks (18 patients, 54.5% [37-72] in cohort 1, 7 patients, 41.2% [15-67] in cohort 2 and 1 patient, 50% in clear cell cohort). Median PFS was 16.5 (CI95% = 8.1-23.3) weeks; 20.6 [8-28.1], 13 [6.4-22.1] and 55.7 [6.6-104.9] weeks for cohorts 1, 2 and clear cell CS respectively. Best objective response according to RECIST 1.1 was progressive disease (PD) in 19 patients (36.5%), stable disease (SD) in 29 (55.8%), partial response in 2 (3.8%) and unknown due to clinical progression for 2 (3.8%). At the time of the analysis there are not enough events to describe OS. The most common Gr 3-5 sirolimus or cyclophosphamide-related adverse events reported were anemia (4 out of 63 patients, 6.3%), neutropenia (3, 4.8%), pneumonia (4, 6.3%), pneumonitis (2, 3.2%), thrombocytopenia (3, 4.8%), and urinary tract infection (3, 4.8%).

Conclusion: With a median PFS of 16.5 weeks and median progression free rate at 16 weeks of 50%, this single-arm phase II study shows a promising result of the combination of sirolimus and cyclophosphamide in advanced or metastatic CS, with an acceptable toxicity. Clinical trial identification: EudraCT: 2013-005155-32, NCT02821507, GEIS-36. Sponsor: Leiden University Medical Center (LUMC), Leiden, The Netherlands. Participating parties: GEIS Group, Grupo Español de Investigación en Sarcomas, University Medical Center Groningen (UMCG), Groningen, The Netherlands. Funding: Pfizer (supply sirolimus), EuroSarc, a European Commission granted FP7 clinical trials network (278742).



1:50 PM - 1:57 PM

Paper #21 #1818717

TARGETING VULNERABILITIES CAUSED BY THE IDH MUTATION IN CHONDROSARCOMA: THE MODEL MATTERS

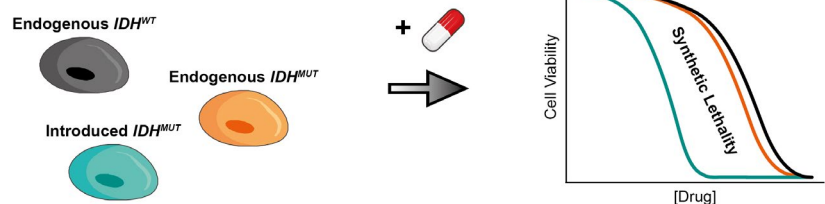
Sanne Venneker; Alwine B. Kruisselbrink; Tessa A.H. Wilpshaar; Ieva Palubeckaite; Pauline M. Wijers-Koster; Hans J. Baelde; René J.M. van Zeijl; Bram Heijs; Karoly Szuhai; Judith V.M.G. Bovée
 Leiden University Medical Center, Leiden, Zuid-Holland, Netherlands

Objective: Approximately 50% of all chondrosarcomas harbour hotspot mutations in IDH1 or IDH2, leading to elevated levels of (D)-2-hydroxyglutarate (D-2-HG). This oncometabolite causes changes in several cellular processes, such as epigenetics, metabolism, DNA repair and growth signalling pathways. Inhibition of the IDH mutant (IDHmut) protein showed disappointing results both in chondrosarcoma cell lines and patients, suggesting that the induced changes may have become static or independent of the IDH mutation over time. In AML and glioma, two tumour types which also frequently harbour IDH mutations, several vulnerabilities caused by the IDH mutation (i.e. synthetic lethal interactions) were identified, including agents that induce DNA damage or target PARP and Bcl-2 family members. However, chondrosarcoma cell lines are variably sensitive to these therapies, irrespective of the IDH mutation status. This difference may be explained by the fact that most of these synthetic lethal interactions were identified in generic cancer cell lines with introduced IDH mutations due to lack of AML and glioma in vitro models, whilst the chondrosarcoma cell lines harbour endogenous IDH mutations. IDH mutations are one of the first alterations in chondrosarcoma, and models with an introduced IDH mutation do not fully represent such an early onset event. Therefore, the aim of this study was to explore if the type of in vitro model (introduced vs. endogenous) should be considered when studying therapeutic vulnerabilities in IDHmut tumours.

Methods: IDH wildtype CH2879 chondrosarcoma cells were lentivirally transduced with an empty vector (EV) or a vector containing the IDH1 promoter and IDH1 R132C mutation. Transduced cells were sorted in low and high GFP fluorescence polyclonal cell populations, representing a low and high IDH1 R132C copy number (CN). Low CN (n=4) and high CN (n=7) single cell clones were derived from the polyclonal cell lines. Established cell lines were characterized for IDH1mut protein expression (western blot), integrated vector copies (RT-PCR and MLPA), and D-2-HG production (LC-MS). Dose-response curves and colony formation assays were performed to assess drug response and radiotherapy sensitivity. If synthetic lethal interactions were identified, western blots were performed to examine the underlying biological mechanism.

Results: Established CH2879 IDH1 R132C single cell clones showed variable IDH1mut protein expression and number of integrated vector copies, but most clones produced D-2-HG whilst culturing over time. Both polyclonal and clonal CH2879 IDH1 R132C cell lines showed synthetic lethal interactions with talazoparib (PARP inhibitor), ABT-737 (Bcl-2/Bcl-xL/Bcl-w inhibitor), and radiotherapy, which were previously not observed in endogenous IDHmut chondrosarcoma cell lines. Of note, the IDHmut single cell clones showed a heterogeneous drug response, especially for ABT-737 treatment (IC50 values from 0.2 to 6 μ M), and some cell lines acquired ABT-737 resistance whilst culturing over time. The anti-apoptotic Bcl-2 family members are highly differentially expressed between single cell clones and expression profiles change whilst culturing over time, which may partly explain the heterogeneous drug response and acquired ABT-737 resistance.

Conclusion: Artificially created IDHmut chondrosarcoma cell lines show the previously reported synthetic lethal interactions, contradicting the results that have been described for endogenous IDHmut chondrosarcoma cell lines. Furthermore, the artificial models show differences in drug sensitivity and may lose the synthetic lethal interactions over time, implying that other factors also influence underlying vulnerabilities caused by IDH mutations. Hence, this study shows that artificial IDHmut models differ in drug response from endogenous IDHmut models. To improve the translation of preclinical findings to clinical trials, endogenous IDHmut models should be used when studying vulnerabilities caused by IDH mutations.

Chondrosarcoma Cell Lines




1:57 PM - 2:04 PM

Paper #22 #1818704

TERT PROMOTER MUTATION IS AN OBJECTIVE CLINICAL MARKER FOR DISEASE PROGRESSION IN CHONDROSARCOMA

Yifan Zhang¹; Yi Chen²; Nelly Seger²; Asle Hesla²; Panagiotis Tsagkozis²; Olle Larsson²; Yingbo Lin²; Felix Haglund¹

¹Department of Pathology and Cancer Diagnostics, Karolinska University Hospital, Stockholm, Sweden and Department of Oncology-Pathology, Karolinska Institute, Solna, Stockholm, SWEDEN;

²Karolinska Institute, Stockholm, Lan, SWEDEN

Objective: Chondrosarcomas are the second most common malignant bone tumor. Activating promoter mutations in Telomerase reverse transcriptase (TERT) was recently described by us and others as a frequent mutation in high-grade chondrosarcoma.

Methods: In this study we investigate the prognostic significance of TERT promoter mutations in 241 chondrosarcomas from 190 patients collected over 24 years (1994 – 2017). The TERT promoter was sequenced after microdissection of 135 chondrosarcomas from 106 patients in addition to data from our previous cohort.

Results: The TERT promoter mutation at -124 C>T was found in 45% of all patients and was significantly associated ($p > 0,001$) with higher tumor grade, shorter metastasis-free survival and disease-specific survival. Additionally, TERT promoter mutated tumors were associated with a more aggressive metastatic pattern. Shorter survival was observed in patients with wild-type primary tumors who developed a mutated metastasis indicative of tumor progression. Primary tumor genetic heterogeneity and altering mutational status between non-synchronous metastatic lesions suggests that chondrosarcoma is a multiclonal disease progressing through a branching evolution.

Conclusion: TERT promoter mutation seems to be a central event in chondrosarcoma progression with association to metastatic disease and disease-related mortality. As an easily analyzed marker, there is future potential to utilize TERT promoter mutation status as a prognostic marker and investigate telomerase-targeted therapy in chondrosarcomas.

Figure 1

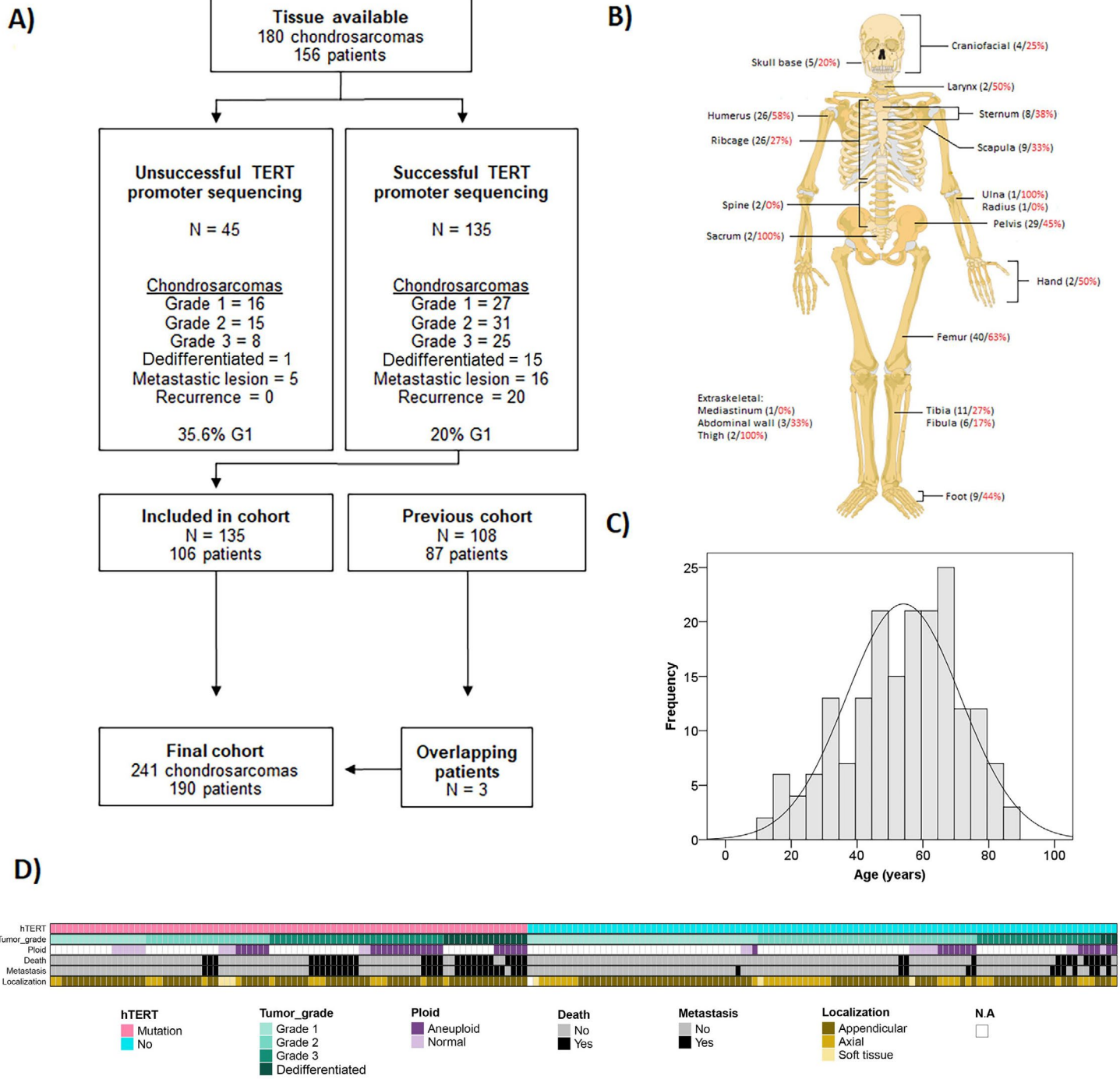


Figure 2

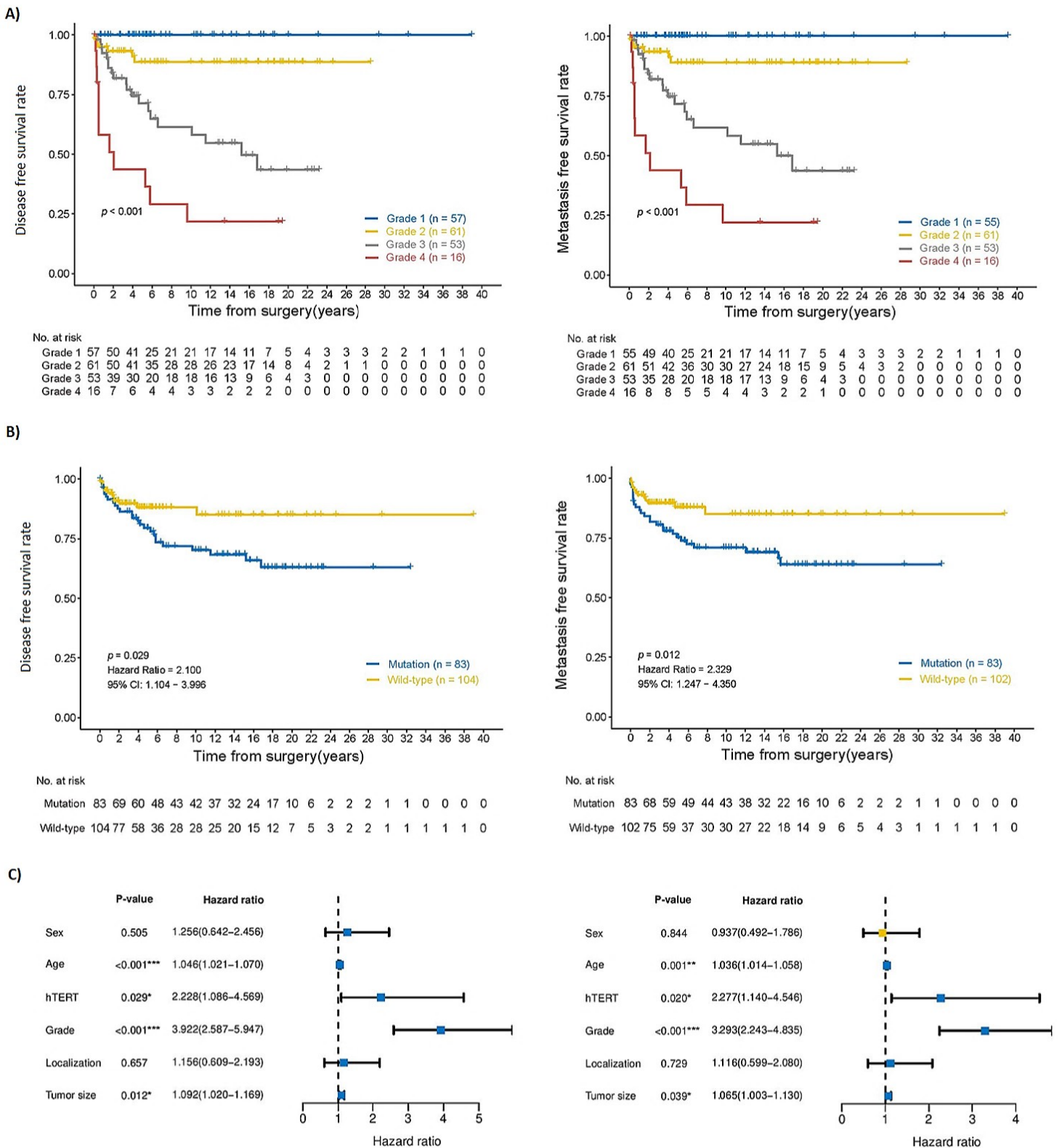
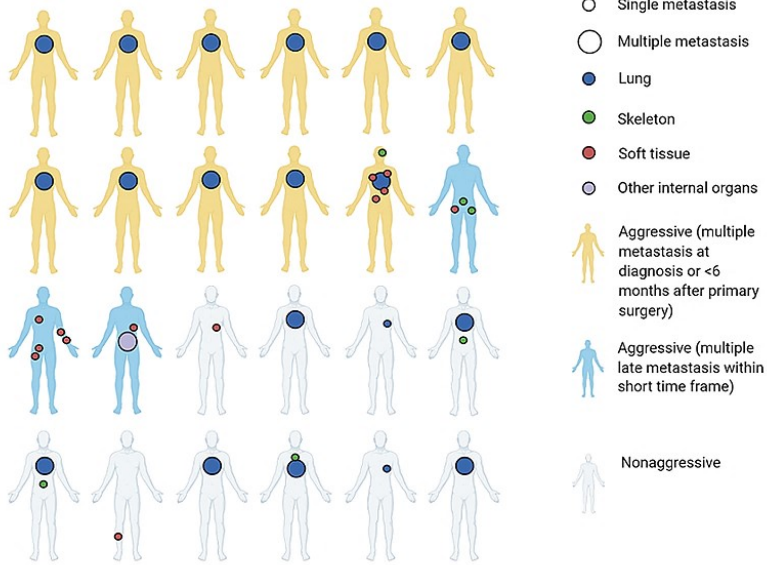


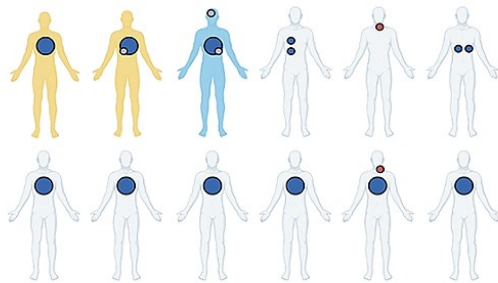
Figure 3

A)

hTERT mutated



hTERT wild type



B)

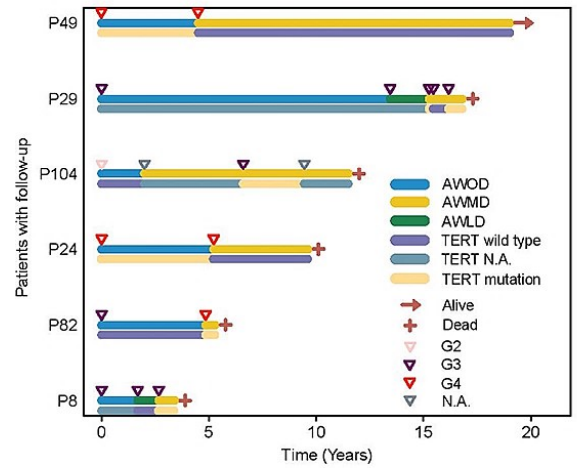
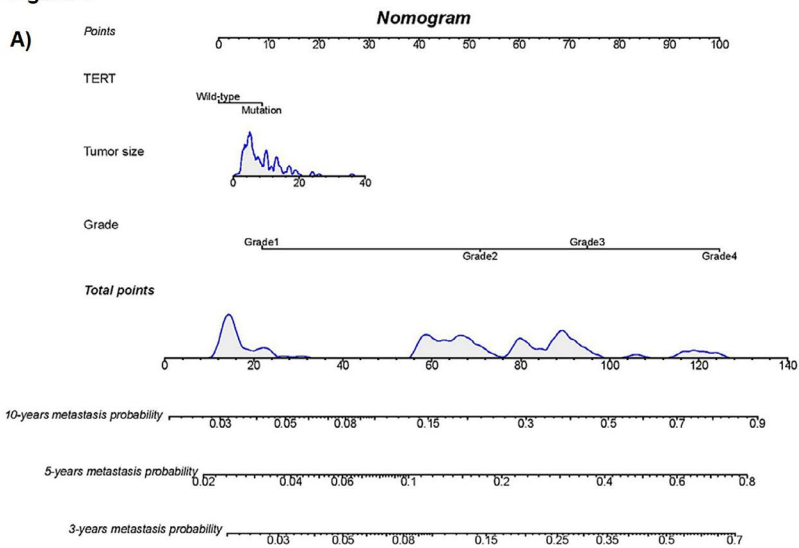
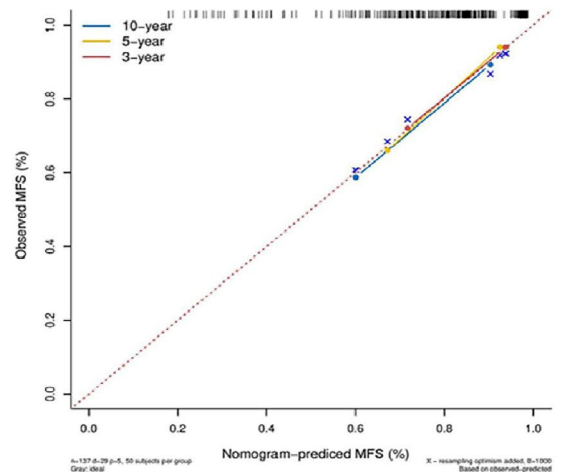


Figure 4

A)



B)





2:04 PM - 2:11 PM

Paper #23 #1818723

**ROTATED MASSIVE AUTOGRAFT RECONSTRUCTION FOR BONE TUMORS:
SAFE AND REPRODUCIBLE TECHNIQUE**

Ana C. Belzarena¹; **Pablo Stoppiello**²; Leticia Gaiero²; Gottardo Bianchi²; Nicolas Casales²; Claudio Silveri²;
¹Miami Cancer Institute, Miami, Florida, UNITED STATES; ²Unidad de Patología Oncológica Musculo Esquelética,
Instituto Nacional de Ortopedia y Traumatología, Montevideo, Montevideo, URUGUAY

Objective: Limb salvage surgery is the current standard of care for limb sarcomas. The main dilemma the oncology orthopedist faces is selecting the most appropriate reconstruction method on a case-by-case basis. Rotating massive frozen autografts could potentially allow tumor treatment without a bone resection, potentially diminishing consolidation time and postoperative complications. Therefore, we asked: 1) what are the rates of complications, local recurrence and metastatic spread for the pedicle frozen rotated massive autograft reconstruction technique for malignant bone tumors? 2) Is this technique reproducible in countries with scarce resources? 3) What is the postoperative function of patients undergoing this reconstruction technique?

Methods: A prospective multicentric study was conducted between 2018 and 2020. Patients with a diagnosis of bone malignant tumor who underwent pedicle frozen rotated massive autograft reconstruction were included. All cases were assessed by the same team of specialists for the feasibility of the technique. Patients with morbid obesity were excluded due to the impossibility of rotating the autograft during the surgical procedure. All patients were assessed preoperatively for adequate planned margins as well as imaging guided osteotomy planning. The surgical technique involved dissecting the tumor and surrounding soft tissue mass with adequate margins that would also allow the rotation of the affected bone. Following, either an osteotomy or a controlled dislocation was performed, and the bone was submerged in liquid nitrogen. Once the autograft had been recycled, reconstruction was executed. Patients were followed clinically and radiographically at 1, 3, 6 and 12 months and then annually.

Results: No patient had local recurrences in our sample. All patients with localized disease at presentation (50%) did not develop metastatic spread during follow up. Twenty percent of patients had postoperative complications. Those included hardware failure (10%) and deep soft tissue infection (10%). All osteotomies underwent complete union in a mean time of 8.2 months (range 7-9, SD 0.5). Autograft survival rate was 88.9%. The mean MSTS/ISOLS functional score was 92.3% (range 63-100, SD 15). After exclusion criteria, ten patients were included for statistical analysis. Sixty percent of patients were male, the mean age for the sample was 40.9 years of age (range 12-82, SD 8.6). Mean follow up time was 15 months (SD 6.0). The most common diagnosis was secondary bone malignancy (50%), and the most common primary bone tumor was osteosarcoma (60%). There was an equal location distribution among femur (50%) and tibia (50%). Six patients (60%) had an osteotomy and reconstruction with plate and screws, three patients underwent reconstruction with a recycled autograft prosthesis composite, and one patient had a coxofemoral arthrodesis.

Conclusion: Pedicle frozen rotated massive autograft reconstruction for bone tumors is a safe and reproducible technique with low complication rates when correctly indicated. Massive pedicle autografts are a novel reconstruction technique that expanded the indications of nitrogen recycled autografts and one more alternative for reconstruction in limb salvage procedures, particularly useful for low resource countries.



9:00 am - 10:00 am

– Session 5 –

DIAGNOSTIC AND SURGICAL TECHNIQUES

9:00 AM - 9:07 AM

Paper #24 ID#1818750

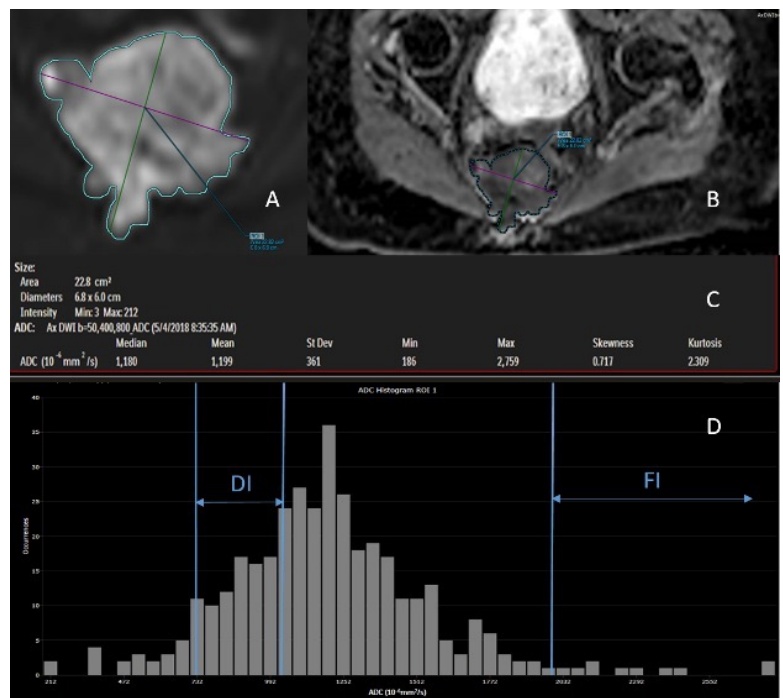
DIFFUSION-WEIGHTED IMAGING FOR DIFFERENTIATION OF SACRAL CHORDOMA AND CHONDROSARCOMA
Raul Valenzuela; Liu Chenglei; William Green; William Murphy; Behrang Amini
MD Anderson Cancer Center, Houston, Texas, UNITED STATES

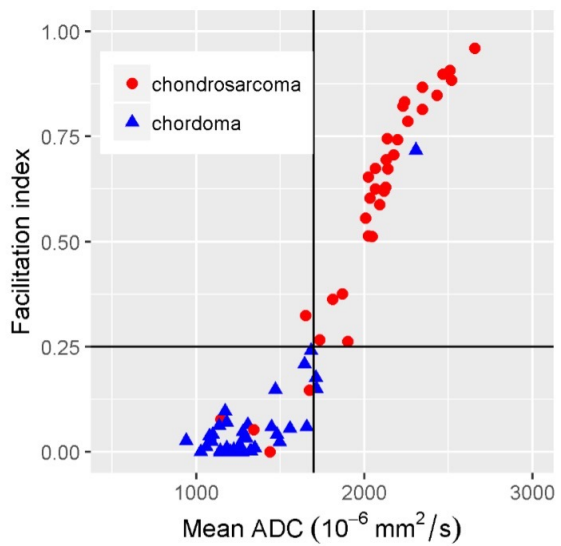
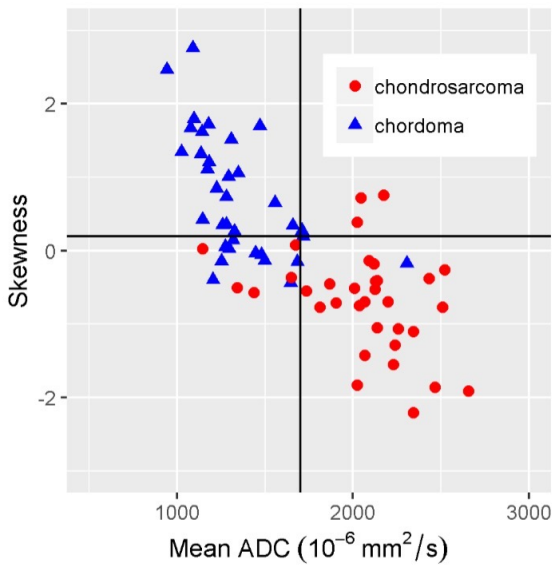
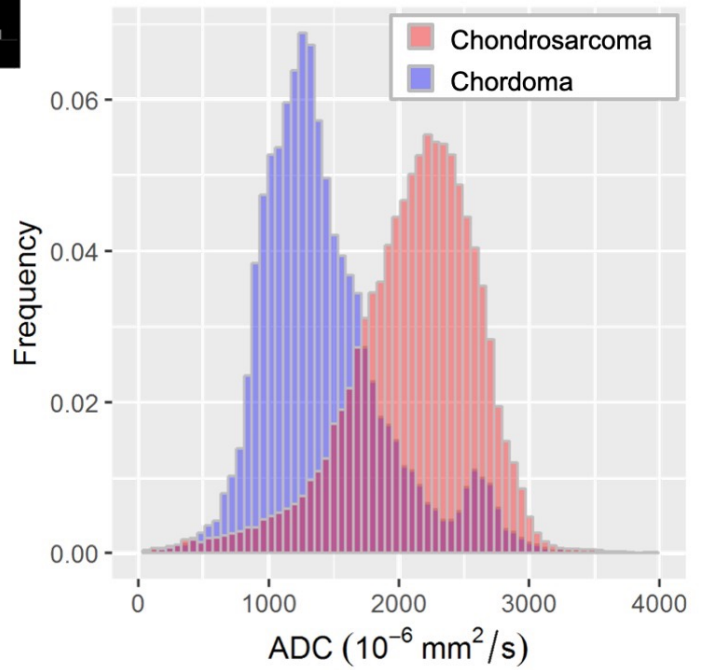
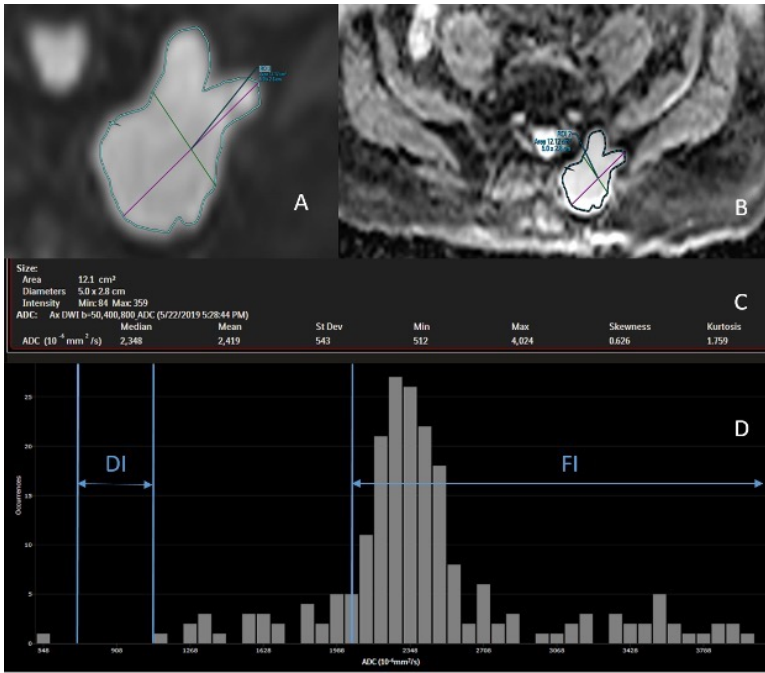
Objective: The overlapping radiographic and MR imaging appearance of sacral chordoma and chondrosarcoma, including bone destruction, lobular shape, presence of calcifications, high T2 signal, and peripheral contrast enhancement, drives the search for an improved imaging method to discriminate from each other. Diffusion-weighted Imaging (DWI) offers the potential to do so.

Methods: 3655 Pelvic MRI exams performed between January 2015 and December 2019 included 262 untreated pelvic chordomas and chondrosarcomas, of which 36 sacral chordomas and 34 sacral chondrosarcomas were segregated for a retrospective review after approval by our Institutional Review Board. An experienced and junior radiologist independently performed image post-processing on all 70 tumors. On DWI b800 sequences, a two-dimensional region of interest (ROI) was manually drawn to contour each lesion at its largest transverse diameter and create a whole-plane apparent diffusion coefficient (ADC) histogram. The histograms were pooled for each tumor type, and their distinct data sets compared. Basic first-order ADC features were extracted, and newly designed facilitation index (FI) (% of pixels with $ADC > 2,000 \times 10^{-6} \text{ mm}^2/\text{s}$) and diffusion index (DI) (% of pixels with $700 < ADC < 1,000 \times 10^{-6} \text{ mm}^2/\text{s}$) were calculated. Intraclass correlation was good to excellent for the two readers.

Results: Utilizing a p-value of < 0.005 , mean ADC, FI, DI, and skew demonstrated significant differences between chordoma and chondrosarcoma. The chordoma ADC histogram is left-sided (positive skew) and has a lower ADC mean and higher kurtosis than the right-sided (negative skew) chondrosarcoma ADC histogram. A FI of 0.25 or higher and a mean ADC of $1700 \times 10^{-6} \text{ mm}^2/\text{s}$ or higher, significantly associated with chondrosarcoma. A Skewness cut point of 0.177 or higher was proven to be statistically significant with Chordoma, although its reproducibility was lower than FI and Mean ADC. Other first-order radiomics features, including SD, kurtosis, and entropy, have proven not to be as helpful.

Conclusion: These findings correlate with the notion that while both tumors are hypercellular with a high nuclear-to-cytoplasmic ratio, the difference in ADC values is attributed to their extracellular matrices' characteristics. DWI can effectively help differentiate sacral chordomas from chondrosarcomas despite their overlapping imaging appearance. To the best of our knowledge, our study is the first to demonstrate the clinical usability of reliable and reproducible ADC-based first-order radiomics for the differentiation of sacral chordoma and chondrosarcoma.







9:07 AM - 9:14 AM

Paper #25 #1818757

DUAL-ENERGY CT VITAL IODINE TUMOR BURDEN AS A QUANTITATIVE RESPONSE PARAMETER IN PATIENTS WITH GIST UNDERGOING TARGETED THERAPY - PROSPECTIVE MULTI-CENTER TRIAL
Peter Hohenberger¹; Mathias Meyer¹; Christina Messiou²; Charlotte Benson²; Hideki Ota³; Stefan Schönberg¹
¹Mannheim University Medical Center, Mannheim, Baden-Württemberg, GERMANY; ²The Royal Marsden NHS

 Foundation Trust, London, England, UNITED KINGDOM; ³Yamagata Prefecture Shinjo Hospital, Shinjo, Yamagata, JAPAN

Objective: Though RECIST 1.1 still remains the reference standard in clinical trials on GIST patients, it does not account for characteristic targeted therapy related response changes, such as hemorrhage, myxoid degeneration, or transient increase in tumor size. Targeted therapy specific tumor metrics have been proposed, such as the modified Choi criteria (mChoi) and the Vascular Tumor Burden (VTB), which attempt to overcome some of the limitations of RECIST 1.1, but lack validation in a prospective setting. Contrast-enhanced dual energy CT (DECT) permits the exact quantification of vital tumor portions, by characterizing and differentiating the total amount of intra-tumoral iodine, from necrotic, myxoid degenerate or hemorrhagic portions. The purpose of this study was to determine, if DECT Vital iodine Tumor Burden (ViTB) allows reliable response assessment in patients with a GIST undergoing targeted therapy, compared to established CT criteria.

Methods: From 5/2014 to 11/2018, 110 patients (m:f ratio 2.1, median age 58.2 years, range 30-77years) with biopsy proven GIST were entered to this prospective, multi-center trial. All patients were treated with tyrosine kinase inhibitors (TKI) imatinib or sunitinib for neoadjuvant (n=17) or metastatic (n=93) disease status. All patients underwent a pre-treatment and 3-month follow-up DECT examination, and response assessment was performed according to RECIST 1.1, mChoi, VTB and DECT ViTB. DECT ViTB used the same cut points for percentage change as RECIST 1.1. Up to 5 target lesions per patient were selected using RECIST 1.1 guidelines. Patients were observed for a minimum of 24 months (median 32 months). Progression-free survival (PFS) in responders (complete, partial response and stable disease) and non-responders (progressive disease) according to each response criteria was compared by using the Cox proportional hazard ratio (HR) and the Harrell c-Indices.

Results: The median PFS was significantly different between non-responders and responders for all response metrics and comparable among the RECIST1.1 (305days; HR=3.5; 95%CI: 2.1-5.9; p<.001) and mChoi criteria (311days; HR=3.2; 95%CI: 1.9-5.2; p<.001). DECT ViTB non-responders (n=45) were 15 times more likely to experience progression of disease (HR=15.0; 95%CI: 8.2-28.0; p<.001) than responders (n=65) on initial DECT follow-up imaging. DECT ViTB allowed a significant better differentiation between non-responders and responders compared to RECIST 1.1, mChoi and VTB (c-Index: 0.77 compared to 0.62-0.70; all p<0.003).

Conclusion: The vital iodine burden assessed by dual-energy CT provides a reliable, consistent method to quantitatively assess the proportion of vital tumor undergoing TKI therapy for metastatic GIST or with treated neoadjuvant intent. ViTB outperformed current CT response assessment criteria such as RECIST 1.1, mChoi and the VTB criteria on a statistically significant basis. As dual-energy CT can be installed with rather low investment, the method could be of use particularly in trials, potentially also in other tumors treated with TKIs.

Table – Progression-Free-Survival of responders and non-responders by response metrics

Response Metrics	N	Median [d]	HR	P-Value	Harrell's C-Index
<i>RECIST1.1 criteria</i>					
Responder	84	399	3.5 (2.1 - 5.9)	<.001*	0.62
Non-Responder	26	94			
<i>mChoi criteria</i>					
Responder	74	430	3.2 (1.9 - 5.2)	<.001*	0.64
Non-Responder	36	119			
<i>VTB criteria</i>					
Responder	74	507	5.9 (3.6 - 9.8)	<.001*	0.70
Non-Responder	36	90			
<i>DECT ViTB criteria</i>					
Responder	65	583	15.0 (8.2 - 28.0)	<.001*	0.77
Non-Responder	45	97			

Note – Vales in parenthesis are 95% confidence interval; HR = Cox regression analysis hazard ratios; RECIST = Response Evaluation Criteria in

Solid Tumors; VTB = Vascular Tumor Burden; DECT = Dual Energy CT; ViTB = Vital iodine Tumor Burden



9:14 AM - 9:21 AM

Paper #26 ID#1818771

FLUORESCENCE GUIDED SURGERY WITH INDOCYANINE GREEN FOR SARCOMA RESECTION- A 39 PATIENT CASE SERIES

Kenneth S. Rankin¹; Corey D. Chan²; Marcus J. Brookes²; Riya Tanwani²; Toni Pringle²; James Knight²; Thomas Beckingsale¹; Timothy Crowley¹; Kanishka M. Ghosh¹; Claire Jones³; Thomas Ness³; Sanjay Gupta⁴; Maniram Ragbir²;

¹North of England Bone and Soft Tissue Tumour Service, Newcastle upon Tyne, England, UNITED KINGDOM;

²Newcastle University, Newcastle upon Tyne, England, UNITED KINGDOM; ³Newcastle Novopath MRC Pathology Node, Newcastle upon Tyne, England, UNITED KINGDOM; ⁴Glasgow Royal Infirmary, Glasgow, Scotland, UNITED KINGDOM

Objective: Resection of bone and soft tissue sarcomas is challenging. Near infrared (NIR) intraoperative fluorescence guided surgical techniques following administration of indocyanine green (ICG) have been used in various surgical settings for the assessment of vascularity of tissue, identification of lymph nodes and solid carcinomas. There have been no reports of NIR fluorescence guidance for open sarcoma surgery, therefore our aim was to perform a case series to collect data on optimal timing and dosage, ability to guide surgery and details on ICG visualisation macroscopically and microscopically.

Methods: Over a period from March 2019 to May 2021, 39 patients with a range of bone and soft tissue sarcoma types were administered with 75mg-100mg of ICG intravenously the 3-18 hours prior to surgery. Six Consultant surgeons (4 orthopaedic and 2 plastic surgeons) from 2 centres performed the cases. The Stryker NIR handheld camera was used intraoperatively to assess tumour fluorescence. The surgeons were asked to report whether the fluorescence if present helped guide the surgery. The tumour specimens underwent standard trimming and processing in the pathology laboratory. Microsections were prepared from selected tumour blocks representing close margins. The microsections were stained with DAPI prior to analysis using the Amersham Typhoon Bioimager and the Zeiss Axioimager. ICG in the sarcoma cells was visualised at the margins of the tumour specimens via the Cy7 channel in both instruments.

Results: There were 39 cases (see table 1), with an age range of 21 to 88 years. There were 15 female and 24 males. There were 27 soft tissue sarcomas and 12 bone sarcomas. There were 30 high grade/ grade 3 sarcomas, four grade 2 and five low/grade 1. Anatomical sites were 22 lower limb, nine upper limb, six pelvis and one each of chest wall and head. The type of surgery was wide excision in 34, amputation in six and 1 one intralesional palliative procedure for a spindle bone sarcoma bone metastasis with pathological fracture. 29 of the high grade tumours and the four grade 2 sarcomas showed evidence of fluorescence. A post-chemotherapy high grade osteosarcoma with over 90% necrosis and two of the low grade sarcomas did not fluoresce. Only two soft tissue sarcoma cases received neoadjuvant radiotherapy due to the preference for post-operative radiotherapy in the participating centres. In both of these cases, there was evidence of tumour fluorescence. In 11 cases, the surgeons reported that the fluorescence helped to guide the surgery (see example in figures 1 and 2). The inadvertent positive margin rate for the series is 7.7%. Grade 3 rapidly growing tumours demonstrated the highest levels of fluorescence and following preparation in the pathology laboratory, the ICG could be visualised in the sarcoma cells at the margins of these tumours (see example in figure 3).

Conclusion: This is the world's first report of fluorescence guided open sarcoma surgery in multiple anatomic sites for a wide range of bone and soft tissue sarcomas. Injection of ICG pre-operatively will cause a range of sarcoma subtypes to fluoresce during surgery. Of note the inadvertent positive margins occurred in three cases, two of which were low grade myxofibrosarcomas that did not fluoresce. Furthermore, the margins of selected high grade tumour specimens can be assessed at a cellular level to detect the ICG. Larger multi-centre studies are warranted to assess which cases would benefit the most from the utilisation of this technology and to further optimise dosage and timing of administration of the ICG. These studies need to include pathology assessments to investigate whether the detection of ICG in sarcoma cells at the margins will facilitate more accurate reporting of positive versus negative margins.

Case no.	Diagnosis	Site	Grade	Neoadjuvant treatment	Operation	ICG	Fluorescent?	Guided the surgery	Margin
1	Chondrosarcoma	Pelvis	3	No	Hindquarter amputation	75mg	Yes	No	1.4mm medial
2	Myxofibrosarcoma	Forearm	3	No	Wide excision	75mg	Yes	Yes	0.8mm deep
3	Sarcoma NOS	Groin	3	No	Wide excision	75mg	Yes	Yes	1.5mm posterior
4	Leiomyosarcoma	Upper arm	2	No	Wide excision	75mg	Yes	No	8mm deep
5	Myxofibrosarcoma	Lower leg	3	No	Wide excision	75mg	Yes	No	Microscopic inadvertent positive margin
6	Synovial sarcoma	Chest wall	3	No	Wide excision	75mg	Yes	No	6mm superior
7	Osteosarcoma	Tibia	High	Chemotherapy	Wide excision	75mg	No	No	0.8mm posteromedial
8	Myxofibrosarcoma	Forearm	1	No	Wide excision	75mg	No	No	Microscopic inadvertent positive margin
9	Sarcoma NOS	Thigh	3	No	Wide excision	75mg	Yes	No	0.5mm deep
10	Myxofibrosarcoma	Knee	1	No	Wide excision	75mg	Yes	No	1mm superficial
11	Pleomorphic rhabdomyosarcoma	Upper arm	3	No	Wide excision	75mg	Yes	Yes	0.4mm deep
12	Chondrosarcoma	Prox femur	3	No	Wide excision	100mg	Yes	No	14mm distal bone
13	Sarcoma NOS	Thigh	3	No	Wide excision	100mg	Yes	Yes	1mm medial
14	Leiomyosarcoma	Shoulder	2	No	Wide excision	75mg	Yes	No	5.6mm deep
15	Recurrent PDS	Cheek	n/a	No	Wide excision	75mg	No	No	0.4mm deep
16	Synovial sarcoma	Thigh	3	No	Wide excision	75mg	Yes	Yes	2mm deep
17	Myxofibrosarcoma	Thigh	3	No	Hip disarticulation	75mg	Yes	No	Expected positive margin
18	Chondrosarcoma	Pelvis	3	No	Hindquarter amputation	75mg	Yes	No	6mm anterior
19	Chondrosarcoma	Pelvis	3	No	Internal hemipelvectomy	75mg	Yes	No	0.2mm multiple
20	Spindle cell sarcoma of bone	Distal femur	High	No	Above knee amputation	75mg	Yes	Yes	14mm anterior
21	Myxofibrosarcoma	Knee	3	No	Above knee amputation	50mg	Yes	Yes	90mm anterior
22	Myxofibrosarcoma	Thigh	3	No	Wide excision	75mg	Yes	No	2mm deep
23	Chondrosarcoma	Shoulder	3	No	Forequarter amputation	75mg	Yes	No	10mm superior
24	Spindle cell sarcoma of bone metastasis	Humerus	3	Palliative chemo	Prox humerus EPR, intralesional	75mg	Yes	Yes	Intralesional palliative
25	Sarcoma NOS	Thigh	3	No	Wide excision	75mg	Yes	No	4.4mm anterior
26	Dediff chondrosarcoma	Humerus	High	No	Shoulder disarticulation	75mg	Yes	Yes	8mm posterior
27	Osteosarcoma	Femur	High	No	Wide excision	75mg	Yes	Yes	1mm posterior
28	Sarcoma NOS	Thigh	3	No	Wide excision	75mg	Yes	No	0.2mm lateral
29	Myxofibrosarcoma	Ankle	3	No	Below knee amputation	75mg	Yes	No	100mm
30	Sarcoma NOS	Buttock	3	No	Wide excision	75mg	Yes	No	8mm deep
31	Pleomorphic rhabdomyosarcoma	Thigh	2	No	Wide excision	75mg	Yes	No	6mm superficial
32	Sarcoma NOS	Pelvis	2	No	Wide excision	75mg	Yes	No	Expected positive margin
33	Myxoid liposarcoma	Thigh	1	Neoadjuvant radiotherapy	Wide excision	75mg	Yes	No	0.4mm lateral
34	Myxofibrosarcoma	Forearm	3	Neoadjuvant radiotherapy	Wide excision	75mg	Yes	No	Negative
35	Leiomyosarcoma	Calf	3	No	Wide excision	75mg	Yes	No	Expected positive margin
36	Sarcoma NOS/LMS	Thigh	3	No	Wide excision	75mg	Yes	No	1.5mm anteromedial
37	Chondrosarcoma	Pelvis	3	No	Wide excision	100mg	Yes	No	0.2mm multiple
38	Myxofibrosarcoma	Lower leg	1	No	Wide excision	75mg	Yes	No	Microscopic inadvertent positive margin
39	Chondrosarcoma	Pelvis	3	No	Wide excision	100mg	Yes	No	1.1mm medial soft tissue

FIGURE 1. Tumour fluorescence on SPY mode

Standard bright light mode

Radial artery highlighted by white arrows

Possible tumour annotated with *

Black and white infrared 'SPY' mode

Radial artery highlighted by white arrows

Definite tumour annotated with *

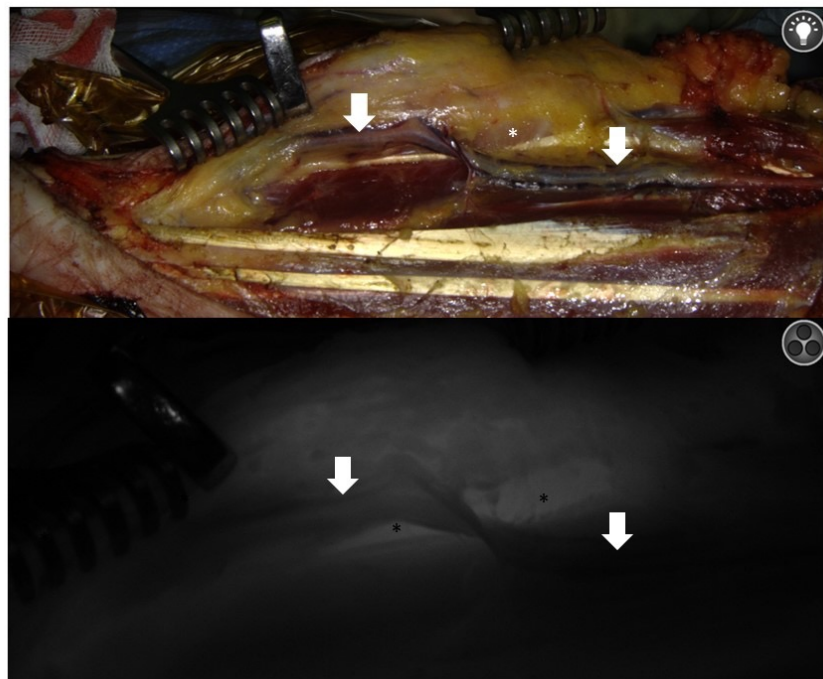


FIGURE 2. Revision of the margin

Standard bright light mode

Radial artery ligated and margin revised (white arrows)

Black and white infrared 'SPY' mode

No tumour visible- clear margin confirmed on pathology

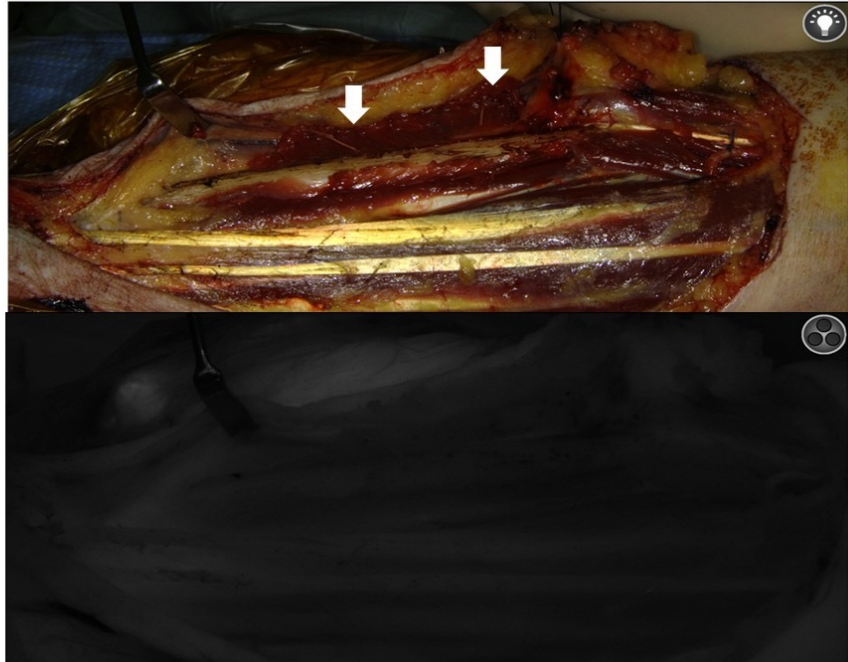
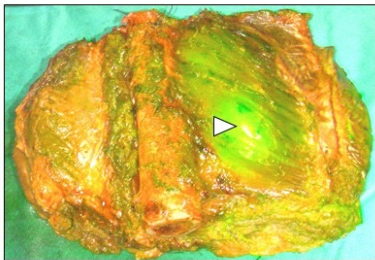
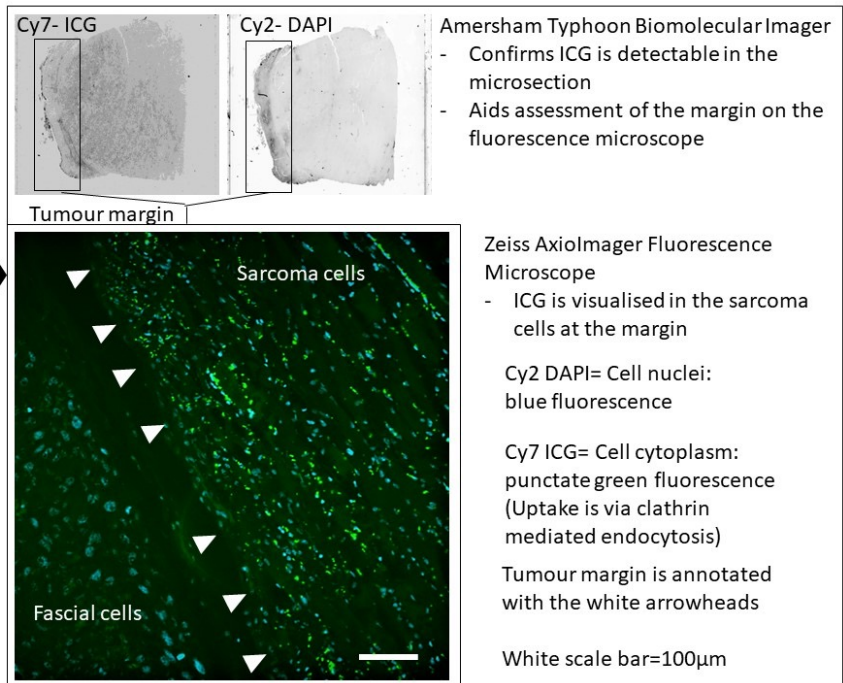


FIGURE 3. Grade 3 soft tissue leiomyosarcoma excised with a section of femoral shaft followed by margin assessment with fluorescence microscopy



High fluorescence in the 'green infrared mode' = close margin (white arrowhead)
 Note ICG uptake in tumours occurs rapidly i.e. less than 30 minutes and is retained due to cellular endocytosis and the enhance permeability and retention effect





9:21 AM - 9:28 AM

Paper #27 ID#1818760

**SENTINEL LYMPH NODE BIOPSY AND FORMAL LYMPHADENECTOMY FOR SOFT TISSUE SARCOMA:
A SINGLE CENTER EXPERIENCE OF 86 CONSECUTIVE CASE**

Russell G. Witt; Yi-Ju Chiang; Derek Erstad MD; Christopher P. Scally; Keila E. Torres; Kelly K. Hunt; Barry W. Feig; Christina L. Roland; Emily Z. Keung

University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES

Objective: Lymph node metastasis (LNM) is a rare occurrence in patients with soft tissue sarcoma (STS) with the incidence ranging from 1.6% to 12% of cases. Due to the rarity of LNM and limited evidence to guide management, practices pertaining to the evaluation, staging, and management of regional lymph node basins in patients with STS vary widely across institutions. As a result, outcomes and prognosis following lymph node surgery for STS are poorly understood. In this study we describe our institutional experience with sentinel lymph node biopsy (SLNB) and formal lymphadenectomy in STS patients. We also report on sarcoma-associated outcomes following regional lymph node basin surgery.

Methods: A single center retrospective chart review was performed for all patients who underwent SLNB and/or formal lymphadenectomy for STS from 1994 to 2018. Clinical characteristics, sarcoma histology, operative course, details of the multimodality treatment, regional and/or distant recurrence-free survival (RFS) and overall survival (OS) were examined. Patients undergoing lymphadenectomy in conjunction with isolated limb perfusion were excluded

Results: Eighty-six patients underwent SLNB (n=34) and/or formal lymphadenectomy (n=60) for STS, with epithelioid sarcoma, clear cell sarcoma, and undifferentiated pleomorphic sarcoma being the most common (Table 1). Median follow-up from the time of regional lymph node basin surgery was 58 months (range 3-258) among SLNB patients and 51 months (range 6-234) among lymphadenectomy patients. At STS diagnosis, all patients who underwent SLNB were without clinical evidence of regional lymph node or distant metastasis. Of these, 8 (23.5%) had a positive sentinel lymph node (SLN) (Table 2). Six patients subsequently underwent completion lymph node dissection at a median of 48 days after SLNB (range 32-371). Among 26 patients with negative SLNs, 2- and 5-year OS were 95.6% and 71.9%, respectively (Table 3). Of these, 8 (30.8%) patients developed regional lymph node recurrence and/or distant metastasis with a median RFS of 25 months (range 1-253). Sixty patients underwent formal lymphadenectomy including 8 who first underwent SLNB, of which 2 had a previous negative SLNB. All patients who underwent formal lymphadenectomy had clinical evidence of nodal disease and 40 (66.6%) had biopsy proven nodal disease. The 2- and 5-year OS following lymphadenectomy was 56.6% and 44.6%, respectively. Viable tumor was identified in the lymphadenectomy specimen of 38 (63.3%) patients. Of 22 patients who were without viable tumor in the lymphadenectomy specimen, 20 (90.9%) received preoperative chemotherapy, 10 (45.5%) had received preoperative radiation, 2 of which were directed at the nodal basin. Twenty-six (43.3%) patients who underwent formal lymphadenectomy developed regional lymph node recurrence and/or distant metastasis with a median RFS of 6 months (range 2-224), and 2- and 5-year OS of 53.8% and 37.6%, respectively. Of the 26 that recurred, 6 (23%) developed regional only disease and 20 (76.9%) distant disease including 5 patients with regional and distant disease (Table 3, Figure 1).

Conclusion: We noted a relatively high SLN positivity rate in this STS cohort with selected histologies. Those patients who had a negative SLNB experienced more favorable RFS and OS rates. In this cohort, RFS and OS rates after formal lymphadenectomy were poor, although patients who developed regional recurrence without distant recurrence had better OS but similar RFS compared to those who recurred distantly. Further investigation is warranted to determine which STS patients with lymph node metastasis, if any, benefit from formal lymphadenectomy.

Table 1: Clinic and pathologic parameters of soft tissue sarcoma patients undergoing sentinel lymph node biopsy and formal lymphadenectomy

	Sentinel Lymph Node Biopsy n=34		Formal Lymphadenectomy n=60	
	N (%)	Median (Range)	N (%)	Median (Range)
Sex				
Female	13 (38.2%)		19 (31.7%)	
Male	21 (61.8%)		41 (68.3%)	
Race				
White	24 (70.6%)		40 (66.7%)	
Black	6 (17.6%)		7 (11.7%)	
Hispanic	3 (8.8%)		8 (13.3%)	
Asian	1 (2.9%)		4 (6.7%)	
Other	0 (0%)		1 (1.7%)	
Median BMI		27 (20.17-47.5)		27.5 (19.3-48)
Median age, years		36 (8-74)		45 (8-87)
Median follow-up from diagnosis, months		58 (3-258)		51 (6-234)
Underwent Sentinel Lymph Node Biopsy	34 (100%)		8 (13.3%)	
Location of Primary Tumor				
Trunk	4 (11.8%)		18 (30.0%)	
Upper Extremity	16 (47.1%)		10 (16.7%)	
Lower Extremity	14 (41.1%)		32 (53.3%)	
Histology				
Angiosarcoma	0 (0%)		2 (3.3%)	
Chondrosarcoma	0 (0%)		2 (3.3%)	
Clear cell sarcoma	11 (32.4%)		8 (13.3%)	
Epithelioid sarcoma	13 (38.2%)		8 (13.3%)	
Ewing Sarcoma	1 (2.9%)		0 (0%)	
Follicular Dendritic Cell Sarcoma	0 (0%)		1 (1.7%)	
Leiomyosarcoma	0 (0%)		2 (3.3%)	
Malignant peripheral nerve sheath tumor	0 (0%)		2 (3.3%)	
Myxoid liposarcoma	0 (0%)		1 (1.7%)	
Myxoid mesenchymal	0 (0%)		1 (1.7%)	
Osteosarcoma	0 (0%)		2 (3.3%)	
Phyllodes	0 (0%)		1 (1.7%)	
Rhabdomyosarcoma	1 (2.9%)		2 (3.3%)	
Spindle cell	0 (0%)		2 (3.3%)	
Synovial sarcoma	2 (5.9%)		5 (8.3%)	
Unclassified	2 (5.9%)		2 (3.3%)	
Undifferentiated pleomorphic sarcoma	4 (11.8%)		19 (31.7%)	

Table 2: Outcomes of sentinel lymph node biopsy and formal lymphadenectomy in patients with soft tissue sarcoma

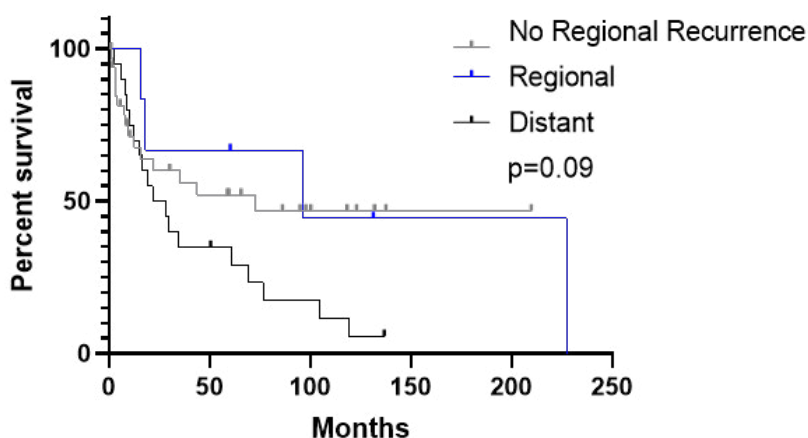
Nodal Basin Dissected	Sentinel Lymph Node Biopsy		Formal Lymphadenectomy	
	N (%)	Median (Range)	N (%)	Median (Range)
Axilla	17 (50.0%)		19 (31.7%)	
Superficial Groin	16 (47.1%)		18 (30.0%)	
Pelvic only	0 (0%)		4 (6.7%)	
Superficial Groin + Pelvic	0 (0%)		19 (31.7%)	
Cervical	1 (2.9%)		0 (0%)	
Number of lymph nodes resected		2 (1-5)		16 (3-62)
Number of lymph nodes with viable tumor				
0	26 (76.5%)		22 (36.7%)	
1	6 (17.6%)		13 (21.7%)	
2 - 3	2 (5.9%)		15 (25.0%)	
>3	0 (0%)		10 (16.7%)	

Table 3 Overall Survival and Recurrence-free survival

Patient cohort	Median OS, months	Median RFS, months	2-year OS	5-year OS
Negative SLNB (n=26)	253	103	95.6%	71.9%
Recurrence after negative SLNB (n=8)	72.0	25	100%	50.0%
Formal Lymphadenectomy (n=60)	35	12	56.6%	44.6%
No regional or distant recurrence (n=34)	72	72	60.1%	52.1%
Regional only recurrence (n=6)	96	6	66.7%	66.7%
Distant recurrence (n=20)	25	6	50.0%	29.1%

SLNB, sentinel lymph node biopsy

Overall Survival





9:28 AM - 9:35 AM

Paper #28 #1818699

DOES SYNOVIAL SARCOMA GRADE PREDICT ONCOLOGIC OUTCOMES, AND DOES A LOW-GRADE VARIANT EXIST?

Michael P. Fice; Abdullah Almajnooni; Charles A. Gusho; Reagan Chapman; Subramanya Mallikarjunappa; Marta Batus; Steven Gitelis; Matthew W. Colman; Ira Miller; Alan T. Blank
Rush University Medical Center, Chicago, Illinois, UNITED STATES

Objective: While historically aggressive, some synovial sarcomas (SS) are clinically indolent. This study sought to determine whether SS grade predicts oncologic outcomes and whether Grade 1 disease might exist. Furthermore, given that some SS follow a more indolent course, we questioned the utility of FNCLCC grading. The current criteria include mitotic activity score, tumor necrosis score, and tumor differentiation score. SS automatically receives a differentiation score of '3'. These tumors are therefore only considered intermediate to high-grade by default, with no low-grade entity by virtue of the system. Anecdotally, some oncology clinicians may see clinically slow-growing SS that on histology show no necrosis or mitoses, thus they may therefore wonder whether these seemingly indolent tumors take on a low-grade clinical course.

Methods: Thirty-five cases (25 Grade 2 and 10 Grade 3) from 2010 to 2019 were retrospectively reviewed. The median age was 37 years at time of diagnosis (interquartile range [IQR], 28-51.5 years), and following the initial oncologic encounter, each case was discussed within a multidisciplinary setting. All patients were then staged and underwent a surgical procedure by a musculoskeletal oncology fellowship trained orthopedic surgeon. Radiation and chemotherapy were offered at the discretion of multidisciplinary team.

Biopsy or non-neoadjuvant treatment resection specimens were interpreted by a musculoskeletal pathologist with sarcoma experience and graded according to FNCLCC guidelines. Of note, each SS receives an automatic high score of '3' for differentiation outright by default, eliminating the possibility of a Grade 1 tumor. Slides were re-reviewed by a musculoskeletal pathologist.

Clinicopathological data were analyzed using descriptive statistics. Continuous variables of interest are represented as the mean or median with range, IQR, or SD. Categorical data are represented as the frequency and percentage of total counts. Kaplan-Meier methods were used to describe overall survival (OS), local recurrence-free survival (RFS), and metastasis-free survival (MFS) with Log-rank methods. To evaluate a theoretical Grade 1 variant, we reassigned each tumor a differentiation score of '2' instead of '3'. Statistical significance was set to a p value of < 0.05, and all statistical analyses were performed on SPSS version 26.0 (IBM Corp, USA).

Results: The median patient age was 37 years (IQR, 28-51.5). The local control rate was 74.3%, and recurrence-free survival was worse in positive compared to negative margin resections ($p = 0.023$). The incidence of metastasis was 21.9% ($n = 7$) at a median 31 ± 31.7 months, and metastasis-free survival was 50.0% in Grade 3 SS compared to 86.5% in Grade 2 ($p = 0.026$). Among a theoretical Grade 1 group, the overall and recurrence-free survival profiles were improved compared to Grade 2 and 3 SS, respectively ($p = 0.014$ and $p = 0.030$). Though eventually, 15.0% ($n = 3$) of Grade 1 SS metastasized.

Conclusion: Tumor grade appears to reliably predict survival as Grade 3 SS had worse metastasis-free and overall survival profiles than Grade 2. Recurrence of these tumors is likely more-so related to margin status. While a theoretical Grade 1 group showed improved survival compared to Grade 2 and 3 SS, no definitive conclusions otherwise could be drawn from the theoretical Grade 1 cohort due to sample size as well as other limitations. Together, these data suggest that although some SS may appear clinically indolent, it is still unclear whether there is a low-grade entity, thus confirming the utility of the conventional FNCLCC diagnostic strategy.

Survival	1-year	3-year	5-year	10-year	p (log-rank)
Overall Survival	97.1	80.8	62.8	57.1	-
Male	94.1	74.3	44.6	37.2	0.017*
Female	93.8	87.1	79.8	79.8	
Extremity	100	90.5	75.1	66.7	0.027*
Non-extremity	90.0	58.3	35.0	-	
Initial metastasis	100	33.3	33.3	-	0.088
No initial metastasis	100	92.3	70.8	63.8	
Radiation	100	85.2	69.2	69.2	0.14
No Radiation	91.7	72.2	49.5	24.8	
Chemotherapy	100	82.9	56.1	56.1	0.82
No Chemotherapy	92.9	77.4	69.6	55.7	
Grade 2	96.0	82.5	77.6	69.9	0.041
Grade 3	100	76.2	25.4	25.4	
Monophasic	95.2	79.6	57.9	49.6	0.71
Biphasic	100	76.2	76.2	76.2	
Recurrence-Free Survival	93.1	81.9	77.0	71.9	-
Extremity	95.5	90.4	90.4	84.0	0.009*
Non-extremity	85.7	53.6	35.7	-	
Negative Margins	95.2	90.5	83.5	83.5	0.023*
Positive Margins	85.7	51.4	51.4	34.4	
Size (0 cm to 5 cm)	100	85.7	85.7	68.6	0.57
Size (> 5 cm)	88.9	88.9	88.9	88.9	
Radiation	95.2	79.8	73.7	67.6	0.49
No Radiation	87.5	87.5	87.5	87.5	
Grade 2	95.0	83.8	83.8	77.4	0.26
Grade 3	88.9	77.8	51.9	51.9	
Monophasic	88.2	88.2	88.2	78.4	0.36
Biphasic	100	88.9	59.3	59.3	
Metastasis-Free Survival	92.3	79.8	74.9	65.5	-
Extremity	90.0	79.7	73.6	64.4	0.79
Non-extremity	100	80.0	80.0	-	
Size (0 cm to 5 cm)	100	85.7	85.7	85.7	0.69
Size (> 5 cm)	85.7	85.7	85.7	57.1	
Chemotherapy	87.5	67.5	67.5	67.5	0.45
No Chemotherapy	100	100	88.9	59.3	
Grade 2	100	93.8	86.5	74.2	0.026*
Grade 3	75.0	50.0	50.0	50.0	
Monophasic	87.5	73.4	65.3	65.3	0.87
Biphasic	100	85.7	85.7	42.9	

Long-term (10-year) survival data may be missing/non-existent. * Significant.

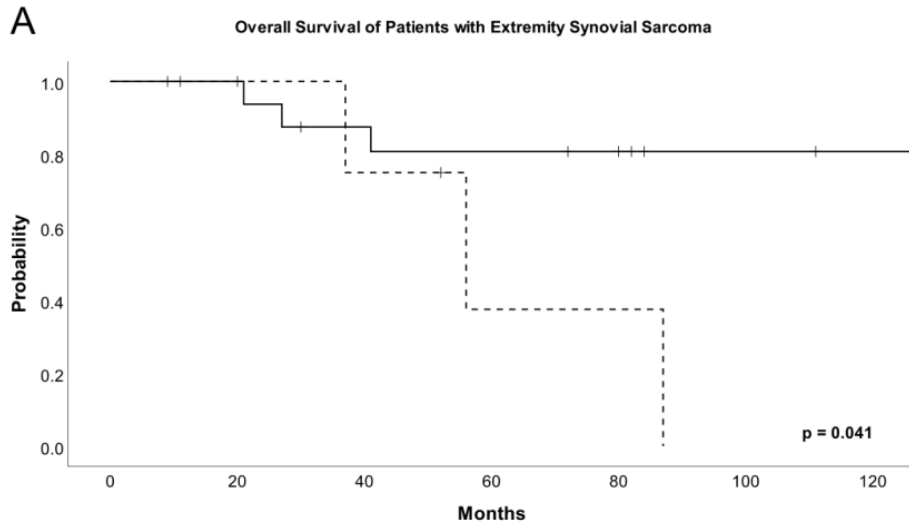


Figure 1A. Kaplan-Meier overall survival for extremity synovial sarcoma only. Survival was improved with limb-salvage (solid line) compared to patients who underwent amputation (dashed line).

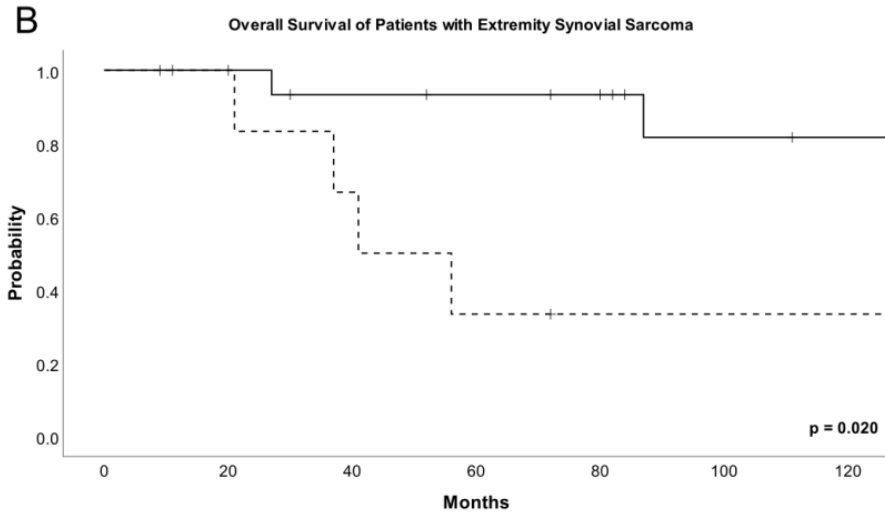


Figure 1B. Kaplan-Meier overall recurrence-free survival of extremity synovial sarcoma only. Recurrence-free survival was better among Grade 2 (solid) compared to Grade 3 (dashed) tumors.

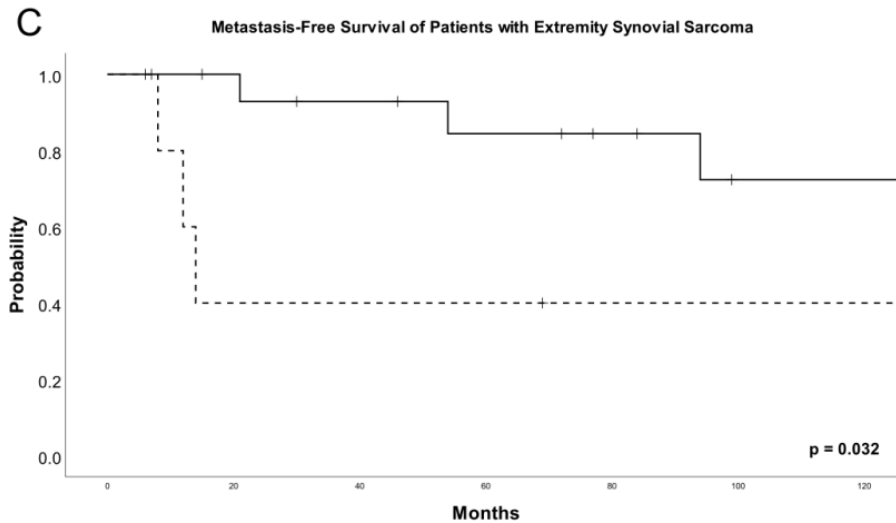


Figure 1C. Kaplan-Meier metastasis-free survival of extremity synovial sarcoma only. Metastasis-free survival was improved in Grade 2 (solid) compared to Grade 3 (dashed) tumors.

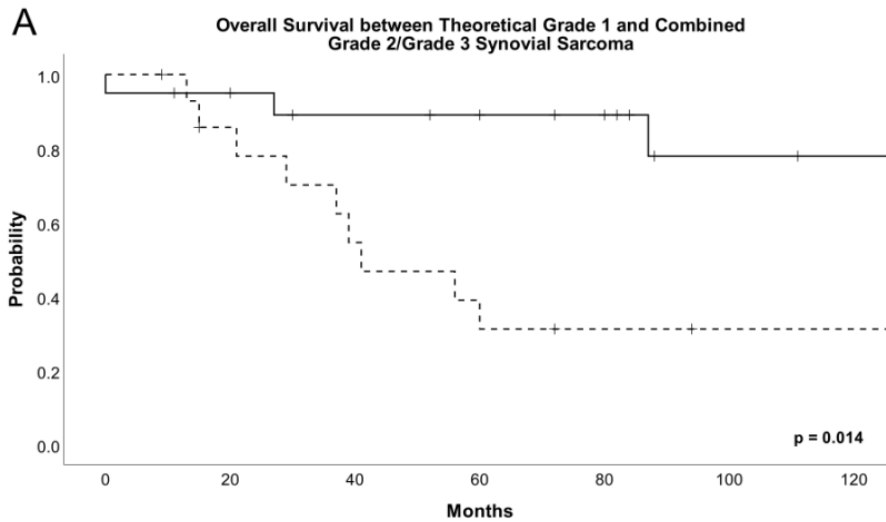


Figure 2A. Kaplan-Meier overall survival for a theoretical Grade 1 Synovial Sarcoma group. Theoretical Grade 1 Synovial Sarcoma (solid line) compared to Grade 2 and Grade 3 Synovial Sarcoma (dashed line).

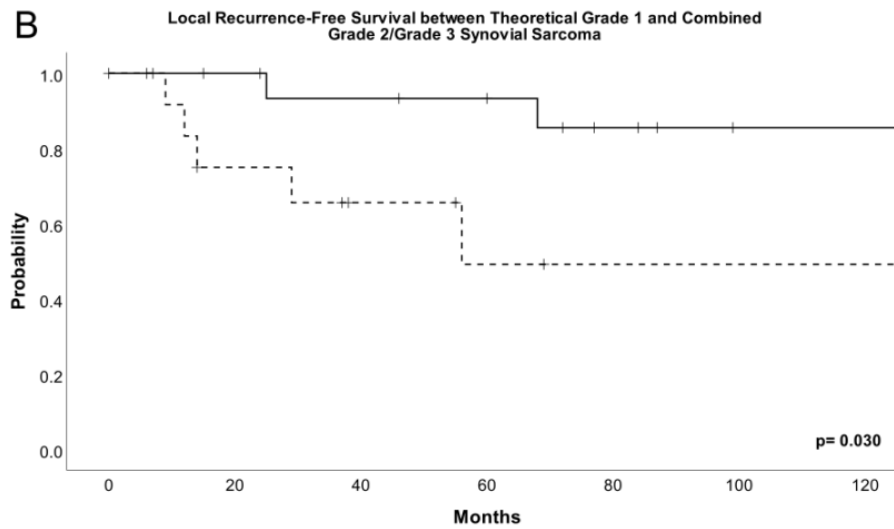


Figure 2B. Kaplan-Meier local recurrence free survival for a theoretical Grade 1 Synovial Sarcoma group. Theoretical Grade 1 Synovial Sarcoma (solid line) compared to Grade 2 and Grade 3 Synovial Sarcoma (dashed line).

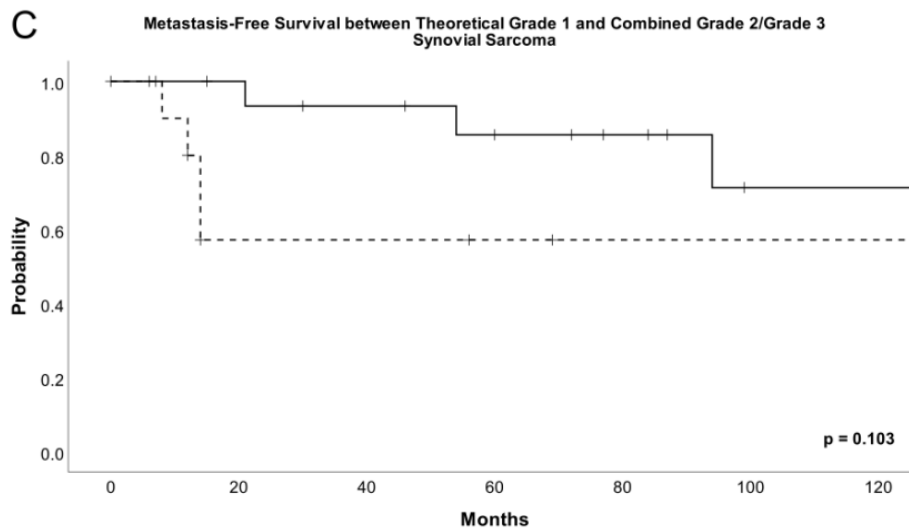
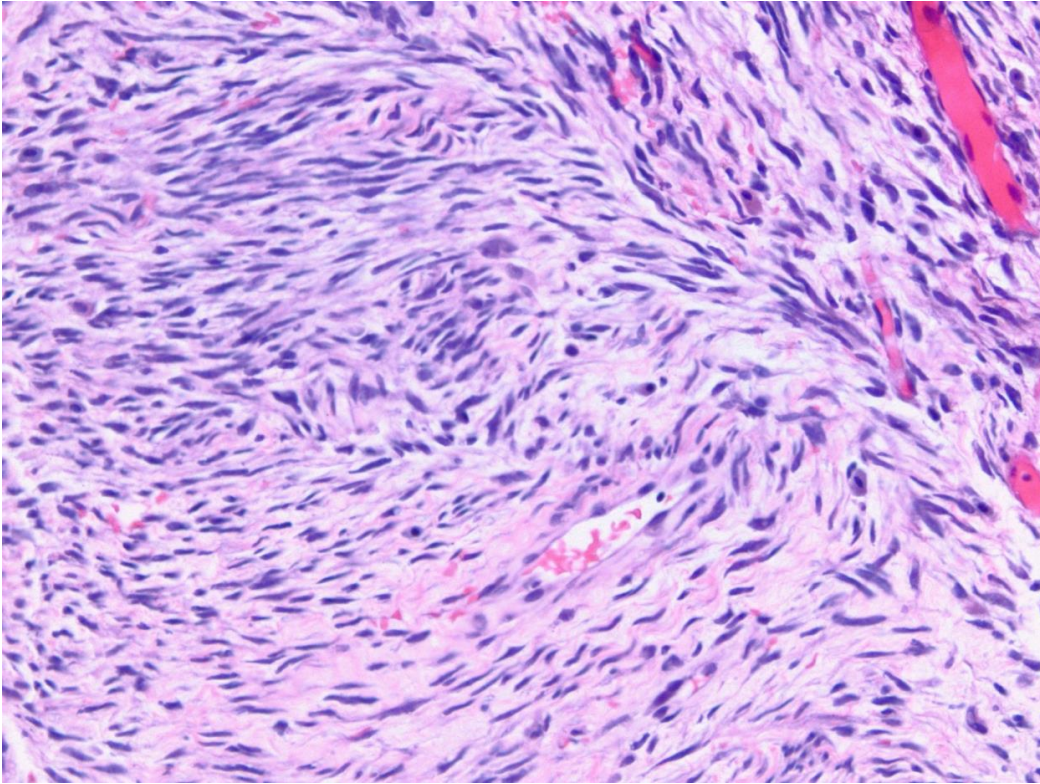
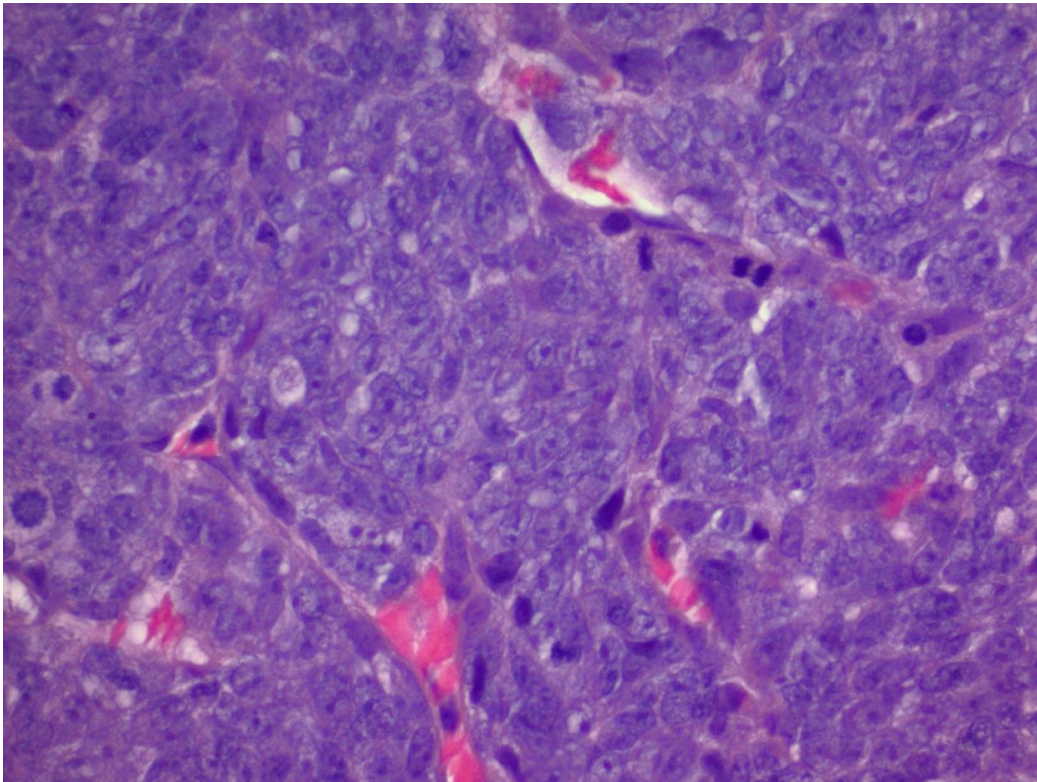


Figure 2C. Kaplan-Meier metastasis free survival for a theoretical Grade 1 Synovial Sarcoma group. Theoretical Grade 1 Synovial Sarcoma (solid line) compared to Grade 2 and Grade 3 Synovial Sarcoma (dashed line).



Experimental grade 1 SS (conventional grade 2) shows low to moderate cellularity. The tumor is composed of delicate and uniform spindle cells with regular chromatin. No mitosis or necrosis is identified.



Poorly differentiated SS shows very high cellularity. The tumor is composed of round to oval epithelioid cells with vesicular chromatin and prominent nucleoli. There is high mitotic activity (up to 44/10HPF), and necrosis (5%; not shown here).



9:35 AM - 9:42 AM

Paper #29 #1818785

DISTRIBUTION AND RATE OF MYXOID LIPOSARCOMA SPINAL METASTASES: IMPACT ON SURVEILLANCE IMAGING

Benjamin M. Vierra¹; Jake Awtry²; Lily V. Saadat²; Jason L. Hornick²; Jyothi P. Jagannathan³; Marco L. Ferrone²; Andrew J. Wagner³; Jiping Wang²; Chandrajit P. Raut³; Mark Fairweather²

¹Harvard Medical School, Boston, Massachusetts, UNITED STATES; ²Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES; ³Harvard Medical School, Dana Farber Cancer Institute, Boston, Massachusetts, UNITED STATES

Objective: Myxoid liposarcomas are characterized by a unique tendency to spread to extra-pulmonary sites with a particular propensity for osseous metastases, including the spine. While magnetic resonance imaging (MRI) is generally preferred over computed tomography (CT) imaging for detection of osseous metastases, the detection rate and utility in patients with myxoid liposarcoma remains unclear. The aim of our study was to investigate the rate and distribution of spinal metastases in patients with myxoid liposarcoma and detection modality.

Methods: Records of all patients with confirmed myxoid liposarcoma treated at our institution were retrospectively reviewed. Metastatic patterns of disease were identified and imaging modality utilization was analyzed.

Results: Between 2000-2020, 164 patients were evaluated at our sarcoma center with myxoid liposarcoma. Most patients (n=124, 75.6%) presented with localized disease with primary sites including extremity (118, 72.0%), trunk (36, 22.0%), abdomen/pelvis (9, 5.5%) and other (1, 0.6%, Table 1). Six (1.7%) patients presented with locally recurrent disease, 24 (14.6%) with metastatic disease, and 10 (6.1%) with primary and metastatic disease concurrently. With a median follow up of 69.2 months, 36 (22.0%) patients developed spinal metastases (Table 2). Of those 36 patients, 26 (72.2%) patients had multifocal spine metastases while 6 (16.7%) patients had isolated thoracic and 4 (11.1%) patients had isolated lumbar metastases. Eight (22.2%) patients had spinal metastases identified on surveillance MRI of the spine, 10 (27.8%) patients had spinal metastases identified on surveillance computed tomography (CT) imaging which then prompted further MRI spine imaging, and 17 (47.2%) patients presented with spine symptoms which prompted imaging. For nine (25.0%) patients, spinal metastases were only visible on MRI spine, while for 22 (61.1%) patients spinal metastases were visible on other forms of imaging including CT, positron emission tomography (PET) scan, or MRI of the pelvis or extremity. At time of diagnosis of spinal metastases, 33 (91.7%) patients had additional sites of non-spinal metastatic disease. Of the 3 patients with spinal metastases with initial isolated metastatic disease, one was detected on surveillance MRI and two were detected after imaging prompted by symptoms. Of those patients with spinal metastases, 31 (86.1%) developed symptoms during their disease course. Surgical intervention was required in 15 (41.7%) patients and 19 (52.8%) were treated with radiation alone. The median overall survival from the time of diagnosis of non-spinal metastases was significantly longer compared to those patients with spinal metastases (8.7 vs. 2.1 years, P<0.001, Fig. 1).

Conclusion: Nearly one quarter of patients in our series developed spinal metastases during their disease course. Detection of asymptomatic isolated spinal metastases by surveillance MRI is rare. Nearly all patients have other sites of non-spinal metastatic disease at the time of diagnosis of spinal metastases. One in five patients were found to have spinal metastases on routine surveillance spine dedicated MRI. Routine surveillance MRI imaging of the spine in patients with localized disease on routine CT imaging likely provides no additional benefit, however, should be considered in those patients with known metastatic disease.

Table 1: Patient Characteristics

<i>Characteristic</i>	n	%
Total Patients	164	100.0
Disease Type at Initial Consultation		
Primary only	124	75.6
Metastatic only	24	14.6
Primary and metastatic	10	6.1
Locally recurrent disease	6	3.7
Location of Primary Disease		
Extremity	118	72.0
Trunk	36	22.0
Abdomen/Pelvis	9	5.5
Other	1	0.6
Pts with Recurrence/Metastases		
Yes	82	50.0
No	82	50.0
Patients with Spine Tumors	36	22.0

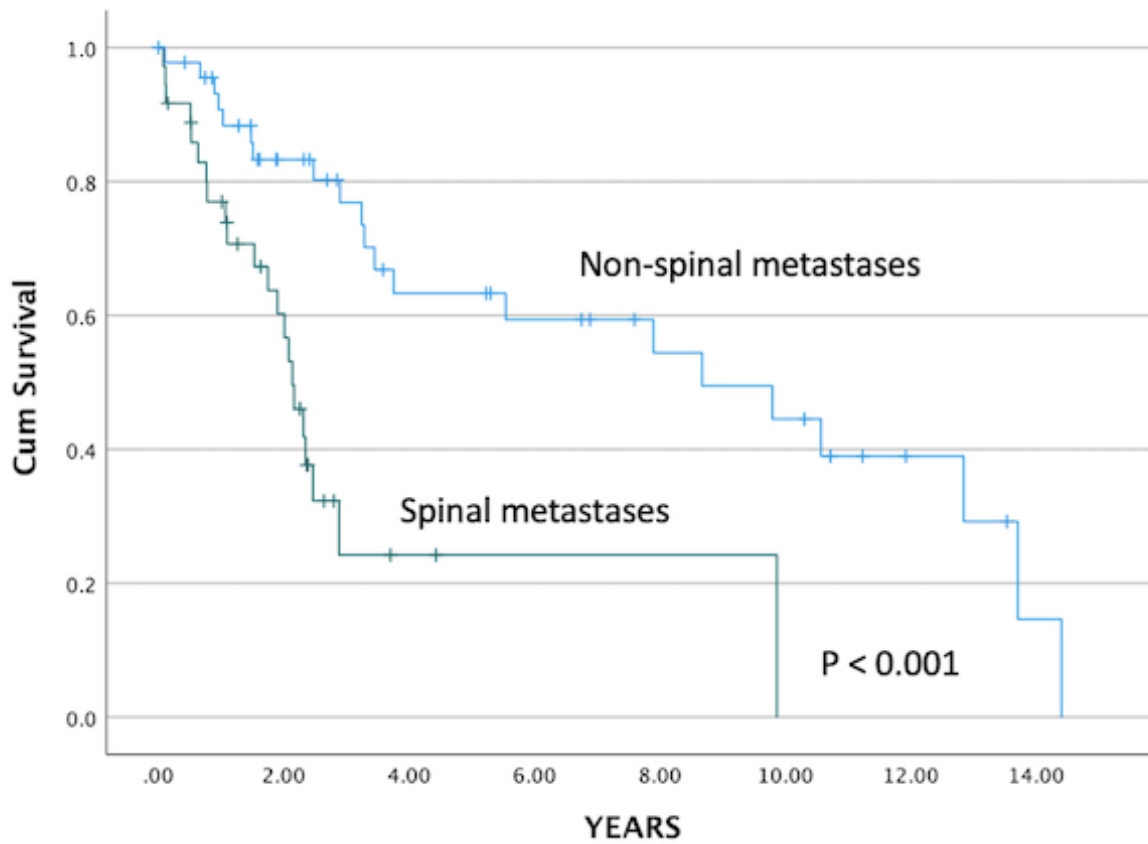


Table 2: Patients with spine tumors

<i>Characteristic</i>	n	%
Total number of patients	164	100.0
Specific location		
Multifocal	26	72.2
Cervical only	0	0.0
Thoracic only	6	16.7
Lumbar only	4	11.1
Sacrum only	0	0.0
Additional non-spine sites of metastases at diagnosis?		
Yes	33	91.7
No	3	8.3
Disease visible on CT imaging?		
Yes	14	38.9
No	17	47.2
Unknown	5	13.9
Diagnosis of spinal metastases		
MRI surveillance imaging	8	22.2
Other imaging surveillance	10	27.8
Symptoms prompting imaging	17	47.2
Unknown	1	2.8
Spine Metastasis only visible on MRI spine		
Yes	9	25.0
No	22	61.1
Unknown	5	13.9
Symptomatic at any time?		
Yes	31	86.1
No	5	13.9
Surgical intervention for spine metastasis		
Yes	15	41.7
No	21	58.3
Radiation to spine metastasis		
Yes instead of surgery	19	52.8
Preoperatively	4	11.1
Preoperatively and postoperatively	2	5.6
Postoperatively	7	19.4
No	4	11.1



ctos®

2021 Virtual Annual Meeting

Oral Presentations

Friday, November 11, 2021



10:00 am - 11:00 am

– Session 6 –

IMMUNOTHERAPY & IMMUNE MICROENVIRONMENT

10:00 AM - 10:07 AM

Paper #30 #1818753

SPEARHEAD-1: A PHASE 2 TRIAL OF AFAMITRESGENE AUTOLEUCEL (FORMERLY ADP-A2M4) IN PATIENTS WITH ADVANCED SYNOVIAL SARCOMA OR MYXOID/ROUND CELL LIPOSARCOMA

Brian Andrew A. Van Tine¹; Sandra P. D'Angelo²; Steven Attia³; Jean-Yves Blay⁴; Sandra Strauss⁵; Claudia Maria Valverde Morales⁶; Albiruni Ryan Abdul Abdul Razak⁷; Kristen N. Ganjoo⁸; Michael J. Wagner⁹; Axel Le Cesne¹⁰; Erin Van Winkle¹¹; Trupti Trivedi¹¹; Swethajit Biswas¹²; Dennis Williams¹¹; Elliot Norry¹¹; Dejka M. Araujo¹³
¹Washington University School of Medicine, St. Louis, Missouri, UNITED STATES; ²Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES; ³The Mayo Clinic, Jacksonville, Florida, UNITED STATES; ⁴Centre Léon Bérard, Lyon, Auvergne, FRANCE; ⁵University College London Hospital, London, England, UNITED KINGDOM; ⁶Vall D'Hebron University Hospital, Barcelona, Catalonia, SPAIN; ⁷Solid Tumor Program and Medical Oncology Lead, Sarcoma Program, Division of Medical Oncology, Princess Margaret Cancer Centre, University Health Network, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, CANADA; ⁸Stanford Cancer Center, Stanford, California, UNITED STATES; ⁹University of Washington/Fred Hutch/Seattle Cancer Care Alliance, Seattle, Washington, UNITED STATES; ¹⁰Institut Gustave Roussy-Gustave Roussy Cancer Center-DITEP, Villejuif, Ile-de-France, FRANCE ¹¹Adaptimmune, Philadelphia, Pennsylvania, UNITED STATES; ¹²Adaptimmune, Abingdon, England, UNITED KINGDOM; ¹³The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES

Objective: SPEARHEAD-1 (NCT04044768) is a Phase 2, open-label trial to evaluate the efficacy and safety of afamitresgene autoleucel (afami-cel) in patients with advanced/metastatic synovial sarcoma or myxoid/round cell liposarcoma (MRCLS).

Methods: Eligible patients are HLA-A*02 positive with MAGE-A4-expressing tumors. Patients undergo leukapheresis for collection of autologous T-cells for processing and manufacture into afami-cel cells. Patients received afami-cel doses between 1–10 × 10⁹ transduced T-cells after receiving lymphodepleting chemotherapy. The primary endpoint is overall response rate per RECIST v1.1 by independent review. An independent Data Safety Monitoring Board reviews ongoing safety and benefit:risk during the interventional phase.

Results: As of March 29, 2021, 37 patients had received afami-cel. Twenty-one patients (57%) were male, the median age was 42 years (range: 24–73), and they had a median of 3 prior systemic lines of therapy (range: 1–12). The median MAGE-A4 antigen expression level (histoscore) was 234 (range: 112–300)[1], and the transduced cell dose ranged from 2.7–9.9 × 10⁹. Thirty-two patients had synovial sarcoma (86%), and the median MAGE-A4 histoscore among this group was 270 (range: 132–300)[1]. At the data cutoff, 33 patients were evaluable for preliminary efficacy having at least one post-infusion scan (29 with synovial sarcoma and 4 with MRCLS). The investigator-assessed responses were: complete response (2 patients; both with synovial sarcoma), partial response (11 patients; 10 synovial sarcoma, 1 MRCLS), stable disease (15 patients; 13 synovial sarcoma, 2 MRCLS), and progressive disease (5 patients; 4 synovial sarcoma, 1 MRCLS). All responses were confirmed. Overall response rate was 39.4% (synovial sarcoma, 41.4%; MRCLS, 25.0%). Median duration of response has not yet been reached and ranged from 4.3 to > 38.0 weeks. Complete and partial responses were observed in patients with MAGE-A4 histoscores ranging from 134–300 (median: 225). The most common AEs (in > 30% of patients) of any grade were neutropenia, lymphopenia, nausea, cytokine release syndrome, leukopenia, fatigue, pyrexia, and anemia. Cytokine release syndrome of any grade occurred in 22/37 (59%) patients; 1 of these events was ≥ Grade 3. No immune effector cell-associated neurotoxicity syndrome (ICANS) has been reported to date. Cytopenia (≥ Grade 3) at 4 weeks post-infusion was observed in 6 patients (anemia 3 patients, neutropenia 2 patients, and thrombocytopenia 1 patient). No treatment-related Grade 5 toxicities have been reported to date. [1] One patient had a missing baseline histoscore at the time of data cut-off (n=36).

Conclusion: These preliminary data demonstrate afami-cel is efficacious in heavily pre-treated patients with synovial sarcoma. Objective responses are reported across a wide range of MAGE-A4 antigen levels, and deep and durable responses have been observed. To date, the safety profile of afami-cel has been favorable, with mainly low-grade cytokine release syndrome and tolerable/reversible hematologic toxicities. This study was sponsored by Adaptimmune (Philadelphia, PA, USA). Writing and editorial support was from Excel Scientific Solutions (Fairfield, CT, USA); funding was provided by Adaptimmune.



10:07 AM - 10:14 AM

Paper #31 #1818726

SAFETY AND EFFICACY OF LETETRESGENE AUTOLEUCEL (LETE-CEL; GSK3377794) IN ADVANCED MYXOID/ROUND CELL LIPOSARCOMA (MRCLS) FOLLOWING HIGH LYMPHODEPLETION (COHORT 2): INTERIM ANALYSIS

Sandra P. D'Angelo¹; Mihaela Druta²; Brian Andrew A. Van Tine³; David Liebner⁴; Scott Schuetze⁵; Aisha N. Hasan⁶; Andrew P. Holmes⁶; Anne Huff⁶; Gurpreet Kapoor⁶; Stefan Zajic⁶; Neeta Somaiah⁷

¹Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES; ²H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida, UNITED STATES; ³Washington University School of Medicine, St. Louis, Missouri, UNITED STATES; ⁴The Ohio State University, Columbus, Ohio, UNITED STATES; ⁵University of Michigan, Ann Arbor, Michigan, UNITED STATES; ⁶GlaxoSmithKline, Collegeville, Pennsylvania, UNITED STATES; ⁷The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES

Objective: Cancer testis antigen NY-ESO-1 is expressed in multiple tumor types, including 80–90% of MRCLS [1,2]. Overall response rates (ORRs) to MRCLS treatment are low (1L, <20%; 2L, <10%) [2]. Lete-cel, an autologous T-cell therapy, targets NY-ESO-1/LAGE-1a+ tumors using a genetically modified, high-affinity T-cell receptor. High-dose lymphodepletion (LD) was linked with better responses in synovial sarcoma [3]; the current study tested this hypothesis in MRCLS.

Methods: This open label, pilot study evaluates lete-cel efficacy and safety in advanced MRCLS following low-dose (Cohort 1 [C1]; 30 mg/m² fludarabine [flu] x 3d + 600 mg/m² cyclophosphamide [cy] x 3d) or high-dose (Cohort 2 [C2]; 30 mg/m² flu x 4d + 900 mg/m² cy x 3d; initiated based on C1 data) LD. Key eligibility: age ≥18 y; HLA-A*02:01; A*02:05, or A*02:06; advanced high-grade NY-ESO-1+ MRCLS (≥30% of cells 2+/3+ by IHC); prior anthracycline; measurable disease; specified washouts; and active/chronic/intercurrent illness restrictions. Stages include screening, leukapheresis, lete-cel manufacture, LD, lete-cel infusion (1– 8 × 10⁹ transduced T cells), follow-up. Response is assessed at wk 4, 8, 12, and 24, then every 3 mo to disease progression/death/withdrawal. The primary efficacy endpoint is investigator-assessed ORR by RECIST v1.1. In C1 (n=10 patients [pts]), lete-cel was well tolerated and linked with 2 confirmed partial responses (PR; ORR, 20%) and stable disease (SD) in 8 pts. Planned interim analysis for C2, shown here, was done once all 10 treated pts had ≥3 post-baseline disease assessments or progressed/died/withdrew. Efficacy data will be correlated with transduced cell kinetics and pharmacodynamics marker profiles.

Results: Durable (1.0–7.8 mo) PR (4/10 pts [ORR, 40%]; 2 ongoing) and prolonged (2.7–10.6 mo) SD (5/10 pts; 3 ongoing) with tumor regression were observed. Treatment-emergent cytopenias occurred in all pts. All experienced T-cell related cytokine release syndrome (5 serious adverse events; 30% Grade 3), with onset ≤5d of infusion and median duration 7.5d. Graft-vs-host disease, immune effector cell–associated neurotoxicity syndrome, pancytopenia, or aplastic anemia were not reported.

Conclusion: A single lete-cel infusion after high LD showed antitumor activity in advanced MRCLS and a manageable safety profile consistent with other lete-cel studies. The trial is active but no longer recruiting (NCT02992743). MRCLS is included in a separate, ongoing lete-cel study (NCT03967223). References: 1. D'Angelo SP, et al. J Clin Oncol 2018;36:15_suppl, 3005. 2. Pollack SM, et al. Cancer Med 2020;9(13):4593–602. 3. D'Angelo SP, et al. J Immunother Cancer 2020;8:P298. Funding: GSK [208469; NCT02992743]. Editorial support was provided by Eithne Maguire, PhD and Frankie Wignall, PhD, of Fishawack Indicia, part of Fishawack Health, and funded by GSK. This abstract was first presented at American Society of Clinical Oncology Annual Meeting on June 4–8, 2021.



10:14 AM - 10:21 AM

Paper #32 #1818746

PHASE II STUDY OF ERIBULIN AND PEMBROLIZUMAB IN PATIENTS WITH METASTATIC SOFT TISSUE SARCOMA

Suzanne George¹; Michael Nathenson¹; Edwin Choy²; Emanuele Mazzola¹; Jeffrey Morgan¹; Gregory M. Cote²; Melissa Hohos¹; Susan Carrozza¹; Sora Limor¹; Kristen Finn²; Julia Digiovanni²; Nicola Bothwick¹; Priscilla Merriam¹; Andrew J. Wagner¹

¹Sarcoma Center, Dana Farber Cancer Institute, Boston, Massachusetts, UNITED STATES;

²Massachusetts General Hospital, Boston, Massachusetts, UNITED STATES

Objective: Eribulin has demonstrated benefit in subsets of soft tissue sarcoma (STS) and may alter the immune microenvironment. Responses to single agent immune check point inhibition (ICI) in STS remains limited. Combination ICI and chemotherapy has shown promise in multiple types of malignancies. We therefore studied the combination of pembrolizumab and eribulin in STS.

Methods: This is a three arm, phase II trial evaluating the combination of pembrolizumab and eribulin. Cohort A, leiomyosarcoma (LMS), has been previously reported (J Clin Oncol 38: 2020 (suppl; abstr 11559)). The current report focuses on Cohort B, liposarcoma (LPS), and Cohort C, other sarcomas, including undifferentiated pleomorphic sarcoma (UPS). Patients (pts) must have received at least one prior therapy, no prior immune check point inhibitors and no prior eribulin. Pts must have ECOG 0 or 1. Eligible patients received eribulin 1.4 mg/m² D1,8 and pembrolizumab 200mg d1, every 21 days. Tumor assessments per RECIST 1.1 were performed at screening and every 6 wks. Pts remained on treatment for up to 2 years or until RECIST 1.1 progressive disease (PD), unacceptable toxicity or death. Primary end point was progression-free survival at 12 weeks (wks), with 60% PFS at 12 wks required to deem the combination promising.

Results: As of May 5, 2021, the trial has met the accrual goal and all patients were evaluable for the primary endpoint of PFS at 12 wks. Thirty-eight patients were enrolled. 20 pts enrolled in cohort B, including 17 pts with dedifferentiated LPS, 2 pts with pleomorphic LPS and 1 pt with myxoid liposarcoma. 18 patients enrolled in cohort C, including 8 pts with UPS and 3 patients with angiosarcoma (AS). At the time of the analysis, 7 pts remain on treatment. Cohort B: Median age 64 (range 32- 78), 11 pts with ECOG 0, median of 1 prior therapy (range 1 – 4). Cohort C: median age 58 (range 29-73) 9 pts with ECOG 0, median of 1 prior therapy (range 1-4). PFS at 12 wks was 69% for cohort B (liposarcoma) with median PFS of 27.4 wks (90% CI 12.4 – unevaluable), and 56% for cohort C (other sarcomas) with median PFS of 12.6 wks (90% CI 7 -38.7). Of the 8 pts enrolled with UPS, 5 pts remained without progression at 12 wks (63%). Of the 3 pts enrolled with AS, all pts remained without progression at 12wks (100%).

In cohort B, there were 3 pts with partial response (all confirmed) for ORR of 15%. In cohort C, there were 6 pts with PR (all confirmed) for ORR of 33%. All three patients enrolled with angiosarcoma experienced PR. Responses and patient characteristics are shown in table A below.

Twenty-two of 38 (58%) pts experienced G3 or higher toxicity, most commonly G3 neutropenia 8 pts (21%), G3 fatigue 4pts (10%), and G3 anemia 4 pts(10%). 1 pt experienced G4 neutropenia, and 1 pt experienced G4 pancreatitis.

Conclusion: The combination of eribulin and pembrolizumab met the primary end point of PFS >60% at 12 wks for liposarcoma. Significant activity was seen in dedifferentiated liposarcoma, unclassified pleomorphic sarcoma and angiosarcoma. No unexpected toxicities were observed. Correlative analysis is ongoing.

Title: PHASE II STUDY OF ERIBULIN AND PEMBROLIZUMAB IN PATIENTS WITH METASTATIC SOFT TISSUE

Table: Characteristics of Patients with RECIST 1.1 Partial Response

COHORT	HISTOLOGY	BEST RESPONSE as of May 2021
C	Angiosarcoma – visceral/splenic	-48 %
C	Angiosarcoma – RT associated	-93 %
C	Angiosarcoma -cutaneous/facial	-59 % (complete pathologic response)
C	Spindle Cell Sarcoma	-60 %
C	SMARCA4 thoracic sarcoma	-66 %
C	UPS	-47 %
B	Dedifferentiated LPS	-69 %
B	Dedifferentiated LPS	-50%
B	Pleomorphic LPS	-61%



10:21 AM - 10:28 AM

Paper #33 #1818738

SAFETY AND EFFICACY FROM A PHASE 1/2 STUDY OF INTRATUMORAL INT230-6 ALONE OR IN COMBINATION WITH IPILIMUMAB [INTENSITY# IT-01; BMS# CA184-592] IN ADULT SUBJECTS WITH METASTATIC SARCOMAS (NCT 03058289)

Ian B. Walters¹; Matthew Ingham²; James S. Hu³; Giles Whalen⁴; Jacob Thomas⁵; Anthony B. El-Khoueiry⁶; Diana Hanna⁶; Anthony Olszanski⁷; Christian F. Meyer⁸; Nilofer S. Azad⁸; Syed Mahmood⁹; Lewis Bender⁹; Lillian L. Siu¹⁰; Albiruni Ryan Abdul Abdul Razak¹⁰

¹Intensity Therapeutics, Inc, Westport, Connecticut, UNITED STATES; ²New York Presbyterian Hospital/Columbia University Medical Center, New York, New York, UNITED STATES; ³USC, Los Angeles, California, UNITED STATES; ⁴UMass Memorial Medical Center, Worcester, Massachusetts, UNITED STATES; ⁵USC Norris Cancer Hospital, Los Angeles, California, UNITED STATES; ⁶Keck School of Medicine of USC, Los Angeles, California, UNITED STATES; ⁷Fox Chase Cancer Center, Philadelphia, Pennsylvania, UNITED STATES; ⁸Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, Maryland, UNITED STATES; ⁹Intensity Therapeutics, Inc., Westport, Connecticut, UNITED STATES; ¹⁰Princess Margaret Cancer Centre, Toronto, Ontario, CANADA

Objective: Sarcomas are a rare and heterogeneous group of solid tumors derived from mesenchymal origin which are primarily treated with systemic chemotherapy with limited benefit. Sarcomas provide a unique opportunity for intratumoral (IT) treatment approaches. INT230-6 is a novel formulation of cisplatin (CIS) and vinblastine (VIN) with an amphiphilic cell penetration enhancer designed specifically for IT administration. The IT-01 trial objectives are to evaluate INT230-6 alone or in combination with the CTLA-4 inhibitor ipilimumab (IPI). In preclinical studies, DfuseRxSM platform increases INT230-6 drug dispersion throughout the tumor, allows drug diffusion into cancer cells, and recruits dendritic, CD4 and CD8 T cells. Further, the addition of IPI has been shown to improve INT230-6 responses in nonclinical models.

Methods: IT-01 is an open-label phase 1/2 study, currently enrolling adult subjects with locally advanced, unresectable or metastatic solid tumors, including sarcoma. INT230-6 dosing is proportional to the injected tumor's volume. INT230-6 was administered IT every 2 weeks for 5 doses as monotherapy or on the same schedule in combination with IPI which was dosed at 3mg/kg IV every 3 weeks for a total of 4 doses. Retreatment or maintenance therapy with INT230-6 was allowed.

Results: 22 subjects with soft tissue sarcomas (14 INT230-6 monotherapy, 8 IPI combination) have been enrolled as of June 1, 2021. Tumor subtypes and demographics for 17 evaluable subjects are listed in Figure 1. The INT230-6 dose injected was up to 175 mL (87.5 mg of CIS, 17.5 mg VIN) in one or more tumors at a single visit, which contains doses exceeding the typical IV doses of the cytotoxic drugs. PK analysis estimates that 95% of INT230-6 active agents remain in the tumor.

The most common (>20%) treatment-emergent adverse events (TEAEs) in evaluable monotherapy subjects (n=13) were localized pain (77%), fatigue (39%), decreased appetite (31%), nausea (31%), and vomiting (23%) most of which were low grade. The most common (>20%) related TEAEs in evaluable IPI combination subjects (n=4) were anemia (50%), fatigue (50%), pruritus (50%), rash maculo-papular (50%), and 1 subject (25%) experienced abdominal pain, chills, colitis, decreased appetite, dyspnea, dysuria, localized tumor-related pain, nausea, and vomiting. There were no related grade 4 or 5 TEAEs in either cohort.

INT230-6 induced tumor regression in both injected and non-injected lesions. Disease control rate (DCR) at the first imaging timepoint at 2 months was 62% for INT230-6 monotherapy subjects (n=13) vs. 50% in IPI combination subjects (n=4). Tumor necrosis, reduction in Ki67 staining and infiltration with CD4 and CD8 T-cells were seen on 28-day biopsies after 2 injections. Following monotherapy, abscopal effects were seen in 4 subjects, with a reduction in longest diameter and tumor volume of 9 uninjected tumors. Early analysis of median overall survival (mOS) of the combined monotherapy and IPI combination population (n=22) has not been reached with a median follow-up of 143 days. In the INT230-6 monotherapy population (n=14), mOS has not been reached with 425 days of median follow-up.

Conclusion: Intratumoral INT230-6 appears well-tolerated in this heterogeneous soft tissue sarcoma population, and early safety with the IPI combination appears favorable. INT230-6 monotherapy treatment resulted in encouraging signs of tumor burden reduction in injected and non-injected lesions, and immune activation. Given the poor cor-

relation of RECIST responses and OS in this population, preliminary analysis of OS from this study compares favorably to historical results from a P1/2 basket sarcoma study with a similar, heavily pretreated, heterogeneous sarcoma population balanced for three prognostic health criteria: albumin and lactase dehydrogenase levels and a subject's number of metastatic sites. Enrollment is ongoing and further follow up will enable design of a confirmatory study.

Figure 1. Baseline Characteristics for All (INT230-6 Monotherapy + Ipilimumab) Subjects with Sarcoma and Chordoma

Age	Median (Min, Max) (years)	65.2 (41.9, 76.9)
Gender	Male, n (%)	13 (76.5%)
	Female, n (%)	4 (23.5%)
ECOG performance status score	0, n (%)	2 (11.8%)
	1, n (%)	14 (82.4%)
	2, n (%)	1 (5.9%)
Total Number of Prior Therapies	Median (Min, Max)	4.0 (2.0, 10.0)
Tumor Types	Chordomas	5
	Leiomyosarcomas	4
	Liposarcomas	3
	Pleomorphic sarcomas	3
	Chondrosarcoma, Mesenchymal chondrosarcoma, Kaposi Sarcoma, Myofibroblastic sarcoma, Malignant chondroid syringoma, Myxofibrosarcoma, & Spindle cell sarcoma	1 each of



10:28 AM - 10:35 AM

Paper #34 #1818766

IMMUNOLOGICAL PROFILING OF PATIENTS WITH SPORADIC DESMOID FIBROMATOSIS UNDER ACTIVE SURVEILLANCE TO IDENTIFY PROGNOSTIC MARKERS

Chiara Colombo; Viviana Vallacchi; Laura Bergamaschi; Federica Perrone; Francesca Rini; Elena Palassini; Sandro Pasquali; Stefano Radaelli; Dario Callegaro; Marco Fiore; Chiara Castelli; Alessandro Gronchi
Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY

Objective: Desmoid fibromatosis (DF) is a locally aggressive rare tumor with high recurrence rate after surgery and unpredictable clinical behaviour. Active surveillance is the strategy of choice for most of DF patients. However, 30% of patients will progress and need one or more active treatments. Biomarkers discriminating aggressive forms of DF are not available and prediction of progressing patients remains challenging. Aim of this study was to identify prognostic inflammatory/immune markers based on previous evidence of a correlation between Wnt/ β -catenin and altered inflammation/immune response.

Methods: Patients with primary sporadic desmoid fibromatosis under active surveillance were included in this study. Tumor and blood samples were prospectively collected at diagnosis and during active surveillance and investigated by 1. transcriptomic analysis of DF biopsies; 2. multiparametric cytofluorimetric analysis and functional profiling of purified PBMCs; 3. RNA profiling of whole blood 4. evaluation of plasma levels of cyto/chemokine and ctDNA of β -catenin variants. Levels of blood analytes were correlated with patients' clinical outcome and integrated with the other immunological parameters.

Results: Immune profile of whole blood and PBMCs of 42 patients showed that granulocytes and monocytes are already altered at the time of DF diagnosis compared to healthy donor (HD, n=17). This results was maintained also at 3 months (n= 26), 6 months (n= 17) and at 9 months (n= 11). DF patients had higher immunosuppressive myeloid subpopulations compared to HD. Specifically, an increasing in activated granulocytes and granulocytic myeloid-derived suppressor cells (PMN-MDSC, m-MDSC, e-MDSC), detected by the differential co-expression of CD15, CD11b, CD16 and Lox1 were observed, concomitantly with a boost of monocyte subsets and monocytic, defined through the co-expression of CD33, CD11b, CD14, CD16, HLA-DR and PDL1. We also observed an up-regulation of the immunosuppressive PMN-MDSC and intermediate inflammatory monocytes in DF with T41A mutation and not in S45F. The evaluation of immune cells, inflammatory cyto/chemokines and adhesion molecules at different time points of active surveillance is ongoing. Correlation between immune profile at each time point of surveillance and status at observation and transcriptomic analysis of DF biopsies is also ongoing.

Conclusion: These preliminary findings, showing a peripheral immune-modulation in DF patients, support the initial hypothesis of an involvement of the immune system in DF onset and maintenance.



10:35 AM - 10:42 AM

Paper #35 #1818731

IMMUNE CHECKPOINT INHIBITORS PROVIDE FAVORABLE RESPONSES IN PATIENTS WITH RECURRENT CHORDOMA

Andrew J. Bishop; Behrang Amini; Heather Lin; Shaan M. Raza; Jason T. Smith; Shreyaskumar Patel; David Grosshans; Ahsan Farooqi; B. Ashleigh Guadagnolo; Devarati Mitra; Kadir Akdemir; Alexander Lazar; Wei-Lien Wang; Justin E. Bird; Laurence D. Rhines; Anthony P. Conley

The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES

Objective: Chordomas are rare, locally aggressive neoplasms of the axial skeleton that are difficult to manage at the time of recurrence. When local therapies are not feasible, systemic therapy is often considered, though largely ineffective to date. However, with the broadening use of immune checkpoint inhibitors (ICI), there has been some interest in their utility for patients with chordoma. Here we report our experience with ICIs in the management of recurrent chordomas to better define responses and outcomes.

Methods: We retrospectively reviewed a cohort of patients with recurrent chordomas who received ICI as part of their treatment between 2016 and 2020. Patients underwent CT or PET/CT imaging at baseline and a serial time points, commonly after every 2-3 cycles. Response was assessed using RECIST 1.1 criteria. The Kaplan-Meier method was used to estimate the duration of response (DOR), progression free survival (PFS), and overall survival (OS). DOR was defined as time from the date of the first documented response to the date of documented progression or death for patients with a complete response (CR), partial response (PR) or stable disease (SD). PFS and OS was defined as the time from treatment initiation to the time of the event. Given that traditional systemic therapies have been ineffective at preventing chordoma progression, clinical benefit was defined as having SD, PR, or CR.

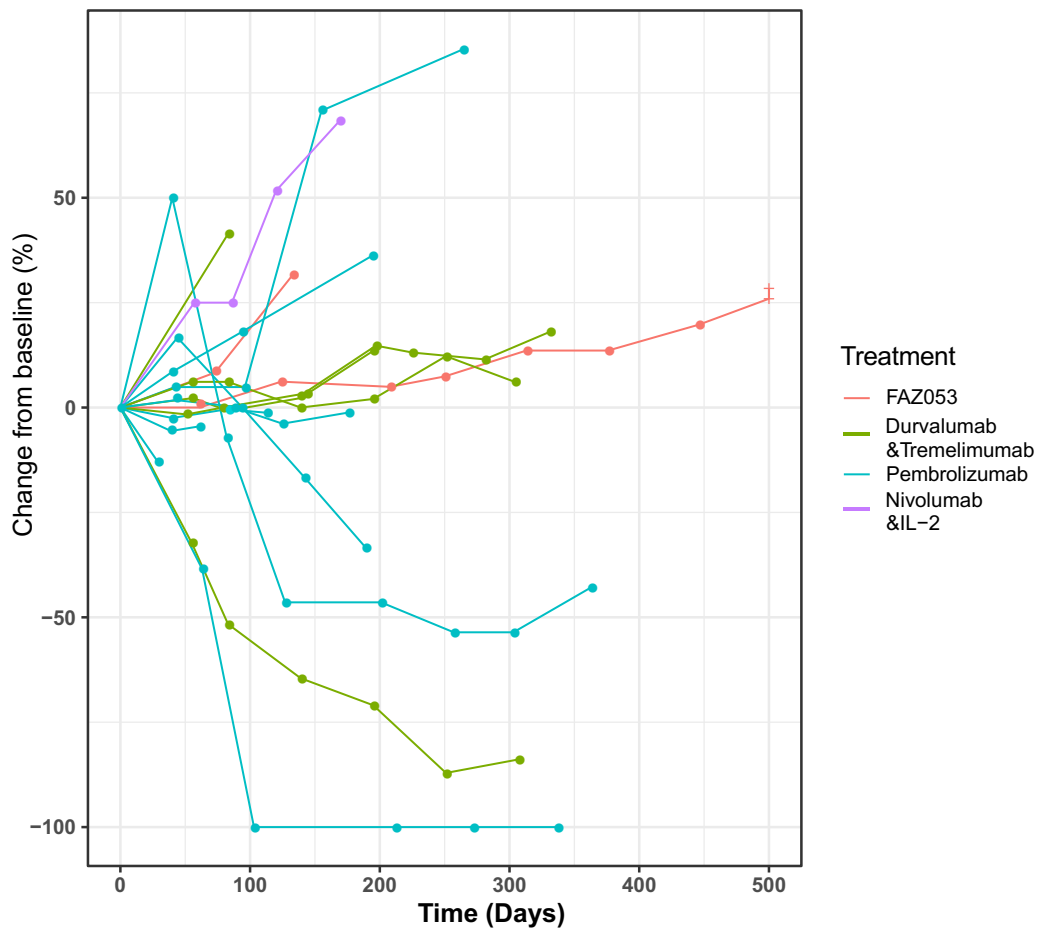
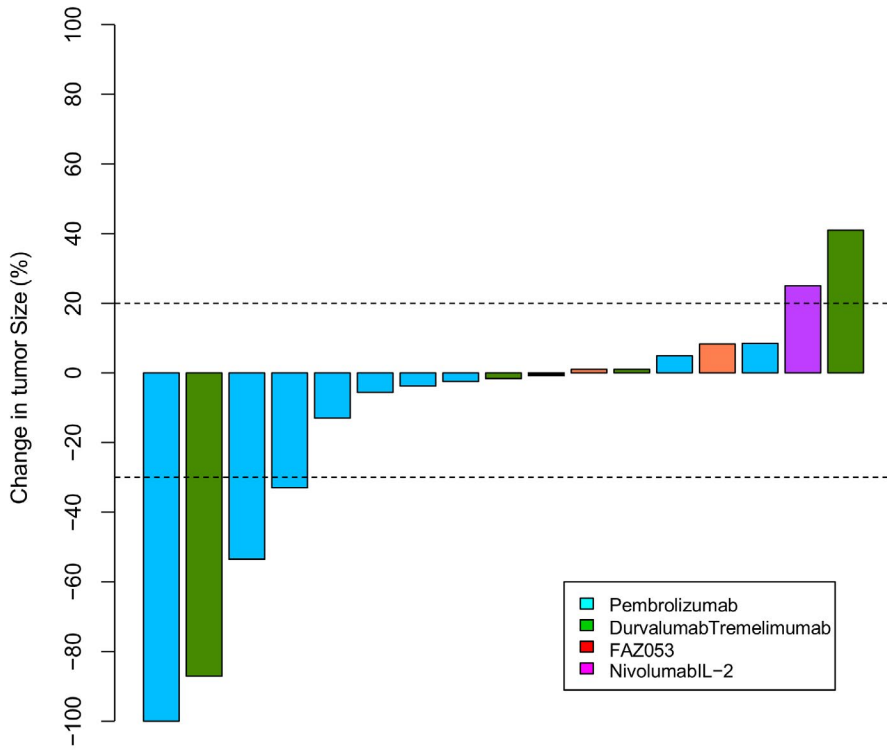
Results: Seventeen patients were evaluated with a median follow-up from the start of ICI of 29 months (m) (95% CI, 13-35 m). The median age at initial diagnosis was 56 years (interquartile range [IQR], 31-65) and 63 years (IQR, 60-69) at the time of ICI initiation. A majority of patients were male (n=13, 76%) and non-Hispanic white (n=13, 76%), and the primary site of involvement was most commonly the sacrum (n=10, 59%; mobile spine, n=5, 29%; base of skull, n=2, 12%). ICI was initiated at the time of locoregional recurrence in 10 patients (59%) and for metastatic disease in 7 (41%). Regarding the types of ICI, the majority received pembrolizumab (n=9, 53%), with others receiving durvalumab/tremelimumab (n=5, 29%), FAZ053 (n=2, 12%), and nivolumab/bempegaldesleukin (n=1, 6%). The median number of cycles delivered was 8 (IQR, 7-12), and the reasons for discontinuation was eventual clinical progression (n=7, 41%) or completion of the recommended course (n=5, 29% vs. toxicity, n=3, 18%; ICI ongoing, n=2, 12%). Additionally, while nearly all (n=16, 94%) received radiation therapy (RT) as part of their care, only 4 (24%) received concurrent RT within 3 m of ICI treatment.

Most patients were alive with disease (n=12, 71%) with a 1-year OS of 87% (95% CI 56-96%) and a median OS that has not yet been reached. The 1-year PFS was 56% with a median PFS of 14 m (95% CI, 5-17). Following ICI initiation, a majority of patients (n=15, 88%) received clinical benefit consisting of a CR (n=1, 6%), PR (n=3, 18%), and SD (n=11, 65%); only 2 patients (n=2) had PD despite ICI (Figure 1 – waterfall plot; Figure 2 – spider plot). Among all responders (n=15), the median DOR was 12 m (95% CI 5-15), with an observed shorter median DOR among patients who achieved only SD (6 m) compared to a CR/PR (13 m) (P=0.7).

Treatment was well-tolerated with two (12%) patients having grade 3/4 immune-related toxicities (colitis, grade 3; myocarditis, grade 4).

Conclusion: Preliminary data suggest ICI are an effective treatment for recurrent chordoma. Nearly all patients had some clinical benefit to ICI with limited toxicities, and responses were relatively durable, though longer among patients achieving a CR/PR compared to SD. These promising data provide support for the prospective evaluation of ICI in patients with chordoma.

From baseline to best response per RECIST





11:00 am - 12:00 pm

– Session 7 –

LOW GRADE AND INDOLENT TUMORS

11:00 AM - 11:07 AM

Paper #36 #1818777

A NATIONWIDE PROSPECTIVE CLINICAL TRIAL ON ACTIVE SURVEILLANCE IN PATIENTS WITH NON-INTRA-ABDOMINAL DESMOID-TYPE FIBROMATOSIS; THE GRAFITI TRIAL

Anne-Rose W. Schut¹; Milea Timbergen¹; Danique van Broekhoven¹; Thijs van Dalen²; Winan J. van Houdt³; Han Bonekamp⁴; Stefan Sleijfer¹; Dirk J. Grünhagen¹; Cornelis Verhoef¹; Frits van Coevorden³; Lukas Been⁵; Robert Van Ginke⁵; Marc Bemelmans⁶; Jos A. van der Hage⁷; Sander Dijkstra⁷

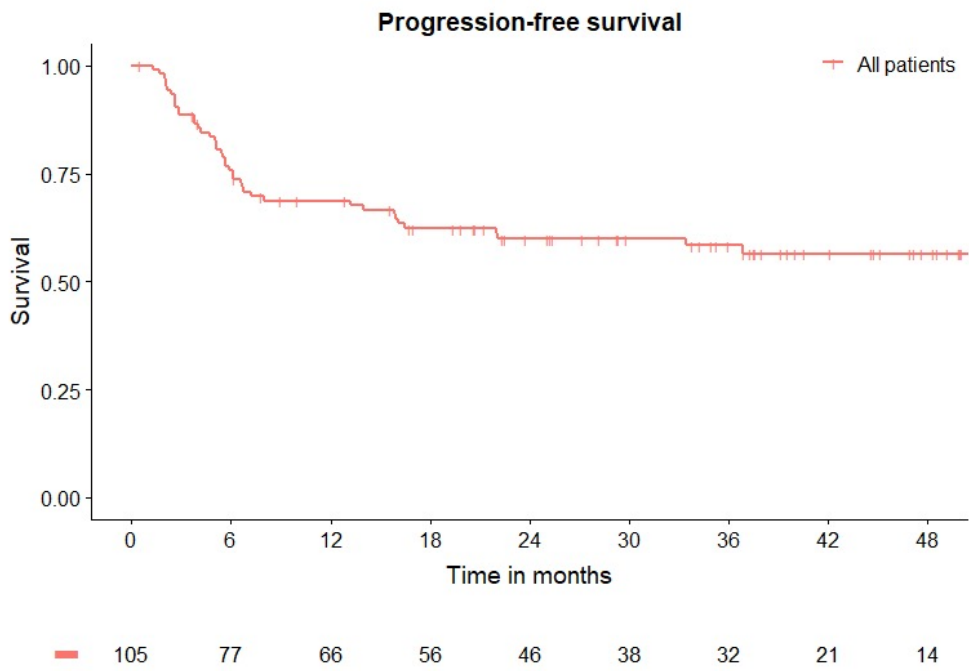
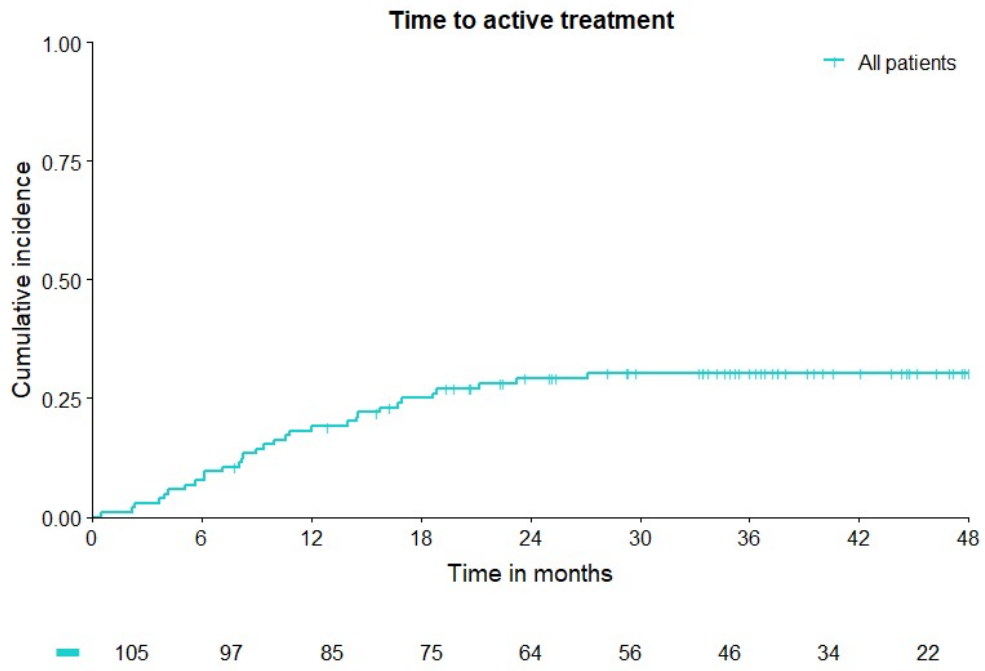
¹Erasmus Medical Center, Rotterdam, Zuid-Holland, NETHERLANDS; ²UMC Utrecht, Utrecht, Utrecht, NETHERLANDS; ³The Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS; ⁴Radboud University Medical Center, Nijmegen, Gelderland, NETHERLANDS; ⁵University Medical Center Groningen, Groningen, Groningen, NETHERLANDS; ⁶Maastricht University Medical Center, Maastricht, Limburg, NETHERLANDS; ⁷Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS

Objective: Desmoid-type fibromatosis (DTF) has a highly variable clinical course, displaying phases of progressive growth, stabilization or even spontaneous regression without treatment. The unpredictable biological behaviour and high recurrence rates after surgical resection have led to a shift to a more conservative approach. Active surveillance (AS) is currently recommended as primary treatment. The aim of this study was to assess tumour behaviour and the efficacy of AS in DTF patients.

Methods: In this multicentre prospective cohort study (NTR4714) adult patients with extra-abdominal or abdominal wall DTF were followed during an initial AS approach for 3 years. Tumour behaviour was assessed according to the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. by MRI. Cumulative incidence of the need to switch to an active treatment and progression-free survival (PFS) were calculated by the Kaplan-Meier method. Cox regression analyses were conducted to identify factors predictive for switch to active treatment. A planned interim analysis was performed after 1 year of follow-up on the first 20 patients to validate the safety of the study.

Results: A total of 105 patients started with an initial AS approach (80% females). Median age was 37 years (interquartile range (IQR) 32-47) and median tumour size at baseline was 4.1 cm (IQR 3.0-6.6). Most common tumour locations were abdominal wall (35%) and trunk (24%). A specific CTNNB1 mutation was found in 98 patients, of whom 57 patients had a T41A mutation and 14 patients had a S45F mutation. During follow-up, 31 patients switched to some form of active treatment. Cumulative incidence of switch to an active treatment at 1 and 3 years were 18.2% (95% confidence interval (CI) 10.4-25.2) and 30.4% (95% CI 20.8-38.8) respectively. Median time to start active treatment was not reached at a median follow-up of 33.7 months. Univariable analysis showed that larger tumour size (≥ 5 cm; HR=2.38 [95% CI 1.15-4.90]) and S45F CTNNB1 mutation (HR=6.24 [95% CI 1.92-20.3]) were risk factors for a switch to active treatment. Multivariable analysis identified only S45F CTNNB1 mutation as predictive factor (HR=4.64 [95% CI 1.38-15.8]). During follow-up, 32% had stable disease, 28% regressed and 40% demonstrated progressive disease (PD). PFS at 3 years was 58.3% (95% CI 49.2-69.1%) and median time to PFS was not reached. In 13 of 21 progressive patients who continued AS the desmoid tumour decreased after initial progression. After regression according to RECIST was observed, none of the patients developed SD or PD. In all patients, first progression or switch to active treatment occurred within the first 3 years. After 3 years, none of the patients who continued AS and with follow-up available (n=34) switched to an active treatment or developed PD.

Conclusion: This study demonstrated that AS is safe and the majority of DTF patients develop stable or regressive disease, even after initial progression. The insights into the natural behaviour of DTF will help to tailor the follow-up schedule to the individual patient. CTNNB1 mutation status and tumour size could be used to select patients who will benefit from AS or active treatment upfront.





11:07 AM - 11:14 AM

Paper #37 #1818736

SAFETY AND PRELIMINARY EFFICACY OF VIMSELTINIB IN TENOSYNOVIAL GIANT CELL TUMOR (TGCT)

Andrew J. Wagner¹; Albiruni Ryan Abdul Abdul Razak²; Hans Gelderblom³; Amparo Sánchez-Gastaldo⁴; Piotr Rutkowski⁵; Breelyn A. Wilky⁶; Michiel van de Sande³; Mary Michenzie⁷; Marc Vallee⁷; Maitreyi Sharma⁷; Matthew L. Sherman⁷; Rodrigo Ruiz-Soto⁷; William D. Tap⁸

¹Harvard Medical School, Dana-Farber Cancer Institute, Boston, Massachusetts, UNITED STATES; ²Princess Margaret Cancer Centre, University Health Network, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, CANADA;

³Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS; ⁴Hospital Universitario Virgen del Rocío, Sevilla, Andalucia, SPAIN; ⁵Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Mazowieckie, POLAND; ⁶University of Colorado Cancer Center, Aurora, Colorado, UNITED STATES; ⁷Deciphera Pharmaceuticals, LLC, Waltham, Massachusetts, UNITED STATES; ⁸Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES

Objective: Diffuse TGCT is a rare, locally aggressive neoplasm, where overexpression of colony-stimulating factor 1 (CSF1) drives recruitment of macrophages leading to local inflammation and joint destruction. Vimseltinib (DCC-3014) is an oral, highly selective, switch-control kinase inhibitor of CSF1 receptor (CSF1R). We report the safety and efficacy of vimseltinib in patients (pts) with TGCT in the phase 1 arm of the phase 1/2 study (NCT03069469).

Methods: In the phase 1 (dose-escalation) and phase 2 (expansion) study, pts with unresectable TGCT were treated with vimseltinib. Primary objectives of phase 1 were to determine safety, tolerability, and recommended phase 2 dose (RP2D). Antitumor activity was assessed using RECIST version 1.1.

Results: As of Feb 26, 2021, 32 TGCT pts enrolled in phase 1; 24 pts remain on study. Median age was 51 years (range, 23-73), median treatment duration was 6.8 months (range, 1-19), and the most common disease site was the knee in 20 (63%) pts. Treatment-emergent adverse events (AEs) of grade 3-4 in >5% were increases in blood creatine phosphokinase, aspartate aminotransferase (AST), lipase, amylase, and hypertension. Enzyme elevations were consistent with CSF1R inhibitor mechanism of action. Treatment-related grade 3 serious AEs in 2 pts included metabolic encephalopathy and vaginal hemorrhage. Dose-limiting toxicity of asymptomatic grade 3 AST increase in 2 pts (1 each, cohort 5 and 8), both had grade 1 AST increase at baseline. Objective responses were observed in 13 (1 complete, 12 partial responses; 45%) of 29 efficacy-evaluable pts across all phase 1 dose cohorts (Table). Enrollment is ongoing in phase 2; all 16 TGCT pts enrolled to date remain on study.

Conclusion: Vimseltinib was well-tolerated with encouraging and durable antitumor activity across all phase 1 TGCT dose cohorts. The safety profile of vimseltinib remains manageable with longer-term follow-up. Phase 2 safety and preliminary efficacy data at RP2D (30 mg twice weekly) will be presented.

TABLE: Phase 1 TGCT dose cohorts			
	Cohort 5 (n = 8)	Cohort 8 (n = 12)	Cohort 9 (n = 9)
Loading dose	30 mg QD x 5	30 mg QD x 3	20 mg QD x 3
Dose	30 mg twice weekly	10 mg QD	6 mg QD
Objective response rate, n (%)	4 (50)	6 (50)	3 (33)
Median duration on study, mo	6.3	8.3	4.5

mo, months; QD, once daily.



11:14 AM - 11:21 AM

Paper #38 #1818780

**ACTIVITY OF HORMONAL TREATMENT IN STUMP/LOW GRADE UTERINE LEIOMYOSARCOMA:
A MULTICENTRE RESTROSPECTIVE STUDY FROM THE LEIOMYOSARCOMA FOUNDATION ROUND TABLE**

Roberta Sanfilippo¹; Chiara Fabbroni¹; Isabelle Ray-Coquard²; Fatma Guermazi²; Felix Blanc-Durand³; Robin L Jones⁴; Angelo Paolo Dei Tos⁵; Marisa Nucci⁶; Annie Achee⁷; Bernd Kasper⁸; Paul Huang⁹; Hemming Matthew¹⁰; Rebecca A. Gladdy¹¹; Jonathan C. Trent¹²; Salvatore Provenzano¹; Francesco Raspagliesi¹; Scott Okuno¹³; Paolo G. Casali¹
¹Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY; ²Centre Leon Bérard, Lyon, Centre, FRANCE; ³Gustave Roussy, Paris, Centre, FRANCE; ⁴Royal Marsden NHS Foundation Trust, London, England, UNITED KINGDOM; ⁵Università di Padova (UniPD), Padova, Veneto, ITALY; ⁶Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES; ⁷National Leiomyosarcoma Foundation (NLMSF), Denver, Colorado, UNITED STATES; ⁸Mannheim University Medical Center, Mannheim, Hessen, GERMANY; ⁹The Institute of Cancer Research, London, England, UNITED KINGDOM; ¹⁰Department of Medicine, Columbia University School of Medicine, New York, New York, UNITED STATES; ¹¹Princess Margaret Hospital, University Health Network and Mount Sinai Hospital, Toronto; Lunenfeld Tanenbaum Research Institute, Sinai Health System, Toronto, Toronto, Ontario, CANADA; ¹²Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES; ¹³Mayo Clinic, Rochester, Minnesota, UNITED STATES

Objective: STUMP encompass a group of uterine mesenchymal neoplasms in which the clinical behaviour cannot be predicted on morphological grounds. A malignant clinical evolution is seen in approximately 10-20% of cases. When STUMP relapses, the label of “low-grade leiomyosarcoma” is sometimes found to be appropriate, though current histopathological criteria for uterine leiomyosarcoma (so called “Stanford criteria”) would exclude even the existence of low-grade uterine smooth muscle neoplasms. As they express ER and PR, hormonal treatment with LhRH analogue (LhRHa) or aromatase inhibitors (AI) may represent therapeutic options.

Methods: This is an observational, retrospective, international study that includes relapsing or locally advanced patients with an initial diagnosis of STUMP, treated with hormonal therapy at 4 European sarcoma reference centres. Data from Royal Marsden will be added for the final analysis. The radiological responses were evaluated according to RECIST 1.1 criteria.

Results: Thirty patients were included in our analysis: 26 were treated in first line; 5 in second line and two in third line following failure of chemotherapy (gemcitabine and taxotere, adriamycin and dacarbazine or trabectedin). Eight premenopausal patients were treated in the first line with LhRHa, 5 with a combination of LhRHa and an AI, 11 with AI alone, 1 with selective progesterone receptor modulator and one patient entered menopause and didn't received additional treatment. All patients but one were evaluable for response. Overall, we observed 3 complete response (CR), 11 partial response (PR), 13 stable disease (SD) and 5 progression disease (PD). At a median follow up of 43 months, median progression-free survival for patients treated with hormonal therapy at first line was 50 months without significant differences among the groups of treatment, while median OS is not reached.

Conclusion: In our series of patients with low grade uterine leiomyosarcoma we observed a long lasting response to hormonal treatment in around 50% of patients. Therefore, these patients may make up a subgroup with therapeutic and prognostic relevance. “Stanford criteria” may need to be revised in an effort to improve prognostic and therapeutic stratification of uterine smooth muscle neoplasms, possibly shrinking the scope of currently defined STUMP.



11:21 AM - 11:28 AM

Paper #39 #1818719

ADMINISTRATION OF PATIENT REPORTED OUTCOMES QUESTIONNAIRES IN TENOSYNOVIAL GIANT CELL TUMOR MANAGEMENT: EXPERIENCE FROM TENOSYNOVIAL GIANT CELL TUMOR OBSERVATIONAL PLATFORM PROJECT
Xin Ye PhD¹; Nicholas M. Bernthal²; Florence Mercier³; Petra Laeis³; Michiel van de Sande⁴
¹Daiichi Sankyo, Inc., Basking Ridge, New Jersey, UNITED STATES; ²David Geffen School of Medicine at UCLA, Santa Monica, California, UNITED STATES; ³Daiichi Sankyo Europe GmbH, Munich, Bayern, GERMANY;

⁴Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS

Objective: Diffuse tenosynovial giant cell tumor (D-TGCT) is a rare, locally aggressive neoplasm of joint and tendon sheath synovia. As TGCT causes pain, stiffness, limited joint function and has significant impact on quality of life, patient reported outcomes (PROs) can provide valuable insights to monitor disease progression and manage treatment options. The objective of this study is to examine the practicality of administering PRO questionnaires in a global TGCT disease registry and potential factors associated with the completion of PRO questionnaires.

Methods: The TGCT Observational Platform Project (TOPP) is the first non-interventional, observational disease registry, which enrolled D-TGCT patients from 10 West European and 2 US specialized sarcoma centers between November 2016 and March 2019, with prospective follow-up of 2 years. It aimed at describing the clinical behavior of the disease and assessing the disease burden from patient perspective as measured by PRO questionnaires, including brief pain inventory (BPI) scoring, worst stiffness numerical rating scale (NRS), Patient-Reported Outcomes Measurement Information System (PROMIS) physical function and EuroQol-5 Dimension 5 Level (EQ-5D-5L). These PRO questionnaires are collected at baseline and every 6 months during the 2-year follow up periods. The completion rates for PRO questionnaires were examined at each timepoint. Generalized linear mixed logit models were used to explore the factors that might be associated with the completion rate.

Results: Of 183 total patients who entered the study, 176 patients (108 females, 61.4%) were included in the full analysis set (FAS; mean age: 43.5 years; range 18-77). All PRO questionnaires were completed by over 90% of patients at baseline, demonstrating a strong willingness to participation. The completion rates varied from 70%-83% during the 2-year follow up period, which were still considered high for non-interventional studies. The detailed results are presented in Table 1. Patients who had onsite/phone visits and age of ≥ 40 were more likely to complete PRO questionnaires. The type of questionnaires and TGCT disease characteristics including diagnosis type, disease severity and treatments were not associated with the completion rates (Table 2).

Conclusion: Patient perspective plays an important role on TGCT management. Based on the experience from TOPP registry, PRO questionnaires regardless of whether they consist of single item question or multiple questions can be successfully administered and integrated into clinical practice of TGCT management.

Table 1: PRO questionnaire completion rates in TOPP

Questionnaire	Baseline		6 Months		12 Months		18 Months		24 Months	
	(Onsite)		(Remote)		(Onsite/phone)		(Remote)		(Onsite/phone)	
	N	%	N	%	N	%	N	%	N	%
BPI	168	95.5	138	78.4	139	79.0	125	71.0	146	83.0
Worst Stiffness NRS	165	93.8	137	77.8	137	77.8	123	69.9	143	81.3
PROMIS PF	169	96.0	137	77.8	138	78.4	124	70.5	146	83.0
EQ-5D	169	96.0	138	78.4	138	78.4	124	70.5	145	82.4

BPI = brief pain inventory; EQ-5D = EuroQol-5 Dimension; NRS = numerical rating scale; PROMIS PF = Patient-Reported Outcomes Measurement Information System Physical Function; TOPP = TGCT Observational Platform Project.

Table 2: Generalized linear mixed logit models on PRO completion

Variable	Category	Type III p-value	OR [95%CI]	LS estimate of % of completion [95% CI]
Type of questionnaire*	BPI	0.8556	1.015 [0.829; 1.243]	81.36% [77.26%; 84.87%]
	EQ-5D-5L		1.000 [0.818; 1.223]	81.14% [77.01%; 84.67%]
	NRS		0.937 [0.769; 1.141]	80.11% [75.89%; 83.75%]
	PROMIS		Ref	81.14% [77.01%; 84.67%]
Type of visit	No contact with the site	<0.0001	0.495 [0.431; 0.569]	74.30% [69.61%; 78.49%]
	On site/Phone		Ref	85.37% [82.09%; 88.14%]
Gender	F	0.3321	1.246 [0.799; 1.944]	82.27% [77.83%; 85.98%]
	M		Ref	78.83% [72.47%; 84.04%]
Age	< 40 years	0.0099	0.562 [0.363; 0.871]	75.97% [69.63%; 81.33%]
	>= 40 years		Ref	84.90% [80.68%; 88.33%]
Country	Austria	<0.0001	4.255 [1.359; 13.322]	90.02% [76.35%; 96.18%]
	Germany		4.661 [1.587; 13.689]	90.80% [79.15%; 96.25%]
	Spain		0.667 [0.267; 1.671]	58.58% [39.55%; 75.35%]
	France		8.985 [1.062; 76.048]	95.01% [70.46%; 99.35%]
	United Kingdom		0.254 [0.044; 1.452]	35.00% [9.20%; 74.11%]
	Italy		3.657 [1.790; 7.472]	88.57% [82.26%; 92.83%]
	The Netherlands		3.022 [1.602; 5.701]	86.49% [81.18%; 90.48%]
	United States of America		Ref	67.94% [56.31%; 77.70%]
Diagnosis	Primary diagnosis	0.7543	0.932 [0.602; 1.445]	80.47% [75.49%; 84.64%]
	Recurrent disease		ref	81.54% [76.10%; 85.97%]
Severity	Moderate diffuse	0.959	0.963 [0.601; 1.542]	80.76% [74.60%; 85.71%]
	Not assessable		0.904 [0.442; 1.848]	79.76% [67.36%; 88.26%]
	Severe diffuse		Ref	81.34% [76.24%; 85.56%]
TGCT at baseline (1)	Naive (no prior TGCT treatment)	0.8404	0.830 [0.441; 1.564]	78.58% [68.10%; 86.31%]
	Primary diagnosis and at least one prior TGCT treatment		0.979 [0.608; 1.577]	81.22% [75.37%; 85.94%]
	Recurrent disease and at least one prior TGCT treatment		Ref	81.54% [76.09%; 85.98%]
TGCT at baseline (2)	Primary diagnosis without any prior TGCT treatment	0.5587	0.839 [0.465; 1.513]	78.58% [68.13%; 86.29%]
	Refractory patients with any prior TGCT treatment		Ref	81.39% [77.53%; 84.72%]
Time from diagnosis to baseline (months)		0.2922	1.002 [0.999; 1.004]	
Number of symptoms at baseline		0.6353	0.958 [0.804; 1.143]	
TGCT treatment at baseline	TGCT currently being treated or planned to be treated	0.5212	0.866 [0.559; 1.343]	79.95% [74.86%; 84.23%]
	Wait and see		Ref	82.16% [76.85%; 86.46%]
Previous treatment at baseline	No prior treatment / wait and see	0.3678	0.633 [0.322; 1.244]	78.58% [68.12%; 86.30%]
	Only surgery		0.672 [0.401; 1.127]	79.57% [73.90%; 84.27%]
	Only systemic treatment		0.583 [0.246; 1.381]	77.16% [61.20%; 87.85%]
	Surgery and other treatment		Ref	85.29% [79.42%; 89.70%]

Each criterion was tested one by one in a mixed logit model with repeated measurements, adjusted on the type of questionnaire.

* Mixed logit model with repeated measurements with type of questionnaire as covariable only

BPI = brief pain inventory; CI = Confidence Interval; EQ-5D-5L = EuroQol-5 Dimension 5 Level; F = female; LS=Least-Squares; M = male; NRS = numerical rating scale; OR=Odds Ratio; PROMIS = Patient-Reported Outcomes Measurement Information System; Ref = reference group; TGCT = tenosynovial giant cell tumor; TOPP = TGCT Observational Platform Project.



11:28 AM - 11:35 AM

Paper #40 #1818744

THE NATURAL HISTORY OF GANGLIONEUROMA: AN INTERNATIONAL STUDY BY THE TRANSATLANTIC AUSTRALASIAN RETROPERITONEAL SARCOMA WORKING GROUP

Sangkyu Noh¹; Carolyn Nessim²; Emily Z. Keung³; Dirk Strauss⁴; Ferdinando Cananzi⁵; Jun Chen⁶; Rebecca Gladdy⁷; Samuel J. Ford⁸; Piotr Rutkowski⁹; Elisabetta Pennacchioli¹⁰; Kenneth Cardona¹¹; Daphne Hompes¹²; Attila Kollár¹³; Nikolaos Vassos¹⁴; Chandrajit P. Raut¹⁵; Dagmar Adamkova Krakorova¹⁶; Sergio Quildrian¹⁷; Andraz Perhavec¹⁸; Eran Nizri¹⁹; Jeffrey Farma²⁰

¹Western University of Health Sciences, College of Osteopathic Medicine of the Pacific, Del Mar, California, UNITED STATES; ²The Ottawa Hospital, Ottawa, Ontario, CANADA; ³The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES; ⁴The Royal Marsden Hospital NHS Foundation Trust, London, England, UNITED KINGDOM; ⁵Humanitas Clinical and Research Center, Humanitas University, Milan, Lombardia, ITALY; ⁶Peking University International Hospital, Beijing, Beijing, CHINA (PEOPLE'S REPUBLIC); ⁷Mount Sinai Hospital, University Health Network, Toronto, Ontario, CANADA; ⁸University Hospital Birmingham NHS Foundation Trust, Birmingham, England, UNITED KINGDOM; ⁹Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Mazowieckie, POLAND; ¹⁰IEO European Institute of Oncology, Milan, Lombardia, ITALY; ¹¹Winship Cancer Institute, Emory University, Atlanta, Georgia, UNITED STATES; ¹²Department of Surgical Oncology, University Hospitals Leuven, Leuven, Belgium, Leuven, Vlaams-Brabant, BELGIUM; ¹³Inselspital, Universitätsspital Bern, Bern, Bern, SWITZERLAND; ¹⁴Division of Surgical Oncology, Mannheim University Medical Center, University of Heidelberg, Mannheim, Baden-Württemberg, GERMANY; ¹⁵Harvard Medical School, Dana-Farber Cancer Institute, Harvard University, Boston, Massachusetts, UNITED STATES; ¹⁶Masaryk Memorial Cancer Institute, Brno, Jihomoravsky Kraj, CZECH REPUBLIC; ¹⁷Buenos Aires British Hospital; Angel Roffo Institute of Oncology, University of Buenos Aires, Buenos Aires, Buenos Aires, ARGENTINA; ¹⁸Institute of Oncology Ljubljana, Ljubljana, Ljubljana, SLOVENIA; ¹⁹Tel Aviv Sourasky Medical Center, Tel Aviv, Tel Aviv, ISRAEL; ²⁰Fox Chase Cancer Center, Philadelphia, Pennsylvania, UNITED STATES

Objective: Ganglioneuromas (GN) are rare tumors that most often originate from neural crest cells along the sympathetic chain and within the adrenal glands. Data on these tumors are limited to case reports and small single-institution case series. Therefore, the Transatlantic Australasian Retroperitoneal Sarcoma Working Group (TARPSWG) conducted a retrospective, multi-institutional review of GN to increase our understanding of the presentation, natural history, and approaches to management of GN.

Methods: We examined patient demographics, clinicopathologic features, radiological findings, and management of GN. Patients of all ages with pathologically confirmed GN located in the retroperitoneum, abdomen, and pelvis diagnosed between January 1, 2000, and January 1, 2020 were included in the study. Head and neck, mediastinal, and submucosal gastrointestinal tract tumors were excluded.

Results: Overall, 319 patients from 29 institutions and 5 continents were included. The median age at diagnosis was 37 years and 58% of patients were females. Tumor locations included the extra-adrenal retroperitoneum (65%), adrenal glands (20%), pelvis (11%), and peritoneal cavity (3%). Ninety-seven percent of GN presented sporadically and 42% presented with symptoms. At baseline, the median maximum tumor diameter was 7 cm (IQR 5–10) and the median tumor volume was 68 cm³ (IQR 29–213). Major vascular (arterial and/or venous) encasement occurred in 17% (N=54) of patients and 76% of these occurred primarily in the retroperitoneum. Major nerve involvement occurred in 8% of tumors. One hundred three (32%) patients underwent non-operative management and active surveillance while 216 (68%) patients underwent resection with 75% of operative cases achieving an R0/R1 resection. Based upon histopathology, malignant degeneration to neuroblastoma was rare (3%, N=10). Non-operative cases had a median follow-up of 20.9 months (IQR 8.8–39.8), and 94% of GN had stable tumor size with 6% displaying tumor growth. During a median follow-up of 36 months (IQR 12.2–67.7) for resected tumors, 82% of patients were disease-free post-resection. GN recurrences were documented in 6 cases (3%).

Conclusion: To date, this is the largest study describing the demographic, clinicopathologic, and radiologic features of GN. While nearly half of patients present with symptoms, most GN have indolent biology and rarely have malignant transformation to neuroblastoma. Operative management with R0/R1 resection may render patients disease-free with rare recurrences. Overall, this study may inform the development of guidelines for the surveillance and management of ganglioneuroma.

Table 1: Patient Demographics and Clinical Features	Number (%)
Total Number of Patients	319
Median Age at Diagnosis	37
Sex	
Male	133 (42)
Female	186 (58)
Location of Ganglioneuroma	
Retroperitoneal	206 (65)
Adrenal	63 (20)
Pelvic	35 (11)
Intra-abdominal	10 (3)
Presentation	
Symptomatic	134 (42)
Incidental	184 (58)
ASA Grade at Referral	
I	150 (47)
II	105 (33)
III	21 (7)
IV	1 (0.3)
Ganglioneuroma Suspected on Imaging	
Yes	76 (24)
No	190 (60)
Vascular Encasement	
Yes	54 (17)
Major Nerve Involvement	
Yes	26 (8)
History of Peripheral Nerve Tumors	9 (3)
PMHx of Neurofibromatosis Type 1	7
PMHx of Schwannomatosis	1
PMHx of Men2A	1

Table 2: Baseline Tumor Volume	Median in cm ³ (Interquartile Range)
Overall (N=143)	68 (29 – 213)
Sex	
Male (N=66)	66 (29 – 206)
Female (N=77)	76 (28 – 213)
Tumor Location	
Retroperitoneal (N=96)	76 (35 – 213)
Adrenal (N=28)	25 (12 – 75)
Pelvic (N=18)	230 (80 – 269)
Intra-abdominal (N=1)	15
Presentation	
Symptomatic (N=57)	92 (34 – 246)
Incidental (N=86)	58 (23 – 175)
Vascular Encasement	
Yes (N=28)	205 (97 – 337)
No (N=93)	44 (22 – 143)
Nerve Involvement	
Yes (N=12)	58 (20 – 270)
No (N=110)	58 (26 – 192)
Non-resected Tumors (N=62)	96 (34 – 231)
Resected Tumors (N=82)	62 (25 – 175)
R0/R1 (N=66)	62 (25 – 160)
R2 (N=11)	80 (16 – 479)

Table 3: Tumor Management and Follow-Up	Number (%)
Non-Operative Management	103 (32)
Surgery	216 (68)
R0/R1 Resection	161 (75)
R2 Resection	25 (12)
Degeneration to Neuroblastoma	10 (3)
Median Follow-Up	26.4 months (IQR 10.5 – 55.2)
Non-operative management	20.9 months (IQR 8.8 – 39.8)
Surgery	36 months (IQR 12.2 – 67.7)
Status at Last Contact: Non-Operative Management (N=103)	
Disease free post-biopsy	4 (4)
Primary ganglioneuroma still present	88 (85)
Status at Last Contact: Surgery (N=216)	
Recurrence	6 (3)
Disease free post-excision	178 (82)
Primary ganglioneuroma still present	5 (2)
Residual disease	14 (6)
Living Status: No surgery (N=103)	
Alive	99 (96)
Dead	1 (1)
Living Status: Surgery (N=216)	
Alive	203 (94)
Dead	6 (3)



11:35 AM - 11:42 AM

Paper #41 #1818779

DOXORUBICIN-ELUTING BEAD TRANSARTERIAL CHEMOEMBOLIZATION (DEB-TACE) IN EXTRA-ABDOMINAL DESMOID TUMORS: INITIAL EXPERIENCE

DaeHee Kim¹; Mary Lou Keohan²; Mrinal M. Gounder²; Aimee M. Crago²; Joseph P. Erinjeri²

¹The Warren Alpert Medical School of Brown University, Providence, Rhode Island, UNITED STATES;

²Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES

Objective: To evaluate the efficacy and safety of Doxorubicin-eluting bead transarterial chemoembolization (DEB-TACE) in extra-abdominal desmoid fibromatosis patients.

Methods: Eleven female patients (mean age = 40.09 years) with symptomatic, progressively enlarging extra-abdominal desmoid tumors were treated with Doxorubicin DEB-TACE after failing or refusing systemic therapy. Six rectus sheath, one chest wall, three axillary, and one upper extremity desmoid tumor patients were included. The median follow-up period was 154.50±53.46 days (Range: 93 to 261 days). Treatment response was assessed by imaging findings in follow-up MRI as well as maximum subjective pain scores.

Results: All procedures were technically successful without immediate procedure-related complications. The average size of the tumor treated was 161.81±119.97ml. The mean doxorubicin dose was 13.32±7.77mg/m² and the average dose per volume of the tumor was 0.20±0.14 mg/ml. All patients experienced temporary discoloration of skin overlying the tumor which improved over time without additional medical treatment. No higher-grade adverse events were observed. Initial one-month follow-up MRI demonstrated partial to near-complete necrosis of tumor in all patients, ranging from 1.44% to 97.56% (mean necrosis volume of 36.39±31.25%) while there was an improvement of subjective pain scores in 6 out of 11 patients (54.54%). Additional follow-up revealed further overall tumor volume reduction and improved subjective pain scores in 10 out of 11 patients (90.90%). In 10 out of 11 patients (90.90%), the enhancing portions of residual tumors seen on the first month MRI exhibited further volume loss with a mean percentage reduction of -38.10±15.30% in further follow-up imaging ($p=0.0041$). Residual tumors also demonstrated a statistically significant T2 signal intensity decrease with an average percent reduction at -29.58±31.99% on the last available follow-up ($p=0.0217$), suggesting a reduction in cellularity of the tumor.

Conclusion: DEB-TACE may be a safe and effective treatment in symptomatic, non-surgical desmoid patients who fail or refuse systemic therapy.



ctos[®]

2021 *Virtual* Annual Meeting

Oral Presentations

Friday, November 11, 2021



12:40 pm - 1:15 pm

– Young Investigator Awards –

AWARD PAPER

12:40 PM - 12:48 PM

#1862531

SARCOMA CELLULAR ECOSYSTEMS ARE ASSOCIATED WITH PROGNOSIS AND PREDICT IMMUNOTHERAPY RESPONSE

Everett J. Moding; Timothy J. Sears; Neda Nemat-Gorgani; Bogdan A. Luca; Chloe B. Steen; Maggie Y. Zhou; David G. Mohler; Matt van de Rijn; Kristen N. Ganjoo; Greg W. Charville; Nam Bui; Aaron M. Newman
Stanford University School of Medicine, Stanford, California, UNITED STATES

Objective: The sarcoma microenvironment consists of malignant, immune, and stromal cells that contribute to tumor development, progression, and response to therapy. However, large-scale profiling of the diverse cellular states within sarcomas and their patterns of co-occurrence has been challenging in fixed clinical specimens. We applied a novel machine learning framework called EcoTyper to identify and validate fundamental sarcoma cell states and ecosystems associated with patient outcomes and response to immunotherapy.

Methods: EcoTyper purifies cell type-specific gene expression from bulk transcriptomic data using CIBERSORTx (Newman et al. Nat. Biotechnol. 2019), identifies transcriptional states for each cell type that can be validated using single cell RNA-sequencing (scRNA-Seq), and defines tumor ecotypes consisting of co-occurring cell states (Luca et al. AACR 2020). We discovered sarcoma cell states and ecotypes by applying EcoTyper to soft tissue sarcomas profiled by The Cancer Genome Atlas (TCGA). We assessed the association between cell states or ecotypes and patient outcomes from TCGA (n=206) along with an independent validation cohort (Chibon et al. Nat. Med. 2010, n=193) using multivariable Cox proportional hazards models including histology as a covariate. In addition, we analyzed bulk RNA sequencing from formalin fixed paraffin embedded samples in a cohort of patients treated with ipilimumab and nivolumab for metastatic sarcoma (n=30).

Results: We identified 23 transcriptionally-defined cell states in malignant, immune, and stromal cells that were validated in independent scRNA-Seq and bulk gene expression datasets. Cell states reflected known and novel cell phenotypes and many were strongly associated with patient outcomes. By identifying sarcomas with co-occurring cell states, we discovered three sarcoma ecotypes with distinct clinical outcomes. One ecotype (SE3) defined by inflammatory macrophages and epithelial-like malignant cells with upregulated mTORC1 signaling was associated with inferior progression-free survival (PFS) in the discovery cohort (P=0.04) and inferior metastasis-free survival in the independent validation cohort (P=0.0034). However, this ecotype was associated with improved PFS in patients treated with ipilimumab and nivolumab (P=0.002), suggesting this ecotype may enable identification of patients with sarcoma who could benefit from immune checkpoint inhibition.

Conclusion: Using a new computational framework to enable large-scale dissection of the sarcoma microenvironment, we identified novel cell states and cellular communities associated with survival outcomes and response to immune checkpoint inhibition. Further evaluation in prospective clinical cohorts could improve patient stratification and lead to the development of novel therapeutic approaches in sarcomas.



ctos®

2021 Virtual Annual Meeting

Oral Presentations

Friday, November 11, 2021



12:40 pm - 1:15 pm

– Young Investigator Awards –

AWARD PAPER

12:48 PM - 12:56 PM

#1862532

ADJUVANT IMATINIB IN GIST PATIENTS HARBORING EXON 9 KIT MUTATIONS: RESULTS FROM A MULTI-INSTITUTIONAL EUROPEAN RETROSPECTIVE STUDY

Andrea Napolitano¹; Bruno Vincenzi¹; Marta Fiocco²; Olivier Mir³; Piotr Rutkowski⁴; Jean-Yves Blay⁵; Peter Reichardt⁶; Heikki Joensuu⁷; Elena Fumagalli⁸; Margherita Nannini⁹; Antonine Italiano¹⁰; Giovanni Grignani¹¹; Antonella Brunello¹²; Silvia Gasperoni¹³; Tommaso Martino De Pas¹⁴; Giuseppe Badalamenti¹⁵; Maria A. A. Pantaleo¹⁶; Winan J. van Houdt¹⁷; Nikki S. IJzerman¹⁷; Neeltje Steeghs¹⁷

¹Università Campus Bio-Medico di Roma, Roma, Lazio, ITALY; ²The Leiden University Medical Center, Zuid-Holland, NETHERLANDS; ³Gustave Roussy, Villejuif, Ile-de-France, FRANCE; ⁴Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Mazowieckie, POLAND; ⁵Centre Léon Bérard, Lyon, Auvergne, FRANCE; ⁶Helios Klinikum Berlin-Buch, Berlin, Berlin, GERMANY; ⁷Helsinki University Hospital and University of Helsinki, Helsinki, Uusimaa, FINLAND; ⁸Fondazione IRCCS Istituto Nazionale Dei Tumori Di Milano, Milan, Lombardia, ITALY; ⁹IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Emilia-Romagna, ITALY; ¹⁰Institute Bergonié, Bordeaux, Aquitaine, FRANCE; ¹¹Candiolo Cancer Institute FPO-IRCCS, Candiolo, Piemonte, ITALY; ¹²Istituto Oncologico Veneto IOV – IRCCS, Padova, Veneto, ITALY; ¹³University Hospital Careggi, Florence, Toscana, ITALY; ¹⁴IEO - European Institute of Oncology IRCCS, Milan, Lombardia, ITALY; ¹⁵Policlinico “Paolo Giaccone”, University of Palermo, Palermo, Sicilia, ITALY; ¹⁶IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Emilia-Romagna, ITALY; ¹⁷The Netherlands Cancer Institute; Amsterdam, Noord-Holland, NETHERLAND

Objective: Gastrointestinal stromal tumors (GIST) are the most common type of sarcoma arising in the digestive tract and are characterized by the common presence of oncogenic mutations in genes encoding the KIT or PDGFRA receptor tyrosine kinases. The most common KIT mutations are in exon 11 and they are present in approximately 70% of the cases. Exon 9 mutations are detected in 9% of all GIST and 22% of small bowel GIST. An analysis of two randomized trials comparing imatinib 400 mg/d and 800 mg/d in advanced GIST demonstrated a significantly longer progression-free survival (PFS) for patients with KIT exon 9 tumors treated with 800 mg/d. No difference in PFS was observed in patients with exon 11-mutated GIST treated at the two doses. For this reason, imatinib 800 mg/d is often proposed as first-line treatment for metastatic GIST patients with exon 9 mutations where national and institutional policies allow it. The effect of high-dose imatinib (800 mg/d) on survival in the adjuvant treatment of patients with resected KIT exon-9 mutated GIST is however not established. Here, the association of dose and other clinicopathological variables with survival was evaluated in a large multi-institutional European cohort.

Methods: Data from 185 patients were retrospectively collected in 23 European GIST reference centers. Propensity score matching (PSM) and inverse-probability of treatment weighting (IPTW) were used to account for confounders. Results were analysed considering the intended- dose (ID) population, which included all the selected patients based on the imatinib dose they were originally prescribed at the start of the adjuvant treatment (analogous to a prospective intention-to-treat population). Univariate and multivariate unweighted and weighted Cox proportional hazard regression models were estimated for: relapse-free survival (RFS), defined as the interval from curative surgery to the date of radiologically confirmed disease relapse or death, whichever occurred first; modified RFS (mRFS), defined as the interval from the end of adjuvant treatment to the date of radiologically confirmed disease relapse or death, whichever occurred first; imatinib failure-free survival (IFFS), defined as the interval from curative surgery to the date of start of a new systemic treatment other than imatinib, the start of a combination of imatinib with a new systemic treatment, or death resulting from any cause, whichever occurred first. Univariate Cox models were estimated for overall survival.

Results: Of the 185 patients, 131 (70.8%) received a starting dose of 400 mg/d and the remaining 54 (29.2%) a dose of 800 mg/d. Baseline characteristics were partially unbalanced, suggesting a potential selection bias (Table 1). In the ID popula-

tion, the median RFS for the 400 mg/d and 800 mg/d group were respectively 80.6 months (95% CI 62.1-126.2) and 62.0 months (95% CI 49.8-99.0) (Fig 1A). The population for mRFS analysis was represented by a subset of the original ID population who did not include those patients with relapse while on treatment or with adjuvant treatment still ongoing at the time of database lock. It included 90 patients in the 400 mg/d group and 42 patients in the 800 mg/d group. The median mRFS for the 400 mg/d and 800 mg/d group were respectively 106.1 months (95% CI 66.7-infinity) and 30.1 months (95% CI 23.1- infinity). For the analysis of IFFS, the ID population was used. The median IFFS for the 400 mg/d and 800 mg/d group were respectively 135.8 months (95% CI 111.0-infinity) and 91.0 months (95% CI 67.3-infinity) (Fig 2A). PSM and IPTW analyses showed no advantage of imatinib 800 mg/d in RFS (Fig 1B and 1C), mRFS and IFFS (Fig 2B and 2C). In the weighted multivariate Cox models, high-dose imatinib was not associated to the survival outcomes (RFS: HR 1.24, 95% CI 0.79-1.94; mRFS: HR 1.69, 95% CI 0.92-3.10; IFFS: HR 1.35, 95% CI 0.79-2.28). The variables consistently associated with worse survival outcomes were high mitotic index and non- gastric tumor location (Table 2).

Conclusion: In this multi-institutional retrospective case series analysis of 185 KIT exon 9-mutated GIST patients who received adjuvant imatinib either at 400 mg/d or 800 mg/d, depending on institutional policies and/or physician's choice, we did not find any statistically significant and/or relevant difference between the two cohorts in terms of RFS, mRFS, IFFS and OS. Higher mitotic count and non-gastric primary tumor site were associate to survival outcomes. The very fact that up to 30% of these patients are treated in expert centers with a dose of 800 mg/d despite the lack of any prospective study underscores how evidence based medicine is difficult to implement in the field of rare tumors. Our results have been generated by a large collaborative network of more than 20 European centers. Although challenging, such networks could potentially embark on a prospective effort to clarify the role of adjuvant imatinib in KIT exon 9-mutated GIST patients. Currently, there are no open trials specifically recruiting these patients in the adjuvant setting.



ctos®

2021 Virtual Annual Meeting

Oral Presentations

Friday, November 11, 2021



1:15 pm - 2:30 pm

– Session 8 –

ONCOLOGY AND CLINICAL TRIALS

1:15 PM - 1:22 PM

Paper #42 #1818712

LONG-TERM EVALUATION OF NBTXR3, A NOVEL RADIOENHANCER, PLUS RADIOTHERAPY IN PATIENTS WITH LOCALLY ADVANCED SOFT TISSUE CARCINOMA TREATED IN THE PHASE II/III ACT.IN.SARC TRIAL

Sylvie Bonvalot¹; Piotr L. Rutkowski²; Juliette Thariat³; Sébastien Carrère⁴; Anne Ducassou⁵; Marie-Pierre Sunyach⁶; Peter Agoston⁷; Angela Hong⁸; Augustin Mervoyer⁹; Marco Rastrelli¹⁰; Cécile Le Péchoux¹¹; Victor Moreno¹²; Rubi K. Li¹³; Béatrice Tiangco¹⁴; Zsusanna Papai¹⁵

¹Institut Curie, PSL Research University, Paris, Ile-de-France, FRANCE; ²Maria Sklodowska-Curie Institute -Oncology Center, Institute of Oncology, Warsaw, Mazowieckie, POLAND; ³Centre François Baclesse, Caen, France; Department of Radiation Oncology, Centre Lacassagne, Nice, Provence-Alpes-Cote d'Azur, FRANCE; ⁴Centre Regional De Lutte Contre Le Cancer Paul Lamarque, Montpellier, Languedoc-Roussillon, FRANCE; ⁵Institut Claudius Regaud (ICR), Institut Universitaire du Cancer de Toulouse-Oncopole (IUCT-O), Toulouse, Languedoc-Roussillon, FRANCE;

⁶Léon Bérard Cancer Center, Lyon, Rhone-Alpes, FRANCE; ⁷Országos Onkologiai Intézet, Budapest, Budapest, HUNGARY;

⁸Chris O'Brien Lifecare and The University of Sydney, Camperdown, Victoria, AUSTRALIA; ⁹Institut de Cancerologie de l'Ouest- Rene Gauducheau, Saint-Herblain, Pays de la Loire, FRANCE; ¹⁰Istituto Oncologico Veneto IRCCS, Padova, Veneto, ITALY; ¹¹Gustave Roussy, Villejuif, Ile-de-France, FRANCE; ¹²Hospital Fundación Jimenez Diaz, Madrid, Madrid, SPAIN; ¹³St. Luke's Medical Center, Quezon City, Quezon, PHILIPPINES; ¹⁴The Medical City APS Cancer Institute, Pasig City, Rizal, PHILIPPINES; ¹⁵Medical Centre, Hungarian Defence Forces, Budapest, Budapest, HUNGARY

Objective: NBTXR3, a novel radioenhancer activated by radiotherapy (RT), demonstrated superior efficacy, as preoperative treatment, in patients with locally advanced soft tissue sarcoma (LA STS), compared to RT alone. Primary endpoint of pCR rate was 16% vs 8% (p=0.044) and R0 margin rate was 77% vs 64% (p=0.042) (Bonvalot et al. Lancet Oncol. 2019). No modification of the early safety profile of RT was observed, leading to market authorization. Here we report on the long-term safety, limb function and quality of life.

Methods: This phase II/III randomized (1:1), international trial included adult patients with LA STS of the extremity or trunk wall, requiring preoperative RT (NCT02379845). Patients were treated with either a single intratumoral injection of NBTXR3 (volume equivalent to 10% of tumor volume, at 53.3g/L) plus EBRT (arm A), or EBRT alone (arm B) (50 Gy in 25 fractions), followed by surgery. Safety of NBTXR3+RT, as preoperative treatment, was evaluated as a secondary endpoint. We present the safety analyses done in the "all treated population", with data recorded during at least a two-year follow-up. Important parameters related to HR-QoL, including functional outcome were studied using the EQ-5D, RNLI, TESS and MST5 questionnaires.

Results: Patients had at least two-year follow-up and the lost to follow-up rate was very low (1.9%). RT-related SAEs were observed in 11.2% in arm A (10/89) vs 13.3% (12/90) in arm B. Post-treatment AEs, any grade, were observed in 51.7% (46/89) vs 57.8% (52/90) and serious post-treatment AEs in 13.5% (12/89) vs 24.4% (22/90) of patients in arms A vs B. Second primary cancer was observed in 1 patient in arm A and 6 patients in arm B. Long-term safety demonstrated that NBTXR3+RT has no impact on post-surgical wound complications (24.7% vs 36.7%, arms A vs B). The evaluation of late radiation toxicities in limbs such as fibrosis (4.5% vs 7.7%), arthrosis (2.2% vs 0.0%) and edema (6.7% vs 2.2%) showed no significant difference between arms. HR-QoL evaluation yielded no difference in functional outcome. In addition, the intratumoral injection of NBTXR3 did not induce cancer cell seeding at the former tumor site. Sequelae or chronic tissue disturbances at the former tumor localization were similar in both treatment arms, confirming that the increase of energy dose deposit and the physical presence of NBTXR3 did not impact post-treatment limb function.

Conclusion: The long-term safety results demonstrate that the addition of NBTXR3 to EBRT neither added toxicity nor modified the long-term safety of RT. The results presented here associated with the efficacy data reported previously reinforce the favorable benefit-risk ratio of the use of NBTXR3 in patients with LA STS.



1:22 PM - 1:29 PM

Paper #43 #1818754

PROSPECTIVE SINGLE-ARM CONTROLLED TRIAL OF 3-WEEK-COURSE HYPOFRACTIONATED PREOPERATIVE RADIOTHERAPY FOR SOFT TISSUE SARCOMA OF THE EXTREMITY OR TRUNK

B. Ashleigh Guadagnolo; Devarati Mitra; Ahsan Farooqi; Caroline Hempel; Courtney Dorber; Rony Mathai; Wei-Lien Wang; Ravin Ratan; Keila E. Torres; Neeta Somaiah; Kelly K. Hunt; Christopher P. Scally; Emily Z. Keung; Robert Satcher; Justin E. Bird; Patrick Lin; Bryan Moon; Valerae Lewis; Christina L. Roland; Andrew J. Bishop MD
The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES

Objective: The standard pre-operative radiation therapy (RT) dose of 50 Gy in 25 daily fractions for soft tissue sarcoma (STS) contributes to excellent local control and is associated with major wound complications (MWC) in approximately 35% of patients. We sought to prospectively investigate whether a radiobiologically equivalent dose given in a 3-week course of 42.75 Gy in 15 daily fractions confers a higher risk of MWC.

Methods: We conducted a prospective, single-arm, non-randomized trial of hypofractionated preoperative RT consisting of 42.75 Gy in 15 once-daily fractions followed by surgery 4-8 weeks after RT completion for adult patients with non-metastatic, previously un-irradiated STS of the extremity or superficial trunk. Patients were enrolled after biopsy-confirmation of STS between December 18, 2018 and January 6, 2021. The primary outcome of the study was to determine the rate of MWC within 120 days of surgery among patients treated with the trial regimen. The rate of MWC was monitored using a Bayesian stopping rule One-Arm Time-To-Event Simulator that assessed the posterior probability of development of MWC at 120 days post-surgery among patients treated on study compared to the historical prior based upon a rate of 35%. Secondary endpoints include cancer control outcomes and patient reported functional outcomes. Descriptive statistics were used to present baseline characteristics. Significance of difference between proportions was evaluated with the c2 test. The Kaplan-Meier method was used to estimate local control. Multiple logistic regression was used to determine adjusted likelihood of MWC.

Results: We enrolled 120 patients. Median follow-up from the date of surgery was 15 mos (interquartile range [IQR] 8-22). Median age was 60 years (IQR 48-69) and median maximum tumor size was 7.6 cm (IQR 4.5-12.8). A majority of the patients were male (n=70, 58%), non-Hispanic white (n=85, 71%), and had lower extremity (LE) tumors (n=78, 65%; upper extremity (UE), n=20, 17%; trunk, n=22, 18%). Tumor grade was: high in 51% (n=61), intermediate in 23% (n=27), low in 8% (n=9), or not gradeable in 18% (n=22). One patient, whose diagnosis was revised to melanoma after excision, is included for the primary MWC endpoint but not secondary endpoint analyses. All patients received 42.75 Gy (or CGE) in 15 once-daily fractions with either: IMRT (n=57, 48%), 3D-RT (n=55, 46%), electrons (n=5, 4%), or protons (n=3, 3%). None experienced acute skin toxicity of CTCAE v4.0 grade 3 or greater (grade 1: n=72, 60%; grade 2: n=9, 8%). Thirty-seven (31%) patients developed MWC within 120 days of surgery (median: 37 days, IQR 25-59 days). In univariate analyses, fewer patients with UE tumors developed MWC (5%) compared to LE (35%) and truncal tumors (41%) (p=0.02) and those with diabetes mellitus (n=12) were significantly more likely to develop MWC (53% vs. 28%, p=0.04). MWC was not significantly associated with age, tumor size, performance status, body mass index, recurrent presentation, RT modality/technique, or receipt of neoadjuvant chemotherapy. In adjusted analyses, UE tumor was less likely to be associated with MWC (OR: 0.10, 95% CI: 0.13-0.80) and diabetes mellitus had higher likelihood of MWC (OR: 3.31, 95% CI: 1.02-10.71). Four patients (3%) developed local recurrence at a median 11 mos (IQR 4-18) and all were in the RT field. One patient required amputation due to local recurrence. Actuarial 2-year local control is 94%. Sixteen patients (13%) developed distant metastases and 6 patients (5%) were deceased at this analysis: 4 with progressive sarcoma at death and 2 of non-sarcoma causes.

Conclusion: Our prospective non-randomized clinical trial revealed that a moderately hypofractionated pre-operative radiotherapy dosing regimen of 42.75 Gy in 15 once-daily fractions resulted in a MWC rate that was not higher than accepted historical rates. Secondary outcomes will be reported with longer patient follow-up, but early analyses show rates of local recurrence that are consistent with those observed with standard fractionation. These data support that this 3-week regimen may offer a safe, effective, and more convenient alternative to 50 Gy in 25 daily fractions for patients undergoing pre-operative RT for STS.



1:29 PM - 1:36 PM

Paper #44 #1818730

A PHASE IA/IB DOSE-ESCALATION/EXPANSION STUDY OF THE MDM2-P53 ANTAGONIST BI 907828 IN PATIENTS WITH ADVANCED/METASTATIC SARCOMA

Mrinal M. Gounder¹; Manish R. Patel²; Noboru Yamamoto³; Todd M. Bauer⁴; Scott Laurie⁵; Alejandro Perez-Pitarch⁶; Junxian Geng⁷; Jan Cheng⁷; Mehdi Lahmar⁶; Patricia LoRusso⁸

¹Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES; ²Sarah Cannon Research Institute, Florida Cancer Specialists & Research Institute, Sarasota, Florida, UNITED STATES; ³National Cancer Center Hospital, Tokyo, Tokyo, JAPAN; ⁴Sarah Cannon Research Institute Tennessee Oncology, Nashville, Tennessee, UNITED STATES; ⁵The Ottawa Hospital Cancer Centre, Ottawa, Ontario, CANADA; ⁶Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Rheinland-Pfalz, GERMANY; ⁷Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, Connecticut, UNITED STATES; ⁸Yale University School of Medicine, Yale Cancer Center, New Haven, Connecticut, UNITED STATES

Objective: The MDM2-p53 antagonist BI 907828 showed anti-tumor efficacy *in vivo*, particularly in *TP53* wild-type, *MDM2*-amplified de-differentiated liposarcoma patient-derived xenografts and syngeneic models. This study aims to evaluate the safety and anti-tumor activity of BI 907828 in patients with advanced solid tumors.

Methods: NCT03449381 is a Phase I study of BI 907828 monotherapy in patients with solid tumors evaluating two dosing schedules (Arm A: Day 1 of 21-day cycles; Arm B: Days 1 and 8 of 28-day cycles). Dose-limiting toxicities (DLTs), pharmacokinetics (PK) and anti-tumor activity were assessed. For the first 6 months, efficacy assessments were every 6 weeks and 8 weeks in Arms A and B, respectively, then every 12 weeks thereafter until disease progression or the start of subsequent anti-cancer therapy.

Results: As of April 2, 2021, 54 patients (29 in Arm A, 25 in Arm B) had been enrolled, among whom 27 had advanced sarcomas. Patients had received a median of 2 prior therapies (range, 0–11). Five patients experienced DLTs during Cycle 1 in Arm A: one grade 3 nausea (45 mg), one grade 3 thrombocytopenia (45 mg), one grade 3 enterocolitis (60 mg), one grade 4 neutropenia (80 mg), and one grade 4 thrombocytopenia (80 mg). In Arm B, 3 patients experienced DLTs during Cycle 1: one grade 4 thrombocytopenia (45 mg), one grade 4 neutropenia associated with grade 4 thrombocytopenia (60 mg), and one grade 3 neutropenia (60 mg). The maximum tolerated dose was determined as 60 mg in Arm A and 45 mg in Arm B. The most common grade 3/4 adverse events were thrombocytopenia (29.6%) and neutropenia (22.2%). Mean plasma exposures (C_{max} and AUC_{0-inf}) increased with dose. In the 27 patients with sarcoma, the disease control rate (defined as complete response + partial response [PR] + stable disease [SD]) was 88.9%. Three of 7 patients with well-differentiated liposarcoma achieved a PR (all were *MDM2*-amplified); 1 remained on treatment for >2 years. All 11 patients with de-differentiated liposarcoma achieved SD as best overall response; the median progression-free survival was approximately 10.8 months (range, 1.3–21 months). Osteosarcoma, gastrointestinal stromal tumor, rhabdomyosarcoma, dermatofibrosarcoma, leiomyosarcoma, and undifferentiated pleiomorphic sarcoma were among the other sarcoma subtypes included in the study. Of these, disease control was notable in 1 patient with myxoid chondrosarcoma (SD = 10 months), 1 with leiomyosarcoma (SD = 14 months) and 1 with undifferentiated pleiomorphic sarcoma (SD = 18+ months).

Conclusion: BI 907828 showed a manageable safety profile, favorable PK, and early signs of anti-tumor activity in patients with sarcoma, especially *MDM2*-amplified well- or de-differentiated liposarcomas. The Phase Ib dose expansion is ongoing.



1:36 PM - 1:43 PM

Paper #45 #1818752

FINAL ANALYSIS FROM AMPECT, AN OPEN-LABEL PHASE 2 REGISTRATION TRIAL OF NAB-SIROLIMUS FOR PATIENTS WITH ADVANCED MALIGNANT PERIVASCULAR EPITHELIOID CELL TUMORS (PECOMA)

Andrew J. Wagner¹; Vinod Ravi²; Richard F. Riedel³; Kristen N. Ganjoo⁴; Brian Andrew A. Van Tine⁵; Rashmi Chugh⁶; Lee D. Cranmer⁷; Erlinda M. Gordon⁸; Jason L. Hornick⁹; Heng Du⁹; Berta Grigorian¹⁰; Anita N. Schmid¹⁰; Shihe Hou¹⁰; Katherine Harris¹⁰; David J. Kwiatkowski⁹; Neil P. Desai¹⁰; Mark A. Dickson¹¹

¹Harvard Medical School, Dana-Farber Cancer Institute, Boston, Massachusetts, UNITED STATES; ²The University of Texas MD Anderson Cancer Center, Houston, UNITED STATES; ³Duke Cancer Institute, Duke University Medical Center, Durham, North Carolina, UNITED STATES; ⁴Stanford Cancer Center, Stanford, California, UNITED STATES;

⁵Washington University School of Medicine, St. Louis, Missouri, UNITED STATES; ⁶University of Michigan, Ann Arbor, Michigan, UNITED STATES; ⁷Univ Washington/Fred Hutchinson Cancer Res Ctr, Seattle, Washington, UNITED STATES;

⁸Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES; ⁹Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES; ¹⁰Aadi Bioscience, Pacific Palisades, California, UNITED STATES;

¹¹Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES

Objective: Malignant perivascular epithelioid cell tumor (PEComa) is a rare, aggressive sarcoma, with no approved treatment. Cytotoxic chemotherapies have limited benefit in this patient population. Case reports suggest that the PI3K/AKT/mTOR pathway is activated in PEComa and mTOR inhibition may be efficacious in this disease. ABI-009 is a novel albumin-bound intravenous mTOR inhibitor with increased tumor uptake, increased mTOR target suppression and distinct pharmacokinetic profile versus oral mTOR inhibitors. The AMPECT trial is the first prospective study in advanced malignant PEComa (NCT02494570). Previously, we reported the primary analysis results which was preplanned when the last enrolled patient had been treated for 6 months, as well as a 1-year follow-up after the primary analysis. At the time, the median duration of response was not reached, >50% of responders were still on treatment. This will be the presentation of the final analysis from AMPECT.

Methods: Patients with malignant PEComa (confirmed by central pathology review), measurable disease and ECOG performance status of 0 or 1 received nab-sirolimus (100 mg/m² IV, weekly, 2/3 weeks) until progression or unacceptable toxicity. Primary endpoint: objective response rate (ORR) by independent radiology review (IRR), assessed every 6 weeks (RECIST v1.1). Secondary endpoints: duration of response (DOR), progression-free-survival rate at 6 month (PFS₆), median PFS and overall survival (OS), and safety. Exploratory endpoints: investigator-assessed outcomes and mutational status.

Results: The final data analysis is planned in September 2021 and the final long-term efficacy, including updated DOR, mature PFS, and mature OS, and safety analyses will be presented.

Conclusion: The AMPECT study met its primary endpoint with an independently assessed ORR of 39% and produced long-term durable responses. This encouraging response rate, durable responses, disease control, PFS, and OS, as well as manageable toxicities supports that nab-sirolimus may provide benefit to patients with this rare and aggressive sarcoma for which there are no approved therapies.



1:43 PM - 1:50 PM

Paper #46 #1818788

A PHASE 2 STUDY OF TALIMOGENE LAHERPAREPVEC, NIVOLUMAB AND TRABECTEDIN (TNT) IN ADVANCED SARCOMA

Sant P. Chawla; Simranjit Sekhon; Ted Kim; Noufil Adnan; Ania Moradkhani; Victoria T. Chua-Alcala; Ishrat Bhuiyan; Kitty Zheng; Erlinda M. Gordon
Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES

Objective: Background and Purpose: Combination Trabectedin (T) and Nivolumab (N) has been shown to be a safe and effective therapy in soft tissue sarcoma (STS). Intratumoral injection of Talimogene laherparepvec (TVEC) has a local oncolytic effect and increases immune response via enhanced recruitment of antigen-presenting cells, and thereby cytotoxic immune response. This study aims to determine the safety and efficacy of the addition of TVEC to combination trabectedin and nivolumab in advanced sarcoma. Objectives: Primary objective: To assess progression-free survival (PFS); Secondary objectives: (1) To evaluate best overall response during treatment period confirmed in a 6-week follow-up, ²PFS rate at 6 and 9 months, ³Overall survival (OS) rate at 6, 9, and 12 months, ⁴Incidence of conversion from unresectable to the resectable tumor, and ⁵Incidence of treatment-related adverse events (TRAEs).

Methods: Patients and Methods: Eligible patients include patients ≥ 18 years of age with locally advanced unresectable or metastatic STS, measurable disease by RECIST v1.1, and at least one accessible tumor for TVEC intratumoral injection. N (3 mg/kg i.v. q 2 weeks), T (1.2 mg/m² i.v. q 3 weeks) and TVEC (1x10⁸ PFU/ml q 2 weeks depending on tumor size) were administered. A starting dose of TVEC (1x10⁶ PFU/ml) was initially given, followed three weeks later by a full dose (1x10⁸ PFU/ml q 2 weeks depending on tumor size).

Results: Efficacy analysis: There were 36 evaluable subjects under the Modified Intention-to-Treat (MITT) population, having completed the first cycle of TNT and a CT or MRI scan at the 6-week follow-up period. The most common histological subtypes in this group include leiomyosarcoma (n=9), liposarcoma (n=5), spindle cell sarcoma (n=3), pleomorphic sarcoma (n=2), Ewing's sarcoma (n=2), and other (n=5). Median number of prior lines of therapy was 4 (range 1-8). Best Overall Response by RECIST v1.1 = 3 PR, 27 SD, 5 PD. One patient, with previously unresectable disease, was taken for resection and was found to have 100% necrosis on surgical pathology. Disease control rate (CR+PR+SD) was 86.1%. The median PFS was >5.5 (range: 1-18) months; 6-month PFS rate: 62.1%. Median PFS on therapy immediately preceding this trial was 2.0 months (range=1-14 months). There were forty-seven evaluable subjects for OS analysis under the Intention-to-Treat (ITT) population. 46/47 ITT patients received T, N, and TVEC. Only one patient received T and N only (no TVEC). Median OS was >9.0 (range 0-20) months; 6-month OS rate: 73%. Safety analysis: There were 47 evaluable subjects under the ITT population. Twenty-three of 47 (48.9%) of these patients experienced at least one >Grade 3 treatment-related adverse event. The most common grade 3/4 TRAEs include anemia (n=12), increased ALT (n=8), fatigue (n=4), thrombocytopenia (n=4), neutropenia (n=4). There were no grade 3/4 TVEC injection site reactions. 22% of patients in the MITT cohort remain on study.

Conclusion: These results suggest that combination therapy with TNT appears to be as effective as standard therapy, with no new safety signals seen. Furthermore, median PFS exceeded that of the immediately preceding lines of therapy in this heavily pre-treated cohort. As data matures, further efficacy and safety data will be reported.



1:50 PM - 1:57 PM

Paper #47 #1818707

SCOPES, AN INNOVATIVE RANDOMIZED TRIAL FOR EXTREMITY SOFT TISSUE SARCOMA PATIENTS: A MODIFIED PICK-THE-WINNER DESIGN

Lisette Wiltink¹; Astrid Scholten²; Augustinus Krol¹; Winan J. van Houdt²; Yvonne M. Schrage¹; Michiel van de Sande¹; Jos A. van der Hage¹; Judith V.M.G. Bovée¹; Marta Fiocco¹; Rick L. Haas²;

¹The Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS; ²The Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS

Introduction: For most intermediate and high grade sarcomas, surgeons strive to preserve essential neurovascular and bone structures and thus to preserve function. Therefore, the margins are often limited and patients are at risk for local failure after surgery alone. Radiotherapy can reduce this local failure rate.

Preoperative radiotherapy, conventionally applied in 1.8-2 Gy fractions to 50 Gy in 5 weeks, does increase the risk for early complications due to unavoidable irradiation of the normal tissues surrounding the sarcoma mass, particularly for lower extremity lesions. Yet, preoperative radiotherapy allows for tighter resection margins, especially when an R1 status is anticipated. Our own recent cell-line experiments have provided an average α/β ratio of 4.9 Gy, suggestive of a gain of (modest) hypofractionation. We propose a 14 x 3 Gy regimen, based upon 1, this α/β ratio, 2, patients still have to undergo surgery, whereto the normal tissues around the sarcoma should not be exposed to too large fraction sizes.

Prior experience: Several hypofractionation trials have been designed or are currently accruing patients, some of them explore lower total doses, all of them lack comparison to the standard 50 Gy and none of them explored quality of life aspects nor patient reported outcomes.

Results: Prerequisite / statistics: A postoperative wound complication (WC) rate of 42% or above will not be accepted.

Conclusion: Trial design solution: A Simon 2-stage modified, "pick- the-winner" design. (see table)



	Arm A; 25 x 2 Gy		Arm B; 14 x 3 Gy	
Number of patients, 1 st phase	N = 56		N = 56	
Events	≤23 WC	>24 WC	≤23 WC	>24 WC
Decision	Safe, yet sufficient own and literature data; no further patients in arm A	unsafe; stop arm A	Safe; continue to 2 nd phase	Unsafe; stop trial
additional patients, 2 nd phase	none	none	N = 51	none
Total number of patients accrued per arm	56		56 + 51 = 107	56
Events			≤38/107 WC	≥39/107 WC
Decision			Arm B = the winner	Arm B is unsafe



1:57 PM - 2:04 PM

Paper #48 #1818765

SAKK 57/16 NNAB-PACLITAXEL AND GEMCITABINE IN SOFT TISSUE SARCOMA (NAPAGE): RESULTS FROM PHASE IB/II TRIAL

Antonia Digkila¹; Attila Kollár²; Marie-Noelle Kronig²; Christian Britschgi³; Tamara Rordorf³; Markus Joerger⁴; Fatime Krasniqo⁵; Yannis Metaxas⁶; Ilaria Colombo⁷; Daniel Dietrich⁸; Karin Rothgiesser⁹; Karin Ribì¹⁰; Christian Rothermundt⁴

¹CHUV, Lausanne, Vaud, SWITZERLAND; ²Inselspital, Bern University Hospital, University of Bern, Bern, SWITZERLAND; ³University Hospital Zurich, Zurich, SWITZERLAND; ⁴Kantonsspital St. Gallen, St Gallen, Sankt Gallen, SWITZERLAND; ⁵University Hospital of Basel, Bale, Basel-Stadt, SWITZERLAND; ⁶Cantonal Hospital Grison, Chur, Graubunden, SWITZERLAND; ⁷Oncology Institute of Southern Switzerland, Ente Ospedaliero Cantonale, Bellinzona, Ticino, SWITZERLAND; ⁸Swiss Group for Clinical Cancer Research (SAKK) Coordinating Center, Bern, SWITZERLAND; ⁹Swiss Group for Clinical Cancer Research (SAKK) Coordinating Center, Bern, SWITZERLAND; ¹⁰International Breast Cancer Study Group IBCSG (IBCSG), Bern, SWITZERLAND

Objective: To investigate the safety and the activity of the combination of gemcitabine and nab-paclitaxel (nab-pc) in advanced soft tissue sarcoma (STS). (ClinicalTrials.gov identifier: NCT03524898).

Methods: Patients with STS who progressed after a maximum of two lines of standard treatment with ECOG 0-2 and a life expectancy of >3 months and adequate organ function have been included.

The primary endpoint was progression-free rate (PFR) at 3 months (H0: 20%, H1:40%). Secondary endpoints included progression-free survival (PFS), adverse events (AEs), overall survival (OS) and patient-reported outcome (MDASI and FACT/GOG-Ntx). Efficacy analysis was by intention to treat.

Results: Thirty-nine patients in eight Swiss institutions were registered; the first six were treated as part of the dose-de-escalation part of the trial confirming the safety and tolerability of nab-pc 150mg/m² and gemcitabine 1000mg/m² every two weeks, until disease progression or unacceptable toxicity. The initially chosen dose in phase I was tolerable and used for the phase 2 part, since there were no DLTs or discontinuations due to AEs. In total, 56.4% patients had grade 3 STS, 77% were treated in the 2nd line and 23% in the 3rd line setting, respectively. The median age was 60 years (range 22 - 85), 53.8% were female. The most frequent primary locations were the retroperitoneum (20.5%), extremity (15.4%) and uterus (15.4%). STS subtypes are listed in table 1. The 3 months PFR (CR/PR/SD rate) was 56.4% (95% confidence interval (CI): 39.6 - 72.2%). The 3 months and 6 months PFS based on the Kaplan-Meier estimator were 58.4% (95% CI: 41.3 - 72.1%) and 44.6% (95% CI: 28.4 - 59.5%), respectively. Median PFS was 5.3 months (95% CI: 1.4 - 8.2) and median OS was 12.8 months (95% CI: 10.5 - 29.2). (Figure 1 and 2) The most common treatment-related AE was grade 3 neutropenia (15.4%). Other treatment-related AEs (of grade ≥ 3) were rare including grade 4 neutropenia (7.7%), grade 3 anemia (5.1%), grade 3 hypertension (2.6%), grade 3 alanine aminotransferase increased (2.6%). Grade 1 and grade 2 peripheral sensory neuropathy (PNP) occurred in 15.4 and 20.5%, respectively. No grade 3 - 4 PNP was reported. Reasons for treatment discontinuation are listed in table 2. Until now, three patients are still on treatment. Patient-reported symptoms remained stable over the first 3 months except for a significant increase in patient-reported neurotoxicity.

Conclusion: Biweekly nab-paclitaxel and gemcitabine is an active combination in pretreated STS patients with manageable toxicity. This regimen should be considered for further exploration.

Table 1: Baseline characteristics.

Characteristic	N	Summary
Age (years)	39	60 (22 – 85)
Female		21 (53.8%)
STS Grade (FNCLCC)	39	
G2		16 (41.0%)
G3		22 (56.4%)
Gx		1 (2.6%)
ECOG/WHO performance status	39	
0		20 (51.3%)
1		18 (46.2%)
2		1 (2.6%)
Subtypes	39	
Angiosarcoma		1 (2.6%)
Leiomyosarcoma		14 (35.9%)
Liposarcoma		10 (25.6%)
Sarcoma NOS		2 (5.1%)
Synovial Sarcoma		2 (5.1%)
Undifferentiated pleomorphic sarcoma		7 (17.9%)
Other		3 (7.7%)
Sites of metastases	35	
Lung		23 (65.7%)
Liver		11 (31.4%)
Bone		7 (20.0%)
Lymph nodes		11 (31.4%)
Brain		0 (0.0%)
Other		15 (42.9%)

Figure 1: Kaplan-Meier curve for progression-free survival with pointwise 95% confidence intervals (log-log scale).

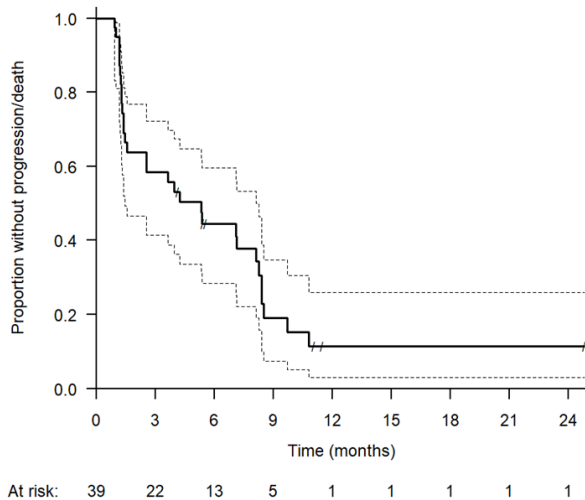
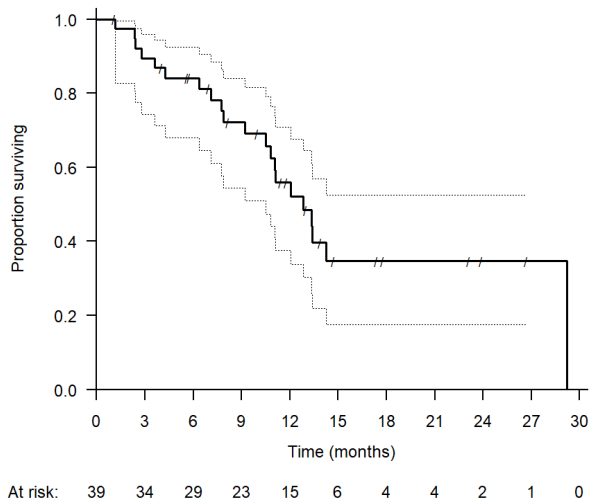


Figure 2: Kaplan-Meier curve for overall survival with pointwise 95% confidence intervals (log-log scale).





2:04 PM - 2:11 PM

Paper #49 #1818775

PHASE I TRIAL OF OLARATUMAB PLUS TRABECTEDIN IN ADVANCED SOFT-TISSUE SARCOMA PATIENTS: OLATRASTS, A SPANISH GROUP FOR RESEARCH ON SARCOMA (GEIS) STUDY

Javier Martin-Broto¹; Claudia M. Valverde²; Rosa Alvarez³; Roberto Diaz⁴; Daniel Bernabeu⁵; Rafael Ramos⁶; César Serrano⁷; Antonio Gutierrez⁶; David Moura⁸; **Nadia Hindi**¹

¹Fundacion Jimenez Diaz University Hospital, Madrid, Madrid, SPAIN; ²Hospital Universitario Vall d'Hebron, Barcelona, Catalonia, SPAIN; ³Gregorio Marañon University Hospital, Madrid, Madrid, SPAIN; ⁴La Fe University Hospital, Valencia, Comunidad Valenciana, SPAIN; ⁵La Paz University Hospital, Madrid, Madrid, SPAIN; ⁶Son Espases University Hospital, Palma de Mallorca, Islas Baleares, SPAIN; ⁷Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Catalonia, SPAIN; ⁸CITIUS III, Seville, Andalucia, SPAIN

Objective: Olaratumab (O) is a monoclonal antibody against human antiplatelet-derived growth factor receptor α (PDGFR α). Its combination with doxorubicin showed encouraging results in a phase II trial, leading to its approval. However, the confirmatory Phase III trial was negative. Trabectedin (T) is an approved second line therapy for advanced soft-tissue sarcoma (STS). This Phase I trial was designed to test the combination of T and O (NCT03985722).

Methods: Adult patients (pts), with progressing, advanced/irresectable and pretreated STS, received the combination of O (1h infusion, d 1, 8 every 21days-d-) followed by T (24-h continuous every 21d) at different dose levels: Level 0 (T 1.1mg/m² + O 15mg/Kg), Level 1 (T 1.3 mg/m² + O 15 mg/Kg), Level 2 (T 1.5mg/m² + O 15mg/Kg), Level 3 (T 1.5 mg/m² + O 20 mg/Kg (cycle 1) and then 15mg/Kg). Previous premedication with dexamethasone and H1 antagonist was administered. Dose escalation followed the 3+3 design. Dose-limiting toxicities (DLTs) were assessed during the 21 first d of therapy. Adverse events (AEs) were evaluated with CTC 5.0. Recommended phase II dose (RP2D) was the main objective. Secondary end-points included: median progression-free survival (PFS), overall response rate (ORR), median overall survival (OS), and correlation with translational findings.

Results: From November 2018 to January 2021, 17 pts (median age 51y, 31-69), 9 female/8 male, with advanced STS (11 liposarcoma, 4 leiomyosarcoma, 2 synovial), were enrolled in the trial. One pt did not complete Cycle 1 due to rapid progression and was not evaluable. The RDP2 was Dose level 3: T 1.5mg/m² + O 20mg/Kg cycle 1 and then 15mg/Kg d 1, 8. Among the 16-DLT evaluable pts, there were no DLTs. Most frequent G3-4 AEs included: neutropenia and GPT increase in 8pts (47%), GOT increase and fatigue in 3pts (18%), anemia, thrombocytopenia, GGT increase in 2 pts (12%) and diarrhea, nausea, vomiting, CPK increase in 1pt each (6%). There were no toxic deaths. Among the 15 evaluable pts (2 not evaluable pts: 1 pt did not complete C1, 1 pt too soon), there were 3 PR (20%), 8 SD (53%) and 4 PD (27%). Median of T cycles were 9 (1-28) with 4 pts still on therapy in the moment of this analysis. With a median follow-up in the alive pts of 16 months-mos- (5-25), 12pts have progressed, with a median PFS of 9.2 mos (95% CI 6-12.3), and 7pts have died, with a median OS of 18.3 mos (95% CI 10.2-26.4).

Conclusion: Trabectedin plus olaratumab was a safe regimen, allowing full doses of both drugs in combination. Its toxicity and efficacy profiles seem favorable in this limited prospective series. Translational analyses are ongoing.



ctos[®]

2021 *Virtual* Annual Meeting

Oral Presentations

Saturday, November 12, 2021



9:00 am - 10:15 am

– Session 9 –

MULTIDISCIPLINARY MANAGEMENT, NEOADJUVANT THERAPY & TREATMENT OF OLIGOMETASTATIC DISEASE

9:00 AM - 9:07 AM

Paper #50 #1818769

QUALITY INDICATORS OF SARCOMA WORK-UP

Bruno Fuchs¹; Philip Heesen¹; Gabriela Studer²; Beata Bode¹; Stefan Breitenstein¹; Javier Martin-Broto³; Alessandro Gronchi⁴; Jean-Yves Blay⁵; Axel LeCesne⁶

¹Swiss Sarcoma Network, Zurich, SWITZERLAND; ²University Hospital, Luzern; Swiss Sarcoma Network, Luzern, SWITZERLAND; ³University of Sevilla, SELNET; Swiss Sarcoma Network, Sevilla, Galicia, SPAIN; ⁴Istituto Tumori, Milano; Swiss Sarcoma Network, Milano, Lombardia, ITALY; ⁵Centre Leon-Berard; Swiss Sarcoma Network, Lyon, Rhone-Alpes, FRANCE; ⁶Gustave Roussy, Paris; Swiss Sarcoma Network, Paris, Centre, FRANCE

Objective: Sarcomas belong to the rare diseases, and its management requires a transdisciplinary approach of several disciplines. Overall progress has been hampered because each single institution and disciplines assess their own data, without common agreement on quality standards. However, to be able to report on quality, a common source of definition on the quality indicators of sarcoma work-up (QI) as well as the capacity of assessing real-world data is a prerequisite.

Methods: The Swiss Sarcoma Network (SSN) created a real-world data platform by combining the management of the weekly sarcomaboard with the sarcoma registry. This platform allows the collection of patient data, the analysis of each parameter in combination, as well as the validation through patient reported outcomes. An international advisory board of world-renowned sarcoma experts defined 8 QI's of sarcoma work-up. These QI's were then programmed into the digital platform such that they can be instantly assessed in real-time.

Results: Herein, we report on the prospective assessment of QI over 18 months starting in January 2020. We found that 93% of all patients underwent some type of imaging before performing the biopsy. 50% of all patients received their biopsy on the day of their first patient contact at the referral center, with an interquartile range of 6 days. Core biopsy was the technique of choice in 84% to establish the diagnosis. From the biopsy, it took a median of 7 days to establish the pathological reference diagnosis, with an interquartile range of 9 days, and 12 days until SB/MDT discussion, with an interquartile range of 13 days. 99% of all patients had a biopsy performed before initiation of treatment. 15% of all patients presented with metastases. From the SB/MDT meeting, it took a median of 23 days until initiation of treatment, with an interquartile range of 33 days.

Conclusion: The definition of QI's and its real-time assessment is possible. These efforts need to be extended to define quality indicators of SB/MDT, including PROMS/PREMs. Such real-world data registry with the capacity to report on QI's in real-time paves the way to create a novel ecosystem for sarcoma patient care in the future.



9:07 AM - 9:14 AM

Paper #51 #1818695

NEOADJUVANT AND ADJUVANT RADIOTHERAPY DECREASES THE RISK OF LOCAL RECURRENCE AND IMPROVES OVERALL SURVIVAL IN A MULTICENTRE COHORT OF 2162 EXTREMITY SOFT TISSUE SARCOMA PATIENTS

Joanna Szkandera¹; Maria Anna Smolle¹; Judith Woelfel¹; Ibtissam Acem²; Michiel van de Sande²; Lee Jays³; Han Bonekamp⁴; Rob Pollock⁵; Johnny Keller⁶; Per-Ulf Tunn⁷; Rick Haas²; Robert Van Ginkel⁸; Cornelis Verhoef⁹; Florian Posch¹; Bernadette Liegl-Atzwanger¹; Dalia Moustafa-Hubmer¹; Philipp Jost¹; Andreas Leithner¹

¹Medical University of Graz, Graz, Steiermark, AUSTRIA; ²Leiden University Medical Centre, Leiden, Zuid-Holland, NETHERLANDS; ³The Royal Orthopaedic Hospital, Birmingham, England, UNITED KINGDOM; ⁴Radboud University Medical Center, Nijmegen, Gelderland, NETHERLANDS; ⁵Royal National Orthopaedic Hospital, London, England, UNITED KINGDOM; ⁶Aarhus University Hospital, Aarhus, Midtjylland, DENMARK; ⁷HELIOS Klinikum Berlin-Buch, Berlin, GERMANY; ⁸University Medical Center Groningen (UMCG), Groningen, Groningen, NETHERLANDS; ⁹Erasmus MC Cancer Institute, Rotterdam, Zuid-Holland, NETHERLANDS

Objective: Both neoadjuvant (NRTX) and adjuvant radiotherapy (ARTX) are considered equivalent regarding their effect on local recurrence (LR) in extremity soft tissue sarcoma (eSTS) patients. However, differing toxicity profiles may be decisive for RTX timing. Based on the knowledge that LR affects survival, the aim of the current study was to independently assess the impact of NRTX and ARTX on LR and overall survival (OS) by applying propensity score (PS) and inverse probability of treatment weight (IPTW).

Methods: Of 2162 patients with eSTS included, 554 (25.6%), 268 (12.4%) and 1341 (62.0%) had received no RTX, NRTX, and ARTX, respectively. Mean patient age 59.2±17.1 years, 45.1% were female (n=976), and median follow-up was 47.2 months. After data imputation using chained equations, two separate analyses were performed, one including patients without and with NRTX (n=821), and one involving patients with or without ARTX (n=1894). Propensity scores and subsequent IPTWs were generated for both models. Univariate and multivariate IPTW-weighted Fine&Gray models (for LR and DM, with death as competing event) and Cox-regression models (for OS) were calculated.

Results: Significant differences regarding grading, tumour size, age, depth, chemotherapy and tumour localisation between patients without or with NRTX were present at baseline that could be adjusted for after IPTW-weighting. Likewise, imbalances between patients receiving and not receiving ARTX in terms of gender, histology, age, depth, and margins were adjusted after IPTW-weighting. In the multivariate IPTW-weighted model for LR, both NRTX (SHR: 0.358; p=0.001, irrespective of tumour size, depth) and ARTX (SHR: 0.850; p=0.010, irrespective of age, size, histology, or localisation) were significantly associated with reduced LR-risk. In the multivariate IPTW-weighted model for OS, NRTX (HR: 0.763; p=0.086, irrespective of age, grading, size, histology, chemotherapy, depth) was marginally associated with an improved OS, whereas ARTX was significantly associated with an improved OS (HR: 0.907; p=0.021), regardless of age, size, grading, histology, chemotherapy, or depth.

Conclusion: Considering the positive effects of both NRTX and ARTX far beyond reduction in LR-risk, radiation therapy may be administered, after carefully weighting against risks and benefit, more deliberately in eSTS patients.



9:14 AM - 9:21 AM

Paper #52 #1818772

THE ROLE OF PERIOPERATIVE CHEMOTHERAPY IN PRIMARY HIGH-GRADE EXTREMITY SOFT TISSUE SARCOMA: A RISK-STRATIFIED ANALYSIS USING PERSARC

Ibtissam Acem¹; Anja Rueten-Budde²; Dirk J. Grünhagen¹; Hans Gelderblom²; Winan J. van Houdt³; Cornelis Verhoef¹; Michiel van de Sande²

¹Erasmus MC Cancer Institute, Rotterdam, Zuid-Holland, NETHERLANDS; ²Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS; ³The Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS

Objective: The level of evidence for perioperative chemotherapy (CTx) in primary soft tissue sarcoma of the extremities (eSTS) is often debated. Recent studies suggested beneficial outcomes of perioperative CTx in a selected group of high-risk patients. Therefore, the aim of this study was to evaluate whether we could identify a group of high-risk patients that may benefit from perioperative CTx based on the predicted PERSARC baseline risk.

Methods: Patients with primary high-grade eSTS surgically treated with curative intent were included in this retrospective cohort study. The effect of anthracycline and ifosfamide-based CTx was investigated in two risk groups (high-risk/low-risk) created using the PERSARC prediction tool. The risk groups were defined as a risk lower and higher than the 66% quantile of the predicted 5-year overall survival (OS) distribution of the cohort. The effect of CTx in these risk groups was investigated using a multivariable Cox proportional hazards model.

Results: This study included 5977 patients with a median follow-up of 4.41 years (95%CI 4.20-4.57). The low-risk group had a predicted 5-year OS of $\geq 75.7\%$ and the high-risk group had a predicted 5-year OS of $< 75.1\%$ at baseline. There was no significant difference in OS between patients who received CTx and patients who did not receive CTx in the low-risk group (HR 0.710; 95%CI 0.434-1.15). However, a significant difference of OS in favor of CTx for high-risk patients was found in the multivariable Cox model with a HR of 0.627 (95%CI 0.480-0.819). The absolute OS difference at 5-year in the high-risk group was 14.9% ($p=0.009$).

Conclusion: This study did not find a beneficial effect of perioperative CTx on OS in the total population of eSTS patients. However, in a selected group of high-risk patients perioperative CTx may be beneficial. The PERSARC tool could be used to identify these high-risk patients.



9:21 AM - 9:28 AM

Paper #53 #1818773

IMMUNE INFILTRATE IN PRIMARY HIGH-RISK SOFT TISSUE SARCOMAS TREATED WITH NEOADJUVANT CHEMOTHERAPY AND SURGERY IN THE ISG-ST5-1001 RANDOMISED TRIAL: A PROGNOSTIC STUDY

Sandro Pasquali¹; Chiara Castelli¹; Paola Collini¹; Cleofe Romagosa²; Silvia Bague³; Jean-Michel Coindre⁴; Angelo Paolo Dei Tos⁵; Marta Barisella¹; Salvatore Lorenzo Renne⁶; Luca Lalli¹; Biagio Eugenio Leone⁷; Viviana Vallacchi¹; Emanuela Palmerini⁸; Vittorio Lorenzo Quagliuolo⁶; Javier Martin-Broto⁹; Antonio Lopez-Pousa³; Giovanni Grignani MD¹⁰; Jean-Yves Blay¹¹; Robert Diaz Beveridge¹²; Franco Domenico Merlo¹³

¹Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY; ²Hospital Universitari Vall d'Hebron, and Universitat Autònoma de Barcelona, Barcelona, Catalonia, SPAIN; ³Hospital de la Santa Creu i Sant Pau, Barcelona, Catalonia, SPAIN; ⁴Institut Bergonié, Bordeaux, Aquitaine, FRANCE; ⁵Università di Padova (UniPD), Padova, Veneto, ITALY; ⁶Humanitas Clinical and Research Center, Milano, Lombardia, ITALY; ⁷Università di Milano Bicocca, Milano, Lombardia, ITALY; ⁸IRCCS Istituto Ortopedico Rizzoli, Bologna, Emilia-Romagna, ITALY; ⁹Hospital Universitario Virgen del Rocío, Sevilla, Andalucía, SPAIN; ¹⁰Candiolo Cancer Institute FPO-IRCCS, Candiolo, Piemonte, ITALY; ¹¹Centre Léon Bérard, Lyon, Auvergne, FRANCE; ¹²Hospital Universitario y Politécnico La Fe, Valencia, Comunidad Valenciana, SPAIN; ¹³AUSL Reggio Emilia, Reggio Emilia, Emilia-Romagna, ITALY

Objective: The sarcoma community is working to define what, in addition to histology, influences the tumour immune infiltrate in soft tissue sarcoma (STS). We report on a planned analysis of the ISG-ST5-1001 study, a prospective trial that compared neoadjuvant anthracycline plus ifosfamide (AI) and histology-tailored (HT) chemotherapy (ChT) regimens in high-risk STS. This correlative study was aimed at characterizing the immune infiltrate after neoadjuvant ChT and investigating any association with disease recurrence.

Methods: Patients registered in the randomized and the non-randomized cohort of the ISG-ST5-1001 clinical trial (ID: NCT01710176) were included if they had tumor tissue from surgical specimens after neoadjuvant ChT and surgery, with or without RT, available for Tissue MicroArray (TMA). The tumour area with the highest lymphocyte infiltrate in each surgical specimen was selected for TMA by pathologists. The following immunohistochemistry (IHC) markers were measured quantitatively: CD3, CD8, PD1, GranzymeB, Foxp3, CD20, CD163, and PDL1. These IHC markers were combined together in a cluster analysis that exploits the Uniform Manifold Approximation and Projection for Dimension Reduction (UMAP) analysis to classify tumours in two groups according to their immune infiltrate. Study treatment regimens were considered as immune-modulating when they included either epirubicin, trabectedin, docetaxel, or gemcitabine and non-immune-modulating when they included the remaining study agents (ifosfamide as single-agent, etoposide). The association of this classification with disease-free survival (DFS) was investigated in a multivariable model.

Results: This analysis included 256 of 435 eligible study patients. A different distribution of immune infiltrate was observed between 'complex' (ck-ST5: leiomyosarcoma, malignant peripheral nerve sheath tumours, undifferentiated pleomorphic sarcoma, pleomorphic liposarcoma, and pleomorphic rhabdomyosarcoma) and 'simple' (sk-ST5: myxoid liposarcoma and synovial sarcoma) ST5 karyotypes. Ck-ST5 displayed higher CD3+ and CD8+ cells infiltrate, which had a heterogeneous distribution within the tumour and were in direct contact with sarcoma cells, compared to sk-ST5. Also, ck-ST5 were enriched in Granzyme B+, CD163+, and PDL1+ cells, which suggested an immune-related expression. CD20+ cells were highly represented in a minority of tumours, where they were organized in tertiary lymphoid-like structure (N=10/256). UMAP analysis identified two clusters of tumours with less (N=133) and more (N=113) immune infiltrate. In a multivariable analysis for DFS adjusting immune infiltrate for existing prognostic features and confounders, patients with more immune infiltrate were at lower risk of disease recurrence (HR=0.55, 95%CI 0.33-0.93, P=0.027) compared to patients with less immune infiltrate. This multivariate model included also having a ck-ST5 (HR=2.65, 95%CI 1.45-4.87, P=0.002), which correlates with shorter DFS, and smaller tumour size after the first cycle of neoadjuvant ChT (HR=0.80, 95%CI 0.71-0.91, P<0.001) and receiving an immune-modulating regimen (HR=0.37, 95%CI 0.16-0.84, P=0.018), which correlates with longer DFS.

Conclusion: In a neoadjuvant high-risk ST5 setting, we found that the post-treatment immune infiltrate substantially varied across sarcoma histologies, with ck-ST5 being marked by the richest immune contexture, and the latter correlated with a halved risk of recurrence. Results on overall survival and further analysis investigating variation of tumour infiltrate according to patient risk stratification based on prognostic nomograms are in progress and will be presented.



9:28 AM - 9:35 AM

Paper #54 #1818694

A MODERATE DOSE OF PREOPERATIVE RADIOTHERAPY MAY IMPROVE RESECTABILITY IN MYXOID LIPOSARCOMA

Jules Lansu¹; *Kirsten van Langevelde*²; *Pètra Braam*³; *Erik van Werkhoven*¹; *Astrid Scholten*¹; *Yvonne M. Schrage*²; *Winan J. van Houdt*¹; *Rick L. Haas*¹

¹Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS; ²Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS; ³Radboud University Medical Center, Nijmegen, Overijssel, NETHERLANDS

Objective: Histotype specific neoadjuvant therapy response data is scarce in soft tissue sarcomas. Although myxoid liposarcomas (MLS) are known for their shrinkage following radiotherapy (RT), it remains unclear how this affects resectability and whether this is predictive for pathologic response. This study aimed to correlate MRI parameters during and after preoperative RT to pathologic response in MLS and to assess the impact of a moderate RT dose on resectability.

Methods: This prospective, multicenter, single-arm, phase 2 trial (DOREMY) explored the radiological effects of preoperative RT to 36Gy in 2Gy fractions in primary non-metastatic MLS. Distance from tumor to the neurovascular bundle (NVB), tumor dimensions, fat fraction and enhancing fraction were determined on repeat MRI scans at baseline, 8 fractions, 16 fractions and preoperatively. The interval between radiotherapy and resection was 4-8 weeks. Pathologic response in the resection specimens was examined by central pathology review. The cumulative percentage of hyalinization, fatty maturation, and necrosis was considered as pathologic response.

Results: A total of 34 patients were included, consisting of 22 (65%) males and 12 (35%) females. The median age was 45 years (IQR 37–52). The tumor location was directly adjacent to the NVB (<1 mm) in 11/34 (32%) patients. All patients underwent RT according to the protocol and subsequent surgery was with one exception performed in all patients. The reason for omitting surgery in this patient was development of intercurrent metastatic disease. Preoperative RT resulted in a median increase of 2 mm (IQR 0-6) of the distance to the NVB (Table 1). Surgical margins were negative and microscopically positive in 32/33 (97%) and 1/33 (3%) patients who underwent surgery.

As compared to baseline, the median change of the tumor volume, craniocaudal diameter and axial diameter at preoperative MRI were -60% (IQR -74–41), -19% (IQR -23–7) and -20% (IQR -29–12), respectively. At preop MRI, but not earlier, relative dimensional tumor changes as compared to baseline, are negatively correlated with the distance to the NVB (volume $b = .506$, $p = 0.012$; craniocaudal diameter $b = -.457$, $p = 0.021$; axial diameter $b = -.512$, $p = 0.011$).

The median fat fraction of 0.1 (IQR 0.0–0.1) and enhancing fraction of 0.8 (IQR 0.6–0.9) at baseline, changed to 0.2 (IQR 0.1–0.5) and to 0.5 (IQR 0.4–0.9) preoperatively, respectively. An example of a patient with a radiologically responding tumor is presented in Figure 1.

Although radiological signs of response in terms of volume, enhancing fraction and fat fraction were not correlated with comprehensive pathologic response, several correlations were identified when the particular pathologic treatment effects were tested separately. Fat fraction correlated with fatty maturation and negatively correlated with hyalinization. Relative volumetric change, as compared to baseline, correlated with necrosis and negatively correlated with hyalinization. Enhancing fraction was correlated with hyalinization and negatively correlated with necrosis.

Conclusion: This cohort suggests that preoperative radiotherapy is beneficial in terms of resectability in approximately half of the at best marginally resectable tumors and that the distance from the tumor to the NVB increases in two-thirds of MLS patients. Tumor shrinkage following a modest dose of preoperative radiotherapy in MLS results in a 2 mm median increase of the distance between the tumor and the NVB. MRI features which were predictive for expressions of pathologic response from fraction 16 onwards, can possibly play a role in further personalization of neoadjuvant treatment strategies in order to improve outcome in MLS.

Table 1. Distance from tumor to the neurovascular bundle (NVB) before, during and after RT and the minimal margin at pathology examination, in millimeters.

MRI Baseline	MRI Fraction 8	MRI Fraction 16	MRI Preoperative	Pathology minimal margin	Radiological Difference
0	NA	1	NA	0	+1*
0	NA	NA	0	1	0
0	0	0	0	+	0
0	0	0	0	0	0
0	0	0	0	0	0
0	NA	NA	0	1	0
0	NA	0	0	1	0
0	0	0	0	0.1	0
0	0	0	1	1	+1
0	1	2	2	1	+2
0	3	3	3	2	+3
1	2	3	3	0.1	+2
2	2	2	NA	2	0*
2	2	3	2	1	+1
2	2	2	5	1	+3
3	5	7	NA	1	+4*
3	4	6	8	1	+5
6	5	6	NA	4	0*
6	5	4	4	0.3	-2
7	7	8	NA	0.2	+1*
7	8	12	9	2	+2
7	7	7	10	2	+3
10	9	11	14	3	+4
11	NA	NA	22	3	+11
14	16	17	26	2	+12
15	20	16	24	3	+9
16	20	29	20	1	+4
16	16	19	22	1	+6
18	13	24	26	3	+8
22	27	34	39	3	+17
23	26	27	NA	3	+4*
3 (0-15)	4 (1-15)	4 (1-17)	5 (2-21)	1 (0.28-2.25)	2 (0-6)

* = represents the difference in distance of the tumor to the NVB between baseline and fraction 16, because no preoperative MRI was performed in these patients. Given the possible underestimation of the difference in distance to the NVB, these values are not taken into account for further descriptive analysis including the presented median difference at the bottom of the right column. + =this patient had microscopically positive surgical margins.

Caption Table 1. Tumors are sorted from small to large distance form tumor to neurovascular bundle (NVB) at baseline MRI. The second, third and fourth column represent the distance from the tumor to the NVB after 8 fractions, 16 fractions and prior to surgery, respectively. The fifth columns shows the minimal pathology margin in mm as reported by the pathologist at pathology examination and the sixth column represents the difference in distance to the NVB between the measurement at baseline and the latest available MRI scan. The row below in bold represents the median value with the inter quartile range (IQR) between the parentheses. In cases with a thoracic wall localization (n=1) and subcutaneous mass (n=2) distance to NVB were deemed irrelevant and excluded from this table.

Figure 1A T1-weighted post contrast images of an illustrative example of a patient with a radiologically responding tumor

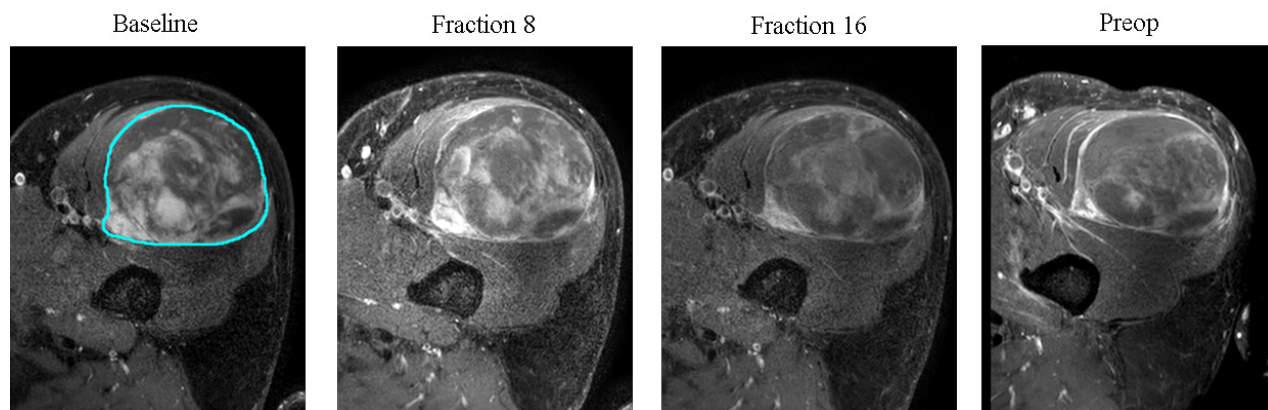
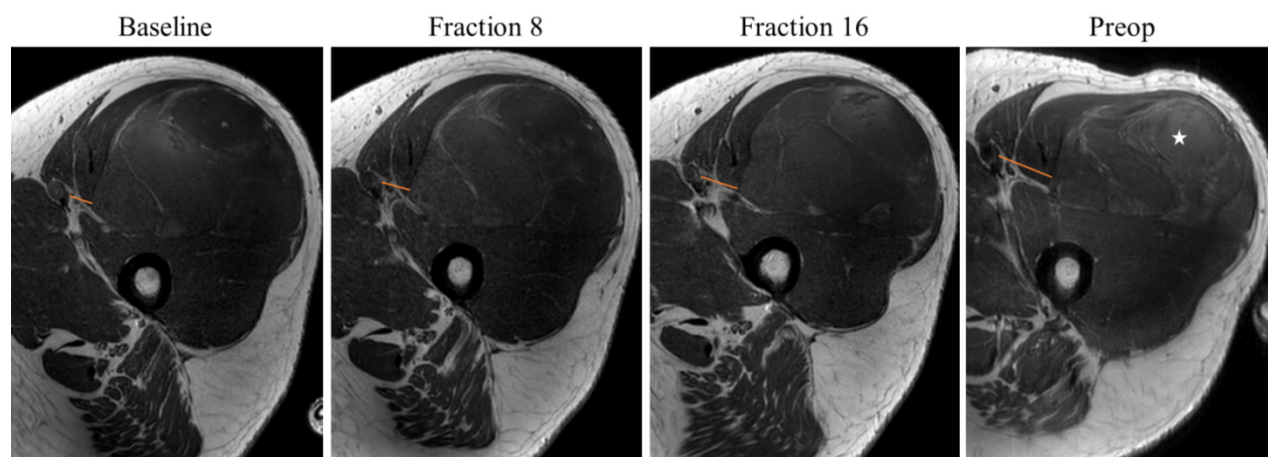


Figure 1B T1-weighted images of the same illustrative example of a patient with a radiologically responding tumor



Captions: **Figure 1A** Axial T1-weighted post contrast images (above) of an example of a radiologically responding intramuscular tumor in the proximal lower extremity. The tumor is delineated with a blue line. In comparison to baseline (left), the decreases in enhancing fraction and tumor volume observed at fraction 8 (middle) and fraction 16 (right). **Figure 1B** Axial T1-weighted images of the same example as presented in *Figure 1*. In comparison to baseline (left), tumor dimensions decrease and the distance of the tumor to the neurovascular bundle increases (in this example the distance from the tumor to the artery is marked with the orange line) over time. Furthermore, the fat fraction gradually increases between baseline and preoperative. The white star in the preoperative image (right) marks a new fat-containing area. In the end, this patient had 90% of pathologic response in the resected specimen, consisting of 20% hyalinization, 20% fatty maturation and 50% necrosis.



9:35 AM - 9:42 AM

Paper #55 #1818748

PRELIMINARY RESULTS OF PHASE II SINGLE-ARM STUDY ON PREOPERATIVE INTENSITY-MODULATED RADIOTHERAPY WITH CONCURRENT ANLOTINIB FOR PATIENTS WITH NON-METASTATIC EXTREMITY AND TRUNK SOFT TISSUE SARCOMA

Ning-Ning Lu¹; Li-Bin Xu²; Hong-Tu Zhang²; Zhen-Guo²; Zhao-Yang²; Ting Liu²; Xin-Xin Zhang²; Meng Li²; Lei Miao Master²; Hao Jing²; Qing Chang²; YiHeBaLi Chi²; Jia-Yu Wang²; Shu-Lian Wang²; Sheng-Ji Yu²

¹Chinese Academy of Medical Sciences, Beijing, Beijing, CHINA (PEOPLE'S REPUBLIC);

²Cancer Hospital, Cancer Institute, Beijing, Beijing, CHINA (PEOPLE'S REPUBLIC)

Objective: Preoperative radiotherapy is one of the recommended treatments for primary extremity and trunk soft tissue sarcoma, however, the pathological remission is relatively low, and survival is not improved. We hypothesized that the addition of Anlotinib will improve the pathological remission rate without significant increase of major wound complications (MWCs).

Methods: A phase II single-arm study was initiated in our center (ChiCTR2000033377). Primary or recurrent non-metastatic extremity or trunk soft tissue sarcoma was enrolled. Patients received preoperative intensity-modulated radiotherapy (IMRT) of 50Gy in 25 fractions with concurrent and sequential Anlotinib (12mg Qd for 2 weeks, for 3 cycles in total), followed by wide resection. NCI-CTC 5.0, RECIST 1.1 criteria, and EORTC-STBSG criteria was used to evaluate acute toxicities, clinical response and pathological remission rate. The primary endpoint was defined as MWCs as per the SR2 criteria within 4 months post-surgery.

Results: From Jul 2020 to May 2021, 19 patients were enrolled. The median onset age was 56 (25-82) years old. More male than female patients were enrolled (1.4 vs. 1). There were 15, 3 and 1 patients with primary untreated, locally relapsed disease and post-operative residual tumor, respectively. The median tumor size was 9.5 (3.7-17.6) cm, with 14 patients (74%) larger than 8cm. Fifteen tumours (79%) were evaluated as unresectable or borderline resectable, which was defined as impossible or difficult to conserve limb with non-R2 wide resection. All except 2 received Anlotinib as per protocol. One refused to take Anlotinib after 3 weeks without any toxicities, another had dose reduction due to Grade 3 hypertension. The observed Grade 3 Anlotinib-related acute toxicity was only hypertension in three patients (15.8%). All the toxicities are shown in Table 2. There were 8 (8/16, 50%) and 8 patients who achieved partial response (PR) and SD at 1 month after the end of radiotherapy, respectively, with the disease control rate of 100%. All the patients who had PR had obvious tumor shrink at the first 1 to 2 weeks during radiotherapy. Three out of 13 patients (23.1%) who underwent wide resection had major wound complications. According to the EORTC-STBSG criteria, 2 patients achieved pathological complete remission (no viable tumor cells). In all, 9 patients (69%) had higher than 10% of hyalinization/fibrosis. All the eleven patients with unresectable or borderline resectable tumor had non-R2 limb-conserving wide resection, with 9 R0 and only 2 R1 resection.

Conclusion: For patients with non-metastatic extremity or trunk primary sarcoma, the combination of Anlotinib and pre-operative radiotherapy is safe and well-tolerated, and achieve favorable clinical and pathological response. The earlier response with addition of Anlotinib make more patients with unresectable or borderline resectable tumor completely resected by limb-conserving wide resection.



9:42 AM - 9:49 AM

Paper #56 #1818789

SAFE MARGIN SURGERY USING PLASTIC RECONSTRUCTION IN EXTREMITIES OR PARIETAL TRUNK SOFT TISSUE SARCOMA: A TERTIARY SINGLE CENTER EXPERIENCE

Laura Samà¹; Jean Philippe Binder²; Lauren Darrigues²; Benoit Couturaud Couturaud²; Benoit Boura²; Sylvie Helfre²; Laurent Chiche²; Nayla Nicolas²; Dimitri Tzanis²; Toufik Bouhadiba²; Julie Perlberg-Samson²; Sylvie Bonvalot
¹Humanitas Clinical and Research Hospital/Humanitas University, Milan, Lombardia, ITALY; ²Institute Curie, Paris, Ile-de-France, FRANCE

Objective: Tertiary centers recruit a large proportion of complex patients affected by locally advanced soft tissue sarcoma (STS). Frequently these patients presented recurrence of STS, previously treated with inadequate surgery or radiotherapy. The objective of this study was to evaluate the results of oncoplastic surgery (OPS) for patients affected by extremity or parietal trunk STS.

Methods: This retrospective study includes patients who underwent a flap reconstruction after sarcoma resection between January 2018 and December 2020 at Institut Curie (Paris, France). Inclusion criteria included: histological diagnosis of STS confirmed by a sarcoma expert pathologist, primary or recurrent disease without metastasis at diagnosis, evaluation by a Multidisciplinary Tumor Board (MDTB) before surgery, and reconstruction with a flap (pedicle or free). Patients treated with skin graft or vacuum-assisted closure (VAC) therapy for wound healing were excluded. The primary endpoint of the study was the evaluation of the impact of reconstructive surgery on the quality of surgical. The secondary endpoint was to quantify the morbidity of OPS and identify predictor factors for wound complications.

Results: Out of 211 patients, 89 (42%) underwent a flap reconstruction after sarcoma resection (Fig.1). Pre-operatively, all patients would have been considered either candidate for amputation (n=9, 10.1%) due to infiltration or encasement of major vessels and/or nerves by the tumour, or eligible for R1/R2 resection (n=80, 89.9%). Nevertheless, a large oncological resection was made possible and performed in all patients with the association of a flap reconstruction. Fifty-three patients (59.5%) received at least one neoadjuvant treatment. Surgery was realized on a pre-irradiated field in 56 (63%) patients (Table 1). Overall, 90 flaps were performed: 72 (80.0%) pedicle flaps and 18 (20.0%) free flaps (Fig.2). The type of flap was: musculocutaneous (63.3%), muscle (25.5%), or fascio-cutaneous (11.1%). The median LOS was 8 days (IQR 6-13 days). Overall, the surgical morbidity rate was 33.3% (30/90 flaps), and the reoperation rate was 15.7% (14/89 patients). No postoperative mortality was recorded. No R2 resections were performed. R0 and R1 margins were achieved in 82 (92.1%) and 7 (7.9%) patients, respectively. The median closest resection margin was 3 mm (IQR 1-6 mm). Among R1 patients, 5 patients had positive margins along preserved critical structures, 2 patients had well-differentiated liposarcomas. The univariate analysis exploring predictors of morbidity (Table 2), showed that tumor size (≥ 10 cm) was significantly correlated to any complications ($p=0.01$) and re-operation for complication ($p=0.03$). Patients with Body Mass Index (BMI) ≥ 30 ($p=0.03$) and STS of lower extremities ($p=0.01$) had significantly more wounds complications.

Conclusion: In a referral sarcoma center, the collaboration between the surgical oncologist and the plastic surgery team should be considered upfront in the surgical plan, allowing the adequate wide OSP with acceptable postoperative morbidity.

Table 1: Patient and tumor characteristics

	N=89
Median Age (IQR)	61 (48-73)
Sex	
• M/F	47 (53%)/42 (47%)
Median BMI (IQR)	25 (22-28.5)
Presentation	
• Primary	48 (54%)
• Re-excision	15 (16.8%)
• Local Recurrence	26 (29.2%)
Pre-irradiated field	
• Yes	14 (15.7%)
○ Local Recurrence	11/14 (78.6%)
○ Radiation induced sarcoma	3/14 (21.4%)
• No	75 (84.3%)
Median size (cm) *	10 (IQR: 9)
Histology	
• UPS	25 (28.1%)
• LMS	10 (11.2%)
• LPS	15 (16.9%)
• Others	39 (43.8%)
Grade	
• 1	15(16.8%)
• 2	30(33.7%)
• 3	18(20.3%)
• Non evaluable **	26(29.2%)
Localization	
• Upper limb	21 (23.6%)
○ Shoulder/axilla/scapula	7/21 (33.3%)
○ Upper arm	6/21 (28.6%)
○ Forearm/hand	8/21 (38.1%)
• Lower limb	49 (55.0%)
○ Groin	5/49 (10.2%)
○ Thigh	33/49 (67.3%)
○ Leg/Foot	11 (22.5%)
• Trunk	19 (21.4%)
○ Thoracic wall	3/19 (15.8%)
○ Abdominal wall	7/19 (36.8%)
○ Breast	4/19 (21.1%)
○ Back	5 (26.3%)
Depth	
• Superficial	26 (29.2%)
• Deep	63 (70.8%)
Neoadjuvant treatment	
• Yes/No	53 (59.5%)/36 (40.5%)
○ Pre op RT alone	33/53 (62.2%)
○ Pre op RT/CT	7/53 (13.2%)
○ Pre op RT+ILP	1/53 (1.9%)
○ Pre op RT/CT +ILP	1/53 (1.9%)
○ Pre op CT alone	9/53 (17.0%)
○ ILP	1/53 (1.9%)
○ Pre op CT+ILP	1/53 (1.9%)

* Size was assessed in patients with primary tumour (n=48)

** Grade was undetermined due in part to preoperative treatment.

UPS: Undifferentiated Pleomorphic Sarcoma; LMS: Leiomyosarcoma; LPS: Liposarcoma; RT: Radiotherapy; CT: Chemotherapy; ILP: Isolated Limb Perfusion; IQR: interquartile range

Table 2: Univariate analysis on morbidity

	Any complication		Re-operation		Wound complication		Necrosis		Seroma		Hematoma	
	N=30	P	N=14	P	N=10	P	N=9	P	N=11	P	N=6	P
Surgical technique		0.17		0.79		0.86		0.21		0.32		0.42
- Free flap N=18	9		4		1		4		4		2	
- Pedicle flap N=72	21		10		9		5		7		4	
Composition of flap		0.13		0.46		0.58		-		0.27		0.94
- Fasciocutaneous N=10	0		0		0		0		0		0	
- Muscle N=23	8		4		5		0		2		2	
- Musculo cutaneous N=57	22		10		5		9		9		4	
Presentation		0.75		0.47		0.57		0.67		0.82		0.67
- Primary N=48	18		9		8		4		7		4	
- Re-excision N=15	1		0		1		0		0		0	
- Local recurrence N=27	11		5		1		5		4		2	
Pre-irradiated field		0.71		0.54		0.17		-		0.52		0.46
- Yes N=56	19		10		4		9		8		3	
- No N=34	11		4		6		0		3		3	
Size (N=48)*	N=18	0.01	N=9	0.03	N=8	0.67	N=4	0.79	N=7	0.28	N=4	0.86
- < 10 N=23	4		1		0		0		2		2	
- ≥ 10 N=25	14		8		8		4		5		2	
Tumor localization		0.12		0.57		0.01		0.21		0.67		0.03
- Upper limb N=21	5		2		0		1		1		4	
- Lower limb N=49	17		9		5		5		9		2	
- Trunk N=20	8		3		5		3		1		0	
Depth		0.69		0.36		0.80		0.68		0.74		0.60
- Superficial N=26	6		2		2		2		2		1	
- Deep N=64	24		12		8		7		9		5	
BMI		0.23		0.31		0.03		0.66		0.01		-
- < 30 N=75	23		13		6		8		6		6	
- ≥ 30 N=15	7		1		4		1		5		0	
Smoking		0.77		0.78		0.41		0.46		0.97		0.42
- Yes												
- No												

* Size was assessed in patients with primary tumour (n=48)

Figure 1: Reconstruction algorithm for extremities and parietal trunk STS

ESTS: extremities soft tissue sarcoma; STS: soft tissue sarcoma; VAC: vacuum-assisted closure

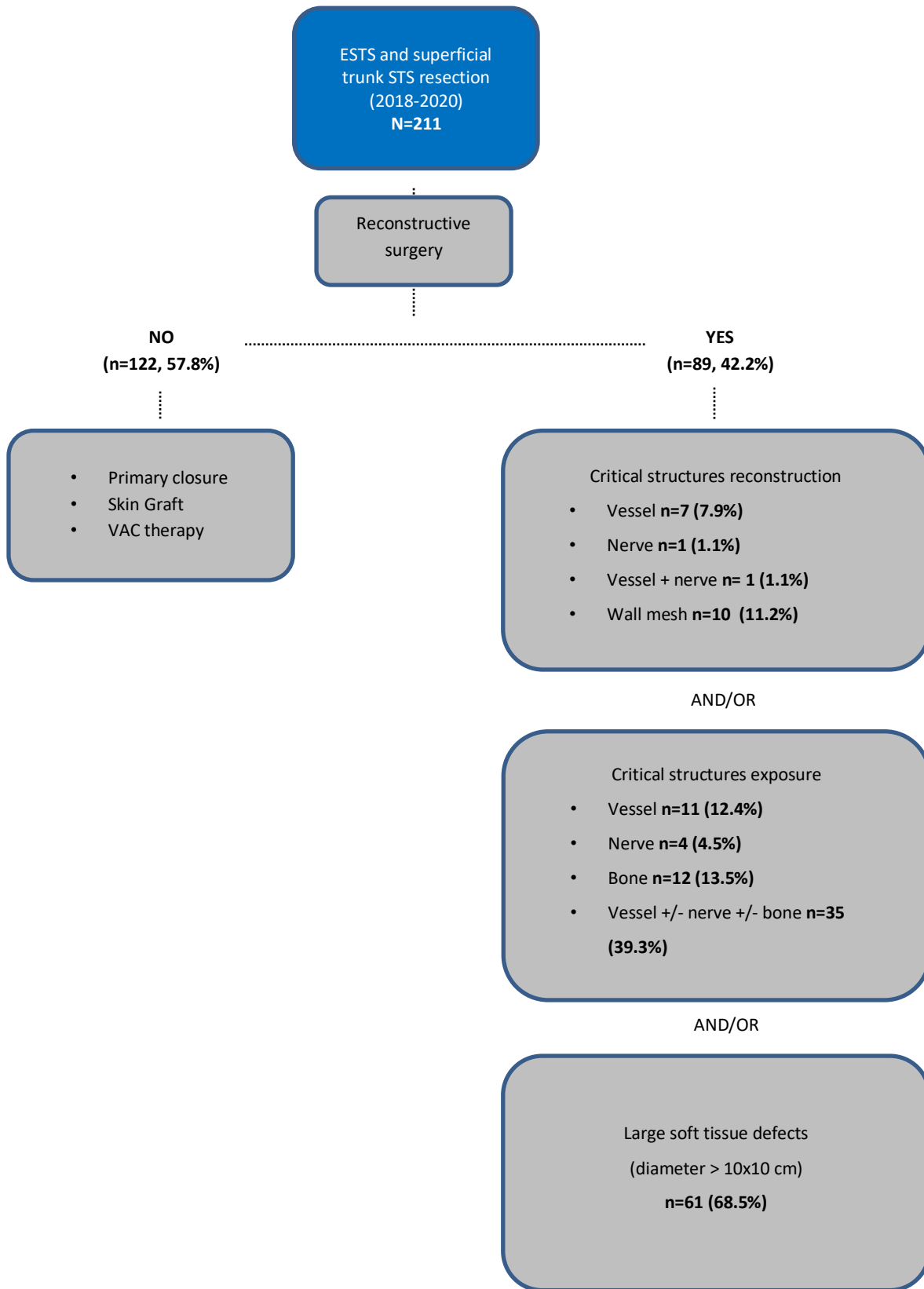
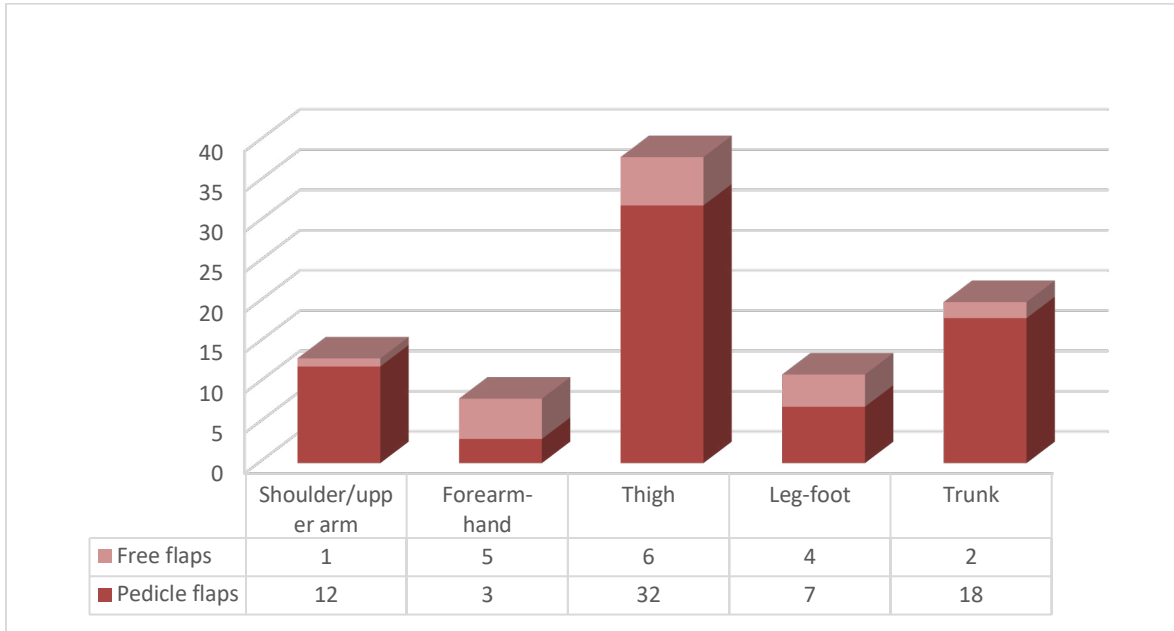


Fig. 2: Anatomical distribution of the surgical reconstructive technique

Overview of the percentages of flap reconstruction types depending on the localization.





9:49 AM - 9:56 AM

Paper #57 #1818729

RESTAGING AFTER NEOADJUVANT RADIOTHERAPY FOR SOFT TISSUE SARCOMA OF THE EXTREMITIES AND TRUNK

Bob Schultze; *Ibtissam Acem; Dirk J. Grünhagen; Cornelis Verhoef*
Erasmus MC Cancer Institute, Rotterdam, Zuid-Holland, NETHERLANDS

Objective: Soft Tissue Sarcomas (STS) of the extremities and the trunk are commonly treated with neoadjuvant radiotherapy (RT) followed by surgery. A course of neoadjuvant RT takes around 5 weeks. In general patients will be operated around 8 weeks following the end of neoadjuvant RT. This raises the question if these patients could develop distant metastases in the period between staging and operation. There is a lack of evidence regarding the value of restaging for distant metastases after neoadjuvant RT. This study assessed the use and value of restaging with chest CT or X-ray after neoadjuvant RT in the treatment of STS of the extremities and trunk.

Methods: This is a single-centre retrospective cohort study. Patients ≥ 18 years, diagnosed or referred between January 2010 and October 2020, with a non-retroperitoneal STS and who were staged with a chest CT or X-ray before and after neoadjuvant RT, were analysed.

Results: A total of 152 patients who were treated with neoadjuvant RT, with curative intention, were included. Staging was performed with an X-ray in three patients (2%, 3/152), the other 149 patients (98%, 149/152) were staged with a CT-scan. Restaging after neoadjuvant RT was done in 91% of all patients. Restaging was performed with an X-ray in four patients (3%, 4/138), the other 134 patients received a CT-scan (97%, 134/138). Median time between staging and restaging was 15.0 weeks [IQR 12.9-16.8]. During restaging, metastases were reported in 29 out of the 138 patients who were restaged (21%, 29/138), compared to the finding of metastases in four patients during staging ($p < 0.001$). In total, a change in strategy was seen in 27 out of 138 patients (20%, 27/138). In 22 out of these 27 patients (81%, 22/27) a change in strategy was seen as a result of newly detected metastases at restaging.

Conclusion: In total, a change in strategy after restaging was seen in 20% (27/138) of the patients. Therefore, restaging after neoadjuvant RT seems advisable.



ctos®

2021 Virtual Annual Meeting

Oral Presentations

Saturday, November 12, 2021



10:15 am - 11:00 am

– Session 10 –

QUALITY OF LIFE AND PATIENTS PERSPECTIVE

10:15 AM - 10:22 AM

Paper #58 #1818703

SETTING THE INTERNATIONAL RESEARCH AGENDA FOR SARCOMA TOGETHER WITH PATIENTS AND CARERS: FIRST RESULTS OF THE SARCOMA PATIENT EURONET (SPAEN) PATIENT INVOLVEMENT AND PRIORITY PROJECT

Olga Husson¹; Kathrin Schuster²; Paul van Kampen³; Carlos Kooops³; Olga Husson¹; Marije Weidema⁴; Richard Davidson⁵; Markus Wartenberg²; Estelle Artzner²; Ornella Gonzato⁶; Natalia Fernandez²; Phil Green²; Bernd Kasper⁷; Kai Pilgermann²; Sami Sandakly²; Lotta Våde²; Roger Wilson⁵; Winette T. A. van der Graaf¹; Gerard van Oortmerssen³

¹Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS; ²Sarcoma Patients EuroNet (SPAEN), Riemerling, Bayern, GERMANY; ³Dutch Sarcoma Patient Platform, Utrecht, Utrecht, NETHERLANDS; ⁴Radboud University Medical Center, Nijmegen, Gelderland, NETHERLANDS; ⁵Sarcoma UK, London, England, UNITED KINGDOM; ⁶Trust Paola Gonzato-Rete Sarcoma, Milan, Lombardia, ITALY; ⁷Mannheim Cancer Center (MCC), University of Heidelberg, Mannheim University Medical Center, Mannheim, Baden-Wurttemberg, GERMANY

Objective: Research in sarcoma has historically been the domain of scientists and clinicians attempting to understand the disease in an effort to develop effective treatments. This traditional approach of placing scientific rigor before the patient's reality is changing. This evolution is reflected in the growth of patient-centered organizations and patient advocacy groups that seek to meaningfully integrate patients into the process of prioritizing research needs and creating alliances wherein patients and researchers can partner together to accomplish research goals. The aims of this study are to identify the unanswered questions regarding sarcoma (for this project also including desmoid fibromatosis (DF)) from patient, carer and clinical perspectives and examine how patients and carers want to be involved in sarcoma research.

Methods: This project is set up by Sarcoma Patients EuroNet (SPAEN) in collaboration with several stakeholders in the sarcoma research field. The project consists of five phases and is partly based on the James Lind Alliance methodology: (1) Identification and invitation of potential partners; ²Awareness raising via international patient advocacy groups, research bodies, sarcoma experts and social media; ³Identifying unanswered research questions (in six areas: diagnosis, treatment, support, health-related quality of life, survivorship and end of life issues) and ways to engage (i.e. meaningful, active collaboration between researchers and patients) patients and carers in research via a sarcoma research priority setting partnership survey. Sarcoma patients, survivors, (bereaved) carers, health care professionals and researchers were able to take part. Answers were analyzed by four team members; ⁴The unanswered research questions that came up in phase 3 will be compared to scientific literature to determine which questions are already answered. The remaining questions will be refined; ⁵A new survey will be sent out to patients, carers, health care professionals and researchers with the aim of prioritizing the unanswered questions for sarcoma research to be addressed in the near future. We describe the findings of phase 3 in this abstract.

Results: In total, 264 sarcoma patients (73%) and carers (27%) from all over the world participated in the online survey. The participants covered the full spectrum of sarcomas: 12% bone sarcoma (BS), 46% soft tissue sarcoma (STS), 27% gastrointestinal stromal tumor (GIST), 8% DF and 6% unknown. The topics mentioned were labeled in accordance with the Common Scientific Outline (CSO) of the International Cancer Research Partnership (icpartnership.org/cso). During the analysis, it became clear that some topics were either potential subjects for research (R); subjects for advocacy (A); or requests for information (I). A list for all three (R, A and I) was constructed, each containing approximately 60 topics. Finally, a reduction in the number of topics was achieved based on the combination of similar topics related to various subtypes of sarcoma. The final list of 24 research questions is shown in Table 1.

With regard to patient and carer involvement 64% were very willing to be actively involved, mainly in the following areas: sharing perspectives, attend research meetings, identify research topics, provide input on study design and research materials and dissemination of research findings.

Conclusion: The first results of this sarcoma research priority exercise identified important research questions, but also important topics for patient advocacy groups and further improvement of information materials. Sarcoma patients and carers

have a strong wish to be involved in multiple aspects of sarcoma research. The next phase will identify the top 10 research priorities per tumor type (BS, STS, GIST, DF). These priorities will provide guidance for research that will achieve greatest value and impact.

Table 1:

1	What are causes of sarcoma?
2	Are preventive measures possible? Can vaccines be developed?
3	Are better diagnostic techniques possible? -Imaging, blood tests, scans, innovative image analysis techniques, Whole Genome Sequencing -Better distinction between subtypes and between benign and malignant
4	What percentage of diagnoses is wrong?
5	What is the risk of taking biopsies?
6	How can we better estimate prognosis and risk?
7	Are there hereditary aspects of sarcomas?
8	Can more research be directed to specific subtypes? -Role of hormones in desmoid tumors -GIST, retroperitoneal liposarcoma, angiosarcoma, TGCT, etc.
9	Is it possible to set up an international registry for research, use of big data analysis
10	What is the effect of mental condition on result of treatment?
11	Are new forms of therapy applicable to sarcomas? -Immunotherapy -Targeted therapy -Combined therapies
12	Is it possible to run more comparative effectiveness studies (e.g. perfusion vs amputation) and determine net clinical benefit (balancing of overall survival and quality of life)?
13	Methods for precision surgery, what is effect of margin on prognosis?
14	Effect of personal characteristics, what have survivors in common?
15	Is it possible to create personalized, risk-based optimization of follow-up schemes?
16	What kind of side effects (pain, effects of TKIs, chemotherapy, radiotherapy, surgery, etc.) can be expected for the different treatment forms?
17	Are there coping strategies to deal with side effects?
18	What are the long-term effects of treatment (e.g. radiation), for example on fertility, intimacy, secondary tumors?
19	What are the benefits of lifestyle, diet, mental condition, integrative healthcare interventions?
20	How should disease related mental suffering (acceptance, anxiety, etc.) be treated (psychotherapy, mindfulness training, psychedelics)?
21	How can sarcoma survivors re-integrate into society?
22	How is end-of-life care organized in different countries?
23	What is happening in the terminal phase, development of the disease, how can quality of life of patient best be supported?
24	How can we come to shared decision making in final life phase? What is role of carers? In case of sedation, should patient be told?



10:22 AM - 10:29 AM

Paper #59 #1818735

SARCOMA UK SUPPORT LINE - 5 YEARS ON

Helen Stradling; Sam Hackett; Carly McDonald BSc
Sarcoma UK, London, England, UNITED KINGDOM

Objective: Introduction: In February 2016 Sarcoma UK, the UK national charity focusing on all types of sarcoma, launched the Sarcoma UK support line (SL). This was introduced following an increase in the number of clinical and complicated calls into the non-clinical staff team. The aim was to provide a free and confidential support line for the sarcoma community. The service is open to anyone who needs information and support including the person with sarcoma, family, friends and health professionals. There are no set time limits to the calls, giving people the time they need to talk though concerns and worries is key to the service. The hope was that while providing useful and accurate information, we could provide support and ensure the pathway for those diagnosed was into the specialist sarcoma services.

Methods: Growth of the service: In the first year the team had 947 contacts (an email or telephone conversation) from 419 individuals. In 2020-21 the team had 2994 contacts from 667 individuals with March 2021 seeing the highest contact of 391 individuals in one month. In the last year 77% of people contacting the team have done so for the first time. Most individuals contact us at least 3 times, we have spoken to some for over 5 years now and followed them through from diagnosis to end of treatment/long term follow up. We also support family members who have been bereaved, with our bereavement calls up by 25% this year. On average our calls last 35 minutes, over the 5 years we have spoken to some people or families for 15 hours. The line is run by 3 healthcare professionals working part time, providing a service from 10-3pm Monday to Friday. We continue to receive international contacts which we answer and signpost to specialist services where we can, email information and signpost to local advocacy support services. The team have now had more than 10,500 contacts from over 2,700 individuals.

Results: Reasons for contact: The top three reasons for contact have remained consistent over the 5 years - support, diagnosis and treatments. This last year has seen an increase in the number of contacts about treatment options increasing by 57% and the team have had contact with 3 times as many people reporting worrying symptoms compared to last year.

Conclusion: Impact of the service: • The team have 'moved' 109 individuals from non-sarcoma specialist hospitals into specialist sarcoma services for their care. • Giving the callers the tools to advocate for themselves through support, accurate information giving and signposting to national guidelines has been key to the support line success. • We have increasingly become a barometer for what is happening across the country, which has enabled us to feedback what we hear to NHSE, the clinical teams and into the policy work the charity does.



10:29 AM - 10:36 AM

Paper #60 #1818762

DEFINING DEPRESSION AND ANXIETY IN ORTHOPAEDIC SARCOMA PATIENTS

Elizabeth Polfer; *Yesne Alici; Ray Baser; John H. Healey; Meredith Bartelstein*

Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES

Objective: Depression and anxiety are common healthcare concerns worldwide. According to the WHO World Health Survey, the 12-month prevalence of depression worldwide is 3.2%. It is estimated that the 12-month prevalence of depression in the United States is 8.6% and is 2.9% for anxiety. Depression results in increased healthcare utilization among cancer patients and increased morbidity and mortality. While prior studies have evaluated depression in patients with carcinoma, there is a paucity of literature evaluating patients with sarcoma. The purpose of this study was to evaluate the prevalence of anxiety and depression in sarcoma patients treated in the orthopaedic clinic and to determine if the disease status influences the depression and anxiety rates.

Methods: This protocol was reviewed by the Human Research Protection Program and determined to meet the criteria for an exempt study as per 45 CFR 46.104(d)(2)(iii). Sarcoma patients were invited to complete the 9-Item Patient Health Questionnaire (PHQ-9) as well as the Generalized Anxiety Disorder Scale (GAD-7) in clinic. Patients were scored per protocol. Specifically, PHQ-9 scores depression as 5–9 mild, 10–14 moderate, 15–19 moderately severe, 20–27 severe. GAD-7 scores anxiety as 5–9 mild, 10–14 moderate, 15–21 severe. The recommended diagnostic cutoff value for both the PHQ-9 and GAD-7 is ≥ 10 based on sensitivity and specificity for the diagnosis of major depressive disorder and generalized anxiety disorder, respectively. As a result, in both cases, patients were referred with scores 10–14 to social work and 15 or higher to psychiatry. Patients with thoughts of self-harm were referred regardless of score. Patients were divided based on disease state—initial management, recurrent disease, metastatic disease, discontinuous no evidence of disease (dNED) (patients with prior recurrence or metastatic lesions who were subsequently treated and now have no evidence of disease), and no evidence of disease (NED). Data were summarized using descriptive statistics. Differences across categories of disease status were testing for statistical significance using Kruskal-Wallis tests for continuous variables and Fisher’s exact tests for categorical variables.

Results: To date, 99 patients have completed surveys. Depressive symptoms were seen in 39 (39.4%) patients at varying levels of severity—19 (19.2%) mild, 13 (13.1%) moderate, 6 (6.1%) moderately severe, 1 (1%) severe. Depression was present in 7 (12.1%) patients with NED, 4 (36.4%) patients in their initial treatment, 4 (57.1%) patients with actively recurrent disease, 2 (22.2%) patients with dNED, and 3 (21.4%) patients with metastatic disease. Symptoms of anxiety were seen in 37 (38.1%) patients—19 (19.6%) mild, 9 (9.3%) moderate, and 9 (9.3%) severe. Anxiety was present in 8 (14.3%) patients with NED, 4 (36.4%) patients in their initial treatment, 4 (57.1%) patients with actively recurrent disease, 1 (11.1%) patients with dNED, and 1 (7.1%) patients with metastatic disease (Table 1). Overall, 26 (26.3%) patients met criteria to be offered referrals and 19 (73.1%) of those accepted the referral. The average age of those without depression was 49 while the average age for those meeting criteria for referral was 41 years old. The average age of those without anxiety was 50 and was 40 years old for those meeting requirements for referral. Nine patients (9.1%) had thoughts of hurting themselves/thinking they were better off dead within two weeks of to the visit.

Conclusion: Depression and anxiety are underrecognized in cancer settings because of the lack of screening and overlap with symptoms of cancer or cancer treatments. As a result, depression and anxiety are frequently underdiagnosed and many patients go without treatment. In cancer patients, depression can lead to increased healthcare utilization, morbidity, and mortality, and anxiety has been linked to increased post-operative complications.

Our study demonstrates that in sarcoma patients, depression and anxiety exist at a higher prevalence than the standard US population: 20.2% vs 8.6%, and 18.6% vs 2.9%, respectively. Depression and anxiety were frequently noted via screening to be at levels high enough to warrant referral to mental health providers. Both were more common among patients at their initial visits and those with actively recurrent disease.

Furthermore, the majority of patients offered referral to mental health accepted this referral. We feel this demonstrates patients are eager for mental help support. When treating sarcoma patients, consideration should be given to potential

concomitant psychiatric diagnoses. Screening, especially at the highest risk timepoints such as at initial diagnosis and at time of recurrence, should be considered.

Table 1. Rates of positive depression and anxiety screens based on PHQ-9 and GAD-7 scores.

Characteristic	N	Overall, N = 99	dNED, N = 9	Initial, N = 11	Metastatic, N = 14	NED, N = 58	Recurrent, N = 7	p-value [†]
Age at Biopsy	97							0.4
Mean (SD)		45.5 (20.0)	43.7 (17.4)	47.1 (20.0)	53.8 (17.1)	42.8 (21.0)	51.6 (18.7)	
Median (IQR)		48.0 (27.5, 63.5)	40.2 (34.3, 60.0)	50.0 (31.7, 65.0)	59.2 (47.4, 63.8)	46.4 (23.6, 61.1)	55.6 (35.9, 66.7)	
Missing		2	0	2	0	0	0	
PHQ-9 Total Score	99							0.12
Mean (SD)		5.0 (5.0)	5.6 (4.9)	7.0 (6.2)	5.5 (4.7)	4.0 (4.5)	8.9 (6.2)	
Median (IQR)		4.0 (1.0, 8.0)	4.0 (2.0, 7.0)	7.0 (1.0, 12.0)	4.5 (2.2, 8.0)	2.6 (0.0, 7.0)	11.0 (4.0, 13.5)	
PHQ-9 Depression Severity, n (%)	99							
Minimal		60 (60.6%)	5 (55.6%)	4 (36.4%)	7 (50.0%)	41 (70.7%)	3 (42.9%)	
Mild		19 (19.2%)	2 (22.2%)	3 (27.3%)	4 (28.6%)	10 (17.2%)	0 (0.0%)	
Moderate		13 (13.1%)	2 (22.2%)	3 (27.3%)	2 (14.3%)	4 (6.9%)	2 (28.6%)	
Moderately Severe		6 (6.1%)	0 (0.0%)	1 (9.1%)	1 (7.1%)	2 (3.4%)	2 (28.6%)	
Severe		1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	
Moderate Depression or Worse, n (%)	99							0.029
Min-Mild Dep		79 (79.8%)	7 (77.8%)	7 (63.6%)	11 (78.6%)	51 (87.9%)	3 (42.9%)	
Mod-Sev Dep		20 (20.2%)	2 (22.2%)	4 (36.4%)	3 (21.4%)	7 (12.1%)	4 (57.1%)	
GAD-7 Total Score	97							0.055
Mean (SD)		4.9 (5.3)	4.6 (5.2)	8.3 (5.2)	3.9 (4.6)	4.0 (4.6)	9.9 (8.3)	
Median (IQR)		3.0 (1.0, 8.0)	2.0 (1.0, 8.0)	9.0 (5.5, 11.5)	2.5 (2.0, 4.0)	3.0 (0.0, 5.0)	10.0 (2.0, 16.5)	
Missing		2	0	0	0	2	0	
GAD-7 Anxiety Severity, n (%)	97							
Minimal		60 (61.9%)	5 (55.6%)	3 (27.3%)	11 (78.6%)	38 (67.9%)	3 (42.9%)	
Mild		19 (19.6%)	3 (33.3%)	4 (36.4%)	2 (14.3%)	10 (17.9%)	0 (0.0%)	
Moderate		9 (9.3%)	0 (0.0%)	3 (27.3%)	0 (0.0%)	5 (8.9%)	1 (14.3%)	
Severe		9 (9.3%)	1 (11.1%)	1 (9.1%)	1 (7.1%)	3 (5.4%)	3 (42.9%)	
Missing		2	0	0	0	2	0	
Moderate Anxiety or Worse, n (%)	97							0.027
Min-Mild Anx		79 (81.4%)	8 (88.9%)	7 (63.6%)	13 (92.9%)	48 (85.7%)	3 (42.9%)	
Mod-Sev Anx		18 (18.6%)	1 (11.1%)	4 (36.4%)	1 (7.1%)	8 (14.3%)	4 (57.1%)	
Missing		2	0	0	0	2	0	
Dep/Anx Referral Offered, n (%)	99	26 (26.3%)	2 (22.2%)	5 (45.5%)	3 (21.4%)	12 (20.7%)	4 (57.1%)	0.2



10:36 AM - 10:43 AM

Paper #61 #1818759

HEALTH-RELATED QUALITY OF LIFE PREDICTS 1-YEAR-SURVIVAL IN SARCOMA PATIENTS - RESULTS OF A GERMAN OBSERVATIONAL STUDY
Martin Eichler¹; Susanne Singer²; Leopold Hentschel¹; Stephan Richter¹; Peter Hohenberger³; Bernd Kasper³;
Dimosthenis Andreou⁴; Daniel Pink⁴; Jens Jakob⁵; Martin Bornhäuser¹; Jochen Schmitt⁶; Markus K. Schuler¹;
¹University Hospital Carl Gustav Carus, Dresden, Sachsen, GERMANY; ²University Hospital Mainz, Mainz, Rheinland-Pfalz, GERMANY; ³Mannheim University Medical Center, University of Heidelberg, Mannheim, Baden-Württemberg, GERMANY;

⁴Helios Klinikum Bad Saarow, Bad Saarow, Brandenburg, GERMANY; ⁵University Hospital Goettingen, Goettingen,

 Niedersachsen, GERMANY; ⁶National Center for Tumor Diseases (NCT/UCC), Dresden, Sachsen, GERMANY

Objective: Health-related quality of life (HRQoL) has been shown to be a predictor for survival in other cancer entities but it was unknown to date whether it is also applies to sarcoma-patients.

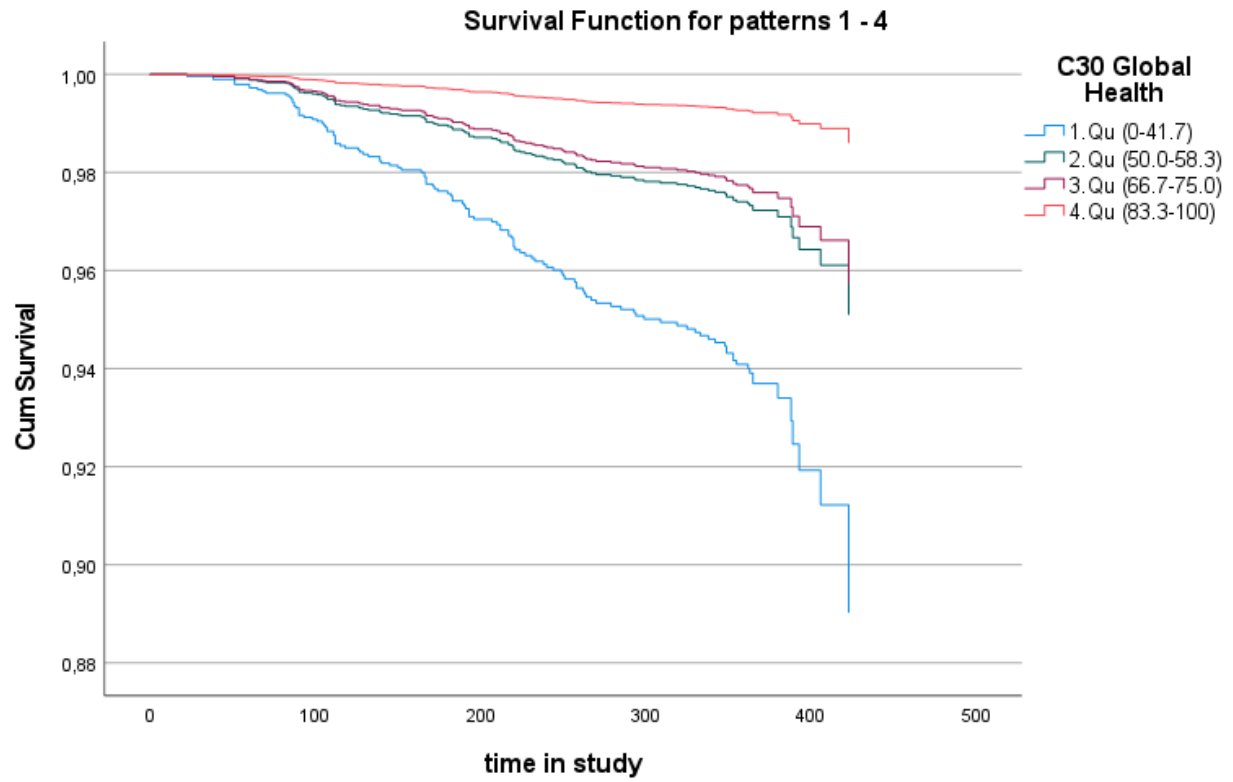
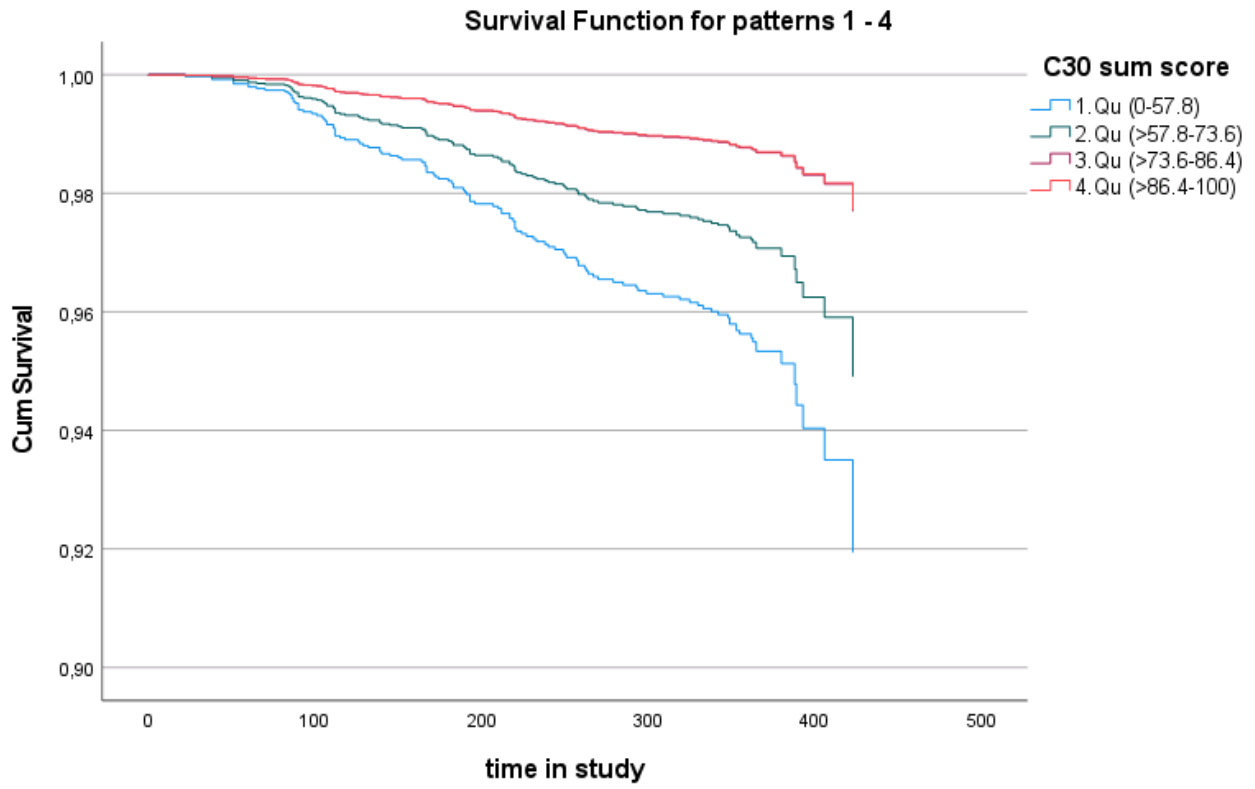
Methods: HRQoL was assessed between 09/2017 and 02/2019 in adult sarcoma patients in 39 study centers in Germany using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30). Vital status was ascertained over the course of one year. We hypothesized that global health, summary score, physical functioning, fatigue, pain, and appetite loss were independently associated with survival. HRQoL domains were analyzed by multivariable cox-regressions including clinical risk factors and stage of disease.

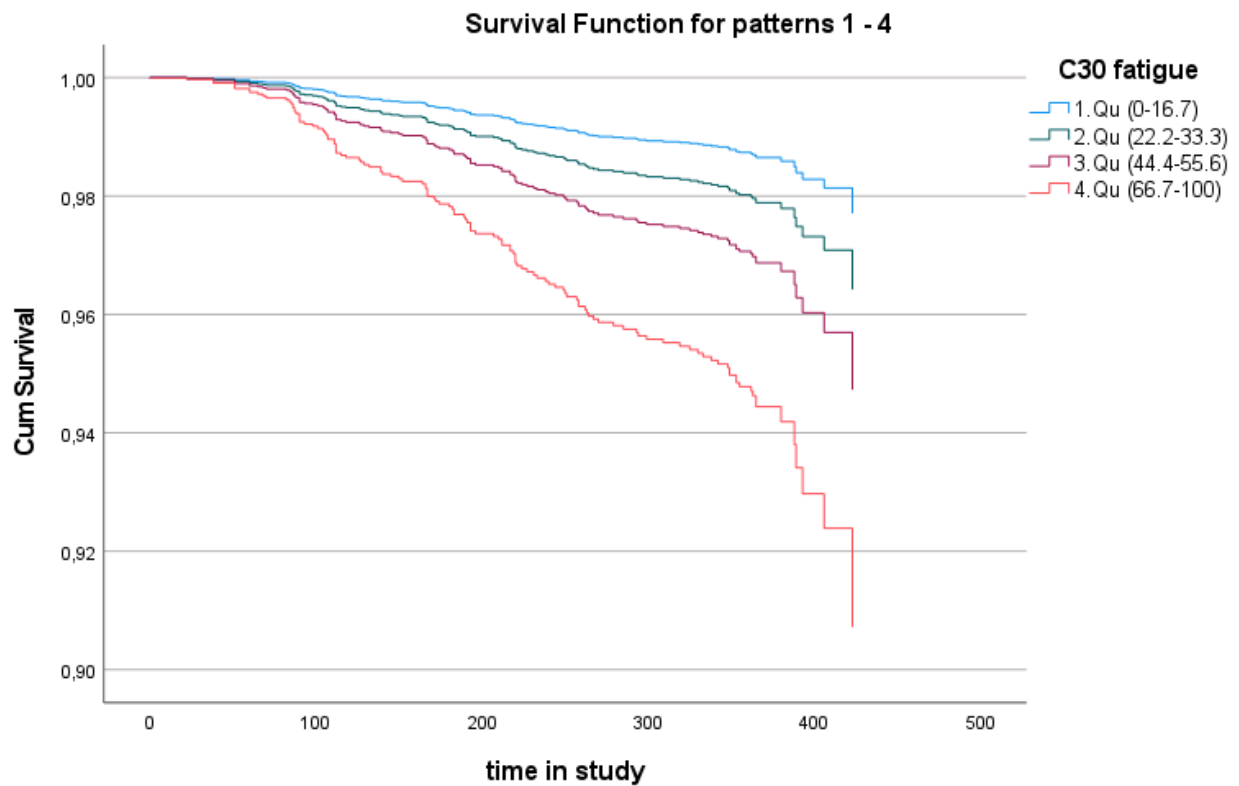
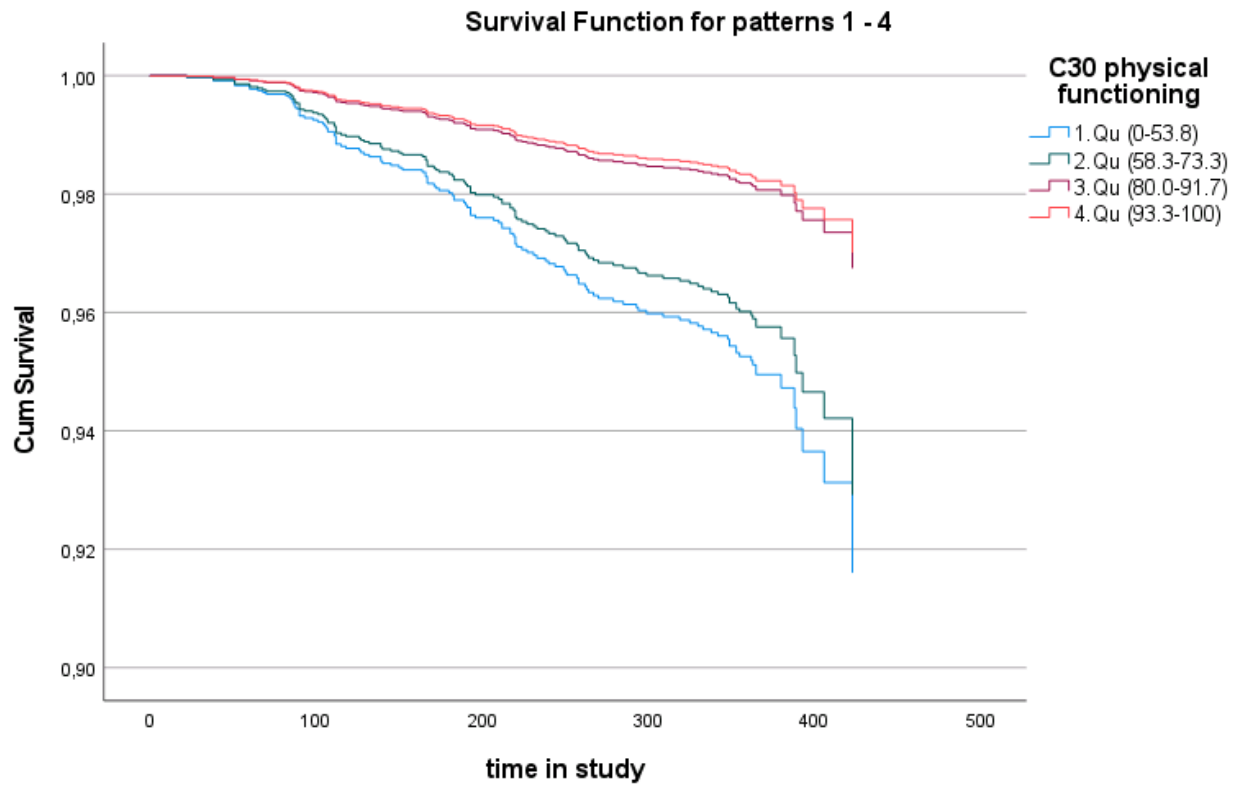
Results: Of 1102 analyzed patients, 126 died during follow-up. The Hazard Ratio (HR) for global health was 0.73 per 10-point increase (95% confidence interval (CI) 0.64-0.85). HR for the summary score was 0.74 (CI 0.64-0.85) and for physical functioning 0.82 (CI 0.74-0.89). There was also evidence that fatigue (HR 1.17, CI 1.10-1.25), appetite loss (HR 1.15, CI 1.09-1.21), and pain (HR 1.14, CI 1.08-1.20) are associated with survival.

Conclusion: All hypothesized HRQoL-domains, namely global health, summary score, physical functioning, fatigue, pain, and appetite loss, were significantly associated with survival. We can therefore add disease-specific evidence to that which already exists in the field of cancer patients in general. Clinicians and care-givers should be aware of the relationship between HRQoL and survival probability.

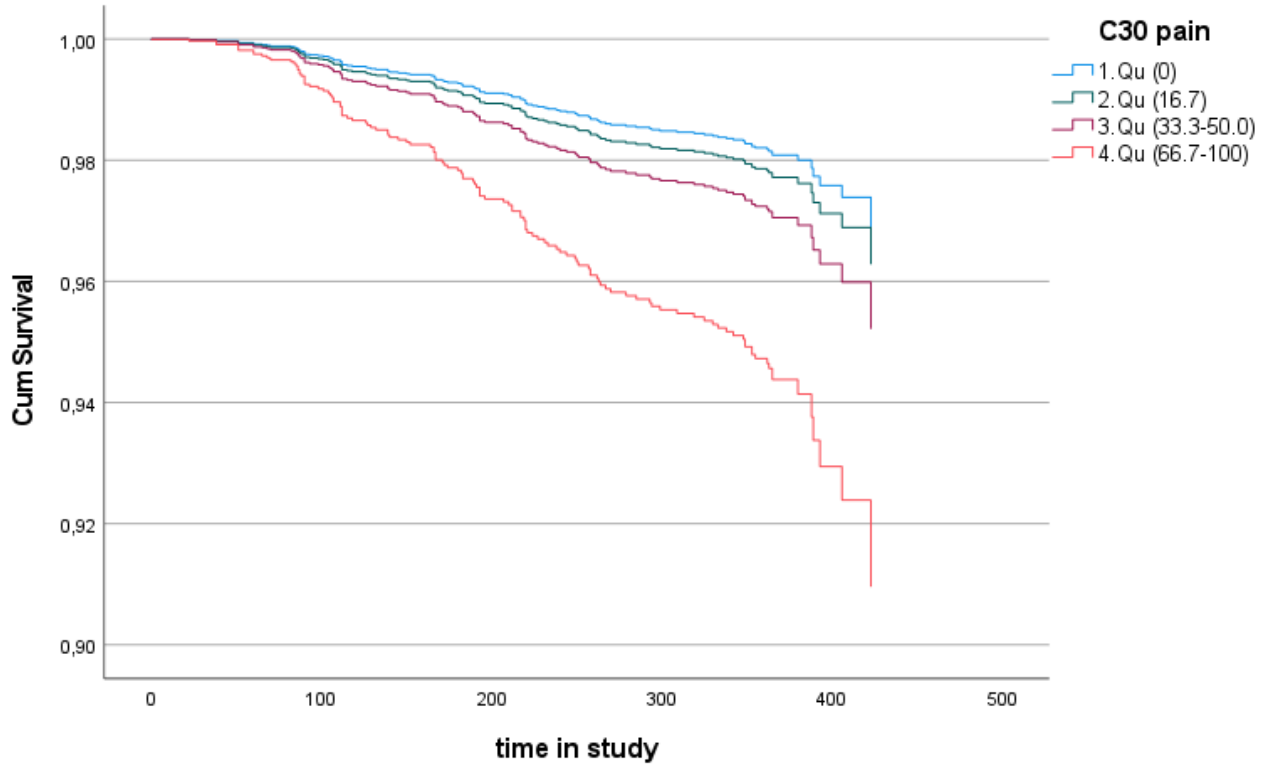
QoL domain	Model – per 10 points HR (95%CI)	Quartiles [range] N (%)		Deceased N (%)	Model HR (95%CI)
C30 summary score	0.74 (0.64-0.85)	4.Qu.[>86.4-100]	271 (25.1)	10 (3.7)	ref.
		3.Qu.[>73.6-86.4]	271 (25.1)	16 (5.9)	1.01 (0.43-2.38)
		2.Qu.[>57.8-73.6]	268 (24.8)	39 (14.6)	2.27 (1.06-4.88)
		1.Qu.[0-57.8]	270 (25.0)	60 (22.0)	3.65 (1.73-7.69)
C30 global health	0.73 (0.64-0.82)	4.Qu.[83.3-100]	262 (23.9)	5 (1.9)	ref.
		3.Qu.[66.7-75.0]	289 (26.3)	26 (9.0)	3.11 (1.12-8.59)
		2.Qu.[50.0-58.3]	264 (24.1)	34 (12.9)	3.58 (1.31-9.78)
		1.Qu.[0-41.7]	282 (25.7)	61 (21.6)	8.29 (3.13-22.00)
C30 physical functioning	0.82 (0.74-0.89)	4.Qu.[93.3-100]	336 (30.5)	16 (4.8)	ref.
		3.Qu.[80.0-91.7]	231 (21.0)	18 (7.8)	1.09 (0.52-2.28)
		2.Qu.[58.3-73.3]	248 (22.5)	32 (12.9)	2.42 (1.23-4.78)
		1.Qu.[0-53.3]	285 (25.9)	60 (21.1)	2.89 (1.52-5.51)
C30 fatigue	1.17 (1.10-1.25)	1.Qu.[0-16.7]	238 (21.6)	9 (3.8)	ref.
		2.Qu.[22.2-33.3]	301 (27.4)	20 (6.6)	1.57 (0.68-3.64)
		3.Qu.[44.4-55.6]	229 (20.8)	27 (11.8)	2.34 (1.04-5.26)
		4.Qu.[66.7-100]	332 (30.2)	70 (21.1)	4.21 (1.98-8.94)
C30 pain	1.14 (1.08-1.20)	1.Qu.[0]	343 (31.2)	24 (7.0)	ref.
		2.Qu.[16.7]	147 (13.4)	12 (8.2)	1.19 (0.56-2.56)
		3.Qu.[33.3-50.0]	334 (30.3)	36 (10.8)	1.55 (0.87-2.74)
		4.Qu.[66.7-100]	277 (25.2)	54 (19.5)	2.99 (1.72-5.19)
C30 appetite loss	1.15 (1.09-1.21)	1.Qu.[0]	722 (65.6)	49 (6.8)	ref.
		2.Qu.[33.3]	208 (18.9)	33 (15.9)	2.10 (1.28-3.44)
		3.Qu.[66.7]	127 (11.5)	31 (24.4)	3.56 (2.12-5.99)
		4.Qu.[100]	44 (4.0)	13 (29.5)	3.43 (1.71-6.88)

Table 1: Results of the multivariable Cox-regression. Variables in the model: sex, age at baseline, employment status at baseline, school education, sarcoma type, tumor site, grading at diagnosis, tumor size at diagnosis, time since diagnosis, tumor recurrence until baseline, metastasis until baseline, disease status at baseline, comorbidities, surgery, chemotherapy, radiotherapy until baseline. Boldface = statistically significant at $p < 0.05$. HR= hazard ratio; 95% CI= 95% confidence interval, ref= reference, n.a. not available.

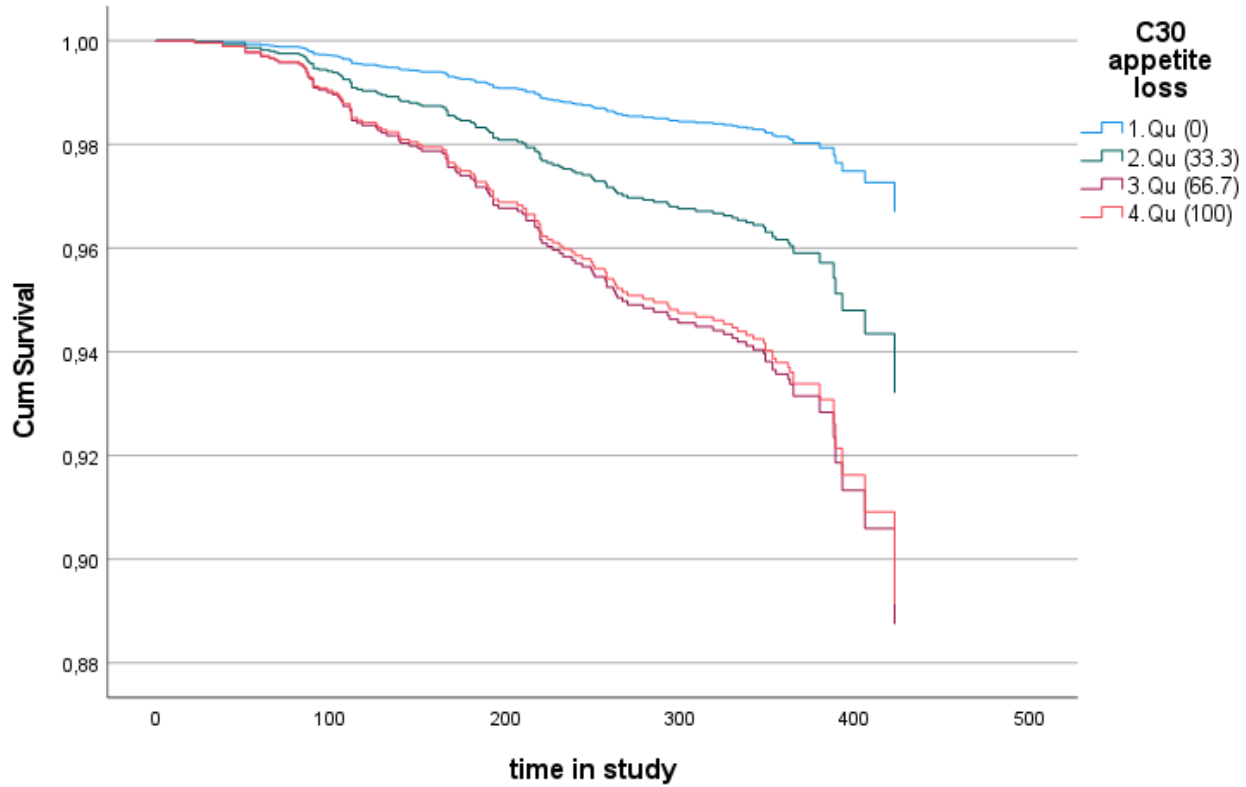




Survival Function for patterns 1 - 4



Survival Function for patterns 1 - 4





ctos[®]

2021 Virtual Annual Meeting

Oral Presentations

Saturday, November 12, 2021



11:00 am - 12:00 pm

– Session 11 –

RETROPERITONEAL SARCOMA

11:00 AM - 11:07 AM

Paper #63 #1818702

ASSOCIATION BETWEEN AGEING AND SHORT-TERM SURVIVAL OUTCOMES IN PATIENTS UNDERGOING SURGERY FOR PRIMARY RETROPERITONEAL SARCOMA

Fabio Tirota¹; **Michael Fadel**¹; **Helene Wilkerson**¹; **Alessandro Parente**²; **James Hodson**²; **Marco Baia**²; **Jonathan Hannay**³; **Max Almond**²; **Myles Smith**³; **Samuel J. Ford**²; **Andrew J. Hayes**³; **Anant Desai**²; **Dirk Strauss**³

¹The Royal Marsden Hospital NHS Foundation Trust, London, England, UNITED KINGDOM; ²University Hospital Birmingham NHS Foundation Trust, Birmingham, England, UNITED KINGDOM; ³The Royal Marsden Hospital NHS Foundation Trust, London, England, UNITED KINGDOM

Objective: Retroperitoneal sarcoma (RPS) can affect patients of any age. Surgical resection is characterised by rates of major postoperative complications (Clavien-Dindo ≥ 3) of approximately 20% and mortality rates of 2%. As a result of the ageing population, numbers of elderly patients presenting with primary RPS are increasing. It is currently unclear whether elderly patients are at increased risk of morbidity or mortality following surgery. Our study aimed to evaluate the association between age and short-term survival outcomes in patients undergoing surgery for RPS.

Methods: Data for patients undergoing surgery for primary RPS between 2008 and 2019 were extracted from a prospectively maintained database at two specialist institutions. Patients were divided into four subgroups of age: <55, 55-64, 65-74, and 75+ years, and demographic factors, postoperative morbidity and one year mortality rates were compared between groups. Comorbidities were quantified using a modified version of the Charlson Comorbidity Index (mCCI), which excluded the age component.

Results: Overall, N=556 patients underwent surgery, at a mean age of 61.4 years (range: 16.6-89.4), comprising N=161, N=139, N=189 and N=69 aged <55, 55-64, 65-74 and 75+ years, respectively. The major complications rate was 19.6%, and was not found to differ significantly between the age groups ($p=0.420$). However, a significant association between age and one year mortality was observed ($p=0.003$). Further assessment found one year mortality rates to be similar for the <55, 55-64 and 65-74 year age groups (9.1% vs. 7.3% vs. 9.3%), but markedly increased in the 75+ year group (23.4%) (Table 1). The distribution of causes of death also differed between groups ($p=0.030$), with all cases of one year mortality in the <55 year group being due to disease recurrence, whilst 33% of deaths in the 75+ year group result were consequences of postoperative complications (Figure 1).

A multivariable analysis identified increasing ECOG ($p=0.026$), mCCI ($p=0.003$), tumour grade ($p<0.001$) and organ resected weighted score ($p<0.001$), as well as tumours located in the right retroperitoneum ($p=0.002$) and lower BMI ($p=0.018$) to be significant independent predictors of one year mortality. After accounting for these factors, the association between age and one year mortality remained significant ($p=0.002$) (Table 2). Comparisons between subgroups found no significant difference between patients aged <55 years and those aged 55-64 ($p=0.346$) or 65-74 ($p=0.485$) years, but a significant increase in mortality for those aged 75+ years ($p=0.015$).

Assessment of the interplay between age and frailty found patients aged <75 years with an ECOG performance score of 2-3 to have similar one year mortality rates to those aged 75+ years with a score of 0-1 (25.0% vs. 21.3%). Likewise, patients aged <75 years with a mCCI of 4+ had similar one year mortality rates to those aged 75+ a mCCI of 2-3 (20.8% vs. 22.4%).

Conclusion: Patients aged 75+ years have a significantly higher risk of one year mortality after surgery, compared to younger patients, largely due to a higher risk of mortality after postoperative complications. In addition, age, comorbidity burden and frailty are independent predictors of one year mortality, with similar effect sizes. As such, elderly, but non-frail patients appear to have similar mortality rates to younger, but frail patients. These findings are particularly relevant in the decision-making process when surgery is being offered to elderly patients with RPS.

Table 1 – Cohort characteristics by age

	Age at Surgery (Years)				p-Value
	<55 (N=161)	55-64 (N=139)	65-74 (N=189)	75+ (N=69)	
Sex (% Male)	71 (44.1%)	75 (54.0%)	114 (61.0%)	43 (62.3%)	0.008
BMI (kg/m ²)	26.2 ± 6.5	27.5 ± 5.9	27.7 ± 5.4	26.8 ± 4.0	0.004
ECOG Performance Status					<0.001*
0	112 (70.4%)	85 (61.2%)	97 (51.9%)	23 (33.8%)	
1	41 (25.8%)	46 (33.1%)	82 (43.9%)	43 (63.2%)	
2-3	6 (3.8%)	8 (5.8%)	8 (4.3%)	2 (2.9%)	
ASA Grade					0.003*
1	37 (23.0%)	24 (17.3%)	16 (8.6%)	6 (8.7%)	
2	92 (57.1%)	81 (58.3%)	117 (62.6%)	41 (59.4%)	
3-4	32 (19.9%)	34 (24.5%)	54 (28.9%)	22 (31.9%)	
CCI – Excluding Age					<0.001*
2	143 (88.8%)	115 (82.7%)	129 (69.0%)	51 (75.0%)	
3	13 (8.1%)	18 (12.9%)	44 (23.5%)	11 (16.2%)	
4+	5 (3.1%)	6 (4.3%)	14 (7.5%)	6 (8.8%)	
Tumour Histology					<0.001
DDLPS	47 (29.2%)	56 (40.3%)	94 (50.3%)	38 (55.1%)	
WDLPS	31 (19.3%)	30 (21.6%)	40 (21.4%)	15 (21.7%)	
LMS	38 (23.6%)	32 (23.0%)	34 (18.2%)	10 (14.5%)	
Others	45 (28.0%)	21 (15.1%)	19 (10.2%)	6 (8.7%)	
Multi-Focal	8 (5.0%)	4 (2.9%)	11 (5.9%)	5 (7.2%)	0.505
Tumour Location					0.483
Right Retroperitoneum	73 (45.3%)	58 (41.7%)	89 (47.6%)	31 (44.9%)	
Left Retroperitoneum	61 (37.9%)	63 (45.3%)	78 (41.7%)	32 (46.4%)	
Others	27 (16.8%)	18 (12.9%)	20 (10.7%)	6 (8.7%)	
Tumour Size (mm)	170 (120-250)	180 (130-267)	200 (128-270)	180 (120-250)	0.157
FNCLCC Tumour Grade**					0.672*
Grade 1	48 (37.2%)	39 (31.5%)	54 (31.0%)	20 (29.4%)	
Grade 2	35 (27.1%)	46 (37.1%)	50 (28.7%)	26 (38.2%)	
Grade 3	46 (35.7%)	39 (31.5%)	70 (40.2%)	22 (32.4%)	
ORWS					0.297*
0-1	64 (39.8%)	46 (33.1%)	50 (26.7%)	23 (33.3%)	
2	44 (27.3%)	36 (25.9%)	67 (35.8%)	21 (30.4%)	
3-4	44 (27.3%)	38 (27.3%)	52 (27.8%)	19 (27.5%)	
5+	9 (5.6%)	19 (13.7%)	18 (9.6%)	6 (8.7%)	
Resection Margins (% R2)	1 (0.6%)	0 (0.0%)	6 (3.2%)	2 (2.9%)	0.075
Chemotherapy					<0.001
No	142 (88.2%)	134 (96.4%)	184 (98.4%)	69 (100.0%)	
Preoperative	18 (11.2%)	5 (3.6%)	2 (1.1%)	0 (0.0%)	
Postoperative	1 (0.6%)	0 (0.0%)	1 (0.5%)	0 (0.0%)	
Radiotherapy					0.006
No	137 (85.1%)	131 (94.2%)	175 (93.6%)	67 (97.1%)	
Preoperative	19 (11.8%)	8 (5.8%)	9 (4.8%)	0 (0.0%)	
Postoperative	5 (3.1%)	0 (0.0%)	3 (1.6%)	2 (2.9%)	
Major Complication	30 (18.6%)	23 (16.5%)	38 (20.3%)	18 (26.1%)	0.420
One Year Mortality	14 (9.1%)	10 (7.3%)	17 (9.3%)	15 (23.4%)	0.003

Continuous variables are reported as mean ± SD, or as median (IQR), with p-values from Kruskal-Wallis tests. Categorical variables are reported as N (column %), with p-values from Chi-square tests, unless stated otherwise. Bold p-values are significant at p<0.05. *p-Value from Kruskal-Wallis test, as the factor is ordinal. ** Excludes patients with tumour histology that was not applicable to grading, or that had received chemo- or radiotherapy preoperatively. CCI=Charlson Comorbidity Index, ORWS=organ resected weighted score.

Table 2 – Associations with one year mortality

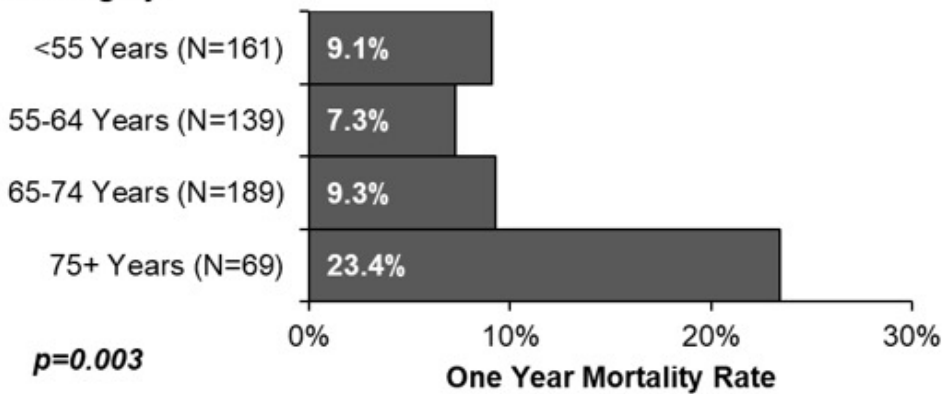
	Univariable		Multivariable	
	OR (95% CI)	p-Value	OR (95% CI)	p-Value
Age at Surgery (Years)		0.006		0.002
<55	-	-	-	-
55-64	0.79 (0.34-1.84)	0.580	0.61 (0.21-1.72)	0.346
65-74	1.02 (0.49-2.15)	0.950	0.72 (0.28-1.83)	0.485
75+	3.06 (1.38-6.80)	0.006	3.81 (1.30-11.2)	0.015
Sex (Female)	0.70 (0.39-1.23)	0.214	-	NS
BMI (per 5kg/m ²)	0.67 (0.49-0.90)	0.009	0.65 (0.46-0.93)	0.018
ECOG Performance Status		0.008		0.026
0	-	-	-	-
1	1.76 (0.97-3.17)	0.061	1.14 (0.56-2.31)	0.720
2-3	4.61 (1.65-12.9)	0.004	5.39 (1.56-18.6)	0.008
ASA Grade		0.026		NS
1	-	-	-	-
2	0.93 (0.39-2.22)	0.862	-	-
3-4	2.07 (0.84-5.06)	0.112	-	-
CCI - Excluding Age		0.035		0.003
2	-	-	-	-
3	1.91 (0.97-3.78)	0.063	2.08 (0.91-4.78)	0.084
4+	2.80 (1.07-7.31)	0.036	7.94 (2.28-27.6)	0.001
Multi-Focal	1.47 (0.49-4.40)	0.493	-	NS
Tumour Location		0.243		0.004
Right Retroperitoneum	-	-	-	-
Left Retroperitoneum	0.60 (0.32-1.11)	0.103	0.29 (0.14-0.63)	0.002
Others	0.97 (0.42-2.24)	0.952	1.12 (0.40-3.11)	0.832
Tumour Size (per 100mm)	0.83 (0.63-1.09)	0.183	-	NS
Tumour Type		<0.001**		NS
DDLPS	-	-	-	-
LMS	0.50 (0.23-1.07)	0.075	-	-
Others	0.99 (0.49-1.97)	0.970	-	-
WDLPS	0%*	NC	N/A***	-
FNCLCC Tumour Grade		<0.001**		0.003
Grade 2	-	-	-	-
Grade 3	3.42 (1.67-6.99)	<0.001	3.96 (1.79-8.77)	<0.001
Preop. Chemo/Radiotherapy	2.61 (0.98-6.94)	0.054	2.47 (0.74-8.24)	0.142
Grade 1	0%*	NC	N/A***	-
ORWS (per Point)	1.37 (1.16-1.62)	<0.001	1.54 (1.23-1.94)	<0.001
Resection Margins (R2)	2.93 (0.58-14.9)	0.194	5.71 (0.89-36.5)	0.066

Results are from binary logistic regression models, with one year mortality as the dependent variable; patients lost to follow up within a year of surgery were excluded throughout (N=18). Univariable models were initially performed, considering each factor separately. A multivariable model was then produced, which used a backwards stepwise approach to variable selection, with all factors in the table considered for inclusion. There were no events in patients with WDLPS or FNCLCC Grade 1 tumours, hence these cases were excluded from the multivariable analysis, along with those with missing data on any of the factors considered, leaving N=382 (N=54 events) in the final analysis. Bold p-values are significant at p<0.05. *Odds ratios were incalculable, as there were no events. **p-Value from a Chi-square test, as an overall p-value could not be produced using binary logistic regression, due to odds ratios being incalculable in one group. ***Patients were excluded from the multivariable model. CCI=Charlson Comorbidity Index, NC=Not calculable; NS=Not selected by the stepwise procedure for inclusion in the final model; OR=Odds ratio; ORWS=Organ resected weighted score.

Figure 1 – One year mortality rates and causes of death by age at surgery

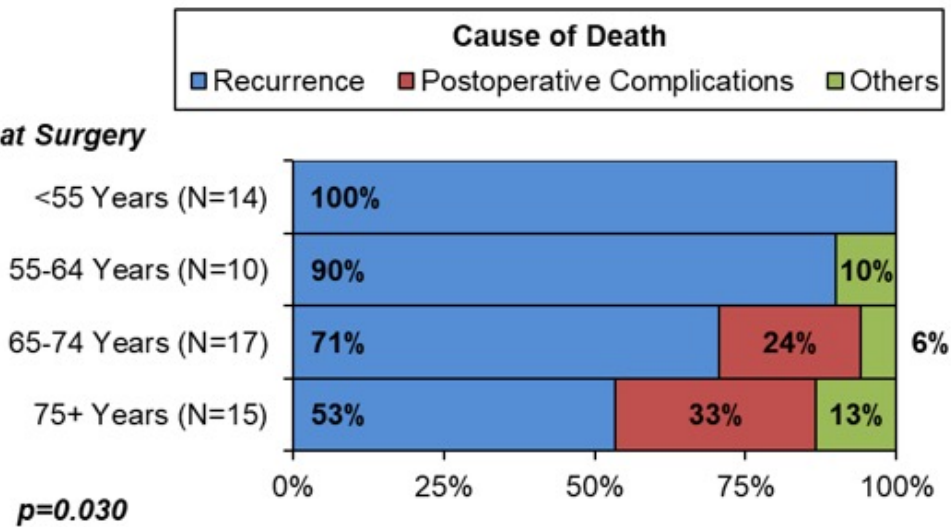
A

Age at Surgery



B

Age at Surgery



The analysis of causes of death includes only those that died within a year of surgery. The p-values are from a Chi-square test for the comparison of the overall mortality rate, and Fisher's exact test for the causes of death.



11:07 AM - 11:14 AM

Paper #64 #1818767

PROGNOSIS PREDICTION IN PATIENTS WITH RETROPERITONEAL SARCOMA: UPDATE OF CURRENT NOMOGRAMS

Dario Callegaro¹; Francesco Barretta¹; Chandrajit P. Raut²; Sally Burtenshaw³; Dirk Strauss⁴; Charles Honoré⁵; Sylvie Bonvalot⁶; Mark Fairweather⁷; Piotr L. Rutkowski⁸; Winan J. van Houdt⁹; Rebecca A. Gladdy¹⁰; Fabio Tirotta⁴; Dimitri Tzanis⁶; Jacek Skoczylas⁸; Rick L. Haas⁹; Rosalba Miceli¹; Carol J. Swallow¹⁰; Alessandro Gronchi¹

¹Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY; ²Harvard Medical School, Dana-Farber Cancer Institute, Harvard University, Boston, Massachusetts, UNITED STATES; ³Mount Sinai Hospital, Toronto, Ontario, CANADA; ⁴The Royal Marsden Hospital NHS Foundation Trust, London, England, UNITED KINGDOM; ⁵Institut Gustave Roussy, Villejuif, Ile-de-France, FRANCE; ⁶Institut Curie, Paris, Ile-de-France, FRANCE; ⁷Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES; ⁸Maria Sklodowska-Curie Institute -Oncology Center, Institute of Oncology, Warsaw, Mazowieckie, POLAND; ⁹The Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS; ¹⁰Princess Margaret Hospital, University Health Network and Mount Sinai Hospital, Toronto; Lunenfeld Tanenbaum Research Institute, Sinai Health System, Toronto, Ontario, CANADA

Objective: Prognostic nomograms for patients with primary RPS provides the individual probability of being alive or developing a tumor recurrence after surgery on the basis of tumor- and patient-characteristics. Nomograms tend to become obsolete with time and need to be updated. In a recent analysis of time-trend outcomes of patients with primary RPS resected at referral centers we observed that long term survival increased over the past 15 years (PMID: 33073340). As a result, the RPS nomograms currently included in the AJCC staging system 8th edition (Sarculator nomograms) systematically underestimated survival probabilities of patients operated upon in a recent time-period (PMID: 33057862). The aim of the present study was to recalibrate the RPS nomogram to take into effect the improved outcomes of RPS patients.

Methods: We updated the prediction of the Sarculator RPS nomogram using a development cohort. The new nomograms were then tested on an independent external validation cohort. All consecutive adult patients with primary localized RPS who had undergone curative-intent resection between 2010 and 2017 at four referral centers in Europe and Canada formed the development cohort. Patients with the same clinical characteristics who had been resected at four other European and US referral centers formed the independent external validation cohort. Patients who underwent macroscopically incomplete resection were not included. Follow-up was updated at May 2021. The Sarculator nomogram endpoints were 7-year OS and DFS. These nomograms were initially tested on the development cohort to assess possible evolutions of the covariates effects or a shift of the baseline hazards. We observed also in this series an underestimation of patient outcomes. Hence, we proceeded by fitting new baseline hazards on the development cohort and externally tested them on the validation cohort. The new nomograms endpoints were 5-yr OS and 5-yr DFS. Performance was assessed in terms of discrimination (Harrell C index) and calibration (calibration plots).

Results: The development and validation cohorts consisted of 837 and 230 patients, respectively. Clinicopathological characteristics are summarized in Table 1. The median follow-up was 75mo (IQR 56-97) for the development cohort and 60mo (IQR 48-79) for the validation cohort. The application of the OS Sarculator nomogram to the development cohort confirmed a systematic underestimation of survival probabilities (Figure 1, all the bars are above the 45-degree line). After the adjustment of the baseline hazard function the nomogram was better calibrated when applied to both the development cohort (Figure 2, bars aligned on the 45-degree line) and the external validation cohort (Figure 3, bars aligned on the 45-degree line, with slight overestimation). In terms of calibration, similar results were observed for the DFS nomogram. When the old nomograms were applied to the development cohort they yielded Harrell C indexes of 0.74 (OS) and 0.68 (DFS). Harrell C indexes of the new OS (DFS) nomogram were 0.74 (0.68) at internal validation and 0.73 (0.71) at external validation.

Conclusion: With the present study we improved the performance of the OS and DFS Sarculator RPS nomograms, especially in terms of calibration, by adjusting the baseline hazard function. We achieved the best calibration when the nomograms were applied to the four higher volume centers while the external validation on lower volume centers, despite improved compared to the old nomograms, resulted in a slight overestimation of patient prognosis, with very good discrimination (Harrell C indexes > 0.70). This further highlight the volume-outcome relationship in RPS. Generalizability of the new nomograms outside referral centers has not been tested. The update will follow in the Sarculator app.

Table 1: clinicopathological characteristics of the development and validation cohorts.

	Development cohort (n=837)	Validation cohort (n=230)	p-value*
Patients per center Median (range)	206 (112-312)	54 (43-80)	0.706
Sex			0.136
Male	448 (53.5)	110 (47.8)	
Female	389 (46.5)	120 (52.2)	
Age (years)			0.025
Median (IQR)	62 (52-69)	61 (52-59)	
Histology			0.002**
WDLPS	194 (23.2)	73 (31.7)	
DDLPS	371 (44.3)	80 (34.8)	
LMS	158 (18.9)	40 (17.4)	
SFT	39 (4.7)	8 (3.5)	
MPNST	15 (1.8)	10 (4.3)	
UPS	24 (2.9)	14 (6.1)	
Other	36 (4.3)	5 (2.2)	
Grade (FNCLCC)			<0.001
I	249 (29.7)	91 (39.6)	
II	363 (43.4)	53 (23.0)	
III	225 (26.9)	86 (37.4)	
Tumor size (cm)			0.820
Median (IQR)	21.5 (15-30)	21.1 (12.5-33.0)	
Multifocality			<0.001
yes	21 (2.5)	20 (8.7)	
no	816 (97.5)	210 (91.3)	
Chemotherapy			0.007
yes	117 (14.0)	17 (7.4)	
no	720 (86.0)	213 (92.6)	
Radiotherapy			0.725
yes	194 (23.2)	56 (24.3)	
no	643 (76.8)	174 (75.7)	
Resected organ score			<0.001
Median (IQR)	3 (2-4)	2 (1-3)	
Tumor rupture			0.126
yes	15 (1.8)	8 (3.5)	
no	822 (98.2)	222 (96.5)	
90-day Clavien-Dindo \geq 3 complications			0.853
yes	167 (20.0)	47 (20.4)	
no	670 (80.0)	183 (79.6)	
Status at last FU			0.421
NED	442 (52.8)	109 (47.4)	
AWD	136 (16.2)	46 (20.0)	
DOD	209 (25.0)	60 (26.1)	
DOC	50 (6.0)	15 (6.5)	

Table legend: IQR, interquartile range; WDLPS, well differentiated liposarcoma; DDLPS, dedifferentiated liposarcoma; LMS, leiomyosarcoma; SFT, solitary fibrous tumor; MPNST, malignant peripheral nerve sheath tumor; UPS, undifferentiated pleomorphic sarcoma; FNCLCC, Federation Nationale des Centres de Lutte Contre le Cancer; FU, follow-up; NED, no evidence of disease; AWD, alive with disease; DOD, dead of disease; DOC, dead of other causes.

* Wilcoxon-Mann-Whitney or Fisher Exact test

** Simulated p-value

Figure 1: calibration plots for validation of the old Sarculator OS nomogram on the development cohort

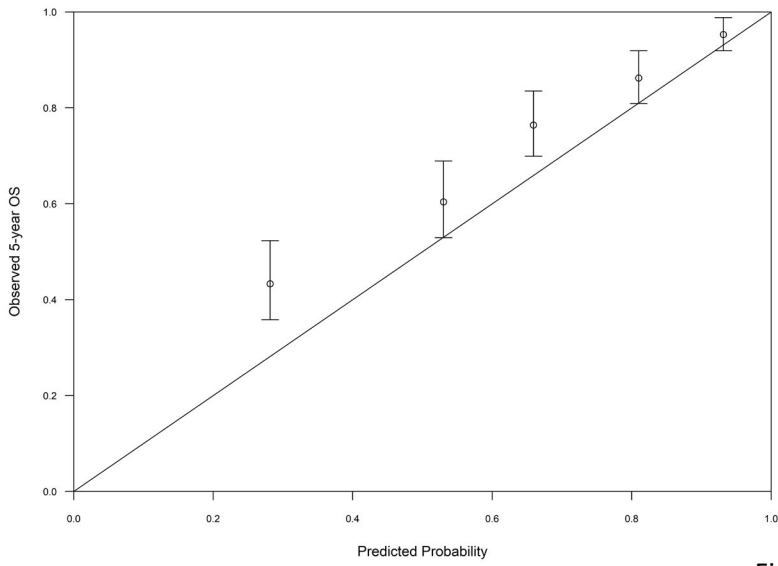


Figure 2: calibration plots for validation of the new Sarculator OS nomogram on the development cohort

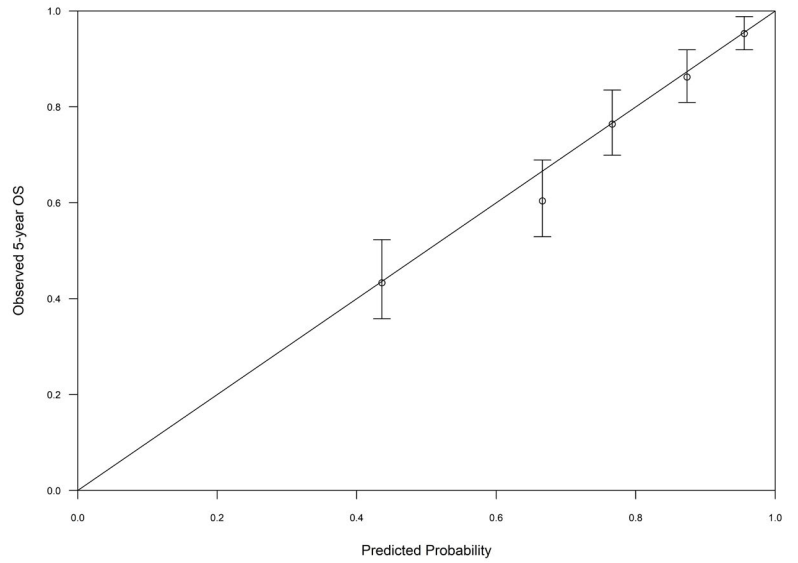
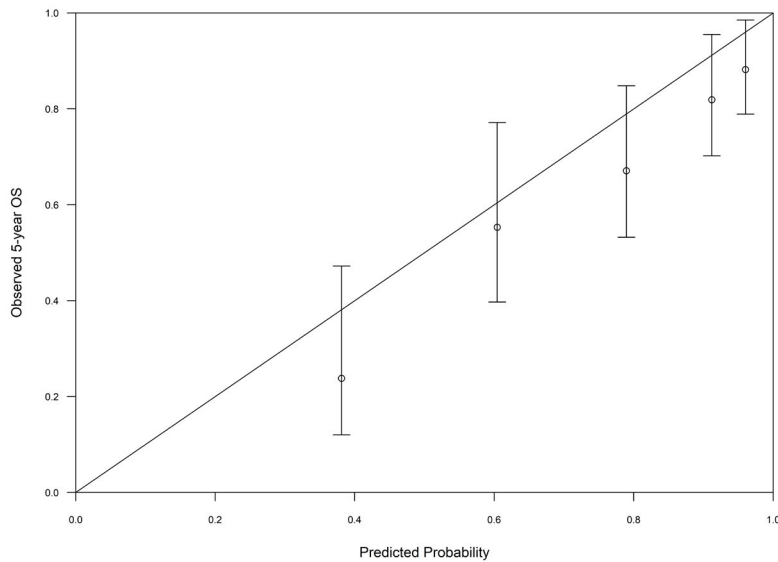


Figure 3: calibration plots for validation of the new Sarculator OS nomogram on the external validation cohort





11:14 AM - 11:21 AM

Paper #65 #1818737

A COMPARISON OF SURVIVAL OUTCOMES AT SPECIALIST VS. NON-SPECIALIST SARCOMA CENTRES, FOR PATIENTS WITH PRIMARY RETROPERITONEAL SARCOMA: AN ENGLISH POPULATION-BASED COHORT ANALYSIS

Fabio Tirotta¹; Shane Collins²; Andrew Bacon³; Anant Desai⁴; Lizz Paley⁵; Dirk Strauss¹; Sandra J. Strauss²

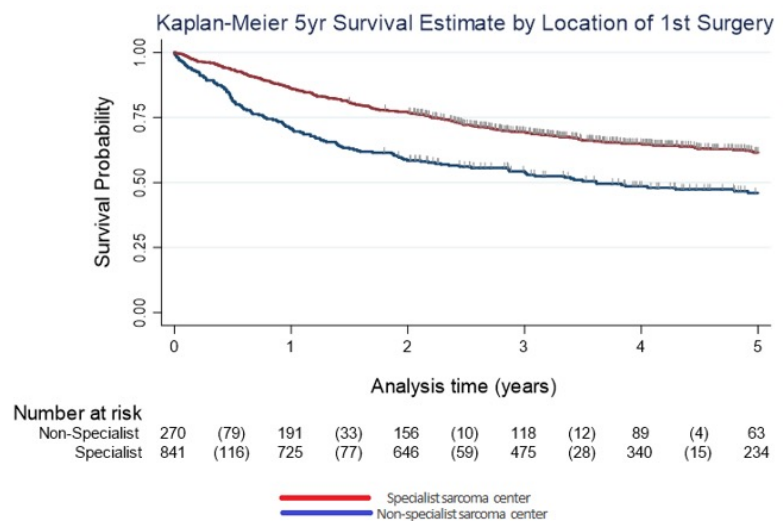
¹The Royal Marsden Hospital NHS Foundation Trust, London, England, UNITED KINGDOM; ²University College London Cancer Institute, London, England, UNITED KINGDOM; ³National Cancer Registration and Analysis Service, Public Health England, London, England, UNITED KINGDOM; ⁴University Hospital Birmingham NHS Foundation Trust, Birmingham, England, UNITED KINGDOM; ⁵National Cancer Registration and Analysis Service, Public Health England, London, England, UNITED KINGDOM

Objective: Primary retroperitoneal sarcomas (RPS) are rare tumours of several well-defined histologic subtypes. Consensus guidelines outline that patients with RPS should be managed within specialist sarcoma centres (SSC). There is, however, a paucity of population-based data that details incidence and outcomes of patients with RPS and the impact of specialist care. The aim of this analysis was to evaluate patterns of care of patients diagnosed with RPS in England and compare outcomes for those undergoing radical surgery in specialist and non-specialist sarcoma centres (N-SSC).

Methods: Data on patients diagnosed with primary RPS between 2013 and 2018 were extracted through Public Health England’s National Cancer Registration and Analysis Service using the national cancer registration dataset for England. The patient cohort was defined using accepted Transatlantic Retroperitoneal Sarcoma Working Group criteria with linked Hospital Episode Statistics (HES) data used to assess the proportion undergoing defined radical surgery. RPS SSC were defined as NHS trusts with a retroperitoneal soft tissue sarcoma multi-disciplinary Team (MDT). Survival was estimated by Kaplan-Meier method and Cox regression analysis.

Results: Between 2013 and 2018, 1,879 patients were diagnosed with RPS, of whom 1,121 (60%) underwent radical surgery within 12 months of diagnosis with a 5-year overall survival (OS) of 58% (CI: 55-61%) compared to 17% (CI: 14-20%) in those who did not undergo surgery (p<0.05). In total, 848 (76%) of 1,121 patients underwent surgery at SSC. Age did not significantly differ between SSC and N-SSC patients (median age 64 [IQR: 53-71] and 62 [IQR: 52-72], p=0.77) as well as comorbidities (Charlson Comorbidity index score 0-1 in 93% and 94% of patients, p=0.48). In contrast, histological subtypes were differently distributed between SSC and N-SSC, with liposarcoma and leiomyosarcoma affecting 57% vs. 30% and 25% vs. 37% of patients (p<0.05), respectively. Patients undergoing surgery in SSC had significantly better 30 day mortality (1.78% [CI:1.08-2.94%] vs. 5.2% [CI:3.1-8.6%], p< 0.05) and 5 year OS than those who received treatment in N-SSC (62% [CI: 58-65%] vs. 46%, [CI: 40-52%], p<0.05) (Figure 1).

Conclusion: Patients with RPS undergoing surgery in SSC have a significantly better acute and long-term survival outcomes than patients operated in N-SSC. The results of this study highlight the importance of managing patients with RPS in SSC.





11:21 AM - 11:28 AM

Paper #66 #1818758

RECLASSIFYING ABDOMINAL NON-UTERINE LEIOMYOSARCOMA: USING A RADIOLOGICAL ANATOMIC APPROACH WITH IMPLICATIONS FOR PATIENT OUTCOMES

Korosh Khalili¹; David Cyr²; Usman Tarique²; Carlo Morosi³; Giorgio Greco³; Rebecca A. Gladdy⁴; Brendan C. Dickson⁵; Dario Callegaro³; Carol J. Swallow⁴

¹University of Toronto, Toronto, Ontario, CANADA; ²Sinai Health System, Toronto, Ontario, CANADA; ³Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY; ⁴Princess Margaret Hospital, University Health Network and Mount Sinai Hospital, Toronto; Lunenfeld Tanenbaum Research Institute, Sinai Health System, Toronto, Ontario, CANADA; ⁵Mount Sinai Hospital, Toronto, Ontario, CANADA

Objective: Primary tumor location is a known prognostic indicator in patients with leiomyosarcoma (LMS), with abdominal tumors portending a worse prognosis. While the IVC is recognized as the most common primary site of abdominal non-uterine (ANU) LMS, we observed a propensity for LMS to originate in veins downstream from sex-hormone producing organs, particularly the ovarian vein. We hypothesize that smaller veins have been under-appreciated as a site of origin. Our purpose here was to classify ANU-LMS using modern high-resolution cross-sectional imaging, and explore any prognostic implications.

Methods: Patients with biopsy-proven primary LMS managed at our center from 2000 through 2020 were identified from an abdominal sarcoma database and automated search of imaging reports. Inclusion criteria: tumor of non-uterine abdominal/pelvic origin, pretreatment cross-sectional (CT/MRI) imaging available for review. Exclusion criteria: history of primary uterine LMS, prior radiation to site of ANU-LMS. Imaging was reviewed by an abdominal radiologist (20 years in practice) who is a member of the abdominal sarcoma group. LMS site of origin was assigned with an increasing confidence rating of 1-5. Tumors originating from the IVC were subclassified as: below right gonadal vein (I); between gonadal vein and liver margin (IIA); between liver margin and hepatic veins (IIB); and at/above hepatic vein (III). Downstream from Sex-Steroid Producing Organ (DSSPO) was defined as originating from ovarian/testicular vein, paratesticular, left renal vein, adrenal vein or IVC IIA. All tumors with low confidence ratings (1-2) were secondarily reviewed with a 2nd external abdominal/sarcoma radiologist (32 years in practice) to reach consensus. Tumor size, location, grade, and ER/PR status and presence of metastases at presentation were noted.

Results: Of 225 patients with ANU-LMS identified from the database, 152 (67.6%) met inclusion/exclusion criteria. 92/152 (61%) were female; median age was 60 (range 22-90). Median tumor size was 7.9 cm (range 1.1-30.3). FNCLCC grade was I in 22/152(15%), II in 61(40%), III in 49(32%). Distant metastases were found at presentation in 23/152 (15%). The 7 most frequent site of origin were ovarian vein 24 (15.8%), IVC IIA 24 (15.8%), renal vein 11 (7.2%), paratesticular 11 (7.2%), IVC IIB 8 (5.2%), indeterminate 8 (5.2%), & adrenal gland/vein 7 (4.6%). In females, IVC (any level) was the most common site (30%), followed by Ovarian Vein (26%), while in males, paratesticular was the most common (18%). Tumor distribution based on organ system was venous (see Figure 1) 84/152 (55.3%), GI 24 (15.8%), genital 11 (7.2%), paratesticular 11 (7.2%), indeterminate 10 (6.6%), urinary 7 (4.6%), adrenal 4 (2.6%), arterial 1 (0.7%). 84/152 (55.3%) of tumors were designated as DSSPO. In univariate analysis of variables associated with distant metastases at presentation (Table 1), large primary tumor size (OR 2.1 (95% CI 1.3-3.4), p=0.004) and non-DSSPO designation (OR 4.3 (95% CI 1.6-11.7), p=0.004) were significant, while patient sex, age, organ system of origin, specific site of origin, and grade were not. On multivariable analysis, both size and DSSPO remained significant predictors of distant metastases at presentation (p=0.01 for both, Table 1). ER/PR status was available in 49/152 (32.2%), being positive in 25/49 (51%) with no significant association found with the studied variables.

Conclusion: Previously under-recognized, the ovarian vein represents the 2nd most common site of AE-LMS in women. For both sexes, tumors arising downstream from sex-hormone producing organs constitute the majority of abdominal extra-uterine LMS. These tumours are associated with a significantly lower risk of metastatic disease at presentation.

Figure 1: Distribution of abdominal non-uterine LMS by organ system

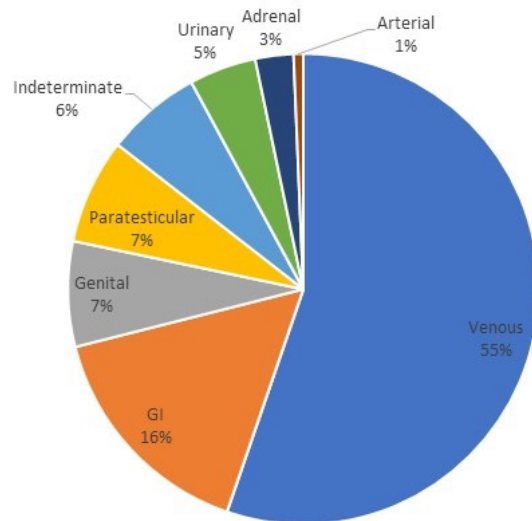


TABLE 1. Univariable and multivariable analysis of factors associated with the presence of distant metastases at presentation

Variables	Univariable analysis		Multivariable analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (years)	1.0 (0.5-2.0)	0.959		
Sex	1.8 (0.8-4.5)	0.180		
Tumor size	2.1 (1.3-3.4)	0.004	1.9 (1.1-3.1)	0.013
Organ system		0.347		
DSSPO	1			
Non-DSSPO	4.3 (1.6-11.7)	0.004	3.7 (1.3-10.3)	0.012
Histologic grade		0.274		
1	0.7 (0.1-3.4)			
2	1.5 (0.3-7.7)			
3	2.9 (0.6-14.4)			



11:28 AM - 11:35 AM

Paper #67 #1818761

WHAT IS THE SIGNIFICANCE OF MICROSCOPIC MARGIN STATUS IN RESECTED PRIMARY RETROPERITONEAL SARCOMA?

Deanna Ng¹; Dario Callegaro²; Brendan C. Dickson³; Dirk Strauss⁴; Sylvie Bonvalot⁵; Chandrajit P. Raut⁶; Charles Honoré⁷; Eberhard Stoeckle⁸; Winan J. van Houdt⁹; Eisar Al-Sukhni³; Shawn Khan³; Rebecca A. Gladdy¹⁰; Marco Fiore²; Mark Fairweather¹¹; Raza Sayyed⁴; Dimitri Tzanis⁵; Yvonne M. Schrage¹²; Alessandro Gronchi²; Carol J. Swallow¹⁰

¹University of Toronto, Toronto, Ontario, CANADA; ²Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY; ³Mount Sinai Hospital, Toronto, Ontario, CANADA; ⁴The Royal Marsden Hospital NHS Foundation Trust, London, England, UNITED KINGDOM; ⁵Institut Curie, PSL Research University, Paris, Ile-de-France, FRANCE; ⁶Harvard Medical School, Dana-Farber Cancer Institute, Harvard University, Boston, Massachusetts, UNITED STATES; ⁷Institut Gustave Roussy, Villejuif, Ile-de-France, FRANCE; ⁸Institut Bergonie, Bordeaux, Aquitaine, FRANCE; ⁹The Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS; ¹⁰Princess Margaret Hospital, University Health Network and Mount Sinai Hospital, Toronto; Lunenfeld Tanenbaum Research Institute, Sinai Health System, Toronto, Ontario, CANADA; ¹¹Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES; ¹²Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS

Objective: The prognostic significance of microscopic margin status following curative resection of primary retroperitoneal sarcoma (RPS) is controversial. We sought to determine the variables that predict for microscopic margin involvement by tumour (R1), and explore the relationship between R1 status and long-term oncologic outcomes.

Methods: The study cohort comprised consecutive patients who underwent curative intent resection of primary RPS at 7 sarcoma referral centers where pathologic evaluation included documentation of microscopic margin status, from 2012 through 2017. Data were extracted from prospectively maintained institutional databases. Patients who had distant metastases at presentation or underwent grossly incomplete resection (R2) were excluded. The primary outcome of interest was Local (extrahepatic abdominal) Recurrence, expressed in a competing risk framework as Crude Cumulative Incidence (CCI LR). Dedifferentiated liposarcoma (DDLPS) was classified as low grade (LG =G1, G2) or high grade (G3).

Results: A total of 587 patients from 7 centers met inclusion criteria. Median follow-up post resection was 52 mos (IQR 35-70). The overall rate of R1 resection was 50% (N=294), and amongst the 7 centers the median R1 rate was 51%. In univariate analysis, factors that were significantly associated with a higher R1 rate (Table 1) were male sex, larger tumour size, multifocality, and specific histologic type, but not patient age or tumour grade. In multivariable analysis, male sex, multifocality and histologic type (LPS, UPS) were independently predictive of R1 status. All instances of intraoperative tumour rupture (n=15/587) had been scored as R1.

In multivariable analysis, factors that were independently associated with a higher LR rate (Table 2) were higher tumour grade (p=0.05), multifocality (p=0.02), histologic type (p

Conclusion: The R1 resection rate for primary RPS was high, and varied by histologic type. R1 status was independently associated with higher LR; this was particularly clear for histologic types where LR is predominant. Preoperative RT may reduce the LR rate associated with R1 resection in patients with WDLPS or LG DDLPS.

Table 1. Univariate and multivariable analyses of factors associated with R1 resection margin

	N	R1 Rate (%)	Univariate			Multivariable		
			OR	95% CI	P value	OR	95% CI	P value
Sex								
Female	286	44						
Male	301	56	1.60 ⁺	(1.16, 2.22)	0.004	1.44 ⁺	(1.00,2.07)	0.05
Tumor size, cm								
<10cm	73	34						
10-20cm	199	51	1.98 [#]	(1.14, 3.49)	0.016	1.11 [#]	(0.56,2.19)	0.76
>20cm	315	53	2.19 [#]	(1.30, 3.78)	0.003	0.90 [#]	(0.44,1.18)	0.77
FNCLCC grade								
1	143	48						
2	251	53	1.21 [%]	(0.80, 1.82)	0.37	1.33 [%]	(0.59,3.03)	0.49
3	168	50	1.07 [%]	(0.67, 1.68)	0.76	1.63 [%]	(0.66,4.18)	0.29
Multifocality								
No	555	48						
Yes	28	79	3.97 [*]	(1.68 ,10.92)	0.003	3.39 [*]	(1.40,9.48)	0.01
Histology								
LMS	101	27						
WDLPS	104	53	3.20 ^{&}	(1.79, 5.80)	<0.001	3.90 ^{&}	(1.50,10.67)	0.006
LG DDLPS	211	58	3.83 ^{&}	(2.30, 6.52)	<0.001	3.68 ^{&}	(1.84,7.66)	<0.001
HG DDLPS	83	57	3.58 ^{&}	(1.94, 6.72)	<0.001	2.22 ^{&}	(1.02,4.99)	0.04
SFT	29	28	1.04 ^{&}	(0.40, 2.57)	0.93	1.00 ^{&}	(0.29,3.10)	0.99
UPS	32	66	5.23 ^{&}	(2.27, 12.64)	0.001	4.55 ^{&}	(1.78,12.32)	0.002
Other	27	44	2.19 ^{&}	(0.90, 5.28)	0.08	2.03 ^{&}	(0.80,5.10)	0.13

Abbreviations: R1, resection with microscopically positive margins; OR, odds ratio for R1 resection margin; CI, confidence interval; LMS, leiomyosarcoma; WDLPS, well-differentiated liposarcoma; LG DDLPS, low grade (G1/G2) dedifferentiated liposarcoma; HG DDLPS, high grade (G3) dedifferentiated liposarcoma; SFT, solitary fibrous tumor; UPS, unclassified pleomorphic sarcoma

⁺ vs Female; [#] vs <10cm; [%] vs Grade1; ^{*} vs Unifocal; [&] vs LMS

Table 2. Univariate and multivariable analyses of factors associated with crude cumulative incidence of local recurrence

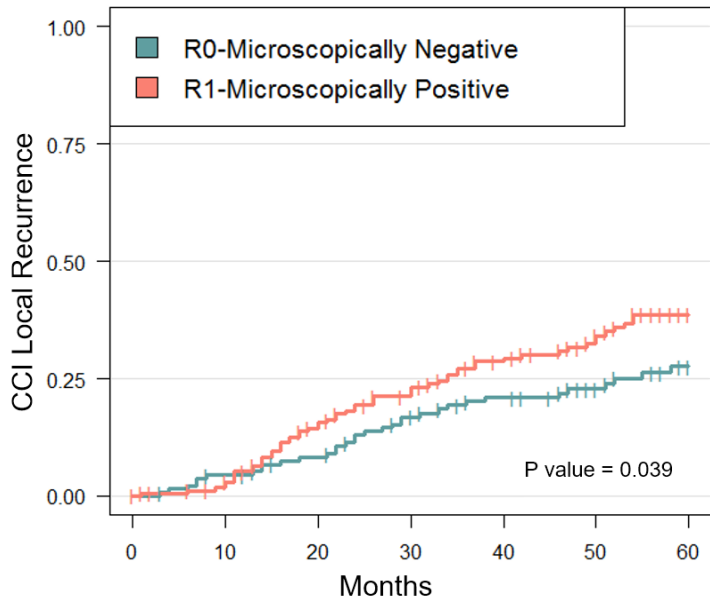
	N	LR Rate (%)	Univariate			Multivariable		
			HR	95% CI	P value	HR	95% CI	P value
Sex								
Female	286	23						
Male	301	38	1.8 ⁺	(1.33, 2.54)	<0.001	1.33 ⁺	(0.95,1.87)	0.09
Tumor size, cm								
<10cm	73	13						
10-20cm	199	29	2.9 [#]	(1.33, 6.30)	0.007	1.90 [#]	(0.81,4.43)	0.14
>20cm	315	36	4.0 [#]	(1.89, 8.46)	<0.001	12.35 [#]	(0.99, 5.56)	0.06
FNCLCC grade								
1	143	18						
2	251	36	1.90 [%]	(1.25, 2.88)	0.003	2.58 [%]	(01.01,6.62)	0.05
3	168	34	1.97 [%]	(1.25, 3.11)	0.004	2.57 [%]	(0.88, 7.47)	0.08
Multifocality								
No	555	29						
Yes	28	61	2.75 [*]	(1.64, 4.60)	<0.001	1.86 [*]	(1.10, 3.19)	0.02
Rupture								
No	572	30						
Yes	15	51	2.44 [^]	(1.07, 5.54)	0.03	2.12 [^]	(0.86, 5.16)	0.1
Margin Status								
R0	294	24						
R1	293	38	1.84 [@]	(1.36, 2.50)	<0.001	1.53 [@]	(1.10, 2.13)	0.01
Histology								
LMS	101	27						
WDLPS	104	53	2.69 ^{&}	(1.23, 5.86)	0.013	3.53 ^{&}	(1.13, 11.01)	0.02
LG DDLPS	211	58	5.06 ^{&}	(2.51, 10.23)	<0.001	2.52 ^{&}	(1.13, 5.64)	0.02
HG DDLPS	83	57	6.14 ^{&}	(2.89, 13.05)	<0.001	3.01 ^{&}	(1.12, 8.12)	0.03
SFT	29	28	3.73 ^{&}	(1.43, 9.70)	0.007	4.43 ^{&}	(1.54, 12.71)	0.006
UPS	32	66	5.55 ^{&}	(2.15, 14.35)	<0.001	3.48 ^{&}	(1.17, 10.34)	0.02
Other	27	44	3.78 ^{&}	(1.39, 10.34)	0.09	2.70 ^{&}	(0.88, 8.23)	0.08

Abbreviations: LR, local (abdominal extra-hepatic) recurrence; HR, Hazard ratio for crude cumulative incidence of local recurrence; CI, confidence interval; R0, resection with microscopically negative margins; R1, resection with microscopically positive margins; LMS, leiomyosarcoma; WDLPS, well-differentiated liposarcoma; LG DDLPS, low grade (G1/G2) dedifferentiated liposarcoma; HG DDLPS, high grade (G3) dedifferentiated liposarcoma; SFT, solitary fibrous tumor; UPS, unclassified pleomorphic sarcoma

⁺ vs Female; [#] vs <10cm; [%] vs Grade1; ^{*} vs Unifocal; [^] vs No rupture; [@] vs R0; [&] vs LMS

Figure 1. Crude Cumulative Incidence of Local Recurrence in patients with WDLPS and LG DD LPS, by microscopic margin status.

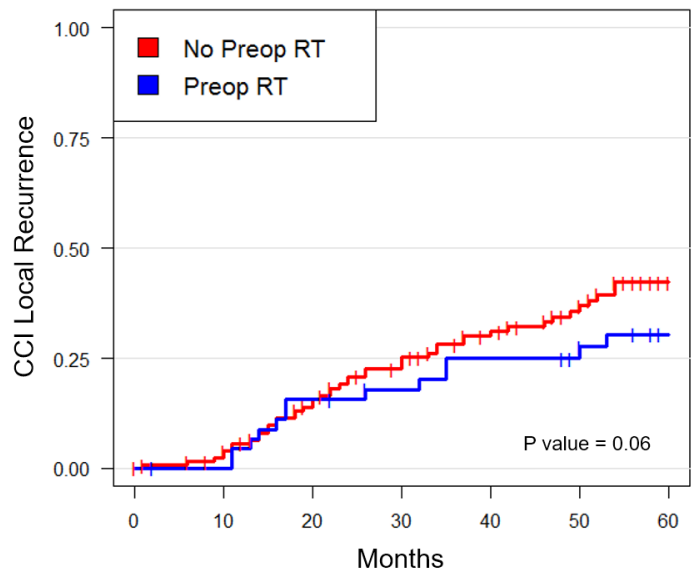
WDLPS + LG DDLPS	All (N=315)	R0 (N=136)	R1 (N=179)
5-year CCI LR (95% CI)	34 (28-40)	27 (19-36)	39 (31-47)



R0	136	131	125	117	109	101	94	88	81	58	52
R1	179	164	151	135	118	109	96	84	76	58	44

Abbreviations: CCI, Crude Cumulative Incidence; LR, local (abdominal extra-hepatic) recurrence; R0, resection with microscopically negative margins; R1, resection with microscopically positive margins

Figure 2. Crude Cumulative Incidence of Local Recurrence in patients with R1 resection, by receipt of preoperative radiation.



No Preop RT	132	122	111	101	86	79	69	57	49	38	27
Preop RT	47	42	40	34	32	30	27	27	27	20	17

Abbreviations: CCI, Crude Cumulative Incidence; R1, resection with microscopically positive margins; RT, radiation therapy



11:35 AM - 11:42 AM

Paper #68 #1818716

RETROPERITONEAL SOFT TISSUE SARCOMA: RECENT OUTCOME IMPROVEMENT AT A SINGLE INSTITUTION

Marco Fiore¹; Max Almond²; Francesco Barretta¹; Stefano Cioffi¹; Dario Callegaro¹; Chiara Colombo¹; Stefano Radaelli¹; Sandro Pasquali¹; Marta Barisella¹; Carlo Morosi¹; Roberta Sanfilippo¹; Claudia Sangalli¹; Rosalba Miceli¹; Paolo G. Casali¹; Alessandro Gronchi¹

¹Fondazione IRCCS Istituto Nazionale dei Tumori; Milan, Lombardia, ITALY; ²University Hospital Birmingham NHS Foundation Trust, Birmingham, England, UNITED KINGDOM

Objective: The shift towards more extended surgery in the early 2000 marked the beginning of a new era in the management of retroperitoneal sarcoma (RPS), resulting in less local recurrences and better survival. Aim of this retrospective observational study was to investigate whether factoring in the biological behavior of different histological types and the introduction of multimodal therapies have been able to further improve the outcome of RPS patients.

Methods: We performed a retrospective analysis of consecutive primary RPS operated at our reference center. Three study periods were compared (2002-2006; 2007-2011; 2012-2016). Primary endpoints were overall survival (OS), crude cumulative incidence (CCI) of local recurrence and distant metastases (LR, DM) for the following histological subgroups: well differentiated (WDLPS), dedifferentiated G2 (G2DDLPS), dedifferentiated G3 liposarcoma (G3DDLPS) and leiomyosarcoma (LMS). Secondary endpoints were postoperative morbidity (Clavien-Dindo grade ≥ 3) and post-relapse OS. Clinico-pathological and treatment characteristics of patients treated in the three study periods were compared using Fisher/Chi-squared tests and the Cochran–Armitage trends test. Survival analysis was made by Kaplan-Meier/Cox PH models or CCI/Fine and Gray models in the competitive risk framework and compared using log-rank/Wald and Gray tests, respectively. Postoperative morbidity was modeled with logistic regression model. Multivariable analyses were performed.

Results: Four hundred and thirty-six patients underwent surgery for primary RPS: 82, 128 and 226 in the first, second and third period, respectively. Median follow-up was 157, 116 and 61 months. Sex, histology, malignancy grade and tumor size did not significantly differ over time. Proportion of complete resection (R0/R1) improved from 93.9% to 98.2% ($p=0.060$), along with an increased median number of resected organs from 2 to 4 ($p<.0001$). Postoperative morbidity percentages did not change significantly (18.3%, 16.4%, 23.5%; $p=0.186$). Overall, 30-day and 90-day postoperative mortality were 0.7% and 2.5%, and did not significantly differ over periods. The administration of radiotherapy and chemotherapy changed according to different histological subtypes (Table 1). A significant improvement of 5-yr OS was observed (63.3% to 74.6%, $p=0.025$), along with a non-significant reduction in CCI LR (18.2% to 16.3%, $p=0.776$) and no change in CCI DM (Figure 1). At multivariable analysis, study period remained a significant adjusted prognostic factor for OS among the other known risk factors (third vs first period HR: 0.28, overall $p<0.0001$). Subgroup analysis revealed these trends to a better prognosis: 1. An improvement in 5-yr OS (from 57.1% to 74.9%, $p=0.277$) and CCI LR (from 42.9% to 30.3%, $p=0.420$) in G2DDLPS, associated with more organs resected and more liberal use of RT in this subtype compared to other histologies (Table 1). 2. A significant improvement of 5-yr OS (from 20.0% to 53.5%, $p=0.010$) and CCI DM (from 66.7% to 13.3%; $p=0.004$) in G3DDLPS, associated with a shift in favor of the use of anthracycline-based chemotherapy in liposarcoma (Table 2). 3. An overall better 2-yr post-relapse OS was also detected (from 47.8% to 64.7%, $p=0.0069$) (Figure 1).

Conclusion: At our institution, five-year OS of patients with DDLPS improved over time, from 2002 on. In G2DDLPS, we speculate that this was mainly associated with a refinement in the surgical approach and use of RT, vis-a-vis a more liberal use of anthracycline-based perioperative chemotherapy in G3DDLPS. The availability of new therapies for recurring tumors may also have played a role. While the importance of proper surgery, possibly combined with preoperative radiotherapy, is paramount in keeping local recurrence rate under a 20% threshold, the role of perioperative therapies for RPS subgroups with high metastatic risk needs to be confirmed by prospective controlled trials.

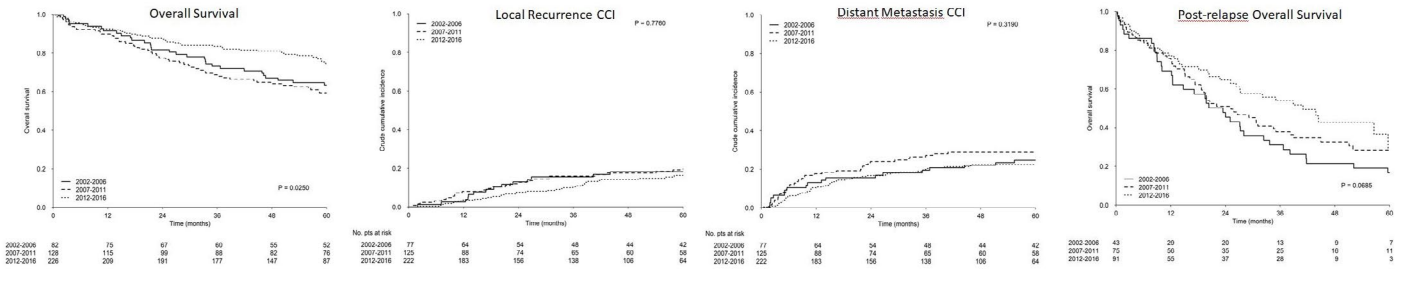


Figure 2. Overall survival, crude cumulative incidence of local recurrence and distant metastasis for main histological subtypes, according to study period.

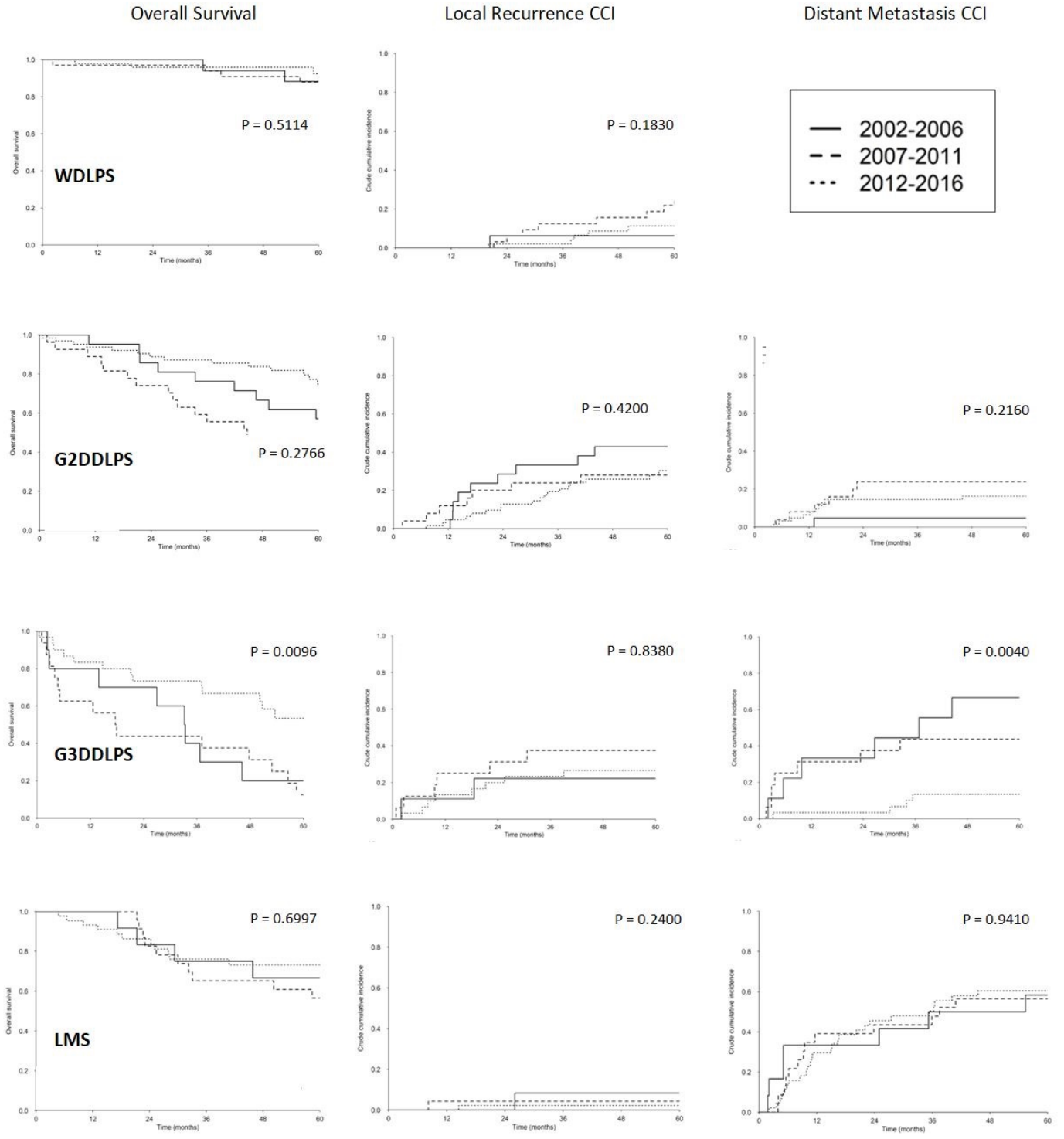


Table 1. Multimodal approach to primary RPS over time, according to histotypes: extent of liberal organ resection, adjuvant/neoadjuvant RT and CT.

		WDLPS			G2DDLPS			G3DDLPS			LMS			Other			
		1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd	1st	2nd	3rd	
Resected organs (median #)	Overall	3			4			4			3			2			
	Per period	1	3	3	3	3	4	3	4	4	2	2	3	1	2	2	
	IQR	1 - 3	3 - 5	3 - 4	2 - 4	2 - 5	4 - 5.5	1.5 - 3.8	4 - 6	4 - 5	2 - 3	2 - 3	2 - 4	0.3 - 2	2 - 3	1 - 3.3	
Radiation Therapy	Overall	12.1%			31.5%			14.3%			20.3%			35.2%			p=.0003
	Per period	23.5%	9.1%	10.2%	19.0%	48.1%	28.6%	30.0%	6.2%	13.3%	33.3%	34.8%	9.1%	50.0%	24.1%	35.0%	
Chemotherapy	Overall	8.1%			26.1%			26.8%			55.7%			31.9%			p<.0001
	Per period	23.5%	12.1%	0.0%	33.3%	59.3%	9.5%	30.0%	25.0%	26.7%	58.3%	65.2%	50.0%	50.0%	27.6%	25.0%	

WDLPS: well differentiated liposarcoma; G2DDLPS: dedifferentiated liposarcoma FNCLCC grade 2; G3DDLPS: dedifferentiated liposarcoma FNCLCC grade 3; LMS: leiomyosarcoma; 1st: period 2002-2006; 2nd: period 2007-2011; 3rd: period 2012-2016

Table 2. Single drugs in CT regimens for DDLPS and LMS over time

	DDLPS			LMS		
	1st	2nd	3rd	1st	2nd	3rd
Anthracycline	40%	45%	80%	57%	46%	72%
Ifosfamide	100%	95%	86%	71%	80%	9%
Dacarbazine	0%	0%	0%	0%	13%	68%
Gemcitabine	0%	0%	7%	14%	13%	14%

DDLPS: dedifferentiated liposarcoma; LMS: leiomyosarcoma; 1st: period 2002-2006; 2nd: period 2007-2011; 3rd: period 2012-2016



1:15 pm - 2:30 pm

– Session 12 –

ULTRA-RARE AND TRANSLOCATION SARCOMAS

1:15 PM - 1:22 PM

Paper #69 #1818698

A ROLE FOR SMARCB1 IN SYNOVIAL SARCOMAGENESIS REVEALS THAT THE SS18-SSX FUSION ONCOPROTEIN INDUCES CANONICAL BAF COMPLEX DESTRUCTION

Jinxu Li¹; Timothy S. Mulvihill¹; Li Li PhD¹; Jared J. Barrott²; Mary Nelson¹; Lena Wagner³; Ian Lock¹; Amir Pozner¹; Sydney L. Lambert¹; Benjamin B. Ozenberger¹; Michael B. Ward¹; Allie H. Grossmann¹; Ting Liu¹; Ana Banito³; Bradley R. Cairns¹; Kevin B. Jones¹

¹Huntsman Cancer Institute, University of Utah, Salt Lake City, Utah, UNITED STATES; ²Idaho State University, Pocatello, Idaho, UNITED STATES; ³Hopp Children's Cancer Center, German Cancer Research Center, Heidelberg, Baden-Wuerttemberg, GERMANY

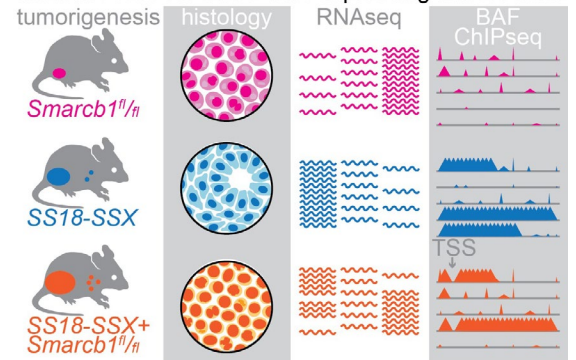
Objective: Reduced protein levels of SMARCB1 (a.k.a. BAF47, INI1, SNF5) have long been observed in synovial sarcoma (SS). As both SMARCB1 protein and the fusion oncoprotein SS18-SSX are known to participate in mammalian SWI/SNF or BAF complexes, multiple models have been developed to explain these two proposed features of BAF complexes, the addition of the SSX tail and the relative reduction in SMARCB1. We sought to ask how these proteins interact in BAF-family complexes in synovial sarcoma.

Methods: Using mouse genetic models, human synovial sarcoma cell lines and recombinant BAF-family complexes, we asked a series of questions with sarcomagenesis experiments, epigenomics, and biochemical assays to determine protein-protein interactions and BAF-family complex subtype distributions.

Results: Combined *Smarcb1* genetic loss with SS18-SSX expression in mice synergized to produce aggressive tumors with histomorphology, transcriptomes, and genome-wide BAF-family complex distributions distinct from SS18-SSX alone, indicating a defining role for SMARCB1 in SS. *Smarcb1* silencing alone in mesenchyme modeled epithelioid sarcomagenesis. In mouse and human SS cells, SMARCB1 was identified within PBAF and canonical BAF (CBAF) complexes, co-incorporated with SS18-SSX in the latter. Recombinant expression of CBAF components in human cells reconstituted CBAF sub-complexes that contained equal levels of SMARCB1, regardless of SS18 or SS18-SSX inclusion. In vivo, SS18-SSX expression led to whole-complex CBAF degradation, rendering increases in the relative prevalence of other BAF-family subtypes, PBAF and GBAF complexes, over time.

Conclusion: *Smarcb1*-loss in mesenchyme generates epithelioid sarcoma not SS. *Smarcb1*-loss synergizes with SS18-SSX to drive tumorigenesis of distinct character, confirming that SMARCB1 protein has a role in SS and is not completely ejected or degraded from BAF-family complexes. Recombinant canonical BAF or the canonical BAF complexes isolated from mouse or human tumor cells readily co-assemble SMARCB1 with SS18-SSX. The reduced level of SMARCB1 protein derives from SS18-SSX-driven canonical BAF complex degradation and relative PBAF and GBAF overabundance, rather than specific degradation of SMARCB1. Thus, SS18-SSX alters BAF subtypes levels/balance and genome distribution, driving synovial sarcomagenesis.

Smarcb1-loss vs. SS18-SSX-expressing tumors differ



synovial sarcoma BAFs retain SMARCB1 with fusion





1:22 PM - 1:29 PM

Paper #70 #1818722

DISCONTINUATION OF LAROTRECTINIB PRIOR TO DISEASE PROGRESSION IN PEDIATRIC SARCOMA: ANALYSIS FROM SCOUT TRIAL

Steven G. DuBois¹; Daniel Orbach²; Catherine M. Albert³; Noah C. Federman⁴; Ramamoorthy Nagasubramanian⁵; Neerav Shukla⁶; Daniel A. Morgenstern⁷; Christian Michel Zwaan⁸; Ricarda Norenberg⁹; Marc Fellous¹⁰; Esther De La Cuesta¹¹; Cornelis M. van Tilburg¹²; Theodore W. W. Laetsch¹³; Leo Mascarenhas¹⁴

¹Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, Massachusetts, UNITED STATES;

²SIREDO Oncology Center (Care, Innovation and Research for Children, Adolescents and Young Adults with Cancer), Institut Curie, PSL University, Paris, Ile-de-France, FRANCE; ³Seattle Children's Hospital, University of Washington, Fred Hutchinson Cancer Research Center, Seattle, Washington, UNITED STATES; ⁴Health Sciences Clinical Professor, Pediatrics and Orthopaedic Surgery, UCLA Medical Center, Los Angeles, California, UNITED STATES;

⁵Nemours Children's Hospital, Orlando, Florida, UNITED STATES; ⁶Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES; ⁷Hospital for Sick Children, Toronto, Ontario, CANADA; ⁸Prinses Maxima Centrum, Utrecht, Utrecht, NETHERLANDS; ⁹Chrestos Concept GmbH & Co. KG, Essen, Nordrhein-Westfalen, GERMANY;

¹⁰Bayer HealthCare Pharmaceuticals, Basel, Basel-Stadt, SWITZERLAND; ¹¹Bayer HealthCare Pharmaceuticals, Inc., Whippany, New Jersey, UNITED STATES; ¹²Hopp Children's Cancer Center Heidelberg (KITZ), Heidelberg University Hospital and German Cancer Research Center (DKFZ), Heidelberg, Baden-Wuerttemberg, GERMANY; ¹³University of Texas Southwestern Medical Center/Children's Health, Dallas, Texas, UNITED STATES; ¹⁴Children's Hospital Los Angeles, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES

Objective: Larotrectinib is a first-in-class, highly selective central nervous system-active tropomyosin receptor kinase (TRK) inhibitor with an objective response rate of 75% and median progression-free survival of 35.4 months in a pooled analysis of 206 adult and pediatric patients with TRK fusion cancer from three clinical trials (Hong et al, ASCO 2021). Larotrectinib is approved for adult and pediatric patients with TRK fusion cancer in over 40 countries. A subset of pediatric patients discontinued larotrectinib without progression, including patients who underwent on-study surgical resection of their tumor or entered a wait-and-see period following response according to physician discretion, as permitted on the pediatric SCOUT study (NCT02637687). The objective of this analysis was to follow outcomes for pediatric patients with TRK fusion sarcoma who discontinued larotrectinib without evidence of prior disease progression.

Methods: Patients with TRK fusion sarcoma in SCOUT who discontinued larotrectinib in the absence of prior on-treatment progressive disease were identified for this post-hoc analysis from data current up to July 20, 2020. Response was investigator assessed according to RECIST v1.1. Patients were actively followed for progression according to protocol.

Results: The analytic cohort included 35 patients: 23 (66%) with infantile fibrosarcomas and 12 (34%) with other soft tissue sarcomas. Median (95% confidence interval [CI]) time to initial larotrectinib discontinuation in all patients was 10.2 (7.4–14.7) months; 9.1 (6.6–12.9) months among patients with locally advanced disease (n=30), and 22.3 (14.7–39.5) months among patients with metastatic disease (n=5). Nineteen patients discontinued larotrectinib in complete response (CR). Thirteen patients had partial response (PR) and three had stable disease (SD). Seventeen patients discontinued larotrectinib without preceding surgical resection. Eighteen patients discontinued larotrectinib after surgery, nine of whom had pathological CR (pCR). Among these nine patients, two were in active follow-up without documented progression at 14.8 and 40.6 months post-surgery and one patient discontinued after surgery and entered active follow-up just before the data cut; the remaining six were followed for survival only. Two of the nine other (non-pCR) patients eventually progressed after surgery, one with no residual tumor (R0) at surgery and one with macroscopic residual tumor (R2) at surgery. Among the 17 non-surgical patients who discontinued, five progressed during the wait-and-see period. Seven (20%) patients (two surgical and five non-surgical) progressed and subsequently resumed larotrectinib treatment. The best response for these patients following resumption of larotrectinib were four CR, one PR, one SD and one unknown. All patients were alive at the time of data cut-off.

Conclusion: In this exploratory analysis, seven of 35 patients (20%) who discontinued larotrectinib had documented subsequent progression. For patients with progressive disease after cessation of larotrectinib, objective responses were achieved in most patients upon resumption of larotrectinib. These results suggest that treatment discontinuation may be feasible in

carefully evaluated or selected patients. However, longer follow-up is necessary to track the durability of the progression-free interval and additional patients are needed to confirm these findings. The optimal duration of treatment with larotrectinib in the pediatric population is a focus of an ongoing Children's Oncology Group (COG) trial (NCT03834961).



1:29 PM - 1:36 PM

Paper #71 #1818755

NAB-SIROLIMUS IN PATIENTS WITH MALIGNANT PECOMA PREVIOUSLY TREATED WITH MTOR INHIBITORS: EMERGING EXPERIENCE FROM AN EXPANDED ACCESS PROGRAM

Mark A. Dickson MD¹; Vinod Ravi MD²; James L. Chen³; Martina C. Murphy⁴; Christopher Y. Thomas⁵; Anita N. Schmid⁶; Andrew J. Wagner⁷

¹Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES; ²The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES; ³Ohio State University, Columbus, Ohio, UNITED STATES;

⁴University of Florida, Department of Medicine, Gainesville, Florida, UNITED STATES; ⁵Wake Forest Baptist Health, Winston-Salem, North Carolina, UNITED STATES; ⁶Aadi Bioscience, Pacific Palisades, California, UNITED STATES;

⁷Harvard Medical School, Dana-Farber Cancer Institute, Boston, Massachusetts, UNITED STATES

Objective: ABI-009 (nab-sirolimus) is a novel albumin-bound intravenous mTOR inhibitor (mTORi) that has demonstrated increased tumor uptake, increased mTOR target suppression, increased tumor suppression and distinct pharmacokinetic profile versus oral mTORi in animal models. In the AMPECT study in advanced malignant PEComa, mTOR-naïve patients treated with nab-sirolimus (NCT02494570) had an independently reviewed ORR of 39% and a duration of response with a median not reached but exceeding 30 months and ongoing (Wagner et al, ASCO 2020). A subset of these patients with TSC1 or TSC2 alterations showed an ORR of 64% (9/14). In other tumor types, including other sarcomas, emerging data in mTOR-naïve patients with TSC1 or TSC2 alterations suggested activity of nab-sirolimus (Dickson et al, ASCO 2021). Here we report emerging data from an expanded access program in patients with prior mTORi exposed malignant PEComa that were subsequently treated with nab-sirolimus.

Methods: Patients with malignant PEComa who had prior treatment with an mTORi received nab-sirolimus 100 mg/m² IV, once weekly for 2 of every 3 weeks at 6 US sites. Alteration status of TSC1 or TSC2 genes was assessed when available, ie, no specific mutational criteria in the TSC1 or TSC2 genes were required for enrollment.

Results: 15 eligible patients were enrolled between 9/2018 and 03/2021. Data cutoff for this abstract was 5/2021. All patients were previously treated with either sirolimus, everolimus or temsirolimus. 6/15 had 3 or 4 previous lines of therapy, including targeted therapy or chemotherapy. 7/15 patients had known alterations in their TSC1 or TSC2 genes. 4/15 patients received 2 prior lines of mTORi treatment, 3/4 had alterations in their TSC1 or TSC2 genes. All 15 patients were evaluable for efficacy; 3/15 (20%) patients had a partial response (PR), 5/15 (33%) had a stable disease (SD), and 7/15 (47%) had progressive disease (PD) as the best response. Duration of treatment at data cutoff ranged from 0.7 to 21.5+ months and 3 patients had ongoing treatment. In the 7 patients with TSC1 or TSC2 alterations, 3/7 (43%) had a PR and 2/7 (29%) had SD and PD, each. Duration of treatment at data cutoff ranged from 1.5 to 21.5+ months and 2 patients had ongoing treatment. Of the 4 patients with 2 lines of prior mTORi, 1 with unknown mutation status had a PD and 3 patients with alterations in their TSC1 or TSC2 genes had clinical benefits (1 PR, 7.4+ months duration of treatment, and 2 SDs, 5.1 and 11.7 months duration of treatment). All 15 patients were evaluable for safety; the most common (>10% [≥ 2 pts]) treatment-related adverse reactions were rash and fatigue (27% each), mucositis and thrombocytopenia (20% each), and anemia, ALT, AST, nausea, and hypertriglyceridemia (13% each). 4 (27%) patients had a treatment-related serious adverse event (anemia, colitis, mucositis, and thrombocytopenia), all of which resolved.

Conclusion: nab-Sirolimus was active with manageable toxicities in patients with malignant PEComa with prior mTORi treatment and achieved clinical benefit including partial responses. This was particularly evident in patients with alterations in their TSC1 or TSC2 genes.



1:36 PM - 1:43 PM

Paper #72 #1818734

INTERIM RESULTS OF AN INTERNATIONAL PHASE 2 STUDY OF THE MICROTUBULE INHIBITOR ERIBULIN, IN PROGRESSIVE METASTATIC ANGIOSARCOMA (AS) AND EPITHELIOID HEMANGIOENDOTHELIOMA (EHE)

Gregory M. Cote¹; Lucille Sebastian²; Edwin Choy¹; Peter Grimison³; Priscilla Merriam⁴; Mandy Ballinger⁵; Alec Colon¹; Subo Thavaneswaran²; Michael Nathenson⁴; Frank Lin⁵; Katherine A. Thornton⁶; Corrie Painter⁷; Esha Jain⁷; John Grady⁵; Michael Millward⁸; Michael Brown⁹; Rosemary Harrup¹⁰; David Espinoza²; George D. Demetri⁴; Suzanne George⁴

¹Massachusetts General Hospital, Boston, Massachusetts, UNITED STATES; ²National Health and Medical Research Council Centre for Clinical Trials, Sydney, New South Wales, AUSTRALIA; ³Chris O'Brien Lifecare, Sydney, New South Wales, AUSTRALIA; ⁴Dana Farber Cancer Institute, Boston, Massachusetts, UNITED STATES; ⁵Garvan Institute, Western Sydney University, Campbelltown, New South Wales, AUSTRALIA; ⁶Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES; ⁷The Broad Institute of MIT and Harvard, Cambridge, Massachusetts, UNITED STATES; ⁸Sir Charles Gairdner Hospital, Perth, Western Australia, AUSTRALIA; ⁹Royal Adelaide Hospital, Adelaide, South Australia, AUSTRALIA; ¹⁰Royal Hobart Hospital, Hobart, Tasmania, AUSTRALIA

Objective: Vascular soft-tissue sarcomas are rare diseases with poor responsiveness to chemotherapy. Taxanes are microtubule stabilizers that are standard of care therapy for metastatic or advanced AS. The largest prospective study to date of 30 AS patients treated with paclitaxel showed a median progression-free survival (PFS) of 12 weeks, and an overall survival (OS) of 33 weeks (Penel et al., 2016). Eribulin, a novel microtubule dynamics inhibitor, has shown clear activity in metastatic breast and sarcoma patients, despite prior failure of taxanes in many of these patients. Moreover, emerging evidence in preclinical models indicates eribulin induces tumor vasculature remodeling as well as altering angiogenesis signaling pathways involved in endothelial cell-pericyte interactions. Here we aimed to determine the single agent activity of eribulin in advanced AS and EHE.

Methods: We conducted an investigator-sponsored multi-site international phase 2 study at Massachusetts General Hospital (MGH, Boston) and through the Molecular Screening and Therapeutics Study (MoST) in Sydney, Australia. Eligibility criteria included a diagnosis of progressive incurable AS and EHE, ECOG performance status 0-2, and adequate organ function. Subjects received 1.4 mg/m² eribulin on days 1 and 8 of a 21-day cycle. Endpoints included PFS and OS, the ratio of time to progression on study compared to prior therapy (TTP2/TTP1), as well as objective response rate (ORR) and clinical benefit rate (CBR: CR or PR or TTP2/TTP1 >1.3). Pre-treatment biopsies were required at MGH and MoST for exploratory analysis of genomics and changes in gene expression by RNAseq, while post-treatment biopsies were performed at MGH.

Results: Enrolment commenced in 2018 and a total of 24 out of 30 planned patients have been enrolled to date (11 MGH; 13 MoST). These have included 11 female patients, with a median age of 65 years (range 40-82) where 21/24 patients had AS (including 6 breast, 4 head and neck). Participants had received a median of 1 prior line of systemic therapy (range 0-6), with 21/24 having previously received a taxane containing regimen. The median time to progression on prior therapy was 14 weeks. After a median follow up of survivors of 17 weeks (range 6-60 weeks), 3/21 evaluable patients had experienced an unconfirmed partial response (one taxane-naïve), and 3 patients a TTP2/TTP1 ratio > 1.3 for an objective response rate of 14% and a clinical benefit rate of 29%. 12 patients experienced PD as best overall response. The median PFS was 7 weeks (range 1-61 weeks), and the median OS was 33 weeks (range 4-127 weeks). The 18 AS patients with prior taxane exposure had similar results to the overall cohort. Of 3 patients with EHE, one experienced TTP2/TTP1 ratio of 1.49, with no objective responses. Safety and tolerability were consistent with previous reports. Of 15 individuals with currently informative data, 9 experienced grade 3/4 adverse events attributed to treatment (4 sepsis, 2 neutropenia, 1 each thrombocytopenia, elevation of liver enzymes, and pain). Results will be updated at CTOS.

Conclusion: These preliminary data suggest clinically meaningful activity of eribulin in a subset of progressive vascular soft-tissue sarcomas, most of whom had received prior taxane therapy. The genomic/RNA expression analysis may help identify patients more likely to derive benefit. Additionally, this study shows that international collaboration enables successful implementation of clinical trials of ultra-rare sarcomas. Together, these data support further exploration of eribulin in angiosarcoma in the taxane-naïve first line setting.



1:43 PM - 1:50 PM

Paper #73 #1818711

EXAMINING STRIPES ON A HERD OF ZEBRAS: IMPACT OF GENOMIC MATCHING FOR ULTRARARE SARCOMAS IN PHASE 1 CLINICAL TRIALS

Justin T. Moyers¹; Jason Roszik¹; Roberto Carmagnani Pestana²; J Andrew Livingston¹; Alejandra Zarzour¹; Vinod Ravi¹; Ravin Ratan¹; Neeta Somaiah¹; Anthony P. Conley¹; Vivek Subbiah¹

¹The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES;

²Hospital Israelita Albert Einstein, São Paulo, Sao Paulo, BRAZIL

Objective: Recently the Connective Tissue Oncology Society published consensus guidelines for the recognition of ultrarare sarcomas (URS). 56 soft tissue and 21 bone sarcoma types were defined as URS on basis of an incidence <1 per 1,000,000. Since, URS comprise up to 20% of the sarcoma population, with few approved histology driven treatments, they may be referred for Phase 1 clinical trials. We evaluated the clinical outcomes of URS vs Common sarcomas (CS) in the context of early phase clinical trials.

Methods: We analyzed clinical and next-generation sequencing (NGS) data from sarcoma patients treated on phase 1 trials at MD Anderson Cancer Center from January 2013 to June 2021. Patients with sarcomas were reviewed for sarcoma subtypes and data was extracted for genomic alterations and the clinical trial enrolment characteristics. We compared objective response rate (ORR), clinical benefit rate defined as objective responses and stable disease for >6months, progression free survival (PFS), and overall survival (OS).

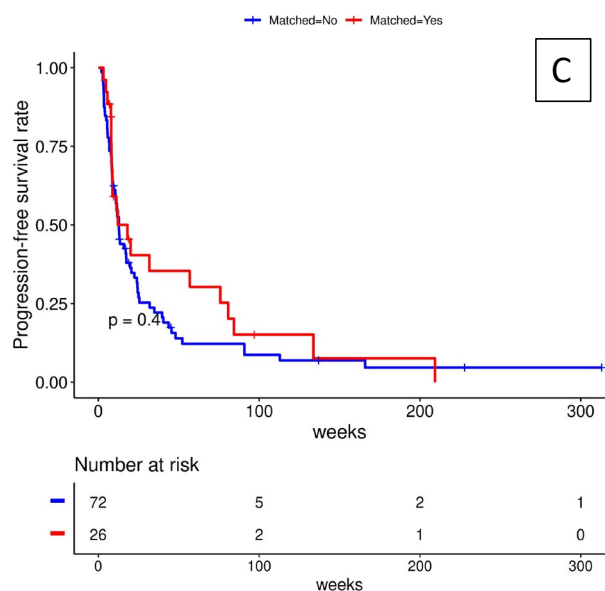
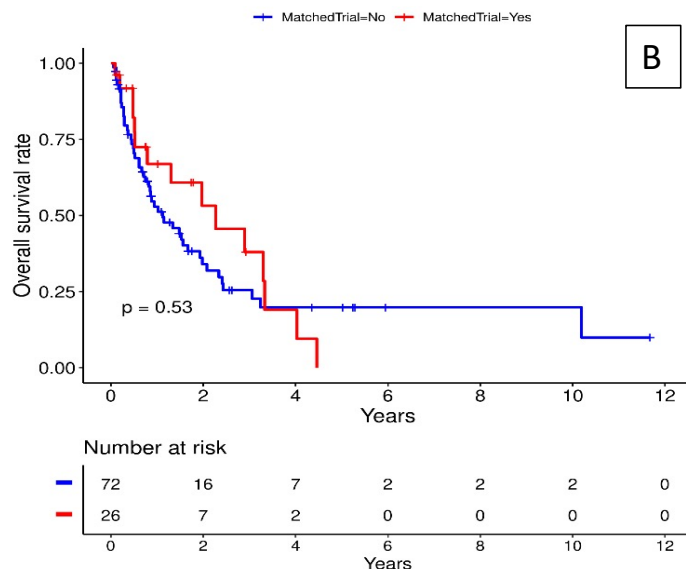
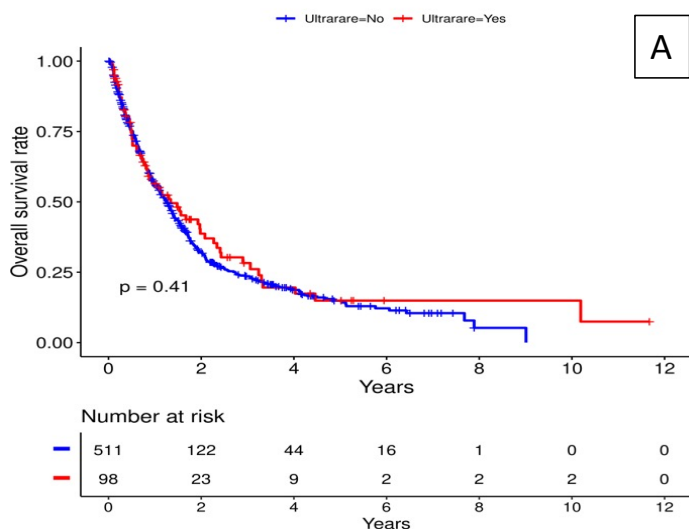
Results: Among 609 sarcomas, 98 (16 %) were classified as URS. Median age at first trial was 43 years (SD: 16y) and had median of 2.0 prior lines of therapy (Range:0-8) and 49% were male. 74 (76%) were soft tissue sarcomas whereas 24 (25%) were bone sarcomas. The most common URS were alveolar soft part sarcoma (n=12), clear cell sarcoma (n=10), and chordoma (n=10) (Table 1). Compared to common sarcomas, mOS was similar 15.0 versus 16.1 months for URS (p=0.41) (Figure 1 Panel A). 12.2% of URS (n=12) achieved objective response compared to 6.8% (n=35) of CS (p=0.067). 26 (27%) of URS were treated on matched trials versus 194 (38%) of common sarcomas (p=0.031).

Clinical NGS was available on 86 (88%) of 98 patients. 26 (27%) patients were treated on matched trials.

PFS for the patients treated on genomically matched trials versus genomically unmatched trials was 0.35 years (95%CI: 0.17-1.55) vs 0.25 yrs (95%CI: 0.21-0.40) (p=0.41) (Figure 1 Panel C). mOS for matched vs unmatched was 27.2 months (95%CI: 15.6-NYR) compared to 13.4 months (95%CI: 9.9-23.8) (p=0.53) (Figure 1 Panel B). Objective response rate was 19% (5/26) on matched trials and 10% (7/72) on unmatched trials (p=0.21). Clinical benefit rate was 39% in matched trials vs 28% in unmatched trials (p=0.31).

Objective responses were seen in clear cell sarcomas with c-met inhibitors (n=2), EZH2/EED inhibitor in epithelioid sarcoma (n=1), MDM2 inhibitor in chordoma (n=1), and ALK in inflammatory myofibroblastic tumor (n=1). Clinical benefit was seen with FGF/FGFR inhibitor in ossifying fibromyxoid tumor (n=1), SHH pathway inhibitor in sclerosing epithelioid fibrosarcoma (n=1), 20S proteasome inhibitor + EGFR-TKI in clear cell sarcoma (n=1), and CDK4/6 inhibitor in low-grade fibromyxoid sarcoma.

Conclusion: While URS were less likely to be enrolled on genomically matched trials, when enrolled on matched trials they showed a trend towards higher OS compared to unmatched patients. Identifying actionable aberrations for targeted therapy will remain an important task treating patients with these ultra rare cancers.



<u>Multiple Cases:</u>	<u>n</u>	<u>Only One case</u>
Alveolar Soft Part Sarcoma	12	Adamantinoma
Clear Cell	10	Clear Cell Chondrosarcoma
Chordoma	10	Dedifferentiated Parosteal Osteosarcoma
Sclerosing Epithelioid Sarcoma	9	Endometrioid stromal sarcoma
Dedifferentiated Chondrosarcoma	9	Fibromyxoid sarcoma low grade
PEComa	6	Giant Cell Tumor of Soft Tissue
Epithelioid Sarcoma	4	Histiocytic Sarcoma
Desmoplastic small round cell tumor	5	Mesenchymal Chondrosarcoma
Alveolar Rhabdomyosarcoma	4	Metastatic Phyllodes Tumor
Extraskelatal myxoid chondrosarcoma	3	Periosteal Osteosarcoma
Epithelioid hemangioendothelioma	3	Pleomorphic rhabdomyosarcoma
Ossifying fibromyxoid tumor	2	Rhabdomyosarcoma, Embryonal
Inflammatory myofibroblastic tumor	2	Round small cell/Ewing-like Sarcoma
Giant Cell Tumor of Bone	2	Spindle Cell Rhabdomyosarcoma
Embryonal Rhabdomyosarcoma	2	Undifferentiated High-grade Pleomorphic Sarcoma of Bone



1:50 PM - 1:57 PM

Paper #74 #1818732

TK216 FOR EWING SARCOMA- INTERIM PHASE 1/2 RESULTS

Ravin Ratan¹; Joseph A. Ludwig¹; Noah C. Federman²; Peter M. Anderson³; Margaret E. Macy⁴; Richard F. Riedel⁵; Lara E. Davis⁶; Najat C. Daw¹; Jade E. Wulff⁷; Aerang Kim⁸; Jeffrey A. Toretsky⁹; Edwina Baskin-Bey¹⁰; James B. Breitmeyer¹⁰; Paul Meyers¹¹

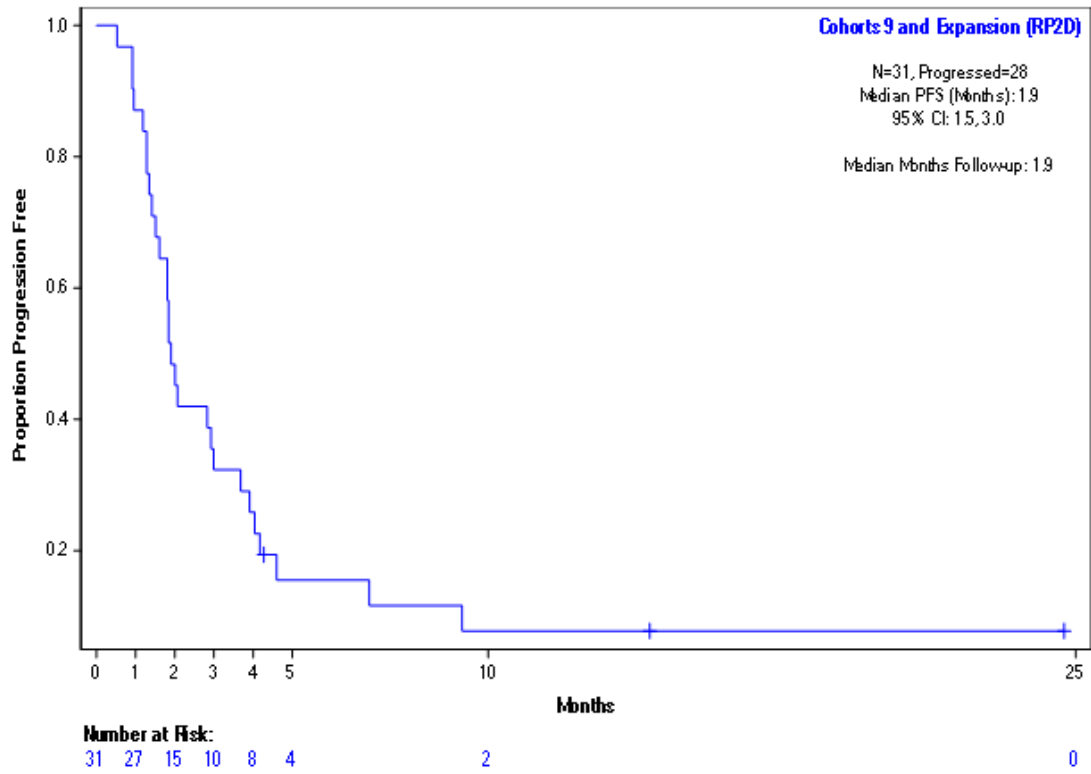
¹University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES; ²UCLA Medical Center, Los Angeles, California, UNITED STATES; ³Cleveland Clinic Foundation, Cleveland, Ohio, UNITED STATES; ⁴University of Colorado and Children's Hospital of Colorado, Aurora, Colorado, UNITED STATES; ⁵Duke Cancer Institute, Duke University Medical Center, Durham, North Carolina, UNITED STATES; ⁶Knight Cancer Institute, Organ Health & Science University, Portland, Oregon, UNITED STATES; ⁷Pediatrics, Texas Children's Hospital, Houston, Texas, UNITED STATES; ⁸Children's National Medical Center, Washington, District of Columbia, UNITED STATES; ⁹Georgetown University, Washington, District of Columbia, UNITED STATES; ¹⁰Oncternal Therapeutics Inc., San Diego, California, UNITED STATES; ¹¹Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES

Objective: Ewing Sarcoma (ES) is a rare cancer of the young with very few treatment options in the relapsed/refractory (R/R) setting. Fusions of the EWS gene and one of five different ETS transcription factors are dominant drivers of ES. TK216 was designed to bind ETS proteins directly, disrupt protein-protein interactions, and inhibit transcription factor function. TK216 plus vincristine (VCR) exerted synergistic activity in non-clinical models. Here, we report updated interim results of the Phase 1/2 trial of TK216 ± vincristine in R/R ES.

Methods: TK216 was administered by continuous IV infusion to adult and pediatric patients (pts) with R/R ES using a 3+3 design. Dosing duration of 7 days was later extended to 10 and 14 days. Dose limiting toxicity was evaluated during Cycle 1. VCR could be added on day 1 after Cycle 2. The MTD for the 14-day infusion was 200 mg/m²/d, which was selected as the recommended Phase 2 dose (RP2D) for the Expansion cohort, with VCR started in Cycle 1.

Results: As of 16APR2021 data cutoff date, a total of 68 R/R ES pts have been enrolled. Thirty-nine pts were treated at the RP2D with median age of 27 years (range 11-77). Median time from initial diagnosis to study start was 3.4 years (range 0.4-18.0). Median prior treatment regimens were 3 (range 1-8). Prior procedures included surgery in 82% and radiation in 87% of pts. All pts treated at the RP2D had metastases: bone only (5%), lung only (54%), lung and bone only (20.5%), and other metastatic (20.5%). The most frequent AEs observed in all 68 treated pts, regardless of causality and severity, included anemia (n=34), neutropenia (n=32), fatigue (n=28), leukopenia (n=26), and pyrexia (n=24). Myelosuppression observed was transient, reversible, and responsive to growth factors. No deaths were attributed to TK216. Thirty-one of 39 pts treated at the RP2D were evaluable for efficacy: the objective response rate (ORR) was 9.7% (3/31 evaluable pts), complete response (CR) in 2 pts (6.5%), partial response (PR) in 1 pt (3.2%), stable disease (SD) in 11 pts (35.5%), and progressive disease (PD) in 17 pts (54.8%), for an overall disease control rate (CR+PR+SD) rate of 45.2%. Median duration of SD was 1.9 months (range: 0.9-9.3). Eight of 11 pts with SD had reductions of target lesions by upwards of 24%. Two complete responses were confirmed. One pt had regression of target lesions after 2 cycles of TK216 alone, then after 6 cycles of TK216 + VCR therapy a residual non-target lesion was removed, for a surgical CR. To date, this pt has been without evidence of disease at 27+ months on study. A second pt had 90% regression of target lesions after 2 cycles, then following 6 cycles of combination therapy had a CR. This pt remains in CR at 16+ months on study to date. Median PFS was 1.9 months (95% CI: 1.5, 3.0) (Figure). Median overall survival (OS) and median 6-month OS rates for all 68 Intent-to-Treat pts was 10.3 months (95% CI: 6.4, 12.6) and 66.4% (95% CI: 52.3%, 77.2%).

Conclusion: TK216 plus VCR was well tolerated and showed encouraging early evidence of anti-tumor activity at the RP2D in this heavily pre-treated/ high tumor burden ES pt population. Investigations are ongoing to characterize the most responsive pt population and intensify TK216 exposure.





1:57 PM - 2:04 PM

Paper #75 #1818713

COMPREHENSIVE ANALYSIS OF INFANTILE SOFT-TISSUE SARCOMAS WITH BCOR ALTERATIONS

Nawal Merjaneh¹; Hee Kim¹; Heather Escoto²; Jonathan Metts³; Anish Ray⁴; Andrew Bukowinski⁵; Zachary LeBlanc⁶; Douglas Fair⁷; Masayo Watanbe⁸; Elizabeth Alva⁹; Kevin Todd¹; Jessica D. Daley⁵; Duncan Hartt⁷; Sara Szabo¹; Joseph Pressey¹

¹Cancer and Blood Diseases Institute/ Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, UNITED STATES;

²Peyton Manning Children's Hospital, Indianapolis, Indiana, UNITED STATES; ³Cancer and Blood Disorders Institute/ Jones Hopkins All Children's Hospital, St Petersburg, Florida, UNITED STATES; ⁴Cook Children's Hospital, Fort Worth, Texas, UNITED STATES;

⁵UPMC Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES;

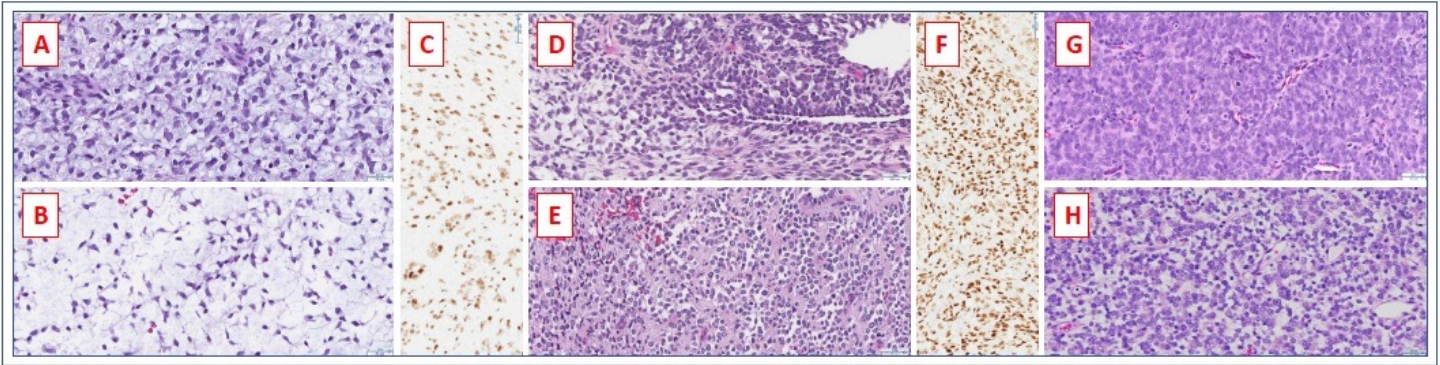
⁶LSU Health Sciences Center New Orleans, New Orleans, Louisiana, UNITED STATES; ⁷University of Utah, Salt Lake City, Utah, UNITED STATES; ⁸Phoenix Children's Hospital, Phoenix, Arizona, UNITED STATES; ⁹University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES

Objective: Alterations of BCL-6 transcriptional corepressor (BCOR) are described in infantile soft tissue sarcomas (STS) including primitive myxoid mesenchymal tumor of infancy (PMMTI) and undifferentiated round cell sarcoma (URCS). Previous reports of this ultra-rare entity describe frequent disease recurrences and often dismal outcomes. In order to further characterize the clinicopathologic features and generate therapeutic recommendations for infantile BCOR-altered tumors, we undertook a detailed analysis of nine patients.

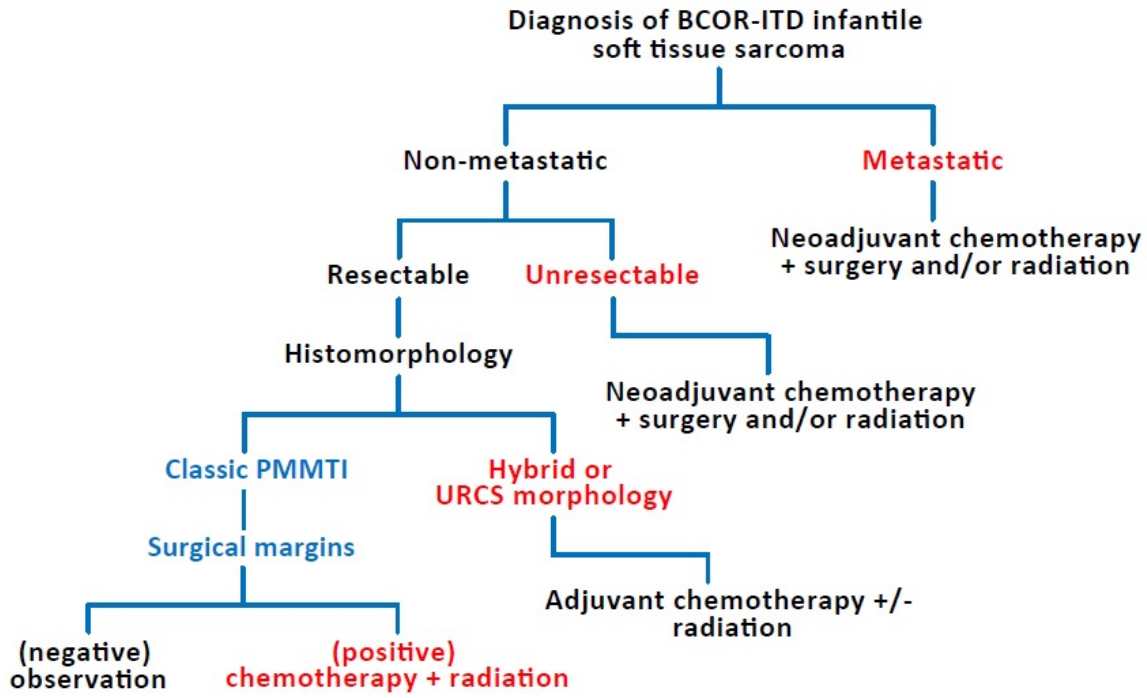
Methods: A retrospective, multi-institutional study of the clinical presentation, radiological features, histologic and molecular findings, and treatment course of infantile soft tissue sarcomas carrying somatic BCOR alterations confirmed by next-generation sequencing was undertaken.

Results: Nine patients aged six weeks to 15 months at initial presentation were identified. Five were male. The most common tumor sites were the trunk (n=5) and extremities (n=2). Radiologically, the tumors were generally lobulated with bright T2/low T1 signal on magnetic resonance imaging. There was no evidence of metastasis to lymph nodes or distant organs at presentation. One tumor carried a BCOR-CCNB3 fusion that manifested a predominant spindle cell morphology. The other cases harbored internal tandem duplication (ITD) of BCOR, including five cases classified as PMMTI with a dominant myxoid background, two cases characterized by a hybrid morphology, and one case classified as URCS. Due to radiological findings and patient age, two cases were initially mistaken for vascular malformations. Four patients were treated with upfront surgery with microscopic or macroscopic residual disease that progressed locally after a median of 2.5 months post-operatively. Multiple locoregional recurrences were observed in both hybrid BCOR-ITD cases, and the patient with URCS recurred with brain metastases. All patients received chemotherapy. The most common regimens used were vincristine/doxorubicin/cyclophosphamide alternating with ifosfamide/etoposide (VDC/IE) every 2-3 weeks, National Wilms Tumor Study Group (NWTS) regimen I, ifosfamide/doxorubicin (ID), and ifosfamide, carboplatin, and etoposide (ICE). Complete radiographic responses were achieved in two patients treated with VDC/IE and one treated with NWTS regimen I. Four patients achieved a partial response with either ID, ICE or VDC/IE regimen. One patient progressed on vincristine/actinomycin, and another progressed on VDC/IE. Seven patients received consolidative radiotherapy. Of those, one patient received definitive radiation for an unresectable retro-orbital tumor. With a median follow-up of 14 months (range 10-48) off therapy, eight patients are alive with no evidence of disease (NED). The patient with URCS remains on therapy.

Conclusion: Based on our findings and a review of published cases, we recommend detailed radiographic staging at diagnosis for all infantile BCOR-altered sarcomas, including brain imaging for cases demonstrating URCS morphology. Due to the likelihood of local recurrence or progression, observation alone is not adequate for the management of microscopic or macroscopic residual disease. Hybrid or URCS morphology predicts a risk of regional or distant disease, respectively. As demonstrated in our accompanying proposed treatment algorithm, aggressive local control, often with radiation, is required for definitive treatment. Systemic chemotherapy is also often necessary for successful therapy. Anthracycline-based regimens and ICE chemotherapy are generally effective.



PMMTI, classic histomorphology (A, B,) hybrid morphology (D, E) and undifferentiated round cell sarcoma (URCS) morphology (G, H). Immunohistochemical stain for BCOR (C, F).



Proposed Treatment Algorithm for BCOR-ITD Infantile Soft Tissue Sarcoma



2:04 PM - 2:11 PM

Paper #76 #1818714

A MULTICENTER RETROSPECTIVE ANALYSIS ON THE EFFECT MUTATIONAL STATUS ON OUTCOMES FOR PATIENTS WITH PECOMA

Lawrence W. Liu¹; Carina Dehner¹; Dana C. Borcharding¹; John S. Chrisinger¹; Jingqin Luo¹; Amanda Parkes²; Nam Bui³; Elizabeth J. Davis⁴; Varun Monga⁵; Mohammed Milhem⁵; Ryan Jones⁶; Angela Hirbe⁷

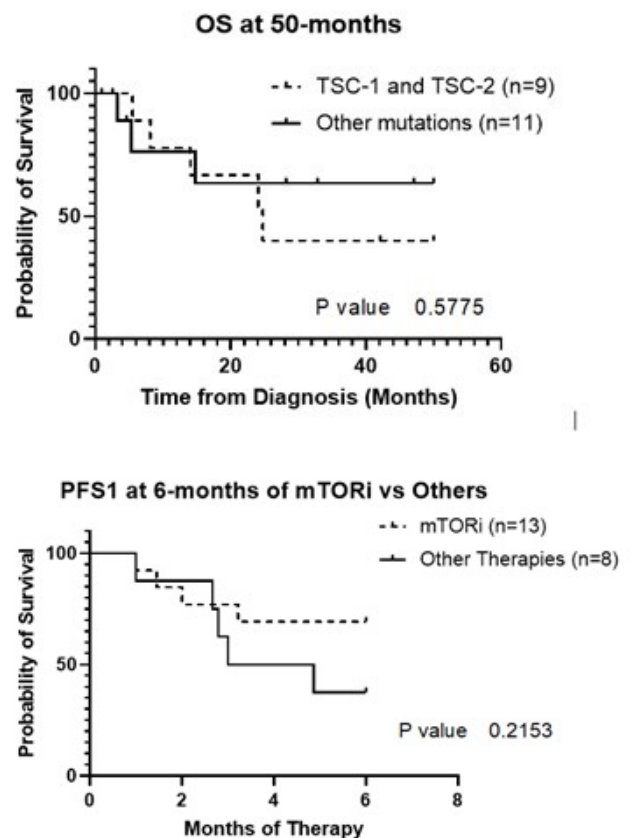
¹Washington University in St. Louis, St. Louis, Missouri, UNITED STATES; ²University of Wisconsin Carbone Cancer Center, Madison, Wisconsin, UNITED STATES; ³Stanford University Department of Oncology, Stanford, California, UNITED STATES; ⁴Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES; ⁵University of Iowa Health Care, Iowa City, Iowa, UNITED STATES; ⁶Tempus, Chicago, Illinois, UNITED STATES; ⁷Siteman Cancer Center, St. Louis, Missouri, UNITED STATES

Objective: Perivascular epithelioid cell neoplasms (PEComas) are mesenchymal tumors with smooth muscle and melanocyte features. They are driven by loss of function from TSC-1 and -2 mutations, leading to overactivation of the mTOR pathway. As such, clinical studies have demonstrated that around 50% of PEComas respond to mTOR inhibitors (mTORi; eg. everolimus), however the nuances regarding response to mTORi based on mutation status and its effect on survival are uncertain. Given this, we sought to examine the impact of TSC-1 and -2 versus other mutations on patient survival and response to mTORi.

Methods: This was a multicenter study conducted at five sites throughout the United States. We identified 49 patients from January 1, 2004, to January 31, 2021, via surgical pathology report with a diagnosis of PEComa. We conducted a retrospective analysis to identify PEComa patients with Next Generation Sequencing (NGS) data and compared outcomes based on mutations. Progression-free survival (PFS) and overall survival (OS) were defined as the date of diagnosis to the date of progression or death or the last imaging scan for PFS and the date of death or last follow-up for OS and were further thresholded at 6 months and 50 months, respectively. Empirical survival probability was estimated via the Kaplan-Meier method and survival differences between groups were compared by log-rank test.

Results: Of the 49 identified PEComa patients, 20 patients had NGS data and were included in the analyses. As seen in Figure 1, there was no significant difference in OS between PEComa patients with TSC-1 and TSC-2 mutations versus those with other mutations (eg., TP53, RB1, MDM2, NF1, MEN1, and others). As seen in Figure 2, there was no significant difference in PFS for first-line therapy (PFS1) between mTORi versus other therapy.

Conclusion: In this multicenter study of PEComas, we identified no significant OS differences based on mutations. We did not find a significant difference in PFS1 with mTORi versus other therapy. Given that our current analysis is limited by the small sample size, we plan to accumulate more data from other sites. Our results support the current recommendation of 1st-line mTORi in PEComas.





Be a part of
something meaningful
**let's work towards
a future option for
desmoid tumors**



Ayala is evaluating investigational new drug AL102 in a Phase 2/3 clinical trial (RINGSIDE) for the treatment of patients with progressing desmoid tumors

**Please attend our
interactive Trial in Progress
poster presentation**

AL102, Oral Gamma-secretase Inhibitor for the Potential Treatment of Desmoid Tumors

Poster #P172, abstract #1818889

Friday, November 12

2:30–3:15 PM EST

**For more information, please visit:
ayalapharma.com/ringside**

Ayala Pharmaceuticals, Inc. is a clinical-stage oncology company focused on developing and commercializing small molecule therapeutics for patients suffering from rare and aggressive cancers. The company has two investigational product candidates under development, AL101 and AL102, targeting the aberrant activation of the Notch pathway with gamma secretase inhibitors to treat a variety of tumors including Desmoid Tumors, Adenoid Cystic Carcinoma, Triple Negative Breast Cancer (TNBC), T-cell Acute Lymphoblastic Leukemia (T-ALL) and Multiple Myeloma (MM) (in collaboration with Novartis).

AL102 is currently in a Pivotal Phase 2/3 clinical trial for patients with progressing Desmoid Tumors (RINGSIDE). **The trial is currently enrolling.**



Poster #001 #1818993

IMMUNE INFILTRATE AND CELL CYCLE / DIFFERENTIATION PROGRAMS ARE INVERSELY CORRELATED IN MYXOID LIPOSARCOMA AND IDENTIFY HIGHER RISK PATIENTS

Andrea Careno, Dr¹; Loris De Cecco, PhD¹; Laura Bergamaschi, Dr²; Marta Barisella, MD³; Paola Collini, MD⁴; Sandro Pasquali, MD, PhD⁵; Chiara Castelli, PhD²; Alessandro Gronchi, MD⁶; Viviana Vallacchi, PhD²

¹Platform of Integrated Biology, Department of Applied Research and Technology Development, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Lombardia, ITALY, ²Immunotherapy of Human Tumors, Department of Research, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Lombardia, ITALY, ³Department of Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ⁴Department of Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Lombardia, ITALY, ⁵Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ⁶Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, Milan, Lombardia, ITALY

Poster #002 #1819047

DISSECTING DRUG RESISTANCE IN GASTROINTESTINAL STROMAL TUMOURS

Leonardo A. Meza-Zepeda, MSc, PhD¹; Sara K. Sara K., MSc¹; Ksenia Khelik, PhD¹; Saikat Das Sajib, MSc¹; Susanne Lorenz, MSc, PhD¹; César Serrano, MD, PhD²; Heidi M. Namløs, MSc, PhD¹,

¹Oslo University Hospital, Oslo, Oslo, NORWAY, ²Sarcoma Translational Research, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Catalonia, SPAIN

Poster #003 #1819027

SOFT TISSUE SARCOMAS HARBOR AN INTRATUMORAL MICROBIOME WHICH IS LINKED WITH PROGNOSIS IN PATIENTS UNDERGOING PREOPERATIVE RADIATION AND SURGERY

Lauren M. Perry, MD, MAS¹; Sylvia M. Cruz²; Louis B. Jones, MD³; Ugur N. Basmaci, BS⁴; Sean J. Judge, MD¹; Steven W. Thorpe, MD¹; Nikhil Joshi, PhD⁵; Blythe P. Durbin-Johnson, PhD⁵; Matthew L. Settles, PhD⁵;

Jonathon A. Eisen, PhD⁵; Robert J. Canter, MD¹, ¹University of California Davis, Sacramento, California, UNITED STATES, ²Division of Surgical Oncology, Department of Surgery, University of California Davis School of Medicine, Sacramento, California, UNITED STATES, ³Dallas Sarcoma Associates, Dallas, TX, UNITED STATES, ⁴University of California Davis School of Medicine, Sacramento, California, UNITED STATES, ⁵University of California Davis, Davis, California, UNITED STATES

Poster #004 #1819043

SIMILARITY ESTIMATION OF PDX MODEL MULTIOMIC PROFILES WITH CORRESPONDING PATIENT TUMORS

Robin Droit, PhD student¹; Maria Eugénia Marques da costa, PhD²; Anne Gomez-Brouchet, Professor³;

Jean-Yves Scoazec, Professor²; Audrey Mohr, PhD²; Pierre Khneisser, Medicine Doctor²;

Tiphaine Adam-de-beaumais, PharmD, PhD²; Marlène Pasquet, Professor³; Birgit Geoerger, MD, PhD⁴;

Antonin Marchais, PhD²; Nathalie Gaspar, MD, PhD⁵

¹Gustave Roussy, Massy, Ile-de-France, FRANCE, ²Gustave Roussy, Villejuif, Ile-de-France, FRANCE,

³CHU Toulouse, Toulouse, Midi-Pyrenees, FRANCE, ⁴Gustave Roussy Cancer Center, Université Paris-Saclay, INSERM U1015, Villejuif, Ile-de-France, FRANCE, ⁵Gustave Roussy Cancer Campus, Villejuif, Ile-de-France, FRANCE

Poster #005 #1819085

SUPER-ENHANCER RADIO-EPIGENOMIC (SERE) PROFILING OF RHABDOMYOSARCOMA: A TRANSLATIONAL STUDY CONCEPT

Prarthana Bangalore Parthasarathy, MD, FAAP; Andrew Muskara; Berkely Gryder; omar Mian; Stacey Zahler Cleveland Clinic Children's, Cleveland, Ohio, UNITED STATES

Poster #006 #1818965

STUDY OF GENE EXPRESSION PROFILE CHANGE AFTER PANOBINOSTAT TREATMENT IN SOFT TISSUE SARCOMA CELL LINES

Yingjun Zhang, Bsc¹; Connie W.C. HUI, Mphi²; Teresa TSE, MbChB, FRCR(Clinical Oncology), FHKCR(Radiology), FHKAM³; Gordon C.H. TANG, MBBS, MRCP³; Qian TAO, PhD²; Eric C.h. WONG, PhD²; Herbert Loong, MBBS, PDipMDPath, MRCP, FRCP Edin, FHKCP, FHKAM(Medicine)⁴,
¹The Chinese University of Hongkong, Hongkong, HONG KONG, ²The Chinese University of Hongkong, HongKong, HONG KONG, ³Prince of Wales Hospital., HongKong, HONG KONG, ⁴The Chinese University of Hong Kong, Hong Kong, HONG KONG

Poster #007 #1819075

AXL AS A POTENTIAL THERAPEUTIC TARGET FOR SOFT TISSUE SARCOMA

Daniela d'Empaire, MSc¹; Hester Boven, Pathologist¹; Ji-Ying Song, Pathologist¹; Winan J. van Houdt, MD PhD MSc²; Winette T. A. van der Graaf, MD PhD¹; Daniel Peeper, Prof Dr¹; Julia Boshuizen, MD PhD³,
¹Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS, ²The Netherlands Cancer Institute, Amsterdam, Noord-Holland, Netherlands, ³OLVG West, Amsterdam, Noord-Holland, NETHERLANDS

Poster #008 #1818966

NOVEL CANDIDATE DRUGS FOR THE TREATMENT OF MALIGNANT PERIPHERAL NERVE SHEATH TUMOR REVEALED BY PROTEOMIC ANALYSIS AND A DRUG SCREENING TEST USING PATIENT-DERIVED CELL LINES

Ryuto Tsuchiya, MD¹; Rei Noguchi, MD, Ph.D²; Yuki Yoshimatsu, Ph.D³; Yooksil Sin, Ph.D⁴; Takuya Ono, graduate student¹; Hideaki Kosako, Ph.D⁵; Akihiko Yoshida, MD, Ph.D⁶; Akira Kawai, MD⁷; Tadashi Kondo, MD, Ph.D¹,
¹Division of Rare Cancer Research, National Cancer Center Research Institute, Chuo-ku, Tokyo, JAPAN, ²Division of Rare Cancer Research, National Cancer Center Research Institute, Tokyo, Tokyo, JAPAN, ³Division of Rare Cancer Research, National Cancer Center Research Institute, 5-1-1 Tsukiji, Chuo-ku, Tokyo, JAPAN, ⁴Division of Rare Cancer Research, National Cancer Center Research Institute, chuo-ku, Tokyo, JAPAN, ⁵Division of Cell Signaling, Fujii Memorial Institute of Medical Sciences, Tokushima University, Tokushima-shi, Tokushima, JAPAN, ⁶Department of Diagnostic Pathology, National Cancer Center Hospital, Chuo-ku, Tokyo, JAPAN, ⁷National Cancer Center Hospital, Chuo-ku, Tokyo, JAPAN

Poster #009 #1819069

DLK1 AS A POSSIBLE THERAPEUTIC TARGET FOR SARCOMA

Ilkyu Han, MD PhD; Han-Soo Kim, MD PhD; Ha Jeong Kim, PhD
Seoul National University Hospital, Seoul, Seoul-t'ukpyolsi, REPUBLIC OF KOREA

Poster #010 #1818952

TARGETING INHIBITION OF EIF4A AND A HIGH THROUGHPUT SCREENING TO IDENTIFY SYNERGISTIC DRUG COMBINATIONS TO TREAT PEDIATRIC AND ADULT SARCOMAS

Long-Sheng Chang, PhD¹; Janet L. Oblinger, PhD²; Xiaohu Zhang, PhD³; hyndavi Anksapuram, BA¹; Marc Ferrer, PhD³; Ryan D. Roberts, MD, PhD⁴; A Douglas Kinghorn, DSc, PhD⁵
¹Nationwide Children's Hospital and The Ohio State University, Columbus, Ohio, UNITED STATES, ²Center for Childhood Cancer & Blood Diseases, Nationwide Children's Hospital, Columbus, Ohio, UNITED STATES, ³National Center for Advancing Translational Sciences, NIH, Bethesda, Maryland, UNITED STATES, ⁴Nationwide Children's Hospital, Columbus, Ohio, UNITED STATES, ⁵Division of Medicinal Chemistry & Pharmacognosy, The Ohio State University College of Pharmacy, Columbus, Ohio, UNITED STATES

Poster #011 #1819058

DEVELOPING A NOVEL MODEL OF NEUROFIBROMATOSIS TYPE 1 ASSOCIATED MALIGNANT PERIPHERAL NERVE SHEATH TUMORS USING INDUCED PLURIPOTENT STEM CELLS

Garrett M. Draper, B.S.; Mahathi Patchava, B.S.; Wendy Hudson; Kyle B. Williams, PhD; David A. Largaespada, PhD, University of Minnesota, Minneapolis, Minnesota, UNITED STATES

Poster #012 #11818919

TARGETING ASPARAGINE METABOLISM INHIBITS TUMOR GROWTH IN LIPOSARCOMA

Kyle D. Klingbeil, MD MS¹; Blake Wilde, PhD²; Sarah Dry, MD³; Joseph Crompton, MD PhD⁴; Fritz C. Eilber, MD³; David Shackelford, PhD⁵; Heather Christofk, PhD²; Brian Kadera, MD⁶
¹UCLA Health, Department of Surgery, Los Angeles, CA, ²UCLA, Department of Biological Chemistry, Los Angeles, California, UNITED STATES, ³UCLA Medical Center, Los Angeles, California, UNITED STATES, ⁴UCLA Health, Los Angeles, California, UNITED STATES, ⁵UCLA Health, Division of Pulmonary and Critical Care Medicine, Los Angeles, California, UNITED STATES, ⁶UCLA Health, Division of Surgical Oncology, Los Angeles, California, UNITED STATES

Poster #013 #1818996

TARGETING SARCOMA PULMONARY METASTASES WITH ANNAMYCIN

Waldemar Priebe, MSc, PhD¹; Rafal Zielinski, PhD²; Krzysztof Grela, MSc³; Roberto Cardenas-Zuniga, PhD¹; Stanislaw Skora, PhD¹; Izabela Fokt, PhD¹; Radjendirane Venugopal, PhD⁴; Maria Poimenidou, BA¹; Lamhamedi Cherradi Salah-Eddine, PhD¹; Joseph A. Ludwig, IV, MD⁵

¹UT MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ²UT MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ³Moleculin Biotech Inc., Houston, Texas, UNITED STATES, ⁴UT MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁵Sarcoma Medical Oncology, University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES

Poster #014 #1818876

TYK2 AS A BIOMARKER AND THERAPEUTIC TARGET IN MALIGNANT PERIPHERAL NERVE SHEATH TUMORS

Dana C. Borcharding, PhD¹; Neha Amin¹; Kevin He¹; Carina Dehner, MD/PhD²; Peter Ruminski, MS¹; Sonika Dahiya, MD¹; John S. Chrisinger, MD³; Taylor Sundby, MD⁴; Kai Pollard, B.S., B.A.⁵; Brigitte C. Widemann, MD⁴; Christine Pratilas, MD⁵; Jack F. Shern, MD⁴; Angela C. Hirbe, MD, PhD⁶, ¹Washington University in St. Louis, St. Louis, Missouri, UNITED STATES, ²Washington University Division of Oncology, St. Louis, Missouri, UNITED STATES, ³Washington University Department of Pathology and Immunology, St. Louis, Missouri, UNITED STATES, ⁴NCI, Bethesda, Maryland, UNITED STATES, ⁵Johns Hopkins University, Baltimore, Maryland, UNITED STATES, ⁶Washington University School of Medicine, St. Louis, Missouri, UNITED STATES

Poster #015 #1819037

CHROMOSOME 8 GAIN IS A COMMON EVENT IN MPNST PATHOGENESIS

Carina Dehner, MD/PhD¹; Chang In Moon²; Xiyuan Zhang, PhD³; Zhaohe Zhou⁴; Chris Miller²; Hua Xu²; Xiaodan Wan²; Kuangying Yang²; Jay Mash²; Sara Gosline⁵; Yuxi Wang²; Xiaochun Zhang²; Abigail Godec⁶; Paul Jones²; Sonika Dahiya, MD⁷; Tina Primeau²; Shunqiang Li²; Kai Pollard, B.S., B.A.⁸; Fausto Rodriguez, MD⁸; Li Ding²; Christine Pratilas, MD⁸; Jack F. Shern, MD³; Angela C. Hirbe, MD, PhD⁹; Himanshi Bhatia, PhD², ¹Washington University Division of Oncology, St. Louis, Missouri, UNITED STATES, ²Washington University, St. Louis, Missouri, UNITED STATES, ³NCI, Bethesda, Maryland, UNITED STATES, ⁴Washington U, St. Louis, Missouri, UNITED STATES, ⁵Pnnl, Benton County, Washington, UNITED STATES, ⁶Michigan State, Grand Rapids, Michigan, UNITED STATES, ⁷Washington University in St. Louis, St. Louis, Missouri, UNITED STATES, ⁸Johns Hopkins University, Baltimore, Maryland, UNITED STATES, ⁹Washington University School of Medicine, St. Louis, Missouri, UNITED STATES

Poster #016 #1818940

ESTABLISHMENT OF A COMPREHENSIVE CLINICALLY- AND GENOMICALLY ANNOTATED BIOSPECIMEN REPOSITORY FROM PATIENTS WITH NEUROFIBROMATOSIS TYPE 1

Kai Pollard, B.S., B.A.¹; Jineta Banerjee, PhD²; Ana Calizo, B.S.¹; Robert Allaway, PhD²; Fausto Rodriguez, MD¹; Christine Pratilas, MD¹

¹Johns Hopkins University, Baltimore, Maryland, UNITED STATES, ²Sage Bionetworks, Seattle, Washington, UNITED STATES

Poster #017 #1818949

IDENTIFICATION OF THERAPEUTIC VULNERABILITIES IN NF1-ASSOCIATED MALIGNANT PERIPHERAL NERVE SHEATH TUMORS DEFICIENT FOR POLYCOMB REPRESSIVE COMPLEX 2

Kyle B. Williams, PhD¹; Alex Larsson, BS²; Justin Tibbits, BS, MS²; Tyler Jubenville, BS³; Helena Sverak, BS²; Christopher L. Moertel, MD²; David A. Largaespada, PhD²

¹University of Minnesota, Minneapolis, Minnesota, UNITED STATES, ²University of Minnesota, Minneapolis, Minnesota, UNITED STATES, ³University of Minnesota, Minneapolis, Minnesota, UNITED STATES

Poster #018 #1819003

PRECLINICAL ASSESSMENT OF PROTEOSTASIS INHIBITION IN RHABDOMYOSARCOMA

Amit J. Sabnis, MD; Jacky Morales, BA; David V. Allegakoen, BS, MS; Leanne Sayles, BS; Alejandro Sweet-Cordero, MD, University of California, San Francisco, San Francisco, California, UNITED STATES

Poster #019 #1819014

CLICK ACTIVATED PROTODRUGS AGAINST CANCER (CAPAC) PLATFORM ENHANCES ANTITUMOR EFFICACY, SAFETY AND PHARMACOKINETICS OF CANCER THERAPEUTICS

Sangeetha Srinivasan, PhD¹; Nathan Yee, PhD¹; Amir Mahmoodi, MS²; Michael Zakharian, MS¹; Wayne M. Saville, MD¹; Jose M. Mejia Oneto, MD/PhD¹

¹Shasqi, Inc., San Francisco, California, UNITED STATES, ²Shasqi, Inc., San Francisco, California, UNITED STATES

Poster #020 #1818953

DEVELOPING AND CHARACTERIZING MODELS OF RESISTANCE TO CYCLIN-DEPENDENT-KINASE 4 (CDK4) INHIBITION IN THE CDK4 AMPLIFIED CANCER, DEDIFFERENTIATED LIPOSARCOMA

James L. Chen, MD¹; Jocelyn Hsu²; Nathan D. Seligson, PharmD³; Colin Stets, BS²; John Hays, MD, PhD¹

¹Ohio State University, Columbus, Ohio, UNITED STATES, ²The Ohio State University, Columbus, Ohio, UNITED STATES,

³University of Florida, Gainesville, Florida, UNITED STATES

Poster #021 #1818939

PATIENT-DERIVED SARCOMA MODELS TOWARDS BETTER CLINICAL OUTCOME OF SARCOMAS

Yuki Yoshimatsu, Ph.D¹; Rei Noguchi, MD, Ph.D²; Ryuto Tsuchiya, MD³; Yooksil Sin, Ph.D⁴; Takuya Ono, graduate student³; Mami Takahashi, Ph.D⁵; Hideaki Kosako, Ph.D⁶; Kaoru Hirabayashi, MD⁷; Kazutaka Kikuta, MD, Ph.D⁸; Iwao Ozawa, MD⁹; Akihiko Yoshida, MD, Ph.D¹⁰; Akira Kawai, MD¹¹; Tadashi Kondo, MD, Ph.D³

¹Division of Rare Cancer Research, National Cancer Center Research Institute, 5-1-1 Tsukiji, Chuo-ku, Tokyo, JAPAN,

²Division of Rare Cancer Research, National Cancer Center Research Institute, Tokyo, Tokyo, JAPAN, ³Division of Rare Cancer Research, National Cancer Center Research Institute, Chuo-ku, Tokyo, JAPAN, ⁴Division of Rare Cancer Research,

National Cancer Center Research Institute, chuo-ku, Tokyo, JAPAN, ⁵Central Animal Division, National

Cancer Center Research Institute, Chuo-ku, Tokyo, JAPAN, ⁶Division of Cell Signaling, Fujii Memorial Institute of

Medical Sciences, Tokushima University, Tokushima-shi, Tokushima, JAPAN, ⁷Division of Diagnostic Pathology,

Tochigi Cancer Center, Utsunomiya-shi, Tochigi, JAPAN, ⁸Division of Musculoskeletal Oncology and Orthopaedic

Surgery, Tochigi Cancer Center, Utsunomiya-shi, Tochigi, JAPAN, ⁹Division of Hepato-Biliary-Pancreatic Surgery,

Tochigi Cancer Center, Utsunomiya-shi, Tochigi, JAPAN, ¹⁰Department of Diagnostic Pathology, National Cancer

Center Hospital, Chuo-ku, Tokyo, JAPAN, ¹¹National Cancer Center Hospital, Chuo-ku, Tokyo, JAPAN

Poster #022 #1818942

IN VITRO DRUG SCREENING OF CIC-REARRANGED SARCOMAS USING SPHEROID AND MONOLAYER CULTURED PATIENT-DERIVED CANCER CELL LINES

Yu Kuwata, Research Associate¹; Yuki Yoshimatsu, Ph.D¹; Rei Noguchi, MD, Ph.D²; Ryuto Tsuchiya, MD³; Yooksil Sin, Ph.D⁴; Takuya Ono, graduate student³; Hiroyasu Nakatani, Ph.D⁵; Akira Kawai, MD⁶; Tadashi Kondo, MD, Ph.D³

¹Division of Rare Cancer Research, National Cancer Center Research Institute, 5-1-1 Tsukiji, Chuo-ku, Tokyo, JAPAN,

²Division of Rare Cancer Research, National Cancer Center Research Institute, Tokyo, Tokyo, JAPAN, ³Division of Rare Cancer Research, National Cancer Center Research Institute, Chuo-ku, Tokyo, JAPAN, ⁴Division of Rare Cancer Research,

National Cancer Center Research Institute, chuo-ku, Tokyo, JAPAN, ⁵Biospecimen Laboratories, Ota-ku, Tokyo, JAPAN,

⁶National Cancer Center Hospital, Chuo-ku, Tokyo, JAPAN

Poster #023 #1819041

SORAFENIB INDUCES FERROPTOSIS AND APOPTOSIS IN DESMOID-TYPE FIBROMATOSIS CELLS

Anne-Rose W. Schut, MD¹; Anne Vriends, MSc¹; Andrea Sacchetti, MSc¹; Milea Timbergen, MD, PhD¹;

Benjamin Alman, MD, PhD²; Mushriq al-Jazrawe, MD, PhD³; Dirk J. Grünhagen, MD PhD⁴; Cornelis Verhoef, MD PhD⁵;

Stefan Sleijfer, MD, PhD¹; Erik Wiemer, PhD¹, ¹Erasmus Medical Center, Rotterdam, Zuid-Holland, NETHERLANDS,

²Duke University, Durham, NC, ³Broad Institute of MIT and Harvard, Cambridge, Massachusetts, UNITED STATES,

⁴Erasmus MC Cancer Institute, Rotterdam, Zuid-Holland, NETHERLANDS, ⁵Erasmus MC Cancer Institute, Rotterdam,

Zuid-Holland, NETHERLANDS

Poster #024 #1818960

PATIENT-DERIVED METASTASIZED ORTHOTOPIC XENOGRAPTS TO GUIDE THERAPEUTIC DECISION MAKING FOR HIGH-GRADE SOFT TISSUE SARCOMA PATIENTS

Suzanne Fischer, MD¹; Elly De Vlieghere, PhD²; David Creyten, MD, PhD³; An Hendrix, PhD, ir.²;

Olivier De Wever, PhD, apr.²; Gwen Sys, MD, PhD³; Lore Lapeire, MD, PhD³,

¹Ghent University, Gentbrugge, Oost-Vlaanderen, BELGIUM, ²Ghent University, Gent, Oost-Vlaanderen, BELGIUM,

³Ghent University Hospital, Gent, Oost-Vlaanderen, BELGIUM

Poster #025 #1819046

XENOSARC: PATIENT-DERIVED XENOGRAFT (PDX) MODELS OF SOFT TISSUE SARCOMA (STS) AND THEIR HISTOPATHOLOGICAL AND MOLECULAR CHARACTERIZATION

Agnieszka Wozniak, PhD¹; Britt Van Renterghem, MSc¹; Luna De Sutter, MD¹; Lore De Cock, MD¹; Che-Jui Lee, MSc¹; Yannick Wang, MD¹; Ulla Vanleeuw, BSc¹; Kimberly Verbeeck, MSc¹; Daphne Hompes, MD, PhD²; Friedl Sinnaeve, MD³; Hazem Wafa, MD³; Baki Topal, MD, PhD⁴; Maria Debiec-Rychter, MD, PhD⁵; Raf Sciote, MD, PhD⁶; Patrick Schöffski, MD⁷

¹Laboratory of Experimental Oncology, Department of Oncology, KU Leuven and Department of General Medical Oncology, University Hospitals Leuven, Leuven Cancer Institute, Leuven, Vlaams-Brabant, BELGIUM,

²Department of Surgical Oncology, University Hospitals Leuven, Leuven, Belgium, Leuven, Vlaams-Brabant, BELGIUM,

³Department of Orthopedic Surgery, University Hospitals Leuven, Leuven, Belgium, Leuven, Vlaams-Brabant, BELGIUM,

⁴Department of Abdominal Surgery, University Hospitals Leuven, Leuven, Belgium, Leuven, Vlaams-Brabant, BELGIUM,

⁵Department of Human Genetics, KU Leuven and University Hospitals Leuven, Leuven, Belgium, Leuven, Vlaams-Brabant, BELGIUM, ⁶Department of Pathology, KU Leuven and University Hospitals Leuven, Leuven, Belgium, Leuven, Vlaams-Brabant, BELGIUM, ⁷General Medical Oncology, University Hospitals Leuven – Campus Gasthuisberg, Leuven, Brabant Wallon, BELGIUM

Poster #026 #1818850

SOCIOECONOMIC AND PREOPERATIVE RISK FACTORS ASSOCIATED WITH LIMB SALVAGE VERSUS AMPUTATION FOR ADULT EXTREMITY BONE SARCOMA PATIENTS WITH MEDICAL INSURANCE

Matthew T. Houdek, MD¹; Michael Stuart, MD¹; Elizabeth P. Wellings, MD¹; Eric R. Wagner, MD²; Denis Asante, MS³; Lindsey Sangaralingham, MPH⁴; Peter S. Rose, MD¹; Steven L. Moran, MD¹

¹Mayo Clinic, Rochester, Minnesota, UNITED STATES, ²Emory University, Atlanta, Georgia, UNITED STATES,

³Optum Labs, Cambridge, Massachusetts, UNITED STATES, ⁴Mayo Clinic Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery, Rochester, Minnesota, UNITED STATES

Poster #027 #1818926

PERFORMANCE OF THE 7TH AND 8TH VERSION OF THE AJCC-CLASSIFICATION FOR SOFT TISSUE SARCOMAS REGARDING PROGNOSTIC ACCURACY

Maria Anna Smolle, MD¹; Michiel van de Sande, MD PhD²; Andrew J. Hayes, PhD³; Marko Bergovec, MD⁴; Henry Smith, MD⁵; Bernadette Liegl-Atzwanger, Prof.⁴; Per-Ulf Tunn, MD⁶; Maya Niethard, MD⁷; Reinhard Windhager, Prof. MD⁸; Joanna Szkandera, MD⁹; Andreas Leithner, Prof. Dr.¹⁰

¹Department of Orthopaedics and Trauma, Medical University Graz, Graz, Steiermark, AUSTRIA, ²Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ³The Royal Marsden Hospital NHS Foundation Trust, London, England, UNITED KINGDOM, ⁴Medical University Graz, Graz, Steiermark, AUSTRIA, ⁵Department of Surgery, Royal Marsden Hospital NHS Foundation Trust, London, London, England, UNITED KINGDOM, ⁶HELIOS Klinikum Berlin-Buch, Berlin, Berlin, GERMANY, ⁷Sarcoma Centre, HELIOS-Klinikum Berlin-Buch, Berlin, Berlin, GERMANY, ⁸Department of Orthopaedics and Traumatology, Medical University of Vienna, Vienna, Wien, AUSTRIA, ⁹Medical University of Graz, Graz, Steiermark, AUSTRIA, ¹⁰Department of Orthopedics and Trauma, Medical University of Graz, Graz, Steiermark, AUSTRIA

Poster #028 #1818946

PATTERNS OF CARE AND FACTORS ASSOCIATED WITH OVERALL SURVIVAL IN PATIENTS WITH LIPOSARCOMA AND SYNCHRONOUS PULMONARY METASTASES.

Wasay Nizam, M.B.B.S¹; Richard Nudotor, MD²; Alexandra C. Istl, MD MPH²; Christian Meyer, MD PhD²; Jonathan Greer, MD²; Fabian Johnston, MD MHS²

¹Johns Hopkins University, Silver Spring, Maryland, UNITED STATES, ²Johns Hopkins Hospital, Baltimore, Maryland, UNITED STATES

Poster #029 #1818857

TREATMENT PATTERNS AND OUTCOMES FOR PRIMARY UTERINE LEIOMYOSARCOMA WITH SYNCHRONOUS ISOLATED LUNG METASTASES: A NATIONAL CANCER DATABASE STUDY OF PRIMARY RESECTION AND METASTASECTOMY

Alexandra C. Istl, MD, MPH; Richard Nudotor, MD; Nerlyne Desravines, MD; Jonathan Greer, MD; Rebecca Stone, MD, MS; Fabian Johnston, MD, MHS

Johns Hopkins Hospital, Baltimore, Maryland, UNITED STATES

Poster #030 #1818943

A NATIONAL CANCER DATABASE STUDY OF CURATIVE INTENT SURGERY IN LEIOMYOSARCOMA PATIENTS WITH SYNCHRONOUS ISOLATED LUNG METASTASES

Alexandra C. Isth, MD MPH¹; Richard Nudotor, MD²; Wasay Nizam, M.B.B.S³; Jonathan Greer, MD¹; Christian Meyer, MD PhD¹; Fabian Johnston, MD MHS¹,

¹Johns Hopkins Hospital, Baltimore, Maryland, UNITED STATES, ²Johns Hopkins Hospital, Baltimore, Maryland, UNITED STATES, ³Johns Hopkins University, Silver Spring, Maryland, UNITED STATES

Poster #031 #1819059

PEDIATRIC RHABDOMYOSARCOMA INCIDENCE AND SURVIVAL - UNITED STATES, 2001-2017

Matthew T. McEvoy, MD¹; M. Fatih Okcu, MD, MPH¹; Shifan Dai, MD, PhD²; David Siegel, MD, MPH²; Philip Lupo, PhD, MPH³,

¹Texas Children's Hospital Cancer Center, Baylor College of Medicine, Houston, Texas, UNITED STATES, ²Division of Cancer Prevention and Control, Centers for Disease Control and Prevention, Atlanta, Georgia, UNITED STATES, ³Texas Children's Cancer Center, Epidemiology Program, Baylor College of Medicine, Houston, Texas, UNITED STATES

Poster #032 #1818884

NON-PRIVATE HEALTH INSURANCE PREDICTS ADVANCED STAGE AT PRESENTATION AND AMPUTATION IN LOWER EXTREMITY HIGH GRADE BONE SARCOMA: AN NCDB STUDY

Muhammad U. Jawad, MD¹; Brad Pollock, MD¹; Elysia Alvarez, MD, MPH¹; Janai Carr-Ascher, MD, PhD¹; R. Lor Randall, MD¹; Steven W. Thorpe, MD²

¹University of California, Davis, Sacramento, California, UNITED STATES, ²University of California Davis, Sacramento, California, UNITED STATES

Poster #033 #1818841

A POPULATION-BASED ANALYSIS OF LYMPH NODE METASTASIS IN EXTREMITY SOFT TISSUE SARCOMA: AN UPDATE

Charles A. Gusho, BS¹; Linus Lee, BE²; Michael P. Fice, MD²; Cristina M. O'Donoghue, MD, MPH²; Steven Gitelis, MD²; Alan T. Blank, MD, MS²,

¹Rush University Medical Center, Milwaukee, Wisconsin, UNITED STATES, ²Rush University Medical Center, Chicago, Illinois, UNITED STATES

Poster #034 #1819074

SOFT TISSUE SARCOMAS IN OCTOGENARIAN PATIENTS: ARE TREATMENT OPTIONS AND ONCOLOGICAL OUTCOMES DIFFERENT? - A SEER RETROSPECTIVE STUDY.

Michael P. Guertin, BS¹; Yonghoon Lee, BA²; Jose M. Ramirez, BS²; Alvin Nguyen, BA³; Juan Pretell-Mazzini, MD⁴

¹University of Miami Miller School of Medicine, Miramar, Florida, UNITED STATES, ²University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES, ³University of Illinois College of Medicine, Chicago, IL, ⁴Miller School of Medicine - University of Miami, Miami, Florida, UNITED STATES

Poster #035 #1818885

MALIGNANT NEOPLASMS OF THE FOOT: PREDILECTION OF HEMATOLOGICAL MALIGNANCIES AND SEX-RELATED AND ETHNIC DISPARITIES IN AMPUTATION

Muhammad U. Jawad, MD¹; Saif Farhan, MD¹; Max R. Haffner, MD¹; Christopher Kreulen, MD, MS¹; Eric Giza, MD¹; Steven W. Thorpe, MD²; R. Lor Randall, MD¹,

¹University of California, Davis, Sacramento, California, UNITED STATES, ²University of California Davis, Sacramento, California, UNITED STATES

Poster #036 #1818917

PRIORITIES AND PROGRESS IN THE FIRST YEAR OF THE MUSCULOSKELETAL TUMOR REGISTRY

Benjamin J. Miller, MD MS¹; Adam Levin, MD MS²; Eric Henderson, MD³

¹University of Iowa, Iowa City, Iowa, UNITED STATES, ²Johns Hopkins, Baltimore, Maryland, UNITED STATES, ³Dartmouth, Lebanon, New Hampshire, UNITED STATES

Poster #037 #1818986

ANALYZING THE TEMPORAL TRENDS IN FIVE-YEAR SURVIVAL FOR PATIENTS WITH OSTEOSARCOMA

Daniel R. Evans, MSc¹; Alexander L. Lazarides, MD²; Isabelle Byers, BA¹; Julia D. Visgauss, MD³; Brian E. Brigman, MD, PhD³; William C. Eward, MD³

¹Duke University School of Medicine, Durham, North Carolina, UNITED STATES, ²Duke University Hospital, Department of Orthopedic Surgery, Durham, North Carolina, UNITED STATES, ³Duke University Hospital, Department of Orthopaedic Surgery, Durham, North Carolina, UNITED STATES

Poster #038 #1818906

IMPACT OF INSURANCE STATUS ON CHONDROSARCOMA DIAGNOSTIC STAGE: IMPLICATIONS FOR DETECTION AND OUTCOMES

Ana C. Belzarena, MD¹; Puja Yatham, BS²; Jacklyn Garcia, BS²; Valeria Fagundo, BS²; Grettel Castro, MPH²; Pura Rodriguez de la Vega, MPH²; Juan Ruiz-Pelaez, MD MMedSci²

¹Miami Cancer Institute, Miami, Florida, UNITED STATES, ²Herbert Wertheim College of Medicine Florida International University, Miami, Florida, UNITED STATES

Poster #039 #1818899

SOFT TISSUE SARCOMA INCIDENCES AND CLINICAL CHARACTERISTICS ARE SIGNIFICANTLY DIFFERENT BETWEEN DIFFERENT GEOGRAPHIC AND ETHNIC POPULATIONS

Tom W. Chen, MD¹; Ruru Chang, PhD²; Axel Le Cesne, MD³; Yuchun Hsieh, MSc⁴; Antonine Italiano, MD⁵; Ya-Wen Yang, MSc⁶; Nicolas Penel, MD⁷; Wen-Chung Lee, MD, PhD⁶; Emmauelle Bompas, MD⁸; Thibaud Valentin, MD⁹; Philippe Anract, MD¹⁰; Nelly Firmin, MD¹¹; Florence Duffaud, MD¹²; K. Arnold Chan, MD PhD¹³; Jean-Yves Blay, MD, PhD¹⁴

¹National Taiwan University Hospital, Taipei, Taipei, TAIWAN (REPUBLIC OF CHINA), ²Institute of Epidemiology and Preventive Medicine, College of Public Health, National Taiwan University, Taipei, Taipei, TAIWAN (REPUBLIC OF CHINA), ³Institut Gustave Roussy-Gustave Roussy Cancer Center-DITEP, Villejuif, Ile-de-France, FRANCE, ⁴Health Data Research Center, National Taiwan University College of Public Health, Taipei, Taipei, TAIWAN (REPUBLIC OF CHINA), ⁵Institute Bergonié, Bordeaux, Aquitaine, FRANCE, ⁶Taiwan Cancer Registry Center, Institute of Epidemiology and Preventive Medicine, National Taiwan University College of Public Health, Taipei, Taipei, TAIWAN (REPUBLIC OF CHINA), ⁷Oscar Lambret Cancer Center, Lille, Nord-Pas-de-Calais, FRANCE, ⁸Institut de Cancérologie de l'Ouest, Saint-Herblain, Pays de la Loire, FRANCE, ⁹IUCT Oncopole, Toulouse, Languedoc-Roussillon, FRANCE, ¹⁰Assistance Publique – Hôpitaux de Paris, Paris, Ile-de-France, FRANCE, ¹¹ICM, Institut du Cancer de Montpellier, Montpellier, Languedoc-Roussillon, FRANCE, ¹²Marseille University Hospital Timone, Marseille, Languedoc-Roussillon, FRANCE, ¹³Graduate Institute of Oncology, National Taiwan University College of Medicine, Taipei, Taipei, TAIWAN (REPUBLIC OF CHINA), ¹⁴Centre Léon Bérard, Lyon, Auvergne, FRANCE

Poster #040 #1818932

IMPACT OF OSTEOARTHRITIS ON SURGICAL TREATMENT PATTERNS AMONG PATIENTS WITH TENOSYNOVIAL GIANT CELL TUMORS

Feng Lin, PhD¹; Kathleen Wilson, MPH²; Matthew Brouillette, MPH²; Winghan J. Kwong, Pharm.D., PhD³; John A. Abraham, MD, FACS⁴

¹Daiichi Sankyo Inc., Basking Ridge, New Jersey, UNITED STATES, ²Custom Data Analytics, Life Sciences, IBM Watson Health, Cambridge, Massachusetts, UNITED STATES, ³Daiichi Sankyo, Inc., Basking Ridge, New Jersey, UNITED STATES, ⁴Rothman Institute and Fox Chase Cancer Center, Philadelphia, Pennsylvania, UNITED STATES

Poster #041 #1818894

THE EPIDEMIOLOGY OF DESMOID TUMORS IN DENMARK

Naushin Hooda, PharmD¹; Marie Anneberg Brahe, MD²; Helene M.L. Svane, PhD, MS³; Jon Fryzek, MPH, PhD⁴; Gina Nicholson, MPH⁴; Jessica White, MS⁵; Badreddin Edris, MS, PhD⁵; Mary Smith, PhD⁵; Michael M. Petersen, MD, PhD⁶; Thomas Baad-Hansen, MD, PhD⁷; Johnny Ø Keller, MD, PhD⁷; Peter H. Jørgensen, MD, PhD⁷; Alma B. Pedersen, DMsc, PhD³

¹EpidStrategies, Vancouver, British Columbia, CANADA, ²Department of Clinical Epidemiology, Aarhus University, Aarhus, Hovedstaden, DENMARK, ³Department of Clinical Epidemiology, Department of Clinical Medicine, Aarhus University and Aarhus University Hospital, Aarhus, Midtjylland, DENMARK, ⁴EpidStrategies, Rockville, Maryland, UNITED STATES, ⁵SpringWorks Therapeutics, Inc., Stamford, Connecticut, UNITED STATES, ⁶Musculoskeletal Tumor Section, Department of Orthopedic Surgery, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Hovedstaden, Denmark, ⁷Department of Orthopedic Surgery, Aarhus University Hospital, Aarhus, Midtjylland, DENMARK

Poster #042 #1818877

A SEER-BASED ANALYSIS OF ALVEOLAR SOFT PART SARCOMA FROM 1975-2018: INCIDENCE, PATTERNS OF PRESENTATION, AND TRENDS IN SURVIVAL

Hari Sankaran, MD MSc¹; Geraldine O'Sullivan Coyne, MD²; Alice P. Chen, MD³; Ana Best, PhD⁴

¹National Institute of Health - NCI, Bethesda, Maryland, UNITED STATES, ²NCI, Bethesda, Maryland, UNITED STATES, ³NCI/NIH, Bethesda, Maryland, UNITED STATES, ⁴NCI, Bethesda, Maryland, UNITED STATES

Poster #043 #1819067

NUCLEAR ORGANIZATION OF MYOGENIC TRANSCRIPTION FACTORS IN PEDIATRIC RHABDOMYOSARCOMA

Kyle L. MacQuarrie, MD/PhD¹; Steven Kosak, PhD²,

¹Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, Illinois, UNITED STATES, ²Northwestern University, Chicago, Illinois, UNITED STATES

Poster #044 #11818901

RADIOMICS AND MACHINE LEARNING PREDICT DIAGNOSIS IN MUSCULOSKELETAL MYXOID SOFT TISSUE TUMORS

Joshua M. Lawrenz, MD; Can Cui, MS; Samuel R. Johnson, BS; Cullen P. Moran, BS; Katherine S. Hajdu, BS; Andrew B. Rees, MD; Benjamin L. Coiner, BS; Brian Bingham, MD; Joanna L. Shechtel, MD; David S. Smith, PhD; John J. Block, MD; Leo Luo, MD; Hakmook Kang, PhD; Jennifer L. Halpern, MD; Herbert S. Schwartz, MD; Benoit Dawant, PhD; Ginger E. Holt, MD

Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES

Poster #045 #1818914

GENOMIC LOSS OF HETEROZYGOSITY REVEALS RARE, CLINICALLY MEANINGFUL SUBTYPES OF LEIOMYOSARCOMA

Nathan D. Seligson, PharmD¹; Joy Tang, MD²; Dexter Jin, PhD³; Monica Bennett, BS⁴; Julia Elvin, MD, PhD³; Kiley Graim, PhD⁵; John Hays, MD, PhD²; Sherri Millis, PhD³; Wayne Miles, PhD²; James L. Chen, MD²,

¹University of Florida, Jacksonville, Florida, UNITED STATES, ²Ohio State University, Columbus, Ohio, UNITED STATES, ³Foundation Medicine Inc, Cambridge, Massachusetts, UNITED STATES, ⁴University of Florida, Jacksonville, Florida, UNITED STATES, ⁵University of Florida, Gainesville, Florida, UNITED STATES

Poster #046 WITHDRAWN

Poster #047 #1818853

COMPARISON OF CLINICOPATHOLOGICAL FEATURES AND OUTCOMES IN PATIENTS WITH PRIMARY LEIOMYOSARCOMA OF BONE AND SOFT TISSUE

Charles A. Gusho, BS¹; Linus Lee, BE²; Alan T. Blank, MD, MS²; Steven Gitelis, MD²

¹Rush University Medical Center, Milwaukee, Wisconsin, UNITED STATES, ²Rush University Medical Center, Chicago, Illinois, UNITED STATES

Poster #048 #1819004

COMPLICATIONS AND POSTOPERATIVE MORTALITY RATE AFTER SURGERY FOR METASTASIS TO FEMUR: ANALYSIS OF A NATIONWIDE DATABASE

Yusuke Tsuda, MD, PhD¹; Liuzhe Zhang, MD²; Sakae Tanaka, MD, PhD²; Hiroshi Kobayashi, MD, PhD²

¹The University of Tokyo Hospital, Tokyo, Tokyo, JAPAN, ²The University of Tokyo Hospital, Bunkyo-ku, Tokyo, JAPAN

Poster #049 #1818844

PULMONARY METASTASECTOMY IN BONE AND SOFT TISSUE SARCOMA WITH METASTASIS TO THE LUNGS

Charles A. Gusho, BS¹; Christopher W. Seder, MD²; Nicolas Lopez-Hisijos, DO²; Linus Lee, BE²; Alan T. Blank, MD, MS²; Marta Batus, MD²

¹Rush University Medical Center, Milwaukee, Wisconsin, UNITED STATES, ²Rush University Medical Center, Chicago, Illinois, UNITED STATES

Poster #050 WITHDRAWN

Poster #051 #1819057

CHARACTERIZATION OF TWO NOVEL PATIENT-DERIVED SPONTANEOUSLY IMMORTALIZED MYXOFIBROSARCOMA CELL LINES FOR DRUGS AND INNOVATIVE TREATMENTS SCREENING

Ania Naila Guerrieri, MSc, PhD¹; Chiara Bellotti, MSc¹; Roberta Laranga, MSc, PhD¹; Barbara Dozza, MSc, PhD¹; Enrico Lucarelli, MSc, PhD¹; Claudia Cocchi, MSc²; Alessandro De Vita, PhD, Pharm D²; Laura Mercatali, MSc, PhD²; Marco Gambarotti, MD³; Tommaso Frisoni, MD, PhD¹; Davide M. Donati, MD, PhD¹; Toni Ibrahim, MSc, MD, PhD¹,
¹IRCCS Istituto Ortopedico Rizzoli, Bologna, Emilia-Romagna, ITALY, ²IRCCS Istituto Romagnolo Per Lo Studio Dei Tumori (IRST) "Dino Amadori", Meldola, Emilia-Romagna, ITALY, ³Istituto Ortopedico Rizzoli, Bologna, Emilia-Romagna, ITALY

Poster #052 #1819045

THERAPEUTIC IMPLICATIONS OF PROSPECTIVE WHOLE GENOME SEQUENCING IN SARCOMA PATIENTS

Luuk J. Schipper, MD¹; Kim Monkhorst, MD, PhD¹; Pia van der Laan, MD¹; Kris G. Samsom, MD¹; Linda J. W. Bosch, PhD¹; Petur Snaebjornsson, MD PhD¹; Hester van Boven, MD PhD¹; Paul Roepman, PhD²; Lizet E. van der kolk, MD PhD¹; Gerrit A. Meijer, MD PhD¹; Emile E. Voest, MD PhD¹; Winan J. van Houdt, MD PhD MSc³; Winette T. A. van der Graaf, MD PhD¹,
¹Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS, ²Hartwig Medical Foundation, Amsterdam, Noord-Holland, NETHERLANDS, ³The Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS

Poster #053 #1819083

THE PERCEPTIONS OF TELEMEDICINE SATISFACTION IN IMMUNOCOMPROMISED PEDIATRIC PATIENTS DURING THE COVID-19 PANDEMIC

Molly M. Aguina¹; Alexandra Arca¹; Ariel Gliksberg, MD²; Paul M. Kent, MD³,
¹Rush University Hospital, Chicago, Illinois, UNITED STATES, ²University of Illinois Hospital, Chicago, Illinois, UNITED STATES, ³Rush University Medical Center, River Forest, Illinois, UNITED STATES

Poster #054 #1818923

HOW COVID-19 AFFECTED THOSE CONTACTING THE SARCOMA UK SUPPORT LINE.

Helen Stradling, MSc, BNurs (Hons); Sam Hackett, BSc (Hons) Oncology Nursing, PgD in Nursing; Carly McDonald, BSc (Hons) Midwifery, PgC Obstetric Ultrasound, Sarcoma UK, London, England, UNITED KINGDOM

Poster #055 #1818862

TREATMENT OF OSTEOSARCOMA PATIENTS IN THE PHILIPPINE GENERAL HOSPITAL DURING THE COVID-19 OUTBREAK

Czar Louie Gaston, MD
University of the Philippines Manila - Philippine General Hospital, Manila, National Capital Region, PHILIPPINES

Poster #056 #1818856

DISPARITIES IN TYROSINE KINASE INHIBITOR USE IN OLDER PATIENTS WITH GASTROINTESTINAL STROMAL TUMOR

Thanh P. Ho, MD¹; Hayley Dykhoff¹; Lindsey Sangaralingham, MPH²; Brittany L. Siontis, MD¹; Travis Grotz, MD¹; Scott Okuno, MD¹; Steven I. Robinson, MD¹
¹Mayo Clinic, Rochester, Minnesota, UNITED STATES, ²Mayo Clinic Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery, Rochester, Minnesota, UNITED STATES

Poster #057 #1818976

A RANDOMIZED PHASE 2 STUDY OF NIVOLUMAB MONOTHERAPY OR NIVOLUMAB COMBINED WITH IPILIMUMAB IN ADVANCED GASTROINTESTINAL STROMAL TUMORS

Arun Singh, MD¹; Joel Hecht²; Lee Rosen, MD²; Xiaoyan Wang, PhD²; Sandra Brackert, NP²; Warren Chow, MD³; Fritz C. Eilber, MD⁴; John Glaspy, MD²; Bartosz Chmielowski, MD PhD²
¹University of California, Los Angeles, Santa Monica, California, UNITED STATES, ²University of California, Los Angeles, Santa Monica, California, UNITED STATES, ³City of Hope Comprehensive Cancer Center, Duarte, California, UNITED STATES, ⁴UCLA Medical Center, Los Angeles, California, UNITED STATES

Poster #058 #1818969

THE ROLE OF NEOADJUVANT IMATINIB IN GIST PATIENTS: A RETROSPECTIVE COHORT STUDY

Sara Renberg, MD¹; Yifan Zhang²; Fredrik Karlsson, MD, PhD³; Robert Bränström, MD, PhD³; Jan Åhlen, MD, PhD³; Li Jalmsell, MD, PhD⁴; Elisabet Lidbrink, MD, PhD⁴; Christina Linder Stragliotto, MD, PhD⁴; Felix Haglund, MD, PhD⁵; Andri Papakonstantinou, MD, PhD⁶

¹Department of Head, Neck, Lung and Skin Tumors, Karolinska University Hospital, Stockholm, Sweden, Stockholm, Stockholms Lan, SWEDEN, ²Department of Pathology and Cancer diagnostics, Karolinska University Hospital, Stockholm, Sweden and Department of Oncology-Pathology, Karolinska Institute, Stockholm, Sweden, Solna, Stockholms Lan, SWEDEN, ³Department of Breast cancer, Endocrine tumors and Sarcoma, Karolinska University Hospital, Stockholm, Sweden and Department of Molecular Medicine and Surgery (MMK), Karolinska Institute, Stockholm, Sweden, Stockholm, Stockholms Lan, SWEDEN, ⁴Department of Breast cancer, Endocrine tumors and Sarcoma, Karolinska University Hospital, Stockholm, Sweden, Stockholm, Stockholms Lan, SWEDEN, ⁵Department of Pathology and Cancer diagnostics, Karolinska University Hospital, Stockholm, Sweden and Department of Oncology-Pathology, Karolinska Institute, Stockholm, Sweden, Stockholm, Stockholms Lan, SWEDEN, ⁶Department of Breast cancer, Endocrine tumors and Sarcoma, Karolinska University Hospital, Stockholm, Sweden and Department of Oncology-Pathology, Karolinska Institute, Stockholm, Sweden, Stockholm, Stockholms Lan, SWEDEN

Poster #059 #1818937

REAL-WORLD EVIDENCE FROM ONLINE PATIENT FORUMS COMPLEMENTING CURRENT MEDICAL PERSPECTIVES: THE EXAMPLE OF GASTROINTESTINAL STROMAL TUMOUR PATIENTS

Anne Dirkson, MSc¹; Suzan Verberne, PhD¹; Gerard van Oortmerssen, PhD²; Wessel Kraaij, PhD¹; Hans Gelderblom, MD, PhD³

¹Leiden Institute of Advanced Computer Science, Leiden University, Leiden, Zuid-Holland, NETHERLANDS, ²Patient Platform Sarcomas & Leiden Institute of Advanced Computer Science, Leiden University, Leiden, Zuid-Holland, NETHERLANDS, ³Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS

Poster #060 #1818912

REAL-WORLD ASSESSMENT OF CLINICAL OUTCOMES IN GIST PATIENTS TREATED WITH SUNITINIB AFTER IMATINIB FAILURE

Virginia Martínez-Marín, MD, PhD¹; Gloria Marquina, MD PHD²; Claudia Maria Valverde Morales, MD³; Mar Galera, MD⁴; Isabel Pajares, MD⁵; Pilar Solis, MD⁶; Nadia Hindi, MD⁷; Maria Angeles Vaz, MD⁸; Eduardo Pujol, MD⁹; Inmaculada Ballester, MD¹⁰; Oscar Reig, MD¹¹; Juana Cano, MD¹²; Alberto Moreno, MD¹³; Rebeca Mondejar, MD¹⁴; Jose Andres Meana, MD¹⁵; Amelia López-Ladrón, MD¹⁶; Roberto Diaz Diaz-Beveridge, MD¹⁷; David Vicente, MD¹⁸; Ana Leon, MD¹⁹; Antonio Fernández-Serra, MD²⁰; César Serrano, MD, PhD²¹

¹H. U. La Paz, Madrid, Madrid, SPAIN, ²H. U. Clínico San Carlos, Madrid, Madrid, SPAIN, ³Vall D'Hebron University Hospital, Barcelona, Catalonia, SPAIN, ⁴H. U. Gregorio Marañón, Madrid, Madrid, SPAIN, ⁵H. U. Miguel Servet, Zaragoza, Aragon, SPAIN, ⁶H. U. Central de Asturias, Oviedo, Asturias, SPAIN, ⁷Fundacion Jimenez Diaz University Hospital, Madrid, Madrid, SPAIN, ⁸H. U. Ramón y Cajal, Madrid, Madrid, SPAIN, ⁹H. U. Lozano Blesa, Zaragoza, Aragon, SPAIN, ¹⁰H. U. Morales Meseguer, Murcia, Murcia, SPAIN, ¹¹H. U. Clinic, Barcelona, Catalonia, SPAIN, ¹²H. General Ciudad Real, Ciudad Real, Castilla-La Mancha, SPAIN, ¹³H. U. Reina Sofía, Cordoba, Andalucia, SPAIN, ¹⁴H. U. La Princesa, Madrid, Madrid, SPAIN, ¹⁵H. U. Alicante, Alicante, Comunidad Valenciana, SPAIN, ¹⁶H. de Valme, Sevilla, Andalucia, SPAIN, ¹⁷H. U. La Fe, Valencia, Comunidad Valenciana, SPAIN, ¹⁸H. U. Virgen Macarena, Sevilla, Andalucia, SPAIN, ¹⁹H. U. Fundación Jiménez Díaz, Madrid, Madrid, SPAIN, ²⁰Fundación Instituto Valenciano de Oncología, Valencia, Comunidad Valenciana, SPAIN, ²¹Sarcoma Translational Research, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Catalonia, SPAIN

Poster #061 #1818927

IMPACT OF ADJUVANT IMATINIB ON BONE AND MUSCLE DENSITY IN PATIENTS WITH RESECTED GASTRO-INTESTINAL STROMAL TUMORS

Claudia Angela Maria Fulgenzi, MD¹; Andrea Napolitano, MD, PhD¹; Eliodoro Faiella, MD²; Laura Messina, MD²; Gennaro Castiello, MD²; Flavia Paternostro, MD²; Marianna Silletta, MD, PhD²; Francesco Pantano, MD, PhD²; Giuseppe Tonini, MD, PhD²; Daniele Santini, MD, PhD²; Bruno Vincenzi, MD, PhD³

¹Campus Bio-Medico, Roma, Lazio, ITALY, ²Campus Bio Medico, Roma, Lazio, ITALY, ³Department of Medical Oncology, Università Campus Bio-Medico di Roma, Rome, Italy, Roma, Lazio, ITALY

Poster #062 #1818973

PSOAS MUSCLE INDEX HAS NO PROGNOSTIC VALUE IN PATIENTS WITH PRIMARY GASTROINTESTINAL STROMAL TUMOR

Steven Hopkins, BA¹; Leah Stockton, MD²; Weier Li, MD²; Elizabeth Handorf, PhD²; Elaine Vo, MD²; Stephanie Greco, MD²,
¹Temple Lewis Katz School of Medicine, Philadelphia, Pennsylvania, UNITED STATES, ²Fox Chase Cancer Center, Philadelphia, Pennsylvania, UNITED STATES

Poster #063 #1819063

NEOADJUVANT IMATINIB IN LOCALLY ADVANCED GASTROINTESTINAL STROMAL TUMOURS (GIST): A SINGLE CENTRE RETROSPECTIVE COHORT ANALYSIS

Georgina E. Wood, MBBS MRCP BSc MSc PhD; Thomas Carter, MBChB MRCP BSc PhD; Michael Luong, BMedMD; Emma Jones, BMBS BSc; Beatrice Seddon, MBBS MRCP FRCR PhD; Palma Dileo, MD; Arjun Shankar, MBBS FRCS MD(Res); Vasilios Karavasilis, MD
London Sarcoma Service, Department of Oncology, University College London Hospitals, London, England, UNITED KINGDOM

Poster #064 #1818875

RIPRETINIB DOSE ESCALATION IN ADVANCED GASTROINTESTINAL STROMAL TUMOR: A REAL-WORLD DATA

Philippos A. Costa, MD¹; Brianna Valdes²; Priscila Barreto Coelho, MD¹; Caroline Hana, MD¹; Steven Bialick, DO, MS³; Andrea Espejo-Freire, MD¹; Luyuan Li, PhD⁴; Jillian Lykon, PharmD, BCOP¹; Emily Jonczak, MD⁴; Gina D'Amato, MD⁵; Ty K. Subhawong, MD¹; Jonathan C. Trent, MD, PhD⁴
¹University of Miami, Miami, Florida, UNITED STATES, ²University of Miami, Miller School of Medicine, Miami, Florida, UNITED STATES, ³University of Miami/Sylvester Comprehensive Cancer Center, Miami, Florida, UNITED STATES, ⁴Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES, ⁵Medical Oncology, Sylvester Comprehensive Cancer Center/University of Miami, Miami, Florida, UNITED STATES

Poster #065 WITHDRAWN

Poster #066 #1819082

HETEROGENOUS INTERTUMORAL KIT MUTATIONS FOUND IN LONG-TERM STAGE 4 GASTROINTESTINAL STROMAL TUMOR SURVIVOR

Seiya Liu¹; Ty K. Subhawong, MD²; Andrew Rosenberg, MD³; Jonathan Trent, MD⁴; Emily Jonczak, MD⁵; Elizabeth Montgomery, MD²; Alan Livingstone, MD⁶; Gina D'Amato, MD⁷
¹University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES, ²University of Miami, Miami, Florida, UNITED STATES, ³Department of Pathology, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES, ⁴Sylvester Comprehensive Cancer Center, Miami, Florida, UNITED STATES, ⁵Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES, ⁶Department of Surgery, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES, ⁷Medical Oncology, Sylvester Comprehensive Cancer Center/University of Miami, Miami, Florida, UNITED STATES

Poster #067 #1818898

A DANISH EXPLORATIVE STUDY OF CIRCULATING TUMOUR DNA PRE- AND POSTOPERATIVE SAMPLES FROM PATIENTS WITH GASTROINTESTINAL STROMAL TUMOUR

Charlotte Margareta Brinch, MD¹; Estrid Høgdall, Prof., PhD, DMSc²; Ninna Aggerholm Pedersen, MD, MSc, PhD³; Pieter de Heer, PhD⁴; Anders Krarup-Hansen, PhD⁵,
¹Department of Oncology, Copenhagen University Hospital, Herlev and Gentofte Hospital, Herlev, Denmark, Copenhagen, Hovedstaden, DENMARK, ²Department of Pathology, Copenhagen University Hospital, Herlev and Gentofte Hospital, Herlev, Denmark, Copenhagen, Hovedstaden, DENMARK, ³Aarhus University Hospital, Aarhus, Denmark, Aarhus, Midtjylland, DENMARK, ⁴Rigshospitalet, Copenhagen, Denmark., Copenhagen, Hovedstaden, DENMARK, ⁵Department of Oncology, Copenhagen University Hospital, Herlev and Gentofte Hospital, Herlev, Denmark, Copenhagen, Hovedstaden, DENMARK

Poster #068 #1819053

INTRAOPERATIVE NEAR-INFRARED FLUORESCENCE IMAGING WITH INDOCYANINE GREEN FOR IDENTIFICATION OF GASTROINTESTINAL STROMAL TUMOURS; PRELIMINARY RESULTS OF A CLINICAL TRIAL

Gijsbert M. Kalisvaart, MD¹; Ruben P. Meijer, MD²; Okker D. Bijlstra, MD²; Hidde A. Galema, MD³; Wobbe O. de Steur, MD²; Henk H. Hartgrink, MD PhD²; Yvonne M. Schrage, MD PhD²; Dirk J. Grünhagen, MD PhD³; Lioe-Fee de Geus-Oei, MD PhD²; Alexander L. Vahrmeijer, MD PhD²; Jos A. van der Hage, MD PhD²
¹LUMC, Leiden, Zuid-Holland, NETHERLANDS, ²Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ³Erasmus MC Cancer Institute, Rotterdam, Zuid-Holland, NETHERLANDS

Poster #069 #1819022

ENGINEERED BONE MARROW: A NOVEL MODEL TO INVESTIGATE EARLY OSTEOSARCOMA PROGRESSION

Steven W. Thorpe, MD¹; Katherine Griffin, BS²; R. Lor Randall, MD³; Kent Leach, PhD³, ¹University of California Davis, Sacramento, California, UNITED STATES, ²University of California, Davis, Davis, California, UNITED STATES, ³University of California, Davis, Sacramento, California, UNITED STATES

Poster #070 #1819018

LONG-TERM INHIBITION OF PARP SENSITIZES A THREE-DIMENSIONAL CHONDROSARCOMA MODEL TO CHEMO- AND RADIOTHERAPY

Ieva Palubeckaite, PhD; Sanne Venneker, MSc; Brendy E. van den Akker; Inge H. Briaire - de Bruijn; Judith V.M.G. Bovée, MD PhD
Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS

Poster #071 #1818979

PROGNOSTIC AND THERAPEUTIC VALUE OF T-LYMPHOKINE-ACTIVATED KILLER CELL-ORIGINATED PROTEIN KINASE (TOPK) IN OSTEOSARCOMA

Pichaya Thanindratarn, MD¹; Zhenfeng Duan, MD, PhD²; Francis J. Hornicek, MD, PhD²; Scott D. Nelson, MD³; Arun Singh, MD⁴; Noah C. Federman, MD⁵; Dylan Dean, MD²
¹Department of Orthopedic Surgery, Chulabhorn Hospital, HRH Princess Chulabhorn College of Medical Science, Chulabhorn Royal Academy, Bangkok, Krung Thep, THAILAND, ²Department of Orthopaedic Surgery, David Geffen School of Medicine at UCLA, Los Angeles, California, UNITED STATES, ³UCLA Medical Center, Santa Monica, California, UNITED STATES, ⁴University of California, Los Angeles, Santa Monica, California, UNITED STATES, ⁵UCLA Medical Center, Los Angeles, California, UNITED STATES

Poster #072 #1818997

UPDATED OUTCOMES FOR PATIENTS WITH COMPLETELY RESECTED PULMONARY RECURRENT OSTEOSARCOMA: A REPORT FROM THE CHILDREN'S ONCOLOGY GROUP

Alexander J. Chou, MD¹; Mark D. Krailo, PhD²; Ruxu Han, MS³; Allen Buxton, MS³; Damon R. Reed, MD⁴; Richard Gorlick, MD⁵; Steven G. DuBois, MD⁶; Michael Isakoff, MD⁷; Katherine A. Janeway, MD⁶; Pooja Hingorani, MD⁵, ¹Weill Cornell Medicine, NY, New York, UNITED STATES, ²Department of Preventive Medicine, Keck School of Medicine of the University of Southern California, Los Angeles, California, UNITED STATES, ³Children's Oncology Group, Monrovia, California, UNITED STATES, ⁴Moffitt Cancer Center, Tampa, Florida, UNITED STATES, ⁵MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁶Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, Massachusetts, UNITED STATES, ⁷Connecticut Children's Medical Center, Hartford, Connecticut, UNITED STATES



Precision that moves

At Blueprint Medicines, we have one common goal: to improve human health. With a focus on developing precision medicines, we are rapidly advancing new therapies that may help people with genomically defined cancers and rare diseases. We combine a deep understanding of the genetic blueprint of disease with a unique scientific approach to enable us to develop new solutions faster, because the need is now.

For information, visit
BlueprintMedicines.com



Poster #073 #1819050

WEEKLY CISPLATIN +/- IMATINIB IN ADVANCED CHORDOMA: A RETROSPECTIVE CASE-SERIES ANALYSIS FROM THE ITALIAN RARE CANCERS NETWORK (RTR)

Giacomo Giulio Baldi, MD¹; Salvatore Lo Vullo²; Giovanni Grignani, MD³; Bruno Vincenzi, MD, PhD⁴; Giuseppe Badalamenti, MD, PhD⁵; Marinella Mastore, MD⁶; Ciriaco Buonomenna, MD⁷; Carlo Morosi, MD⁸; Alessandro Gronchi, MD⁹; Anna Maria Frezza, MD¹⁰; Salvatore Provenzano, MD¹⁰; Noemi Simeone, MD¹⁰; Luigi Mariani²; Paolo G. Casali, MD¹⁰; Silvia Stacchiotti, MD¹⁰

¹Department of Medical Oncology, Hospital of Prato, Prato, Italy, Prato, Toscana, ITALY, ²Unit of Clinical Epidemiology and Trial Organization, IRCCS Fondazione Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY, ³Department of Medical Oncology-Sarcoma Unit, Candiolo Cancer Institute FPO-IRCCS, Candiolo (TO), Italy, Candiolo, Piemonte, ITALY, ⁴Department of Medical Oncology, Università Campus Bio-Medico di Roma, Rome, Italy, Roma, Lazio, ITALY, ⁵Department of Medical Oncology, Policlinico "Paolo Giaccone", University of Palermo, Palermo, Italy, Palermo, Sicilia, ITALY, ⁶Department of Medical Oncology, San Gerardo Hospital, Monza, Italy, Monza, Lombardia, ITALY, ⁷Department of Radiology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, Milan, Lombardia, ITALY, ⁸Department of Radiology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, Milan, Lombardia, ITALY, ⁹Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, Milan, Lombardia, ITALY, ¹⁰Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY

Poster #074 #1818999

EPIGENETIC MODULATION OF NK CELLS TO IMPROVE TUMOR TRAFFICKING AND ENHANCE THERAPEUTIC EFFICACY AGAINST OSTEOSARCOMA

Ariana R. Anjier, MS; Shinji Maegawa, PhD; Vidya Gopalakrishnan, PhD; Juan Bournat, PhD; Donghang Cheng, PhD; Yanwen Yang, PhD; Charles V. Kingsley; Adam Kulp; Eugenie Kleinerman, MD; Nancy Gordon, MD
UT MD Anderson Cancer Center, Houston, Texas, UNITED STATES

Poster #075 #1818980

FIRST-IN-CLASS CDC45-MCM-GINS HELICASE INHIBITORS OFFER THERAPEUTIC POTENTIAL FOR OSTEOSARCOMA TREATMENT

Darcy L. Welch, MS¹; Shengyan Xiang, PhD¹; Xingju Luo, PhD¹; Damon R. Reed, MD²; Mark Alexandrow, PhD¹,
¹H Lee Moffitt Cancer Center and Research Institute, Tampa, Florida, UNITED STATES, ²Moffitt Cancer Center, Tampa, Florida, UNITED STATES

Poster #076 #1818865

IDH1 MUTATION INDUCES HIF-1 α AND CONFERS ANGIOGENIC PROPERTY IN CHONDROSARCOMA JJ012 CELLS

Luyuan Li, PhD; Xiaoyu Hu, MD; Josiane E. Eid, MD; Jonathan C. Trent, MD, PhD
Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES

Poster #077 #1819025

ADVERSE PROGNOSTIC IMPACT OF LOSS OF STAG2 PROTEIN EXPRESSION IN PATIENTS WITH NEWLY DIAGNOSED LOCALIZED EWING SARCOMA: A REPORT FROM THE CHILDREN'S ONCOLOGY GROUP (COG)

David S. Shulman, MD¹; Kelly Klega, BS¹; Alanna J. Church, MD²; Sonja Chen, MD³; Aaron R. Thorner, PhD⁴; Anwasha Nag, PhD⁴; David Hall, MS⁵; Donald A. Barkauskas, PhD⁶; Mark D. Krailo, PhD⁶; Katherine A. Janeway, MD¹; Steven G. DuBois, MD¹; Brian D. Crompton, MD¹

¹Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, MA, ²Department of Pathology, Boston Children's Hospital and Harvard Medical School, Boston, Massachusetts, UNITED STATES, ³Department of Pathology and Laboratory Medicine, Rhode Island Hospital, Providence RI, Providence, Rhode Island, UNITED STATES, ⁴Center for Cancer Genomics, Dana-Farber Cancer Institute, Boston, Massachusetts, UNITED STATES, ⁵Children's Oncology Group, Monrovia, California, UNITED STATES, ⁶Department of Preventive Medicine, Keck School of Medicine of the University of Southern California, Los Angeles, California, UNITED STATES

Poster #078 #1819068

METASTATIC LUNG COLONIZATION BY OSTEOSARCOMA CELLS IS A MULTI-STEP PROCESS REQUIRING COOPERATION BETWEEN TUMOR SUBPOPULATIONS WITH DISTINCT PHENOTYPES

Ryan D. Roberts, MD, PhD¹; James B. Reinecke, MD, PhD¹; John M. Hinckley¹; Sanjana Rajan¹; Amy Gross²; Maren Cam, PhD¹,

¹Nationwide Children's Hospital, Columbus, Ohio, UNITED STATES, ²Center for Childhood Cancer, Nationwide Children's Hospital, The Ohio State University James Comprehensive Cancer Center, Columbus, Ohio, UNITED STATES

Poster #079 #1818849

FACTORS ASSOCIATED WITH ONCOLOGIC OUTCOME IN PATIENTS WITH SCAPULAR CHONDROSARCOMA

Matthew T. Houdek, MD; Elizabeth P. Wellings, MD; Chad W. Parkes, MD; Adam J. Tagliero, MD; Peter S. Rose, MD, Mayo Clinic, Rochester, Minnesota, UNITED STATES

Poster #080 #1818868

SAFETY AND EFFICACY OF MULTIPLE TYROSINE KINASE INHIBITOR THERAPY FOR PEDIATRIC/ADOLESCENT AND YOUNG ADULT PATIENTS WITH RELAPSED OR REFRACTORY OSTEOSARCOMAS: SINGLE-INSTITUTION RETROSPECTIVE STUDY

Masanaka Sugiyama, MD; Ayumu Arakawa, MD; Nami Shirakawa, MD; Kayoko Tao, MD; Kazuki Tanimura, MD; Miho Nakajima, MD; Yuko Watanabe, MD; Tadashi Kumamoto, MD; Junnosuke Maniwa, MD; Akihiro Yoneda, MD; Shintaro Iwata, MD; Eisuke Kobayashi, MD; Akira Kawai, MD; Chitose Ogawa, MD
National Cancer Center Hospital, Chuo-ku, Tokyo, JAPAN

Poster #081 #1818925

TYROSINE KINASE INHIBITORS IN RECURRENT BONE TUMOURS. A REAL WORLD EXPERIENCE

Tushar Vora, MD¹; Sarah Cohen-Gogo, MD, PhD²; David Malkin, MD, FRCP(C)²; Daniel A. Morgenstern, MB BChir, PhD³; Paul Nathan, MD, M.Sc., FRCPC²; Avram Denburg, MD, M.Sc., PhD, FRCPC²; Furqan Shaikh, MD, M.Sc., PhD, FRCPC²; Jack Brzezinski, MD²; Anita Villani, MD²; Sevan Hopyan, MD, PhD, FRCSC²; Jay S. Wunder, MSc., MD⁴; Peter C. Ferguson, MD, PhD, FRCSC⁵; Kim M. Tsoi, MD, PhD⁶; Albiruni Ryan Abdul Razak, MD, MB, MRCPI⁷; Abha A. Gupta, MD, M.Sc., FRCPC⁸; Hagit Peretz Soroka, PhD⁹

¹Hospital for Sick Children, Princess Margaret Cancer Center, University of Toronto, Toronto, Ontario, CANADA,

²Hospital for Sick Children and University of Toronto, Toronto, Ontario, CANADA, ³Hospital for Sick Children, Toronto, Ontario, CANADA, ⁴The Lunenfeld-Tanenbaum Research Institute, Toronto, Ontario, CANADA, ⁵Division of Orthopaedic Surgery, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, CANADA, ⁶University of Toronto, Mount Sinai Hospital, Toronto, Ontario, CANADA, ⁷Division of Medical Oncology, Princess Margaret Cancer Centre, University Health Network, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, CANADA, ⁸Hospital for Sick Children and Princess Margaret Cancer Center and University of Toronto, Toronto, Ontario, CANADA, ⁹Princess Margaret Cancer Center, Canadian Sarcoma Research and Clinical Collaboration (CanSaRCC), Toronto, Ontario, CANADA

Poster #082 #1818989

PRESENTING CHARACTERISTICS AND SURVIVAL OF EWING SARCOMA OF THE PELVIS

Jeffrey Brown, BS¹; Kyla Rakoczy, BS¹; John Groundland, MD²

¹University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES,

²Huntsman Cancer Institute, Salt Lake City, Utah, UNITED STATES

Poster #083 #1818967

ESTABLISHMENT OF SIMPLE SCREENING SYSTEM FOR MOLECULAR TARGET THERAPY IN OSTEOSARCOMA

Keita Sasa, MD¹; Tsuyoshi Saito, MD, PhD²; Taisei Kurihara, M.D, PhD²; Nobuhiko Hasegawa, MD, PhD²; Kei Sano, MD, PhD²; Daisuke Kubota, MD, PhD²; Keisuke Akaike, MD, PhD²; Taketo Okubo, MD, PhD²; Takuo Hayashi, MD, PhD²; Tatsuya Takagi, MD, PhD²; Muneaki Ishijima, MD, PhD²; Yoshiyuki Suehara, MD, PhD²

¹Juntendo University, Bunkyo-ku, Tokyo, JAPAN, ²Juntendo University, Bunkyo-ku, Tokyo, JAPAN

Poster #084 #1819038

AN EXPLORATORY PILOT TRIAL EVALUATING TUMOR INFILTRATING LYMPHOCYTES THERAPY ON RELAPSED OSTEOSARCOMA

Yingqi Hua, MD, PhD¹; Chongren Wang, MD²; Hongliang Fang, PhD³; Yafei Jiang, MD²; Mengxiong Sun, MD²; Dongqing Zuo, MD²; Xiaojun Ma, MD²; Suxia Xue, MD³; Wei Sun, MD²; Yu Lv, MD²; Jing Xu, PhD²; Zhengdong Cai, MD²; Xiaowen He, PhD, MD³

¹Shanghai General Hospital, Shanghai Jiao Tong University, Shanghai, Shanghai, CHINA (PEOPLE'S REPUBLIC),

²Shanghai General Hospital, School of Medicine Shanghai Jiao Tong University, Shanghai, Shanghai, CHINA (PEOPLE'S REPUBLIC), ³Origincell Technology Group Co., Ltd, Shanghai, Shanghai, CHINA (PEOPLE'S REPUBLIC)

Poster #085 #1818959

CLINICAL OUTCOME OF EXTRA-AXIAL CHORDOMA: AN INTEGRATIVE DATA ANALYSIS

Toshihiko Nishisho, MD, PhD¹; Toki Shunichi, MD²; Ryo Miyagi, MD³; Koichi Sairyō, MD, PhD²

¹Tokushima Pref. Miyoshi Hospital, Tokushima, Tokushima, JAPAN, ²Tokushima University, Tokushima, Tokushima, JAPAN,

³Tokushima Prefectural Central Hospital, Tokushima, Tokushima, JAPAN

Poster #086 #1819023

PATHOGENIC GERMLINE VARIANT OF PALB2 IN A PATIENT WITH EWING SARCOMA: IMPACT OF PALB2 LOSS ON RESPONSE TO DNA DAMAGE

Jessica D. Daley, MD¹; Sreya Dey²; Noah Brown, MD³; Elena Kessler, MS, CGC⁴; Julia Meade, MD⁵; Elena Mukherjee, MS⁶; Alexandra Superdock, MD⁷; James Cooper, MD⁵; Kelly M. Bailey, MD, PhD⁵

¹UPMC Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES, ²University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES, ³University of Michigan, Ann Arbor, Michigan, UNITED STATES, ⁴UPMC, Pittsburgh, Pennsylvania, UNITED STATES, ⁵University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES, ⁶University of Pittsburgh Dept of Pediatrics, Pittsburgh, Pennsylvania, UNITED STATES, ⁷UPMC Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES

Poster #087 #1818933

CAN LOW-GRADE CHONDROSARCOMA IN FLAT BONES BE TREATED WITH INTRALESIONAL CURETTAGE AND CRYOTHERAPY?

Kwangwon Park, MD, PhD¹; John Krumme, MD²; Moses Adebayo, MD³; Brock Adams, MD⁴; Robert Henshaw, MD⁴

¹Arnold Palmer Children's Hospital, Oviedo, Florida, UNITED STATES, ²University of Missouri, Leawood, Kansas, UNITED STATES, ³Howard University Hospital, Washington, District of Columbia, UNITED STATES, ⁴Washington Hospital Center, Washington, District of Columbia, UNITED STATES

Poster #088 #1818848

PREOPERATIVE SARCOPENIA IS ASSOCIATED WITH LOCAL TUMOR RECURRENCE BUT NOT WOUND COMPLICATIONS FOLLOWING SACRAL TUMOR RESECTION

Matthew T. Houdek, MD; Elyse Brinkmann, MD; Doris E. Wenger, MD; Joshua D. Johnson, MD; Syed M. Karim, MD; Daniel Blezek, PhD; Peter S. Rose, MD

Mayo Clinic, Rochester, Minnesota, UNITED STATES

Poster #089 #1819084

PRELIMINARY SAFETY RESULTS OF A PILOT STUDY OF HIGH DOSE PEMETREXED FOR CHORDOMA

Kamlesh K. Sankhala, MD¹; Tiffany Juarez, MD²; Jose Carrillo, MD³; Naveed Wagle, MD³; Akanksha Sharma, MD⁴; Judy Truong, PAC³; Minhdan Nguyen, PAC³; Annie Heng, RN³; Jaya Gill, RN³; Raffi Nersesian, Clinical Research³; Santosh Kesari, MD, PhD³

¹NextGen Oncology, Cedars Sinai Medical Center, Beverly Hills, California, UNITED STATES, ²Saint John's Cancer Institute and Pacific Neuroscience Institute at Providence Saint John's Health Center, Santa Monica, CA, Santa Monica, California, UNITED STATES, ³Saint John's Cancer Institute and Pacific Neuroscience Institute at Providence Saint John's Health Center, Santa Monica, CA, Santa Monica, California, UNITED STATES, ⁴Saint John's Cancer Institute and Pacific Neuroscience Institute at Providence Saint John's Health Center, Santa Monica, CA, Santa Monica, California, UNITED STATES

Poster #090 #1818985

TETRAVALENT DEATH RECEPTOR 5 AGONIST INBRX-109 IN EWING SARCOMA: PLANNED PHASE 1 COHORT EXPANSION GUIDED BY PRECLINICAL DATA

Emily Rowell, PhD¹; Vasily Andrianov, MD²; Analeah Heidt, PhD³; Klaus Wagner, MD, PhD³; Chase Deveraux³; Will Crago³; Brendan Eckelman, PhD³; Quinn Deveraux, PhD³; Victoria T. Chua-Alcala, MD⁴; Joseph Chao, MD⁵; Warren Chow, MD⁵; Rashmi Chugh, MD⁶; Anthony P. Conley, MD⁷; Vivek Subbiah, MD⁸

¹Inhibrx, inc., La Jolla, California, UNITED STATES, ²Inhibrx Inc., La Jolla, California, UNITED STATES, ³Inhibrx, Inc., La Jolla, California, UNITED STATES, ⁴Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES, ⁵City of Hope Comprehensive Cancer Center, Duarte, California, UNITED STATES, ⁶University of Michigan, Ann Arbor, Michigan, UNITED STATES, ⁷MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁸The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES

Poster #091 #1819036

MORE TO CONSIDER: THE MISDIAGNOSIS OF ACUTE LYMPHOBLASTIC LEUKEMIA AS EWING'S SARCOMA

Lauren Riggs¹; Madeline Link¹; Paul M. Kent, MD²

¹Rush University Medical Center, Chicago, Illinois, UNITED STATES, ²Rush University Medical Center, River Forest, Illinois, UNITED STATES

Poster #092 #1819010

PRESENCE OF TUMORAL STEM CELLS AS A PROGNOSTIC FACTOR IN OSTEOSARCOMA OSTEOBLASTIC IN ADULTS

Miguel Angel Clara-Altamirano, MD, MSc¹; Claudia HS Caro-Sanchez, MD, MSc¹; Alethia Alvarez-Cano, MD, MSc²; Carlo C Cortés-González, PHD¹; Silvio A Namendys-Silva, MD, MSc¹; Dorian Y. Garcia-Ortega, MD, MSc, FACS³

¹Instituto Nacional de Cancerología, Tlalpan, Distrito Federal, MEXICO, ²Christus Muguerza, Monterrey, Nuevo Leon, MEXICO, ³Instituto Nacional de Cancerología, Mexico, Distrito Federal, MEXICO

Poster #093 #1819062

SUCCESSFUL TREATMENT OF A CHILD WITH SYMPTOMATIC BRACHIAL PLEXUS OSTEOSARCOMA METASTASIS WITH MICROSPHERE EMBOLIZATION

Rhea M. Nambiar¹; Madeline Link²; Paul M. Kent, MD³

¹Rush University Medical Center, Boston, Massachusetts, UNITED STATES, ²Rush University Medical Center, Chicago, Illinois, UNITED STATES, ³Rush University Medical Center, River Forest, Illinois, UNITED STATES

Poster #094 #1818838

APATINIB PLUS IFOSFAMIDE AND ETOPOSIDE (IE) FOR RELAPSED OR REFRACTORY OSTEOSARCOMA: A RETROSPECTIVE STUDY IN TWO CENTERS IN CHINA

Lu Xie, MD¹; Jie Xu, MD¹; Xin Sun, MD¹; Xiaowei Li, MD¹; Kuisheng Liu, MD¹; Xin Liang, PhD¹; Zuli Zhou, MD¹; Hongqing Zhuang, MD²; Kunkun Sun, MD¹; Jin Gu, MD³; Wei Guo, MD and PhD¹

¹Peking University People's Hospital, Beijing, Beijing, CHINA (PEOPLE'S REPUBLIC), ²Peking University Third Hospital, Beijing, Beijing, CHINA (PEOPLE'S REPUBLIC), ³Peking University Shougang Hospital, Beijing, Beijing, CHINA (PEOPLE'S REPUBLIC)

Poster #095 #1819072

THE THERAPEUTIC REGIMEN INCLUDING BEVACIZUMAB, SORAFENIB AND CYCLOPHOSPHAMIDE PROVIDES CLINICAL BENEFIT FOR THE TREATMENT OF CHILDREN AND YOUNG ADULTS WITH RECURRENT OR REFRACTORY OSSEOUS SARCOMAS

Jessica L. Bodea, MD; Sara M. Federico, MD

St. Jude Children's Research Hospital, Memphis, Tennessee, UNITED STATES

Poster #096 #1818929

SUCCESSFUL COMBINATION OF DENOSUMAB AND SCLEROTHERAPY FOR SYMPTOMATIC LARGE RECURRENT SPINAL ANEURYSMAL BONE CYST IN A CHILD

Paul M. Kent, MD¹; Sreekumar Madassery, MD²

¹Rush University Medical Center, River Forest, Illinois, UNITED STATES, ²Rush University Medical Center, Chicago, Illinois, UNITED STATES

Poster #097 #1818847

ACTIVATION OF EFFICIENT DNA REPAIR MECHANISMS AFTER PHOTON AND PROTON IRRADIATION OF HUMAN CHONDROSARCOMA CELLS

Birgit Lohberger, PhD MSc¹; Sylvia Kerschbaum-Gruber, PhD MSc²; Tobias Madl, Prof. Dr.³; Karl Kashofer, PhD MSc⁴; Andreas Leithner, Prof. Dr.⁵; Dietmar Georg, Prof. Dr.²

¹Medical University Graz, Department of Orthopedics and Trauma, Graz, Steiermark, AUSTRIA, ²Department of Radiation Oncology, Medical University of Vienna; MedAustron Ion Therapy Center, Wiener Neustadt,, Vienna, Wien, AUSTRIA, ³Gottfried Schatz Research Center for Cell Signaling, Metabolism and Aging Molecular Biology and Biochemistry, Medical University of Graz,, Graz, Steiermark, AUSTRIA, ⁴Institute of Pathology, Medical University of Graz, Graz, Steiermark, AUSTRIA, ⁵Department of Orthopedics and Trauma, Medical University of Graz, Graz, Steiermark, AUSTRIA

Poster #098 #1818839

COMPLETE REMISSION OF METASTATIC OSTEOSARCOMA USING COMBINED MODALITY THERAPY: A RETROSEPTIVE ANALYSIS OF UNSELECTED PATIENTS IN CHINA

Lu Xie, MD¹; Jie Xu, MD¹; Xiaowei Li, MD¹; Zuli Zhou, MD¹; Hongqing Zhuang, MD²; Xin Sun, MD¹; Kuisheng Liu, MD¹; Xingyu Liu, MD¹; Kunkun Sun, MD¹; Jin Gu, MD³; Wei Guo, MD and PhD¹

¹Peking University People's Hospital, Beijing, Beijing, CHINA (PEOPLE'S REPUBLIC), ²Peking University Third Hospital, Beijing, Beijing, CHINA (PEOPLE'S REPUBLIC), ³Peking University Shougang Hospital, Beijing, Beijing, CHINA (PEOPLE'S REPUBLIC)

Poster #099 #1818859

FACTORS INFLUENCING RISK FOR DEEP SURGICAL WOUND COMPLICATIONS IN PEDIATRIC PATIENTS AFTER LIMB SALVAGE SURGERY FOR OSTEOSARCOMA

Lindsay J. Talbot, MD¹; Aaron Ross, MS²; Andrew Miller, BS²; Xiaoqing Wang, PhD¹; Zhaohua Lu, PhD¹; Carla Cartwright, RDN, LDN, CNSC¹; Karen Ringwald-Smith, RDN, CSP, LDN¹; Madison Tyler, RDN, CSP, LDN¹; Najat C. Daw³; Fariba Navid, MD⁴; Hafeez Abdelhafeez, MD⁵; Michael Neel, MD¹; Michael Bishop, MD¹

¹St. Jude Children's Research Hospital, Memphis, Tennessee, UNITED STATES, ²University of Tennessee School of Medicine, Memphis, Tennessee, UNITED STATES, ³Pediatrics, MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁴Keck School of Medicine, Los Angeles, California, UNITED STATES, ⁵St. Jude Children's Research Hospital, Memphis, Tennessee, UNITED STATES

Poster #100 #1818944

CLINICAL OUTCOMES OF PATIENTS TREATED WITH CARBON FIBER NAILS: AN INTERNATIONAL STUDY

Santiago A. Lozano-Calderon, MD, PhD¹; Zeger Rijs, MD²; Nelson Merchan, MD¹; Caleb Yeung, MD¹; Emily Berner, BS¹; Vania Oliveira, MD, PhD³; Giuseppe Bianchi, MD⁴; Eric Staals, MD⁴; Debora Lana, MD⁵; Davide Donati, MD⁴; Ortal Segal, MD⁶; Stefano Marone, MD⁷; Raimondo Piana, MD⁷; Simone De Meo, PhD⁷; Pietro Pellegrino, MD⁷; Nicola Ratto, MD⁷; Carmine Zoccali, MD, PhD⁸; Maurizio Scorianz, MD⁹; Guido Scoccianti, MD⁹;

Domenico A. Campanacci, MD⁹; Lorenzo Andreani, MD¹⁰; Silvia de Franco, MD¹⁰; Michele Boffano, Dr/ MD-MSc¹¹; Thomas Cosker, FRCS¹²; Varunprasanth Sethurajah¹²; Manuel Peleteiro Pensado, MD, PhD¹³; Irene Barrientos Ruiz, MD¹³; Esperanza Holgado Moreno, MD¹³; Eduardo J. Ortiz-Cruz, MD, PhD¹³; Michiel van de sande, MD, PhD²

¹Massachusetts General Hospital, Boston, Massachusetts, UNITED STATES, ²Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ³Centro Hospitalar Universitário do Porto, Portugal / Oporto University Hospital Center, Portugal, Porto, Porto, PORTUGAL, ⁴IRCCS Istituto Ortopedico Rizzoli, Bologna, Emilia-Romagna, ITALY, ⁵Ospedale Maggiore Trauma Center, Bologna, Emilia-Romagna, ITALY, ⁶Tel Aviv Sourasky Medical Center, Tel Aviv, Tel Aviv, ISRAEL, ⁷Centro Traumatologico Ortopedico, Turin, Piemonte, ITALY, ⁸IRCCS Regina Elena National Cancer Institute, Rome, Lazio, ITALY, ⁹Careggi University Hospital, Florence, Toscana, ITALY, ¹⁰University Hospital of Pisa, Pisa, Toscana, ITALY, ¹¹Regina Margherita Children's Hospital, Turin, Piemonte, ITALY, ¹²Nuffield Orthopaedic Centre, Oxford, England, UNITED KINGDOM, ¹³Hospital Universitario La Paz, Madrid, Madrid, SPAIN

Poster #101 #1818995

CLINICAL OUTCOMES OF PATIENTS TREATED WITH CARBON FIBER PLATES: AN INTERNATIONAL STUDY

Zeger Rijs, MD¹; Santiago A. Lozano-Calderon, MD, PhD²; Emily Berner, BS²; Nelson Merchan, MD²; Caleb Yeung, MD²; Vania Oliveira, MD, PhD³; Giuseppe Bianchi, MD⁴; Eric Staals, MD⁴; Debora Lana, MD⁵; Davide Donati, MD⁴; Ortal Segal, MD⁶; Stefano Marone, MD⁷; Raimondo Piana, MD⁷; Simone De Meo, PhD⁷; Pietro Pellegrino, MD⁷; Nicola Ratto, MD⁷; Maurizio Scorianz, MD⁸; Guido Scoccianti, MD⁸; Amber Weekhout, BSc¹;

Domenico A. Campanacci, MD⁸; Lorenzo Andreani, MD⁹; Silvia de Franco, MD⁹; Michele Boffano, Dr/ MD-MSc¹⁰; Thomas Cosker, FRCS¹¹; Varunprasanth Sethurajah¹¹; Manuel Peleteiro Pensado, MD, PhD¹²; Irene Barrientos Ruiz, MD¹²; Esperanza Holgado Moreno, MD¹²; Eduardo J. Ortiz-Cruz, MD, PhD¹²; Michiel van de sande, MD, PhD¹

¹Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ²Massachusetts General Hospital, Boston, Massachusetts, UNITED STATES, ³Centro Hospitalar Universitário do Porto, Portugal / Oporto University Hospital Center, Portugal, Porto, Porto, PORTUGAL, ⁴IRCCS Istituto Ortopedico Rizzoli, Bologna, Emilia-Romagna, ITALY, ⁵Ospedale Maggiore Trauma Center, Bologna, Emilia-Romagna, ITALY, ⁶Tel Aviv Sourasky Medical Center, Tel Aviv, Tel Aviv, ISRAEL, ⁷Centro Traumatologico Ortopedico, Turin, Piemonte, ITALY, ⁸Careggi University Hospital, Florence, Toscana, ITALY, ⁹University Hospital of Pisa, Pisa, Toscana, ITALY, ¹⁰Regina Margherita Children's Hospital, Turin, Piemonte, ITALY, ¹¹Nuffield Orthopaedic Centre, Oxford, England, UNITED KINGDOM, ¹²Hospital Universitario La Paz, Madrid, Madrid, SPAIN

Poster #102 #1818907

ROLE OF 3D PRINTED IMPLANTS IN THE DEFECT RECONSTRUCTION IN PATIENTS WITH CHEST WALL TUMORS

Aslan Valiev, PhD; Pavel Kononets, PhD; Timur Charatishvili, Prof; Nikolay Petrochenko, PhD; Alexander Salkov, Fellow, Federal State Budgetary Institution

N.N. Blokhin National Medical Research Center of Oncology of the Ministry of Health of the Russian Federation (N.N. Blokhin NMRCO), Moscow, Moskva, RUSSIA

Poster #103 #1818971

RESTORATION OF PELVIC RING CONTINUITY IN INTERNAL HEMIPELVECTOMY DEFECTS WITH THE VASCULARIZED FIBULA OSSEOUS FREE FLAP

Max Vaynrub, MD; Leslie N. Kim, MD; Farooq Shahzad, MBBS, MS
Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES

Poster #104 #1818887

INTRAMEDULLARY NAIL VERSUS PLATE FIXATION OF METASTATIC LESIONS OF THE HUMERUS

Danielle Greig, MD¹; Rishi Trikha, MD¹; Erik J. Geiger, MD²; Nicholas M. Bernthal, MD²; Brooke Crawford, MD³

¹University of California, Los Angeles, Santa Monica, California, UNITED STATES, ²David Geffen School of Medicine at UCLA, Santa Monica, California, UNITED STATES, ³University of California, Los Angeles, Los Angeles, California, UNITED STATES

Poster #105 #1819066

LONG-TERM OUTCOMES AND DIFFERENCES IN THERAPY FOR PEDIATRIC AND ADULT EWING SARCOMA PATIENTS IN BRITISH COLUMBIA, CANADA

Christine Simmons, FRCPC, MD, MSc¹; Omar Hajjaj, BSc²; Lauren Corke, BSc²; Caron Strahlendorf, FRCPC, FCP, MB³; Sarah Hamilton, MD, FRCPC⁴

¹BC Cancer - Vancouver, Vancouver, British Columbia, CANADA, ²BCCA Vancouver, Vancouver, British Columbia, CANADA, ³BC Children's Hospital, Vancouver, British Columbia, CANADA, ⁴BC Cancer Agency, Vancouver, British Columbia, CANADA

Poster #106 #1818843

DEDIFFERENTIATED CHONDROSARCOMA: A REVIEW OF THE CLINICOPATHOLOGICAL FEATURES AND OUTCOMES OF 16 CASES TREATED AT A SINGLE INSTITUTION

Charles A. Gusho, BS¹; Athan Zavras, BS²; Ira Miller, MD, PhD²; Matthew W. Colman, MD²; Linus Lee, BE²; Steven Gitelis, MD²; Alan T. Blank, MD, MS²

¹Rush University Medical Center, Milwaukee, Wisconsin, UNITED STATES, ²Rush University Medical Center, Chicago, Illinois, UNITED STATES

Poster #107 WITHDRAWN

Poster #108 #1819061

DETECTION OF DNA COPY-NUMBER CHANGES IN CIRCULATING TUMOUR DNA IN PATIENTS WITH UPS AND LPS BY ULTRA LOW-PASS WHOLE GENOME SEQUENCING AND DIGITAL DROPLET PCR

Heidi M. Namløs, PhD¹; Marie K. Gillstrøm, MSc¹; Justine Abdelli, MSc¹; Nitin Sharma, PhD¹; Ksenia Khelik, PhD¹; Ola Myklebost, PhD²; Kjetil Boye, MD, PhD¹; Leonardo A. Meza-Zepeda, MSc, PhD¹

¹Oslo University Hospital, Oslo, Oslo, NORWAY, ²University of Bergen, Bergen, Hordaland, NORWAY

Poster #109 #1818892

TOWARDS ELIMINATING LOCAL TUMOUR RECURRENCE: DETECTION OF SATELLITE TUMOUR CELLS IN PERI-TUMOURAL EDEMA IN MYXOFIBROSARCOMA AND UNDIFFERENTIATED PLEOMORPHIC SARCOMA USING TARGETED GENE SEQUENCING

Miguel Alfonso V. Principe¹; Nalan Gokgoz, Ph.D²; Patrick Prochazka³; Peter C. Ferguson, MD, PhD, FRCSC⁴; Simin Dewji, MD⁵; Jay S. Wunder, MSc., MD²; Irene L. Andrulis, Ph.D²; Brendan C. Dickson, MD MSc⁶; Kim M. Tsoi, MD, PhD⁷

¹Lunenfeld-Tanenbaum Research Institute, Toronto, Ontario, CANADA, ²The Lunenfeld-Tanenbaum Research Institute, Toronto, Ontario, CANADA, ³The Lunenfeld-Tanenbaum Research Institute, Toronto, Ontario, CANADA, ⁴Division of Orthopaedic Surgery, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, CANADA, ⁵Department of Laboratory Medicine and Pathobiology, Toronto, Ontario, CANADA, ⁶Mount Sinai Hospital, Toronto, Ontario, CANADA, ⁷University of Toronto, Mount Sinai Hospital, Toronto, Ontario, CANADA

Poster #110 #1818871

CIRCULATING TUMOUR DNA DETECTION: A POTENTIAL TOOL FOR SARCOMA MANAGEMENT

Paige E. Darville-O'Quinn¹; Nalan Gokgoz, PhD²; Kim M. Tsoi, MD, PhD³; Jay S. Wunder, MSc., MD²; Irene L. Andrulis, PhD²

¹Lunenfeld Tanenbaum Reseach Institute, Aurora, Ontario, CANADA, ²The Lunenfeld-Tanenbaum Research Institute, Toronto, Ontario, CANADA, ³University of Toronto, Mount Sinai Hospital, Toronto, Ontario, CANADA

Poster #111 #1819051

CIRCULATING TUMOR DNA (CTDNA) LANDSCAPE IN BONE AND SOFT TISSUE SARCOMAS

Gabriel Tinoco, MD, FACP¹; David Liebner, MD¹; Lesli Kiedrowski, MS, MPH, CGC²; Leslie Bucheit, MS, CGC²

¹The Ohio State University, Columbus, Ohio, UNITED STATES, ²Guardant Health, Redwood City, California, UNITED STATES

Poster #112 #1818978

UPREGULATION OF LCP1 IN CHONDROSARCOMA CORRELATES WITH AGGRESSIVE BEHAVIOR AND POOR PROGNOSIS

Caleb A. Watson¹; Emily Peairs, MS¹; John Martin, PhD¹; Trudy Zou, MS¹; Jianhong Ou, PhD¹; Julia D. Visgauss, MD³,
¹Duke University School of Medicine, Durham, North Carolina, UNITED STATES, ²University of Pittsburgh School of
Medicine, Durham, North Carolina, UNITED STATES, ³Duke University Hospital, Department of Orthopaedic Surgery,
Durham, North Carolina, UNITED STATES

Poster #113 #1818840

THE PROGNOSTIC SIGNIFICANCE OF LYMPHOVASCULAR TUMOR INVASION IN LOCALIZED HIGH-GRADE OSTEOSARCOMA: OUTCOMES OF A SINGLE INSTITUTION OVER TEN YEARS

Charles A. Gusho, BS¹; Ira Miller, MD, PhD²; Bishir Clayton, MD²; Linus Lee, BE²; Matthew W. Colman, MD²;
Steven Gitelis, MD²; Alan T. Blank, MD, MS²
¹Rush University Medical Center, Milwaukee, Wisconsin, UNITED STATES, ²Rush University Medical Center, Chicago,
Illinois, UNITED STATES

Poster #114 #1818886

COMPARISON OF NEXT GENERATION SEQUENCING IN ADOLESCENT AND YOUNG ADULT VERSUS OLDER ADULT PATIENTS WITH METASTATIC OR UNRESECTABLE SARCOMA

Amanda Parkes, MD, University of Wisconsin Carbone Cancer Center, Madison, Wisconsin, UNITED STATES

Poster #115 #1818893

PHOTOACOUSTIC MICROSCOPY OF UNDECALCIFIED BONE

Brooke Crawford, MD, FAAOS¹; Rui Cao, PhD²; Scott D. Nelson, MD³; Yu Liang, MD⁴; Yilin Luo, PhD²; Yide Zhang, PhD²;
Lihong Wang, PhD²
¹UCLA, Los Angeles, California, UNITED STATES, ²California Institute of Technology, Pasadena, California, UNITED
STATES, ³UCLA Medical Center, Santa Monica, California, UNITED STATES, ⁴City of Hope Cancer Center, Duarte,
California, UNITED STATES

Poster #116 #1819079

THE SARCOMA MICROBIOME AS A NOVEL PROGNOSTIC TOOL

Gabriel Tinoco, MD, FACP¹; Marium Husain, MD¹; Rebecca Hoyd, Biostatistician¹; Malvenderjit Jagjit Singh,
Biostatistician¹; James L. Chen, MD²; David Liebner, MD¹; Daniel Spakowicz, PhD¹
¹The Ohio State University, Columbus, Ohio, UNITED STATES, ²Ohio State University, Columbus, Ohio, UNITED STATES

Poster #117 #1818988

VALIDATION OF MDM2 FLUORESCENCE IN SITU HYBRIDIZATION TESTING IN THE DIAGNOSIS OF WELL-DIFFERENTIATED ADIPOCYTIC NEOPLASMS: A RETROSPECTIVE REVIEW

Ashley N. Flaman, MD, FRCPC¹; Brendan C. Dickson, MD MSc²; Elizabeth G. Demicco, MD PhD³
¹University of Toronto / Mount Sinai Hospital, Toronto, Ontario, CANADA, ²Mount Sinai Hospital, Toronto, Ontario,
CANADA, ³Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, Ontario, CANADA

Poster #118 #1819030

A REPORT ON THE REVIEW OF ARCHIVED OSTEOSARCOMA AND EWING SARCOMA SPECIMENS AT THE BIOPATHOLOGY CENTER - BONE SARCOMA COMMITTEE, CHILDREN'S ONCOLOGY GROUP

Archana Shenoy, MD¹; Sonja Chen, MD²; Jonathan Bush, MD³; Alyaa Al-Ibraheemi, MD⁴; Jessica L. Davis, MD⁵;
Mark D. Krailo, PhD⁶; Damon R. Reed, MD⁷; Katherine A. Janeway, MD⁸
¹Nationwide Childrens Hospital, Columbus, Ohio, UNITED STATES, ²Brown University, Providence, Rhode Island, UNITED
STATES, ³British Columbia Children's Hospital, Vancouver, British Columbia, CANADA, ⁴Boston Children's Hospital,
Boston, Massachusetts, UNITED STATES, ⁵Oregon Health & Science University, Portland, Oregon, UNITED STATES,
⁶Department of Preventive Medicine, Keck School of Medicine of the University of Southern California, Los Angeles,
California, UNITED STATES, ⁷Moffitt Cancer Center, Tampa, Florida, UNITED STATES, ⁸Dana-Farber/Boston Children's
Cancer and Blood Disorders Center, Boston, Massachusetts, UNITED STATES

Poster #119 #1818948

CELL-CYCLE PHASE PROGRESSION ANALYSIS IDENTIFIES DISTINCT PHENOTYPES OF PROGNOSTIC SIGNIFICANCE IN SARCOMA

Mark M. Cullen, MD¹; Alexander L. Lazarides, MD²; Etienne M. Flamant, BA³; Patricia D. Pittman, MD⁴; Harrison R. Ferlauto, MD⁵; David L. Kerr, IV, MD¹; Daniel Evans, BS, MSc³; Zuwei Su, PhD⁴; Kai Stoeber, PhD⁶; David G. Kirsch, MD, PhD⁷; Nicole A. Larrier, MD, MS⁷; Lars M. Wagner, MD⁸; Julia D. Visgauss, MD¹; Brian E. Brigman, MD, PhD¹; Richard F. Riedel⁹; Jason A. Somarelli, PhD⁹; Dianna M. Cardona, MD⁴; William C. Eward, MD¹

¹Duke University Hospital, Department of Orthopaedic Surgery, Durham, North Carolina, UNITED STATES,

²Duke University Hospital, Department of Orthopedic Surgery, Durham, North Carolina, UNITED STATES

³Duke University School of Medicine, Durham, North Carolina, UNITED STATES, ⁴Duke University Hospital, Department of Pathology, Durham, North Carolina, UNITED STATES, ⁵Icahn School of Medicine at Mt. Sinai, Department of Orthopaedic Surgery, New York, New York, UNITED STATES, ⁶University of Cambridge, London, England, UNITED KINGDOM, ⁷Duke University Hospital, Department of Radiation Oncology, Durham, North Carolina, UNITED STATES, ⁸Duke University Hospital, Department of Pediatrics, Durham, North Carolina, UNITED STATES, ⁹Duke Cancer Institute, Duke University Medical Center, Durham, North Carolina, UNITED STATES

Poster #120 #1818981

THE EFFICACY OF MOLECULAR ANALYSIS IN THE DIAGNOSIS OF BONE AND SOFT TISSUE TUMORS: A 15 YEARS MONO-INSTITUTIONAL EXPERIENCE

Marco Gambarotti, MD¹; Stefania Benini, Bsci¹; Gabriella Gamberi, Bsci¹; Stefania Cocchi, Bsci¹; Giovanna Magagnoli, Bsci¹; Marta Sbaraglia, MD²; Alberto Righi, MD¹; Angelo Paolo Dei Tos, MD³

¹Rizzoli Orthopaedic Institute, Bologna, Emilia-Romagna, ITALY, ²Azienda Ospedaliera Università di Padova (UniPD), Padova, Veneto, ITALY, ³Università di Padova (UniPD), Padova, Veneto, ITALY

Poster #121 #1818938

FIBROBLAST ACTIVATION PROTEIN EXPRESSION IN SARCOMAS

Jacquelyn Crane, MD¹; Danielle S. Graham, MD²; Christine Mona, PhD²; Scott D. Nelson, MD³; Alireza Samiei, MD²; David Dawson, MD²; Sarah Dry, MD²; Joseph Crompton, MD PhD⁴; Matthias Benz, MD²; Johannes Czernin, MD²; Fritz C. Eilber, MD²; Thomas Graeber, PhD⁵; Jeremie Calais, MD²; Noah C. Federman, MD²

¹Stanford University, Cupertino, California, UNITED STATES, ²UCLA Medical Center, Los Angeles, California, UNITED STATES, ³UCLA Medical Center, Santa Monica, California, UNITED STATES, ⁴UCLA Health, Los Angeles, California, UNITED STATES, ⁵UCLA, Los Angeles, California, UNITED STATES

Poster #122 #1818998

MAGNETIC RESONANCE IMAGING EVIDENCE OF JOINT EFFUSION IS ASSOCIATED WITH INTRA-ARTICULAR TUMOR EXTENSION

Max Vaynrub, MD; John Nolan, MD; Mohammad El Amine, MD; Anton Becker, MD PhD; Sinchun Hwang, MD
Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES

Poster #123 #1819060

OPTICAL COHERENCE TOMOGRAPHY FOR SURGICAL MARGIN ASSESSMENT IN SOFT TISSUE SARCOMA

Laura E. Selmic, BVetMed (Hons), MPH¹; John Alexander, MD²; Joel Mayerson, MD²; Thomas Scharschmidt, MD²; Valerie Grignol, MD²; Joal Beane, MD²; Raphael Pollock, MD²; David Konieczkowski, MD, PhD²; O. Hans Iwenofu, MD²,
¹The Ohio State University College of Veterinary Medicine, Columbus, Ohio, UNITED STATES, ²James Cancer Hospital, The Ohio State University, Columbus, Ohio, UNITED STATES

Poster #124 #1818896

ANTIBIOTIC PROPHYLAXIS IN MEGAPROSTHETIC RECONSTRUCTIONS: IS CEFAZOLIN THE CERTAIN CHOICE?

Isabelle S. Byers, BA¹; Daniel Evans, BS, MSc¹; Nicole Levine, MD²; Alexander L. Lazarides, MD²; Julia D. Visgauss, MD³; Brian E. Brigman, MD, PhD³; Nicholas Turner, MD, MHSc⁴; William C. Eward, MD³

¹Duke University School of Medicine, Durham, North Carolina, UNITED STATES, ²Duke University Hospital, Department of Orthopedic Surgery, Durham, North Carolina, UNITED STATES, ³Duke University Hospital, Department of Orthopaedic Surgery, Durham, North Carolina, UNITED STATES, ⁴Duke University Hospital, Department of Infectious Disease, Durham, North Carolina, UNITED STATES

Poster #125 #1818915

MULTI-OMIC PREDICTORS OF CLINICAL OUTCOMES FOLLOWING CURATIVE INTENT SURGICAL RESECTION IN SOFT-TISSUE SARCOMAS

Nathan D. Seligson, PharmD¹; Yan W. Asmann, PhD²; Tariq Almerey, MD²; Steven Attia, DO²; Sanjay Bagaria, MD²

¹University of Florida, Jacksonville, Florida, UNITED STATES, ²The Mayo Clinic, Jacksonville, Florida, UNITED STATES

Poster #126 #1818931

EXTRA-PLEURAL PNEUMONECTOMY (EPP) IN CHILDREN AND ADULTS WITH ADVANCED SARCOMA

Abha A. Gupta, MD, MSc, FRCPC¹; Hagit Peretz Soroka, PhD²; Agostino Pierro, MD³; Tom Waddell, MD⁴;

Reto Baertschiger, MD³; Marcelo Cypel, MD⁴; Marc de Perrot, MD⁴; Caroline Rodrigues, Undergraduate Student²

¹Division of Medical Oncology, Princess Margaret Cancer Centre, University Health Network, University of Toronto, The Hospital for Sick Children, Canadian Sarcoma Research and Clinical Collaboration (CanSaRCC), Toronto, Ontario, CANADA, ²Princess Margaret Cancer Center, Canadian Sarcoma Research and Clinical Collaboration (CanSaRCC), Toronto, Ontario, CANADA, ³The Hospital for Sick Children, Toronto, Ontario, CANADA, ⁴University Health Network, Toronto, Ontario, CANADA

Poster #127 #1819015

CANDIDATE BIOMARKERS FOR SPECIFIC INTRAOPERATIVE IMAGING OF SOFT TISSUE SARCOMAS

Zeger Rijs, MD¹; Naweed Shifai, BSc²; Peter Kuppen, PhD²; Alexander L. Vahrmeijer, MD PhD¹;

Judith V.M.G. Bovée, MD PhD¹; Cornelis Sier, PhD²; Michiel van de Sande, MD PhD¹; Pieter van Driel, MD PhD³

¹Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ²LUMC, Leiden, Zuid-Holland, NETHERLANDS, ³Isala hospital, Zwolle, Overijssel, NETHERLANDS

Poster #128 #1819011

FREE FLAP RECONSTRUCTION AFTER RADICAL RESECTION OF LIMB AND TRUNCAL SARCOMAS

Sergio Quildrian, MD¹; Gabriela vega, MD²; Walter Nardi, MD³; Jorge Chapela, MD⁴; Anabella Daffinoti, MD⁵

¹Buenos Aires British Hospital; Angel Roffo Institute of Oncology, University of Buenos Aires, Buenos Aires, Buenos Aires, ARGENTINA, ²Angel H Roffo Institute of Oncology, Tucuman, Tucuman, ARGENTINA, ³Buenos Aires British Hospital, Buenos Aires, Ciudad Autonoma de Buenos Aires, ARGENTINA, ⁴Angel H Roffo Institute of Oncology, Buenos Aires, Buenos Aires, ARGENTINA, ⁵Angel H Roffo Institute of Oncology, Buenos Aires, Ciudad Autonoma de Buenos Aires, ARGENTINA

Poster #129 #1819039

PRELIMINARY RESULTS OF THE USE OF A BONE TRANSPORT NAIL AFTER TUMOR RESECTION

Lee M. Zuckerman, MD

City of Hope National Medical Center, Duarte, California, UNITED STATES

Poster #130 #1818846

TO WHAT EXTENT DOES PLASTIC AND RECONSTRUCTIVE SURGICAL ASSISTANCE WITH COMPLEX CLOSURE HELP AVOID AMPUTATION FOLLOWING RESECTION OF DISTAL LOWER EXTREMITY SOFT TISSUE SARCOMAS?

Charles A. Gusho, BS¹; Johnathon R. McCormick, MD²; Linus Lee, BE²; Gordan Derman, MD²; Deana Shenaq, MD²;

Amir Dorafshar, MD²; Georgios Kokosis, MD²; Matthew W. Colman, MD²; Steven Gitelis, MD²; Alan T. Blank, MD, MS²

¹Rush University Medical Center, Milwaukee, Wisconsin, UNITED STATES, ²Rush University Medical Center, Chicago, Illinois, UNITED STATES

Poster #131 #1818842

A MODIFIED HARRINGTON TECHNIQUE FOR PERIACETABULAR RECONSTRUCTION IN ADVANCED METASTATIC BONE DISEASE AND A DISCUSSION OF ALTERNATIVE TREATMENT OPTIONS

Charles A. Gusho, BS¹; Linus Lee, BE²; Reagan Chapman, MS²; Alan T. Blank, MD, MS²

¹Rush University Medical Center, Milwaukee, Wisconsin, UNITED STATES, ²Rush University Medical Center, Chicago, Illinois, UNITED STATES

Poster #132 #1818908

FROZEN SECTION MARGIN ASSESSMENT IN ONCOLOGY ORTHOPEDICS

Ana C. Belzarena, MD¹; Pablo Stoppiello, MD²; Leticia Gaiero, MD²; Gottardo Bianchi, MD²; Nicolas Casales, MD²;

Claudio Silveri, MD²

¹Miami Cancer Institute, Miami, Florida, UNITED STATES, ²Unidad de Patología Oncológica Musculo Esquelética, Instituto Nacional de Ortopedia y Traumatología, Montevideo, Montevideo, URUGUAY

Poster #133 #1819070

MAJOR AMPUTATIONS FOR EXTREMITY SARCOMAS: OLD-FASHIONED SURGERY OR CHANCE OF TREATMENT? A TERTIARY REFERRAL CENTER EXPERIENCE

Laura Samà, MD¹; Simone Ricchitelli, MD²; Marta Tassan Mangina, Student³; Manuela Cammelli, Student³; Ilaria Santori, Student³; Laura Ruspi, MD⁴; Federico Sicoli, MD⁵; Ferdinando Cananzi, MD⁶; Vittorio Lorenzo Quagliuolo, MD⁵

¹Humanitas Clinical and Research Hospital/Humanitas University, Milan, Lombardia, ITALY, ²Humanitas Clinical and Research Center/Humanitas University, Milan, Lombardia, ITALY, ³Humanitas University, Milan, Lombardia, ITALY, ⁴Humanitas Clinical and Research Center, Rozzano (MI), Lombardia, ITALY, ⁵Humanitas Clinical and Research Hospital, Milan, Lombardia, ITALY, ⁶Humanitas Clinical and Research Center, Humanitas University, Milan, Lombardia, ITALY

Poster #134 #1818872

CLINICAL RESULTS OF PATIENTS UNDERGOING UNPLANNED EXCISIONS OF SOFT TISSUE SARCOMAS

Sei Morinaga; Norio Yamamoto; Katsuhiko Hayashi; Akihiko Takeuchi, MD, PhD; Shinji Miwa; Kentaro Igarashi; Hirotaka Yonezawa; Yohei Asano; Shiro Saito; Hiroyuki Tsuchiya

Department of Orthopedic Surgery, Kanazawa University School of Medicine, Kanazawa, Ishikawa, JAPAN

Poster #135 #1818984

SPECIFIC DETECTION OF THE SS18-SSX FUSION PROTEIN AND INTERACTING PARTNERS IN SYNOVIAL SARCOMA TISSUES AND MODELS

Ainiah Rushdiana Raquib, B.Sc; Torsten Nielsen, MD, PhD

University of British Columbia, Vancouver, British Columbia, CANADA

Poster #136 WITHDRAWN

Poster #137 WITHDRAWN

Poster #138 #1819065

IMMUNE AND CANCER TESTIS ANTIGEN LANDSCAPE IN SARCOMA

Anne C. Grand'Maison, MD¹; Robert J. Seager, PhD²; Yong Hee Lee, MPH²; Mary K. Nesline, MS²; Jeffrey Conroy, PhD²; Sarabjot Pabla, PhD²

¹Roswell Park Comprehensive Cancer Center, Buffalo, New York, UNITED STATES, ²OmniSeq Inc, Buffalo, New York, UNITED STATES

Poster #139 #1819040

DISSECTING THE ROLE OF THE TUMOR MICROENVIRONMENT IN RESPONSE TO CHEMOTHERAPY IN LIPOSARCOMA: TRANSLATIONAL AND CLINICAL IMPLICATIONS

Alessandro De Vita, PhD, Pharm D¹; Fausti Valentina, MD²; Federica Recine, MD³; Silvia Vanni, MSc, PhD²; Giacomo Miserocchi, MSc⁴; Marcella Tazzari, PhD, Pharm D⁵; Martine Bocchini, MSc⁵; Silvia Carloni, MSc, PhD⁵; Chiara Liverani, MSc, PhD²; Chiara Spadazzi, MSc²; Claudia Cocchi, MSc¹; Roberto Casadei, MD⁶; Francesca Brandolini, MD⁶; Giorgio Ercolani, MD⁷; Davide Cavaliere, MD⁷; Alberto Bongiovanni, MD²; Federica Pieri, MD⁸; Anna Farnedi, MSc⁸; Nada Riva, MD²; Lorena Gurrieri, MD²; Toni Ibrahim, MSc, MD, PhD⁹; Laura Mercatali, MSc, PhD¹

¹IRCCS Istituto Romagnolo Per Lo Studio Dei Tumori (IRST) "Dino Amadori", Meldola, Emilia-Romagna, ITALY, ²Osteoncology and Rare Tumors Center, IRCCS Istituto Romagnolo Per Lo Studio Dei Tumori (IRST) "Dino Amadori", Meldola, Italy, Meldola, Emilia-Romagna, ITALY, ³Medical Oncology Unit, Azienda Ospedaliera San Giovanni Addolorata, Roma, Italy, Roma, Lazio, ITALY, ⁴Osteoncology and Rare Tumors Center, IRCCS Istituto Romagnolo Per Lo Studio Dei Tumori (IRST), Meldola, Emilia-Romagna, ITALY, ⁵Immunotherapy, Cell Therapy and Biobank Unit, IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) "Dino Amadori", Meldola, Italy, Meldola, Emilia-Romagna, ITALY, ⁶Orthopedic Unit, Morgagni-Pierantoni Hospital, Forlì, Italy, Forlì, Emilia-Romagna, ITALY, ⁷Unit of Surgery and Advanced Oncologic Therapies, Morgagni-Pierantoni Hospital, Forlì, Italy, Forlì, Emilia-Romagna, ITALY, ⁸Pathology Unit, Morgagni-Pierantoni Hospital, Forlì, Italy, Forlì, Emilia-Romagna, ITALY, ⁹IRCCS Istituto Ortopedico Rizzoli, Bologna, Emilia-Romagna, ITALY

Poster #140 #1818909

GENOMIC AND TRANSCRIPTOMIC CORRELATES OF RESPONSE TO IMMUNE CHECKPOINT BLOCKADE-BASED THERAPY IN ANGIOSARCOMA

Evan Rosenbaum, MD¹; Cristina Antonescu, MD¹; Shaleigh Smith, MS¹; Martina Bradic, PhD¹; Allison Richards, PhD¹; Mark Donoghue, PhD¹; Daniel Kashani, MD²; Ciara Kelly, MD¹; Benjamin Nacev, MD, PhD¹; Jason Chan, MD, PhD¹; Ping Chi, MD, PhD³; Mark A. Dickson, MD¹; Mary Lou Keohan, MD⁴; Mrinal M. Gounder, MD⁴; Katherine A. Thornton, MD¹; Samuel Singer, MD, PhD¹; William D. Tap, MD¹; Sandra P. D'Angelo, MD¹

¹Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES, ²SUNY Downstate Medical College, New York, New York, UNITED STATES, ³Human Oncology and Pathogenesis Program/Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES, ⁴Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES

Poster #141 #1818900

TRABECTEDIN + NIVOLUMAB IN PRETREATED PATIENTS WITH ADVANCED LIPO- AND LEIOMYOSARCOMAS: FIRST RESULTS OF THE "L-GROUP" FROM THE NITRASARC-TRIAL OF THE GERMAN INTERDISCIPLINARY SARCOMA GROUP (GISG-15)

Daniel Pink, MD, PhD¹; Dimosthenis Andreou, MD, PhD²; Anne Flörcken, MD³; Alexander Golf, MD⁴; Stephan Richter, MD, PhD⁵; Torsten Kessler, MD⁶; Martin Kortüm, MD⁷; Christian Andreas Schmidt, MD⁸; Bernd Kasper, MD, PhD⁹; Eva Wardelmann, MD¹⁰; Jeanette Bahr⁸; Daniel W. Müller, MD¹¹; Disorn Sookthai¹¹; Marcin Ostrzyzek, MD¹¹; Salah-Eddin Al-Batran, MD¹¹; Peter Reichardt, MD¹²

¹Helios Klinikum Bad Saarow, Universitätsmedizin Greifswald, Bad Saarow, Brandenburg, GERMANY, ²Helios Klinikum Bad Saarow, Bad Saarow, Brandenburg, GERMANY, ³Charité-Universitätsmedizin Berlin, Berlin, GERMANY, ⁴Universitätsklinikum Tübingen, Tübingen, Baden-Württemberg, GERMANY, ⁵University Hospital Carl Gustav Carus, University Cancer Center/Medical Department I, Dresden, Dresden, Sachsen, GERMANY, ⁶University Hospital Muenster, Münster, Nordrhein-Westfalen, GERMANY, ⁷Universitätsklinikum Würzburg, Würzburg, Bayern, GERMANY, ⁸Universitätsmedizin Greifswald, Greifswald, Mecklenburg-Vorpommern, GERMANY, ⁹University of Heidelberg, Mannheim University Medical Center, Mannheim Cancer Center, Sarcoma Unit, Mannheim, Germany, Mannheim, Baden-Württemberg, GERMANY, ¹⁰Universitätsklinikum Münster, Münster, Nordrhein-Westfalen, GERMANY, ¹¹Institut für Klinische Krebsforschung IKF GmbH at Krankenhaus Nordwest, Frankfurt, Hessen, GERMANY, ¹²Oncology and Palliative Care, Sarcoma Center, Helios Klinikum Berlin-Buch, Berlin, Berlin, GERMANY

Poster #142 #1819006

SAINT: AN EXPANDED PHASE 2 STUDY USING SAFE AMOUNTS OF IPILIMUMAB (I), NIVOLUMAB (N), AND TRABECTEDIN (T) AS FIRST-LINE TREATMENT OF ADVANCED SOFT TISSUE SARCOMA [NCT03138161]

Erlinda M. Gordon, MD¹; Ted T. Kim, BS²; Noufil Adnan, MD¹; Victoria Chua, MD³; Ishrat Bhuiyan, BS³; Sonu Thomas, MD⁴; Simranjit Sekhon, MD⁵; Don A. Brigham, PhD³; Victoria T. Chua-Alcala, MD⁵

¹Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES, ²Sarcoma Oncology Center, Santa Monica, California, UNITED STATES, ³Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES, ⁴Sarcoma Oncology Research Center, Santa Monica, CA, ⁵Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES

Poster #143 #1818895

CHARACTERIZATION OF MECA-79, CD1A, STAT1, AND LAMP3 IN THE INFLAMMATORY MICROENVIRONMENT IN MYXOFIBROSARCOMA AND UNDIFFERENTIATED PLEOMORPHIC SARCOMA

Ashley N. Flaman, MD, FRCPC¹; Elizabeth G. Demicco, MD PhD²; Brendan C. Dickson, MD MSc³; Nalan Gokgoz, PhD⁴; Jay S. Wunder, MSc., MD⁴; Irene L. Andrulis, PhD⁴

¹University of Toronto / Mount Sinai Hospital, Toronto, Ontario, CANADA, ²Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, Ontario, CANADA, ³Mount Sinai Hospital, Toronto, Ontario, CANADA, ⁴The Lunenfeld-Tanenbaum Research Institute, Toronto, Ontario, CANADA

Poster #144 #1819044

PERIPHERAL IMMUNE LANDSCAPE OF SOFT TISSUE SARCOMA: CELLULAR, PROTEOMIC AND TRANSCRIPTOMIC ANALYSIS

Jani Sofia J. Almeida, MSc¹; Paulo Rodrigues Santos²; Patrícia Couceiro³; Luana Madalena Sousa³; Tânia Fortes Andrade³; Ruben Fonseca⁴; Manuel Santos Rosa¹; Paulo Freitas Tavares⁴; José Manuel Casanova⁴

¹Institute of Immunology, Fac Medicine Univ Coimbra, Portugal, Coimbra, Coimbra, PORTUGAL, ²Immunology and Oncology Laboratory, Center for Neurosciences and Cell Biology & Institute of Immunology, Fac Medicine Univ Coimbra, Portugal, Coimbra, Coimbra, PORTUGAL, ³Immunology and Oncology Laboratory, Center for Neurosciences and Cell Biology, Univ Coimbra, Portugal, Coimbra, Coimbra, PORTUGAL, ⁴Bone and Soft Tumor Unit, Coimbra Hospital and University Centre, Coimbra, Portugal, Coimbra, Coimbra, PORTUGAL

Poster #145 #1818982

NY-ESO-1 EXPRESSION PROFILING AND PREVALENCE ASSESSMENT OF TUMOR BIOPSIES FROM PHASE I/II TCR T CELL THERAPY CLINICAL TRIALS IN ADVANCED SYNOVIAL SARCOMA OR MYXOID ROUND CELL LIPOSARCOMA

Erika Klohe, BS, MBA; Alexandra Gyurdieva, MS; Gurpreet Kapoor, PhD; Jaegil Kim, PhD; Ellie Corigliano, PhD, GlaxoSmithKline, Collegeville, Pennsylvania, UNITED STATES

Poster #146 #1818968

SPEARHEAD-1: PRELIMINARY TRANSLATIONAL INSIGHTS FROM A PHASE 2 TRIAL OF AFAMITRESGENE AUTOLEUCEL (FORMERLY ADP-A2M4) IN PATIENTS WITH ADVANCED SYNOVIAL SARCOMA OR MYXOID/ROUND CELL LIPOSARCOMA

Sandra P. D'Angelo, MD¹; Steven Attia, DO²; Jean-Yves Blay, MD, PhD³; Kristen N. Ganjoo, MD⁴; Axel Le Cesne, MD⁵; Claudia Maria Valverde Morales, MD⁶; Albiruni Ryan Abdul Razak, MD, MB, MRCP⁷;

Sandra Strauss, BA, MBBS, MRCP (UK), PhD⁸; Brian A. Van Tine, MD, PhD⁹; Michael J. Wagner, MD¹⁰; Natalie Bath, MSc¹¹; Gareth Betts, PhD¹¹; Robyn Broad, PhD¹¹; Ian Donaldson, PhD¹¹; Chris Evans, DPhil¹²; Alasdair Gunn, PhD¹¹; Ashley Liddle, MSc¹¹; Cheryl McAlpine, PhD¹¹; Karen Miller, PhD¹¹; Jean-Marc Navenot, PhD¹²; Paul Noto, PhD¹²; Stavros Rafail, PhD¹²; William Spinner, PhD¹¹; Alex Tipping, PhD¹³; Erin Van Winkle, BS¹²; Ruoxi Wang, PhD¹¹; Swethajit Biswas, ChB (Hons), MRCP (UK), DPhil (Oxon)¹¹; Elliot Norry, MD¹²; Dennis Williams, PharmD¹²; Dejka M. Araujo, MD¹⁴

¹Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES, ²The Mayo Clinic, Jacksonville, Florida, UNITED STATES, ³Centre Léon Bérard, Lyon, Auvergne, FRANCE, ⁴Stanford Cancer Center, Stanford, California, UNITED STATES, ⁵Institut Gustave Roussy-Gustave Roussy Cancer Center-DITEP, Villejuif, Ile-de-France, FRANCE, ⁶Vall D'Hebron University Hospital, Barcelona, Catalonia, SPAIN, ⁷Division of Medical Oncology, Princess Margaret Cancer Centre, University Health Network, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, CANADA, ⁸University College London Hospital, London, England, UNITED KINGDOM, ⁹Washington University School of Medicine, St. Louis, Missouri, UNITED STATES, ¹⁰University of Washington/Fred Hutch/Seattle Cancer Care Alliance, Seattle, Washington, UNITED STATES, ¹¹Adaptimmune, Abingdon, England, UNITED KINGDOM, ¹²Adaptimmune, Philadelphia, Pennsylvania, UNITED STATES, ¹³Adaptimmune, Philadelphia, England, UNITED KINGDOM, ¹⁴The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES

Poster #147 #1819007

GALLANT: A PHASE 2 STUDY USING METRONOMIC GEMCITABINE, DOXORUBICIN, NIVOLUMAB AND DOCETAXEL AS SECOND/THIRD LINE THERAPY FOR ADVANCED SARCOMA: TRIAL IN PROGRESS [NCT04535713]

Sant P. Chawla, MD¹; Noufil Adnan, MD²; Ted T. Kim, BS³; Victoria T. Chua-Alcala, MD¹; Simranjit Sekhon, MD¹; Ishrat Bhuiyan, BS⁴; Ania Moradkhani, NP¹; Erlinda M. Gordon, MD²

¹Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES, ²Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES, ³Sarcoma Oncology Center, Santa Monica, California, UNITED STATES, ⁴Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES

Poster #148 #1818858

T-REGULATORY CELLS PREDICT CLINICAL OUTCOME IN SOFT TISSUE SARCOMA PATIENTS

Joanna Szkandera, MD¹; Maria Anna Smolle, MD²; Laurin Herbsthofner, PhD³; Mark Goda, Student⁴; Iva Brcic, MD⁴; Marko Bergovec, MD⁴; Susanne Scheipl, MD⁴; Barbara Prietl, PhD³; Martin Pichler, Prof.⁴; Armin Gerger, Prof.⁴; Christopher Rossmann, MD⁴; Jakob Riedl, MD⁴; Martina Tomberger, Technical assistant³; Pablo Lopez-Garcia, Dr.³; Amin El-Heliebi, PhD⁴; Andreas Leithner, Prof.⁴; Bernadette Liegl-Atzwanger, Prof.⁴

¹Medical University of Graz, Graz, Steiermark, AUSTRIA, ²Department of Orthopaedics and Trauma, Medical University Graz, Graz, Steiermark, AUSTRIA, ³CBmed GmbH, Graz, Steiermark, AUSTRIA, ⁴Medical University Graz, Graz, Steiermark, AUSTRIA

Poster #149 #1818955

NATURAL KILLER AND CYTOTOXIC T CELL IMMUNE INFILTRATES ARE ASSOCIATED WITH SUPERIOR OUTCOMES IN SOFT TISSUE SARCOMAS

Sylvia M. Cruz¹; Sean J. Judge, MD²; Morgan A. Darrow, MD³; Cordelia Dunai, PhD⁴; Shuai Chen, PhD⁵; Steven W. Thorpe, MD²; Robert J. Canter, MD²

¹Division of Surgical Oncology, Department of Surgery, University of California Davis School of Medicine, Sacramento, California, UNITED STATES, ²University of California Davis, Sacramento, California, UNITED STATES, ³Pathology and Laboratory Medicine, University of California Davis School of Medicine, Sacramento, California, UNITED STATES, ⁴Dermatology, University of California Davis School of Medicine, Sacramento, California, UNITED STATES, ⁵Public Health Sciences, University of California Davis, Sacramento, California, UNITED STATES

Poster #150 #1818918

PHASE 2 STUDY OF ATEZOLIZUMAB IN ADVANCED CLEAR CELL SARCOMA (CCS)

Alice P. Chen, MD¹; Abdul Rafah Naqash, MD²; Geraldine O'Sullivan Coyne, MD²; Nancy Moore, RN²; Elad Sharon, MD, MPH²; Anthony P. Conley, MD³; Elizabeth J. Davis, MD⁴; Priscilla Merriam, MD⁵; Jared Foster, PhD⁶; Naoko Takebe, MD PhD²; Kristin K. Fino, PhD⁷; Katherine V. Ferry-Galow, PhD⁷; Ralph E. Parchment, PhD⁷; James H. Doroshow, MD¹

¹NCI/NIH, Bethesda, Maryland, UNITED STATES, ²NCI, Bethesda, Maryland, UNITED STATES, ³MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁴Vanderbilt University Cancer Center, Nashville, Tennessee, UNITED STATES, ⁵Dana Farber Cancer Institute, Boston, Massachusetts, UNITED STATES, ⁶NCI CTEP, Bethesda, Maryland, UNITED STATES, ⁷Frederick National Laboratory for Cancer Research, Fredrick, Maryland, UNITED STATES

Poster #151 #1818880

PHASE II STUDY OF THE ANTIBODY-CYTOKINE FUSION PROTEIN L19TNF PLUS DACARBAZINE FOR PRETREATED PATIENTS WITH ADVANCED OR METASTATIC SOFT TISSUE SARCOMA: RESULTS OF THE RUN-IN PART

Torsten Kessler, MD¹; Daniel Pink, MD, PhD²; Peter Reichardt, MD³; Emanuela Palmerini, MD⁴; Piotr Rutkowski, MD, PhD⁵; Teresa Hemmerle, PhD⁶; Dario Neri, Prof.⁷; Christoph Schliemann, MD¹

¹University Hospital Muenster, Münster, Nordrhein-Westfalen, GERMANY, ²Helios Klinikum Bad Saarow, Universitätsmedizin Greifswald, Bad Saarow, Brandenburg, GERMANY, ³Oncology and Palliative Care, Sarcoma Center, Helios Klinikum Berlin-Buch, Berlin, Berlin, GERMANY, ⁴IRCCS Istituto Ortopedico Rizzoli, Bologna, Emilia-Romagna, ITALY, ⁵Department of Soft Tissue/Bone Sarcoma and Melanoma; Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Mazowieckie, POLAND, ⁶Philgogen S.p.A., Siena, Toscana, ITALY, ⁷Philogen S.p.A., Siena, Toscana, ITALY

Poster #152 #1819008

PHASE 1 STUDY OF ESCALATING DOSES OF EX VIVO EXPANDED, AUTOLOGOUS NATURAL KILLER CELLS IN PATIENTS WITH PATHOLOGICALLY CONFIRMED CANCER REFRACTORY TO CONVENTIONAL THERAPY [NCT03941262]

Sant P. Chawla, MD¹; Simranjit Sekhon, MD¹; Noufil Adnan, MD²; Ted T. Kim, BS³; Victoria T. Chua-Alcala, MD¹; Ania Moradkhani, NP¹; Steven Cha, MD⁴; Erlinda M. Gordon, MD²

¹Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES, ²Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES, ³Sarcoma Oncology Center, Santa Monica, California, UNITED STATES, ⁴NK-Gen Biotech, Santa Ana, California, UNITED STATES

Poster #153 #1818863

RADIATION-INDUCED SARCOMAS RESPONDING TO PEMBROLIZUMAB

Benjamin C. Powers, MD¹; Julie Hamlin, APRN²; Dana Smith, RN²; Tiffany Verhulst, RN²

¹The University of Kansas Health System, Leawood, Kansas, UNITED STATES, ²The University of Kansas Health System, Overland Park, Kansas, UNITED STATES

Poster #154 #1818855

INTERIM SAFETY AND EFFICACY RESULTS FROM A PHASE 1/2 STUDY OF BA3011, A CAB-AXL-ADC, IN PATIENTS WITH ADVANCED SARCOMA OR OTHER SOLID TUMORS

Breelyn A. Wilky, MD¹; Mihaela Druta, MD²; Jordi Rodón, MD³; Anthony P. Conley, MD³; Gerald Falchook, MD⁴; Howard Burriss, MD⁵; Matthew Ingham, MD⁶; Inderjit Mehmi, MD⁷; Eric Sievers, MD⁸

¹University of Colorado School of Medicine, Aurora, CO, ²H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida, UNITED STATES, ³MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁴Sarah Cannon Research Institute at HealthONE, Denver, Colorado, UNITED STATES, ⁵Sarah Cannon Research, Nashville, Tennessee, UNITED STATES, ⁶New York Presbyterian Hospital/Columbia University Medical Center, New York, New York, UNITED STATES, ⁷The Angeles Clinic and Research Institute, A Cedars-Sinai Affiliate, Los Angeles, California, UNITED STATES, ⁸BioAtla, Inc., San Diego, California, UNITED STATES

Poster #155 #1818902

METHODS FOR EXTRACTION AND EXPANSION OF TUMOR-INFILTRATING LYMPHOCYTES FROM HUMAN SARCOMA CORE NEEDLE BIOPSIES AND RESECTED TISSUE

Cristiam Moreno Tellez, MD¹; Kyle Powers, BS²; Allison Christians, BA²; Jing Liu, PhD²; Brian A. Van Tine, MD, PhD³; Jacqui Toeniskoetter⁴; Eduardo Davila, PhD²; Breelyn A. Wilky, MD²

¹University of Colorado School of Medicine, Parker, Colorado, UNITED STATES, ²University of Colorado School of Medicine, Aurora, Colorado, UNITED STATES, ³Washington University School of Medicine, St. Louis, Missouri, UNITED STATES, ⁴Washington University, St. Louis, Missouri, UNITED STATES

Poster #156 #1818934

CHARACTERIZATION OF TUMOR INFILTRATING IMMUNE CELLS FROM ADULT SOFT TISSUE SARCOMAS

Jacky H.K Chen, HBSc¹; Jay S. Wunder, MSc., MD²; Kim M. Tsoi, MD, PhD³; Nalan Gokgoz, PhD²; Irene L. Andrulis, PhD²,

¹Lunenfeld Tanenbaum Research Institute, Mount Sinai Hospital, Toronto, Ontario, CANADA, ²The Lunenfeld-Tanenbaum Research Institute, Toronto, Ontario, CANADA, ³University of Toronto, Mount Sinai Hospital, Toronto, Ontario, CANADA

Poster #157 #1818910

DETERMINING THE CONTRIBUTIONS OF PD-L1 AND CO-EXPRESSED GENES TO THE UPS ANTI-TUMOUR MICROENVIRONMENT

Victoria S. Coward¹; Maisha Syed, MSc²; Nalan Gokgoz, Ph.D²; Jay S. Wunder, MSc., MD²; Irene L. Andrulis, PhD²

¹The Lunenfeld-Tanenbaum Research Institute, Toronto, Ontario, CANADA, ²The Lunenfeld-Tanenbaum Research Institute, Toronto, Ontario, CANADA

Poster #158 #1818970

DESMOID TUMOR AND MOLECULAR TESTING FROM PATIENT REPORTED DATA IN AN INTERNATIONAL NATURAL HISTORY STUDY

Maneesh Kumar, MD, PhD¹; Danielle Braggio, PhD, BCMAS²; Amanda L. Lucas³; Lynne Hernandez⁴; Kelly Mercier, PhD⁵

¹Desmoid Tumor Research Foundation, Cedar Rapids, Iowa, UNITED STATES, ²Desmoid Tumor Research Foundation, Houston, Texas, UNITED STATES, ³Desmoid Tumor Research Foundation, Jacksonville Beach, Florida, UNITED STATES, ⁴Desmoid Tumor Research Foundation, Philadelphia, Pennsylvania, UNITED STATES, ⁵Desmoid Tumor Research Foundation, Cary, North Carolina, UNITED STATES

Poster #159 #1818874

IS MOH'S MICROGRAPHIC SUGERY REALLY SUPERIOR TO WIDE LOCAL EXCISION FOR DERMATOFIBROSARCOMA PROTUBERANS (DFSP)? A MULTICENTER INTERNATIONAL STUDY

Matthew T. Houdek, MD¹; Kim M. Tsoi, MD, PhD²; Katerine Mallett, MD¹; Matthew R. Claxton, BS¹; Sarah Almubarak, BS²; Peter C. Ferguson, MD²; Peter S. Rose, MD¹; Jay S. Wunder, MD²

¹Mayo Clinic, Rochester, Minnesota, UNITED STATES, ²University of Toronto, Mount Sinai Hospital, Toronto, Ontario, CANADA

Poster #160 #1818990

DESMOID TUMOURS IN FAMILIAL ADENOMATOUS POLYPOSIS PATIENTS: FAVOURABLE OUTCOMES WITH MULTIDISCIPLINARY MANAGEMENT

Eisar Al-Sukhni, MD¹; Harini Suraweera, MSc²; Kara Semotiuk, MS, (C)CGC³; Carol J. Swallow, MD PhD FRCSC FACS²; Savtaj Brar, MD MSc FRCSC⁴; Albiruni Ryan Abdul Abdul Razak, MD, MB, MRCP⁵; Abha A. Gupta, MD, M.Sc., FRCPC⁶; Rebecca A. Gladdy, MD PhD FRCSC FACS²

¹Mount Sinai Hospital, Toronto, Ontario, CANADA, ²Department of Surgical Oncology, Princess Margaret Hospital, University Health Network and Mount Sinai Hospital, Toronto; Lunenfeld Tanenbaum Research Institute, Sinai Health System, Toronto, Toronto, Ontario, CANADA, ³Zane Cohen Centre for Digestive Diseases/Mount Sinai Hospital, Toronto, Ontario, CANADA, ⁴Department of Surgical Oncology, Princess Margaret Hospital, University Health Network and Mount Sinai Hospital, Toronto, Ontario, CANADA, ⁵Division of Medical Oncology, Princess Margaret Cancer Centre, University Health Network, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, CANADA, ⁶Hospital for Sick Children and Princess Margaret Cancer Center and University of Toronto, Toronto, Ontario, CANADA

Poster #161 #1818890

EVALUATION OF PRIMARY SPORADIC DESMOID TYPE FIBROMATOSIS MANAGEMENT AND THE UNDERLYING FACTORS INFLUENCING VARIED OUTCOMES, A SINGLE SOFT TISSUE SARCOMA UNIT SERIES.

Misbah Khan¹; Anant Desai, MD²

¹University Hospitals Birmingham, London, England, UNITED KINGDOM, ²University Hospital Birmingham NHS Foundation Trust, Birmingham, England, UNITED KINGDOM

Poster #162 #1819042

MARGINAL RESECTION OF NON-COELOMIC ATYPICAL LIPOMATOUS TUMOURS/WELL-DIFFERENTIATED LIPOSARCOMAS IS ASSOCIATED WITH A LOW RATE OF LATE LOCAL RELAPSE: IMPLICATIONS FOR FOLLOW UP PROTOCOLS

Gausihi Sivarajah, MBBS FRACS¹; Andrew J. Hayes, PhD²; Hayden Snow, MBBS, FRACS³; Myles Smith, PhD²; Dirk Strauss, MD²

¹Royal Marsden NHS Trust, London, England, UNITED KINGDOM, ²The Royal Marsden Hospital NHS Foundation Trust, London, England, UNITED KINGDOM, ³Peter MacCallum Cancer Centre, Melbourne, Victoria, AUSTRALIA

Poster #163 #1818920

SURGICAL MARGIN FOR PHOSPHATURIC MESENCHYMAL TUMORS IN SOFT TISSUES: AN ANALYSIS OF THE RADIOLOGICAL-HISTOPATHOLOGICAL CORRELATION

Hiroshi Kobayashi, MD, PhD¹; Noahiro Makise, MD, PhD¹; Nobuaki Ito, MD, PhD¹; Liuzhe Zhang, MD¹; Yuki Ishibashi, MD¹; Masachika Ikegami, MD, PhD¹; Yusuke Shinoda, MD, PhD¹; Toru Akiyama, MD, PhD²; Tetsuo Ushiku, MD, PhD¹; Sakae Tanaka, MD, PhD¹

¹The University of Tokyo Hospital, Bunkyo-ku, Tokyo, JAPAN, ²Jichi Medical Center, Omiya-shi, Saitama, JAPAN

Poster #164 WITHDRAWN

Poster #165 #1819029

MANAGEMENT OF DESMOID-TYPE FIBROMATOSIS IN TWO CENTERS FROM ARGENTINA

Sergio Quildrian, MD¹; Anabella Daffinoti, MD²; Francisco Colazo, MD³; Diego Prost, MD²; Walter Nardi, MD³; Sonia Patron Costas, MD²; Nahir Queiro, MD³; Gonzalo Cervelo, MD²; Julieta Gerino, MD²; Fernando Carrizo, MD²; Julieta Arbat, MD²; Pablo Desanzo, MD³; Luciana Bella Quero, MD³; Cintia Novas, MD³; Carlos Silva, MD³; Gabriela Cinat, MD²; Jorge Chapela, MD⁴

¹Buenos Aires British Hospital; Angel Roffo Institute of Oncology, University of Buenos Aires, Buenos Aires, Buenos Aires, ARGENTINA, ²Angel H Roffo Institute of Oncology, Buenos Aires, Ciudad Autonoma de Buenos Aires, ARGENTINA, ³Buenos Aires British Hospital, Buenos Aires, Ciudad Autonoma de Buenos Aires, ARGENTINA, ⁴Angel H Roffo Institute of Oncology, Buenos Aires, Buenos Aires, ARGENTINA

Poster #166 #1818924

RANDOMIZED PLACEBO-CONTROLLED DOUBLE BLIND PHASE II STUDY OF ZALTOPROFEN FOR PATIENT WITH DIFFUSE-TYPE AND UNRESECTABLE LOCALIZED TENOSYNOVIAL GIANT CELL TUMORS

Akihiko Takeuchi, MD, PhD¹; Makoto Endo²; Akira Kawai, MD³; Yoshihiro Nishida⁴; Ryu Terauchi⁵; Akihiko Matsumine⁶; Hisaki Aiba, MD⁷; Tomoki Nakamura⁸; Susumu Tandai⁹; Toshifumi Ozaki¹⁰; Manabu Hoshi¹¹; Kenichi Yoshimura¹²; Akihiro Nomura¹³; Toshinori Murayama¹³; Hiroyuki Tsuchiya¹, ¹Department of Orthopedic Surgery, Kanazawa University School of Medicine, Kanazawa, Ishikawa, JAPAN, ²Department of Orthopaedic Surgery, Kyushu University, Fukuoka, Fukuoka, JAPAN, ³National Cancer Center Hospital, Chuo-ku, Tokyo, JAPAN, ⁴Department of Orthopedic Surgery, Nagoya University Graduate School of Medicine, Nagoya, Aichi, JAPAN, ⁵Department of Orthopaedics, Kyoto Prefectural University of Medicine Graduate School of Medicine, Kyoto, Kyoto, JAPAN, ⁶Department of Orthopaedics and Rehabilitation Medicine, University of Fukui, Fukui, Fukui, JAPAN, ⁷Department of Orthopaedic Surgery, Nagoya City University Graduate School of Medical Sciences, Nagoya, Aichi, JAPAN, ⁸Department of Orthopaedic Surgery, Mie University Graduate School of Medicine, Tsu, Mie, JAPAN, ⁹Department of Orthopaedic Surgery, Asahikawa Medical University, Asahikawa, Hokkaido, JAPAN, ¹⁰Department of Orthopaedic Surgery, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Science, Okayama, Okayama, JAPAN, ¹¹Department of Orthopaedic Surgery, Osaka City University Graduate School of Medicine, Osaka, Japan, Osaka, Osaka, JAPAN, ¹²Future Medical Center, Hiroshima University Hospital, Hiroshima, Hiroshima, JAPAN, ¹³Innovative Clinical Research Center (iCREK), Kanazawa University Hospital, Kanazawa, Ishikawa, JAPAN

Poster #167 #1818851

A PROSPECTIVE REAL-WORLD STUDY OF THE DIFFUSE-TYPE TENOSYNOVIAL GIANT CELL TUMOR PATIENT JOURNEY: A 2-YEAR OBSERVATIONAL ANALYSIS

Nicholas M. Bernthal, MD¹; Geert Spierenburg, MD²; John H. Healey, MD, FACS³; Silvia Stacchiotti, MD⁴; Emanuela Palmerini, MD⁵; Sebastian Bauer, MD⁶; Erik J. Geiger, MD¹; Zachary Burke, MD¹; Bart Schreuder, MD, PhD⁷; Andreas Leithner, MD, PhD⁸; Javier Martin-Broto, MD, PhD⁹; Francois Gouin, MD, PhD¹⁰; Hans Gelderblom, MD, PhD²; Eric L. Staats, MD⁵; Julio Lopez-Bastida, MSc, PhD¹¹; Elisabeth Beyerlein, MSc¹²; Xin Ye, PhD¹³; Petra Laeis, PhD¹²; Michiel van de Sande, MD PhD²

¹David Geffen School of Medicine at UCLA, Santa Monica, California, UNITED STATES, ²Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ³Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES, ⁴Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY, ⁵IRCCS Istituto Ortopedico Rizzoli, Bologna, Emilia-Romagna, ITALY, ⁶West German Cancer Center, University of Duisburg-Essen, Essen, Nordrhein-Westfalen, GERMANY, ⁷Radboud University, Nijmegen, Gelderland, NETHERLANDS, ⁸Medical University of Graz, Graz, Steiermark, AUSTRIA, ⁹Fundacion Jimenez Diaz University Hospital, Madrid, Madrid, SPAIN, ¹⁰Center Leon Berard, Lyon, Rhone-Alpes, FRANCE, ¹¹University Castilla-La Mancha, Talavera de la Reina, Castilla-La Mancha, SPAIN, ¹²Daiichi Sankyo Europe GmbH, Munich, Bayern, GERMANY, ¹³Daiichi Sankyo, Inc., Basking Ridge, New Jersey, UNITED STATES

Poster #168 #1819071

CLINICAL RECOGNITION AND LOCAL RECURRENCE RATES OF ABC SECONDARY TO GCT

Ahmet Salduz, MD, PhD candidate¹; Michael Russel, MD²; Benjamin J. Miller, MD MS²

¹Istanbul University, İstanbul, Istanbul, TURKEY, ²University of Iowa, Iowa City, Iowa, UNITED STATES

Poster #169 #1819034

THE RECURRENCE RATE OF DIFFUSE TENOSYNOVIAL GIANT CELL TUMOUR OF THE KNEE FOLLOWING STAGED OPEN SYNOVECTOMY

Stefan A. St George, MD; Paul Clarkson, MB ChB, University of British Columbia, Vancouver, British Columbia, CANADA

Poster #170 WITHDRAWN

Poster #171 #1818882

A PHASE 4, MULTICENTER STUDY TO EVALUATE DISCONTINUATION AND RE-TREATMENT IN SUBJECTS WITH TENOSYNOVIAL GIANT CELL TUMOR PREVIOUSLY TREATED WITH PEXIDARTINIB

Silvia Stacchiotti, MD¹; Jason Jiang, MD, PhD²; Florence Mercier, MSc³; Hamim Zahir, PhD²; Margaret Wooddell, PhD, MPH, MBA²

¹Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY, ²Daiichi Sankyo, Inc., Basking Ridge, New Jersey, UNITED STATES, ³Daiichi Sankyo Europe GmbH, Munich, Bayern, GERMANY

Poster #172 #1818889

AL102, ORAL GAMMA-SECRETASE INHIBITOR FOR THE TREATMENT OF DESMOID TUMORS

Bernd Kasper, MD, PhD¹; Jason Kaplan, MD²; Gary Gordon, MD, PhD³; Mrinal M. Gounder, MD⁴

¹University of Heidelberg, Mannheim University Medical Center, Mannheim Cancer Center, Sarcoma Unit, Mannheim, Germany, Mannheim, Baden-Wurttemberg, GERMANY, ²Ayala Pharmaceuticals, Highland Park, Illinois, UNITED STATES, ³Ayala Pharmaceuticals, Northbrook, Illinois, UNITED STATES, ⁴Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES

Poster #173 #1818930

PHASE 2 BASKET STUDY TO EVALUATE THE ANTITUMOR ACTIVITY AND SAFETY OF LENVATINIB IN CHILDREN, ADOLESCENTS, AND YOUNG ADULTS WITH RELAPSED OR REFRACTORY SOLID MALIGNANCIES

Samuel Abbou, MD¹; Nicolas André, MD, PhD²; Alba Rubio San-Simón, MD³; Edita Kabickova, MD, PhD⁴; Peter Múdry, PhD⁵; Wayne Nicholls, FRACP⁶; Kyung-Nam Koh, MD, PhD⁷; Alexey Maschan, MD⁸; Tezer Kutluk, MD, PhD⁹; Mercedes García Lombardi, MD¹⁰; Isabelle Aerts, MD¹¹; Nadège Corradini, MD¹²; Michela Casanova, MD¹³; Csongor Kiss, MD, PhD, DSc¹⁴; Nicholas G. Gottardo, MBChB, FRACP, PhD¹⁵; Jodi McKenzie, PhD¹⁶; Xuan Deng, PhD¹⁷; Rohini Singh, MD¹⁷; Behzad Bidadi, MD¹⁸; Hyoung Jin Kang, MD, PhD¹⁹

¹Gustave Roussy, Villejuif, Ile-de-France, FRANCE, ²Hôpital de la Timone, Aix-Marseille University, Marseille, Provence-Alpes-Cote d'Azur, FRANCE, ³Hospital Universitario Niño Jesús, Madrid, Madrid, SPAIN, ⁴Pediatric Hematology and Oncology, University Hospital Motol and Charles University, 2nd Medical School, Prague, Stredocesky kraj, CZECH REPUBLIC, ⁵Univeristy Hospital Brno – Children's Hospital, Brno, Moravskoslezsky kraj, CZECH REPUBLIC, ⁶Queensland Children's Hospital and University of Queensland, Brisbane, Queensland, AUSTRALIA, ⁷Asan Medical Center Children's Hospital, University of Ulsan College of Medicine, Seoul, Seoul-t'ukpyolsi, REPUBLIC OF KOREA, ⁸Federal Research and Clinical Centre of Pediatric Hematology, Oncology and Immunology, Moscow, Moskva, RUSSIA, ⁹Hacettepe University Faculty of Medicine & Cancer Institute, Ankara, Ankara, TURKEY, ¹⁰Hospital de Niños Ricardo Gutierrez, Buenos Aires, Buenos Aires, ARGENTINA, ¹¹Institut Curie, Paris, Ile-de-France, FRANCE, ¹²Institute of Pediatric Hematology and Oncology (IHOPE), Lyon, Auvergne, FRANCE, ¹³Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ¹⁴University of Debrecen, Debrecen, Hajdu-Bihar, HUNGARY, ¹⁵Perth Children's Hospital, Perth, Western Australia, AUSTRALIA, ¹⁶Eisai Inc., Woodcliff Lake, New Jersey, UNITED STATES, ¹⁷Merck & Co., Inc., Kenilworth, New Jersey, UNITED STATES, Kenilworth, NJ, ¹⁸Merck & Co., Inc., Kenilworth, New Jersey, UNITED STATES, ¹⁹Seoul National University College of Medicine, Seoul National University Cancer Research Institute, Wide River Institute of Immunology, Seoul National University Children's Hospital, Seoul, Seoul-t'ukpyolsi, REPUBLIC OF KOREA

Poster #174 #1819017

TRABECTEDIN CLINICAL ACTIVITY AND IMPACT ON SYMPTOM BURDEN AND QUALITY OF LIFE IN PATIENTS WITH ADVANCED SOFT TISSUE SARCOMA: RESULTS OF THE GREEK REAL-WORLD BEYOND-STS STUDY

Stefania Kokkali, MD, MSc¹; Ioannis Boukovinas, MD, PhD, PharmaD²; Epaminondas Samantas, MD, PhD³; Pavlos Papakotoulas, MD, PhD⁴; Ilias Athanasiadis, MD, PhD⁵; Charalampos Andreadis, MD, PhD⁶; Parisi Makrantonakis, MD, PhD⁷; George Samelis, MD, PhD⁸; Eleni Timotheadou, MD, PhD⁹; George Vassilopoulos, MD, PhD¹⁰; Christos Papadimitriou, MD, PhD¹¹; Dimitrios Tzanninis, MD¹²; Ioannis Kotsantis, MD, PhD¹³; Kiki Karvounis-Marolachakis, BSc¹⁴; Theodora Theodoropoulou, BSc, MSc¹⁴; Amanda Psyrris, MD, PhD¹³

¹Saint-Savvas Cancer Hospital, Athens, Athens, Attiki, GREECE, ²Medical Oncology, Bioclinic of Thessaloniki, Thessaloniki, Thessaloniki, GREECE, ³Third Oncology Clinic, AgioiAnargiroi Athens General Hospital, Athens, Attiki, GREECE, ⁴First Chemotherapeutic Oncology Department, Theagenion Anti-Cancer Hospital of Thessaloniki, Thessaloniki, Thessaloniki, GREECE, ⁵Oncology Department, Hygeia Athens Private Hospital, Athens, Attiki, GREECE, ⁶Third Department of Clinical Oncology and Chemotherapy, Theagenion Anti-Cancer Hospital of Thessaloniki, Thessaloniki, Thessaloniki, GREECE, ⁷Second Department of Clinical Oncology and Chemotherapy, Theagenion Anti-Cancer Hospital of Thessaloniki, Thessaloniki, Thessaloniki, GREECE, ⁸Oncology Department at Hippocraton General Hospital of Athens, Athens, Attiki, GREECE, ⁹Department of Medical Oncology, Papageorgiou Hospital, Aristotle University of Thessaloniki, Thessaloniki, Thessaloniki, GREECE, ¹⁰Department of Hematology, Larissa University Hospital, Larissa, Larisa, GREECE, ¹¹Oncology Unit, Aretaieion University Hospital, National and Kapodistrian University of Athens, Athens, Attiki, GREECE, ¹²Medical Oncology Unit of Athens Medical Center, Athens, Attiki, GREECE, ¹³Division Medical Oncology, Attikon University General Hospital of Athens, Haidari, Attiki, GREECE, ¹⁴Medical Department, Genesis Pharma SA, Athens, Chalandri, Attiki, GREECE

Poster #175 #1818869

THE SURVEILLANCE AFTER EXTREMITY TUMOR SURGERY (SAFETY) TRIAL: RESULTS OF THE PILOT STUDY AND SUCCESSFUL INTERNATIONAL EXPANSION

Michelle Ghert, MD, FRCSC¹; The SAFETY, Investigators²

¹McMaster University, Oakville, Ontario, CANADA, ²McMaster University, Hamilton, Ontario, CANADA

Poster #176 #1818941

OUTCOMES RELATED TO THE TREATMENT OF SARCOMAS WITH ANTHRACYCLINES AND/OR IFOSFAMIDE DURING PREGNANCY

Amanda Parkes, MD¹; Yeonhee Park, PhD²; Kristi Posey, PA³; Sonia Godbole, MD⁴; Keith Skubitz, MD⁵; Steven I. Robinson, MD⁶; Mark Agulnik, MD⁷; Brian A. Van Tine, MD, PhD⁴; Angela C. Hirbe, MD, PhD⁴; J Andrew Livingston, MD³

¹University of Wisconsin Carbone Cancer Center, Madison, Wisconsin, UNITED STATES, ²University of Wisconsin-Madison Department of Biostatistics and Medical Informatics, Madison, Wisconsin, UNITED STATES, ³MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁴Washington University School of Medicine, St. Louis, Missouri, UNITED STATES, ⁵University of Minnesota, Minneapolis, Minnesota, UNITED STATES, ⁶Mayo Clinic, Rochester, Minnesota, UNITED STATES, ⁷City of Hope, Duarte, California, UNITED STATES

Poster #177 #1818864

SIX+ YEARS OF BENEFIT WITH SINGLE AGENT PAZOPANIB IN UNRESECTABLE METASTATIC UNDIFFERENTIATED PLEOMORPHIC SARCOMA

Benjamin C. Powers, MD¹; Mark Myron, MD²; Julie Hamlin, APRN²; Tiffany Verhulst, RN²; Dana Smith, RN²

¹The University of Kansas Health System, Leawood, Kansas, UNITED STATES, ²The University of Kansas Health System, Overland Park, Kansas, UNITED STATES

Poster #178 #1819013

FRAGILITY INDEX OF CLINICAL TRIALS FOR SYSTEMIC TREATMENT OF SOFT TISSUE SARCOMA

Abdulazeez Salawu, MBBS, PhD, MRCP(UK)¹; Brooke Wilson, MD²; Albiruni Ryan Abdul Razak, MD, MB, MRCP¹,

¹Division of Medical Oncology, Princess Margaret Cancer Centre, University Health Network, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, CANADA, ²Princess Margaret Cancer Centre, Toronto, Ontario, CANADA

Poster #179 #1819078

PRELIMINARY EFFICACY FROM AN ONGOING PHASE 1 DOSE ESCALATION STUDY OF SECLIDEMSTAT (SP-2577) IN ADVANCED SARCOMAS AND OTHER SOLID TUMORS

Sant P. Chawla, MD¹; Victoria T. Chua-Alcala, MD¹; Jasgit Sachdev, MD²; David Wages, MD³; David Stenehjem, MD⁴; Daniela Santiesteban⁵; Nadeem Mirza, MD, MPH⁵; Simranjit Sekhon, MD⁶; Erlinda M. Gordon, MD⁷; Michael Gordon, MD²

¹Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES, ²HonorHealth Research Institute, Scottsdale, Arizona, UNITED STATES, ³Doc Wages LLC, Southborough, Massachusetts, UNITED STATES, ⁴University of Minnesota, Duluth, Minnesota, UNITED STATES, ⁵Salarius Pharma, Houston, Texas, UNITED STATES, ⁶Sarcoma Oncology Center, Tracy, California, UNITED STATES, ⁷Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES

Poster #180 #1818913

SAFETY AND RECOMMENDED PHASE 2 DOSE OF NEXT GENERATION NY-ESO-1-SPECIFIC TCR T-CELLS IN HLA-A*02 PATIENTS WITH SYNOVIAL SARCOMA OR NON-SMALL CELL LUNG CANCER: MASTER PROTOCOL (SUBSTUDIES 1 AND 2)

Adam J. Schoenfeld, MD¹; Mehmet Altan, MD²; Taofeek K. Owonikoko, MD, PhD, MSCR³; Sandra P. D'Angelo, MD¹; Brian H. Ladle, MD, PhD⁴; Jonathan Noujaim, MD⁵; Kai He, MD, PhD⁶; David Liebner, MD⁶; Adrian G. Sacher, MD⁷; John B.A.G. Haanen, PhD⁸; Jeffrey Yachnin, MD, PhD⁹; Chao Huang, MD¹⁰; Brian A. Van Tine, MD, PhD¹¹; Aisha N. Hasan, MD¹²; Thomas Faitg, PhD¹³; Emily Butler, PhD¹³; Aiman Shalabi, PharmD¹³; Steven Attia, DO¹⁴; Dejka M. Araujo, MD¹⁵

¹Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES, ²MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ³Winship Cancer Institute of Emory University, Atlanta, Georgia, UNITED STATES, ⁴Johns Hopkins University, Baltimore, Maryland, UNITED STATES, ⁵Institut D'Hématologie-Oncologie, Hôpital Maisonneuve-Rosemont, Montreal, Province du Québec, CANADA, ⁶The Ohio State University, Columbus, Ohio, UNITED STATES, ⁷Princess Margaret Cancer Centre, Toronto, Ontario, CANADA, ⁸Antoni van Leeuwenhoek Ziekenhuis, Amsterdam, Noord-Holland, NETHERLANDS, ⁹Karolinska Institutet, Stockholm, Uppsala Lan, SWEDEN, ¹⁰University of Kansas Medical Center, Kansas City, Kansas, UNITED STATES, ¹¹Washington University School of Medicine, St. Louis, Missouri, UNITED STATES, ¹²GlaxoSmithKline, Collegeville, Pennsylvania, UNITED STATES, ¹³GlaxoSmithKline, Philadelphia, Pennsylvania, UNITED STATES, ¹⁴The Mayo Clinic, Jacksonville, Florida, UNITED STATES, ¹⁵The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES

Poster #181 #1818922

EMACTUZUMAB: TARGET MEDIATED DRUG DISPOSITION

David J. Kerr, MD DSc¹; Jean-Pierre Delord, MD²; Carlos Gomez Roca, MD²; Antonine Italiano, MD³; Sandra P. D'Angelo, MD⁴; Michael Cannarile⁵; Georgina Meneses-Lorente⁵; Christophe Le Tourneau⁶; Jean-Yves Blay, MD, PhD⁷; Axel Mescheder, MD⁸

¹University of Oxford, Oxford, England, UNITED KINGDOM, ²IUCT-Oncopole, Toulouse, Provence-Alpes-Cote d'Azur, FRANCE, ³Institute Bergonié, Bordeaux, Aquitaine, FRANCE, ⁴Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES, ⁵F. Hoffmann-La Roche, SWITZERLAND; ⁶Institut Curie, Paris, FRANCE ⁷Centre Léon Bérard, Lyon, Auvergne, FRANCE, ⁸SynOx Therapeutics, Dublin 1, Dublin, IRELAND

Poster #182 #1819001

FIRST-IN-HUMAN TRIAL OF SQ3370 IN RELAPSED OR REFRACTORY SOFT TISSUE SARCOMA AND OTHER SOLID TUMORS: PROOF-OF-CONCEPT FOR CLICK CHEMISTRY-BASED CAPAC PLATFORM

Alexander Guminski, MD/PhD¹; Vivek Bhadri, MD²; Nam Bui, MD³; James Strauss, MD⁴; Robert Steffner, MD⁵; Kathleen Batty, MD¹; Madeline Strach, MD⁶; Michael Zakharian, MS⁷; Steven Smith, PhD⁷; Sangeetha Srinivasan, PhD⁷; Wayne M. Saville, MD⁷; Jose M. Mejia Oneto, MD/PhD⁷; Nathan Yee, PhD⁷; Vivek Subbiah, MD⁸

¹Royal North Shore Hospital, St Leonards, New South Wales, AUSTRALIA, ²Chris O'Brien Lifehouse, Camperdown, New South Wales, AUSTRALIA, ³Stanford University Department of Oncology, Stanford, California, UNITED STATES, ⁴Mary Crowley Cancer Research, Dallas, Texas, UNITED STATES, ⁵Stanford Cancer Institute, Palo Alto, California, UNITED STATES, ⁶Chris O'Brien Lifehouse, Camperdown, New South Wales, AUSTRALIA, ⁷Shasqi, Inc., San Francisco, California, UNITED STATES, ⁸The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES

Poster #183 #1818911

IGNYTE-ESO: LETETRESGENE AUTOLEUCEL (LETE-CEL; GSK3377794) SAFETY AND ACTIVITY IN HLA-A*02+ PATIENTS WITH SYNOVIAL SARCOMA OR MYXOID/ROUND CELL LIPOSARCOMA (SUBSTUDIES 1 AND 2): A MASTER PROTOCOL

Sandra P. D'Angelo, MD¹; Jonathan Noujaim, MD²; Fiona Thistlethwaite, MD, PhD³; Albiruni Ryan Abdul Abdul Razak, MD, MB, MRCP⁴; Silvia Stacchiotti, MD⁵; Warren Chow, MD⁶; John B.A.G. Haanen, PhD⁷; Anna Chalmers, MD⁸; Steven I. Robinson, MD⁹; Brian A. Van Tine, MD, PhD¹⁰; Kristen N. Ganjoo, MD¹¹; Melissa L. Johnson, MD¹²; Victoria L. Chiou, MD¹³; Thomas Faitg, PhD¹³; Mary Woessner, MD¹³; Laura Pearce, MS¹³; Aiman Shalabi, PharmD¹³; Jean-Yves Blay, MD, PhD¹⁴; George D. Demetri, MD¹⁵

¹Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES, ²Institut D'Hématologie-Oncologie, Hôpital Maisonneuve-Rosemont, Montreal, Province du Québec, CANADA, ³The Christie NHS Foundation Trust and University of Manchester, Manchester, England, UNITED KINGDOM, ⁴Division of Medical Oncology, Princess Margaret Cancer Centre, University Health Network, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, CANADA, ⁵Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY, ⁶City of Hope Comprehensive Cancer Center, Duarte, California, UNITED STATES, ⁷Antoni van Leeuwenhoek Ziekenhuis, Amsterdam, Noord-Holland, NETHERLANDS, ⁸Huntsman Cancer Institute, University of Utah, Salt Lake City, Utah, UNITED STATES, ⁹Mayo Clinic, Rochester, Minnesota, UNITED STATES, ¹⁰Washington University School of Medicine, St. Louis, Missouri, UNITED STATES, ¹¹Stanford Cancer Center, Stanford, California, UNITED STATES, ¹²Sarah Cannon Research Institute, Nashville, Tennessee, UNITED STATES, ¹³GlaxoSmithKline, Philadelphia, Pennsylvania, UNITED STATES, ¹⁴Centre Léon Bérard, Lyon, Auvergne, FRANCE, ¹⁵Dana-Farber Cancer Institute and Ludwig Center at Harvard University, Boston, Massachusetts, UNITED STATES

Poster #184 #1818975

TRIAL IN PROGRESS: NIVOLUMAB AND RELATLIMAB IN PATIENTS WITH ADVANCED CHORDOMA

Arun Singh, MD¹; Bartosz Chmielowski, MD PhD²; Sandra Brackert, NP²; Anahis Hagopian²; John Glaspy, MD²; Noah C. Federman, MD³; Brooke Crawford, MD⁴; Nicholas M. Bernthal, MD⁵

¹University of California, Los Angeles, Santa Monica, California, UNITED STATES, ²University of California, Los Angeles, Santa Monica, California, UNITED STATES, ³UCLA Medical Center, Los Angeles, California, UNITED STATES, ⁴University of California, Los Angeles, Los Angeles, California, UNITED STATES, ⁵David Geffen School of Medicine at UCLA, Santa Monica, California, UNITED STATES

Poster #185 #1818883

PHASE 1 STUDY OF CABOZANTINIB IN COMBINATION WITH TOPOTECAN-CYCLOPHOSPHAMIDE FOR PATIENTS WITH RELAPSED EWING SARCOMA OR OSTEOSARCOMA

Kevin Campbell, MD¹; Wendy London, PhD²; David S. Shulman, MD³; Brian Crompton, MD²; Kelly Klega, PhD²; Kerri Cavanaugh, RN²; Natalie Collins, MD²; Suzanne Shusterman, MD²; Katherine A. Janeway, MD³; Steven G. DuBois, MD³

¹Dana-Farber Cancer Institute, Brookline, Massachusetts, UNITED STATES, ²Dana-Farber Cancer Institute, Boston, Massachusetts, UNITED STATES, ³Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, Massachusetts, UNITED STATES

Poster #186 #1819077

A PHASE 1B/2 STUDY OF LIPOSOMAL ANNAMYCIN (ANN) IN PATIENTS WITH PREVIOUSLY TREATED SOFT-TISSUE SARCOMAS (STS) WITH PULMONARY METASTASES

Sant P. Chawla, MD¹; Robert Shepard, MD²; Cynthia Abbate²; Simranjit Sekhon, MD³; Victoria T. Chua-Alcala, MD¹; Ted Kim⁴; Noufil Adnan, MD⁵; Waldemar Priebe, MD⁶; Sandra Silberman, MD²; J. Paul Waymack, MD⁷; Erlinda M. Gordon, MD⁵

¹Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES, ²Moleculin, Houston, Texas, UNITED STATES, ³Sarcoma Oncology Center, Tracy, California, UNITED STATES, ⁴Sarcoma Oncology Center, Santa Monica, California, UNITED STATES, ⁵Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES, ⁶University Of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁷Moleculin Biotech, Houston, Texas, UNITED STATES

Poster #187 #1818897

A POST HOC ANALYSIS OF THE EPAZ TRIAL: THE ROLE OF GERIATRIC VARIABLES IN ELDERLY SOFT TISSUE SARCOMA (STS) PATIENTS ON TOXICITY

Rainer Hamacher, MD¹; Xiaofei Liu, PhD²; Markus K. Schuler, MD, PhD³; Leopold Hentschel, Dipl. Psych⁴; Patrick Schöffski, MD⁵; Hans-Georg Kopp, MD⁶; Sebastian Bauer, MD⁷; Bernd Kasper, MD, PhD⁸; Lars Lindner, MD⁹; Jens-Markus Chemnitz, MD¹⁰; Martina Crysandt, MD¹¹; Alexander Stein, MD¹²; Björn Steffen, MD¹³; Stephan Richter, MD, PhD⁴; Gerlinde Egerer, MD¹⁴; Philipp Ivanyi, MD¹⁵; Annegret Kunitz, MD¹⁶; Viktor Grünwald, MD¹⁷;

¹Department of Medical Oncology, Sarcoma Center, West German Cancer Center, University Hospital Essen, Essen, Nordrhein-Westfalen, GERMANY, ²Institute for Biostatistics, Hannover Medical School, Hannover, Niedersachsen, GERMANY, ³University Hospital Carl Gustav Carus/ Medical Department I, Dresden, Berlin, Berlin, GERMANY,

⁴University Hospital Carl Gustav Carus, University Cancer Center/Medical Department I, Dresden, Dresden, Sachsen, GERMANY, ⁵General Medical Oncology, University Hospitals Leuven – Campus Gasthuisberg, Leuven, Brabant Wallon, BELGIUM, ⁶Robert Bosch Centrum für Tumorerkrankungen Stuttgart, Stuttgart, Baden-Württemberg, GERMANY,

⁷Medical Oncology, University Hospital Essen Westdeutsches Tumorzentrum, Essen, Nordrhein-Westfalen, GERMANY, ⁸University of Heidelberg, Mannheim University Medical Center, Mannheim Cancer Center, Sarcoma Unit, Mannheim, Germany, Mannheim, Baden-Württemberg, GERMANY, ⁹Department of Medicine III, University Hospital, Ludwig Maximilian University Munich, Munich, Bayern, GERMANY, ¹⁰Community Hospital Middle Rine / Department of Hematology, Oncology, Clinical Infectious Diseases, Clinical Immunology, Hemostaseology and Medical Intensive Care, University Hospital Cologne, Koblenz, Rheinland-Pfalz, GERMANY, ¹¹University Hospital RWTH Aachen, Aachen, Nordrhein-Westfalen, GERMANY, ¹²University Hospital Hamburg-Eppendorf, Hamburg, Hamburg, GERMANY,

¹³University Hospital Frankfurt, Frankfurt, Hessen, GERMANY, ¹⁴University Hospital Heidelberg, Heidelberg, Baden-Württemberg, GERMANY, ¹⁵Clinic for Hematology, Hemostasis, Oncology and Stem Cell Transplantation, Medical School Hannover, Hannover, Niedersachsen, GERMANY, ¹⁶Vivantes Clinic Berlin-Spandau /Department of Hematology, Oncology and Tumor Immunology, University Hospital Charite Berlin, Berlin, Berlin, GERMANY, ¹⁷Interdisciplinary Genitourinary Oncology at the West-German Cancer Center, Clinic for Internal Medicine (Tumor Research) and Clinic for Urology, University Hospital Essen, Essen, Nordrhein-Westfalen, GERMANY

Poster #188 #1818994

A PHASE III, MULTI-CENTRE, RANDOMIZED, DOUBLE-BLIND, GROUP COMPARATOR TRIAL TO ASSESS THE SAFETY AND EFFICACY OF EMACTUZUMAB VS PLACEBO IN PATIENTS WITH TENOSYNOVIAL GIANT CELL TUMOURS (TANGENT)

Axel Mescheder, MD¹; Jean-Yves Blay, MD, PhD²; Nicole LeBoeuf, MD, MPH³; Hans Gelderblom, MD, PhD⁴; Michiel van de Sande, MD PhD⁴; David Kerr, CBE MD DSc FRCP FRCGP FACP FMedSci⁵; Simon Cook, CSci, MIMBS⁶; Rowena Abbey, BSc hons⁷; Ulrich Granzer, PhD⁸; Kevin Carroll, PhD⁹; Jerry Kenna, PhD¹⁰; Ray Barlow, PhD¹¹; Broes Naeye, PhD¹¹

¹SynOx Therapeutics, Dublin 1, Dublin, IRELAND, ²Centre Léon Bérard, Lyon, Auvergne, FRANCE, ³Harvard Medical School, Cambridge, Massachusetts, UNITED STATES, ⁴Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ⁵University of Oxford, Oxford, England, UNITED KINGDOM, ⁶Celleron Therapeutics, Oxford, England, UNITED KINGDOM, ⁷SynOx Therapeutics Ltd, Dublin, Dublin, IRELAND, ⁸Granzer Regulatory Consulting & Services, Munich, Bayern, GERMANY, ⁹KJC Statistics Ltd., Stoke on Trend, England, UNITED KINGDOM, ¹⁰Kenna Consulting, Macclesfield, England, UNITED KINGDOM, ¹¹SynOx Therapeutics, Dublin, Dublin, IRELAND

Poster #189 #1819002

NEOADJUVANT THERAPY INCREASES BOTH MYELOID AND LYMPHOID CELLS IN THE SARCOMA TUMOR MICROENVIRONMENT

Laura Riobobos, PhD¹; Peter Goff, MD PhD²; Teresa Kim, MD¹; Bonnie LaFleur, PhD³; Matthew B. Spraker, MD PhD⁴; Kimberly Smythe, BS⁵; Yuzheng Zhang, M.S.⁶; Qianchuan He, PhD⁶; Wendy M Blumenschein, PhD⁷; Natalie A. LaFranzo, PhD⁸; Seth M. Pollack, MD⁹

¹University of Washington, Seattle, Washington, UNITED STATES, ²Universtiy of Washington, Seattle, WA, ³University of Arizona, Tucson, Arizona, UNITED STATES, ⁴Washington University, St. Louis, Missouri, UNITED STATES, ⁵FHCRC, Seattle, Washington, UNITED STATES, ⁶Fred Hutchinson Cancer Research Center, Seattle, Washington, UNITED STATES, ⁷Merck & Co. Inc., Kenilworth, New Jersey, UNITED STATES, ⁸Cofactor Genomics, San Francisco, California, UNITED STATES, ⁹Northwestern University, Chicago, Illinois, UNITED STATES

Poster #190 #1819012

OUTCOMES FOLLOWING DEFINITIVE TREATMENT OF LOCALIZED MALIGNANT PERIPHERAL NERVE SHEATH TUMOUR (MPNST) ARE SIGNIFICANTLY WORSE FOR PATIENTS WITH NF1

Abha A. Gupta, MD, MSc, FRCPC¹; Hagit Peretz Soroka, PhD²; Peter C. Ferguson, MD, PhD, FRCSC³; Jay S. Wunder, MSc., MD⁴; Kim M. Tsoi, MD, PhD⁵; Carol J. Swallow, MD PhD FRCSC FACS⁶; Rebecca A. Gladdy, MD PhD FRCSC FACS⁶; Savataj Brar, MD, MSc, FRCSC⁷; Peter Chung, MD⁸; Charles Catton, MD FRCPC⁸; Philip Wong, MD MSc MDCM FRCPC⁸; Elizabeth G. Demicco, MD PhD⁹; Brendan C. Dickson, MD MSc¹⁰; Albiruni Ryan Abdul Razak, MD, MB, MRCP¹¹; Anthony Griffin, MSc¹²; David Shultz, MD PhD¹³; Rachel Aubrey, BSc¹⁴

¹Division of Medical Oncology, Princess Margaret Cancer Centre, University Health Network, University of Toronto, The Hospital for Sick Children, Canadian Sarcoma Research and Clinical Collaboration (CanSaRCC), Toronto, Ontario, CANADA, ²Princess Margaret Cancer Center, Canadian Sarcoma Research and Clinical Collaboration (CanSaRCC), Toronto, Ontario, CANADA, ³Division of Orthopaedic Surgery, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, CANADA, ⁴The Lunenfeld-Tanenbaum Research Institute, Toronto, Ontario, CANADA, ⁵University of Toronto, Mount Sinai Hospital, Toronto, Ontario, CANADA, ⁶Department of Surgical Oncology, Princess Margaret Hospital, University Health Network and Mount Sinai Hospital, Toronto; Lunenfeld Tanenbaum Research Institute, Sinai Health System, Toronto, Toronto, Ontario, CANADA, ⁷Department of Surgical Oncology, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, CANADA, ⁸Department of Radiation Oncology, Princess Margaret Hospital, University Health Network, Toronto, Toronto, Ontario, CANADA, ⁹Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, Toronto, Ontario, CANADA, ¹⁰Mount Sinai Hospital, Toronto, Ontario, Canada, ¹¹Division of Medical Oncology, Princess Margaret Cancer Centre, University Health Network, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, CANADA, ¹²Division of Orthopaedic Surgery, Department of Surgery, Sinai Health System, Toronto, Ontario, CANADA, ¹³Department of Radiation Oncology, Princess Margaret Hospital, University Health Network, University of Toronto, Toronto, Ontario, CANADA, ¹⁴Princess Margaret Cancer Center, Canadian Sarcoma Research and Clinical Collaboration (CanSaRCC), McMaster University, Toronto, Ontario, CANADA

Poster #191 #1818972

TRANSCUTANEOUS OXYGEN AS A PREDICTOR OF WOUND HEALING COMPLICATIONS IN PREOPERATIVELY RADIATED SOFT TISSUE SARCOMA

Lukas M. Nystrom, MD¹; Benjamin J. Miller, MD MS²; Yuxuan Jin, MS¹; Nathan Mesko, MD¹; Jeremy White, MD³; Andre Spiguel, MD⁴

¹Cleveland Clinic, Cleveland, Ohio, UNITED STATES, ²University of Iowa, Iowa City, Iowa, UNITED STATES, ³University of Oklahoma, Oklahoma City, Oklahoma, UNITED STATES, ⁴University of Florida, Gainesville, Florida, UNITED STATES

Poster #192 #1818866

WHAT FACTORS DO NEW PATIENTS CONSIDER IMPORTANT WHEN SELECTING AN ORTHOPEDIC ONCOLOGIST?

Linus Lee, BE¹; Charles A. Gusho, BS²; Vishal Patel, BS¹; Alan T. Blank, MD, MS¹

¹Rush University Medical Center, Chicago, Illinois, UNITED STATES, ²Rush University Medical Center, Milwaukee, Wisconsin, UNITED STATES

Poster #193 #1819020

BRAIN METASTASES FROM ADULT SARCOMA: THE EXPERIENCE OF THE HELLENIC GROUP OF SARCOMA AND RARE CANCERS (HGSR).

Stefania Kokkali, MD, MSc¹; Louiza Vini, MD, PhD, FRCR²; Anastasia Stergioula, MD³; Anastasios Kyriazoglou, MD, PhD⁴; Nikolaos Vassos, MD, PhD, FACS, FICS, MHBA⁵; Ioannis Boukovinas, MD, PhD, PharmaD⁶

¹Saint-Savvas Cancer Hospital, Athens, Athens, Attiki, GREECE, ²"Iatriko" Hospital of Athens, Athens, Attiki, GREECE, ³Department of Radiation Oncology, "Iaso", Department of Tomotherapy-Stereotactic Radiosurgery "Iatropolis", Athens, Athens, Attiki, GREECE, ⁴Oncology Unit, Department of Clinical Therapeutics, General Hospital Alexandra, Athens, Athens, Attiki, GREECE, ⁵Division of Surgical Oncology, Mannheim University Medical Center, University of Heidelberg, Mannheim, Baden-Wuerttemberg, GERMANY, ⁶Medical Oncology, Bioclinic of Thessaloniki, Thessaloniki, GREECE

Poster #194 #1819033

IMMUNE CORRELATES IN SOFT TISSUE SARCOMA UNDERGOING NEOADJUVANT RADIATION AND DUAL CHECKPOINT BLOCKADE

Adrienne Victor, MD, MSc; Numbereye Numbere, MD, MBBS; Deepak Sahasrabudhe, MD
University of Rochester, Rochester, New York, UNITED STATES

Poster #195 #1818951

NOVEL ACCELERATED HYPOFRACTIONATED RADIOTHERAPY IN SOFT TISSUE SARCOMA, UTILIZING SIMULTANEOUS INTEGRATED BOOST

Matthew N. Mills, MD; Justin Miller, CMD, RT; Vladimir Feygelman, PhD; Arash Naghavi, MD
H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida, UNITED STATES

Poster #196 #1819081

THE UTILIZATION OF STEREOTACTIC BODY RADIOTHERAPY IN THE MANAGEMENT OF SOFT TISSUE SARCOMA LIVER AND PULMONARY METASTASIS

Aqeel Ashraf, B.Med.Sc., BMBCh; Nasra AlBusaidi, MD; Paul Ramia, MD; Simon Gauvin, MD; Neil Kopek, MD; Sinziana Dumitra, MD, MSc (Epi), FRCS(C)
McGill University, Montreal, Province du Québec, CANADA

Poster #197 #1819055

CIVASHEET® USE FOR RECURRENT SOFT TISSUE SARCOMA: A SINGLE INSTITUTION EXPERIENCE

Crystal S. Seldon, MD¹; Julie Grossman, MD²; Gautam Shrivastava, ScM³; Melanie Fernandez, BA²; Sheila Conway, MD⁴; Andrew Rosenberg, MD PhD⁵; Alan Livingstone, MD⁵; Dido Franceschi, MD²; Jonathan C. Trent, MD, PhD⁶; Matthew Studenski, PhD²; Raphael Yechieli, MD²

¹University of Miami, Homestead, Florida, UNITED STATES, ²University of Miami, Miami, Florida, UNITED STATES,

³University of Miami, Miami, Georgia, UNITED STATES, ⁴University of Miami/Jackson Memorial Hospital, Miami, Florida, UNITED STATES, ⁵University of Miami, University of Miami, Florida, UNITED STATES, ⁶Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES

Poster #198 #1818977

ASSESSING RADIOGRAPHIC AND PATHOLOGICAL RESPONSE IN MYXOID LIPOSARCOMA PATIENTS TREATED WITH PREOPERATIVE RADIOTHERAPY

Robert Gao, MD; Ivy A. Petersen, MD; Michael Haddock, MD; Andrew Folpe, MD; William Harmsen, MS; Safia Ahmed, MD
Mayo Clinic, Rochester, Minnesota, UNITED STATES

Poster #199 #1819009

MANAGEMENT OF MYXOFIBROSARCOMA: IMPACT OF TUMOR DEPTH AND ROLE OF PREOPERATIVE RADIATION IN LOCAL CONTROL

Maya Abdou; Ivy A. Petersen, MD; William Harmsen, MS; Matthew T. Houdek, MD; Brittany A. Looker, PA-C, MS; Michael Haddock, MD; Safia Ahmed, MD
Mayo Clinic, Rochester, Minnesota, UNITED STATES

Poster #200 #1818921

EFFICACY OF VMAT RADIOTHERAPY FOR SOFT TISSUE SARCOMA OF THE EXTREMITIES

Anna K. Lawless, BSc, MPH, MBBS¹; Nonga Fangupo, MRadTher, BMedHlthSc²; Reuben Patrick Estoesta, MHSc(MRS), BAppSc(RT)²; Gino Perez, BAppSc(RT), BSc(Nurs)²; Samara Alzaidi, PhD³; Robin Hill, PhD, MSc, BSc(Hons)⁴; Angela Hong, MBBS, MMed, PhD, FRANZCR⁵

¹Chris O'Brien Lifecare, Sydney, Australia, Sydney, NSW, New South Wales, AUSTRALIA, ²Chris O'Brien Lifecare, Sydney, Australia, Sydney, New South Wales, AUSTRALIA, ³Department of Radiation Oncology, Chris O'Brien Lifecare, Sydney, Australia, Sydney, New South Wales, AUSTRALIA, ⁴Department of Radiation Oncology, Chris O'Brien Lifecare, Sydney, Australia, Institute of Medical Physics, School of Physics, University of Sydney, Sydney, Australia, Sydney, New South Wales, AUSTRALIA, ⁵Department of Radiation Oncology, Chris O'Brien Lifecare, Sydney, Australia, Faculty of Medicine and Health, The University of Sydney, Sydney, Australia, Camperdown, Victoria, AUSTRALIA

Poster #201 #1819064

A PHASE II STUDY ON THE NEO-ADJUVANT COMBINATION OF PAZOPANIB AND RADIOTHERAPY IN PATIENTS WITH HIGH-RISK, LOCALIZED SOFT TISSUE SARCOMA

Milan Van Meekeren, PhD¹; Judith V.M.G. Bovée, MD PhD¹; Frits van Coevorden, MD, PhD²; Winan J. van Houdt, MD PhD MSc³; Anne Miek Koenen⁴; Aisha Miah⁵; Shane Zaidi⁵; Andrew J. Hayes, PhD⁶; Khin Thway, MD, PhD⁷; Augustinus Krol, MD PhD⁸; Marta Fiocco, PhD⁸; Hans Gelderblom, MD, PhD¹; Neeltje Steeghs, MD, PhD⁹; Rick L. Haas, MD PhD³

¹Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ²The Netherlands Cancer Institute, Amsterdam, Zuid-Holland, NETHERLANDS, ³The Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS, ⁴Netherlands Cancer Institute, Amsterdam, Zuid-Holland, NETHERLANDS, ⁵The Royal Marsden NHS Foundation Trust, London, England, UNITED KINGDOM, ⁶The Royal Marsden Hospital NHS Foundation Trust, London, England, UNITED KINGDOM, ⁷Royal Marsden Hospital, London, England, UNITED KINGDOM, ⁸The Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ⁹Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS

Poster #202 #1818854

LACK OF RADIOSENSITIVITY PREDICTS POOR ONCOLOGIC OUTCOME IN EXTREMITY MYXOID LIPOSARCOMA

Matthew T. Houdek, MD; Katerine Mallett, MD; Steven I. Robinson, MD; Brittany L. Siontis, MD; Safia Ahmed, MD; Ivy A. Petersen, MD; Peter S. Rose, MD
Mayo Clinic, Rochester, Minnesota, UNITED STATES

Poster #203 #1818881

PREOPERATIVE CHEMORADIATION THERAPY IN THE MANAGEMENT OF LOCALIZED SOFT TISSUE SARCOMAS

Brittany L. Siontis, MD; Judith Jebastin Thangaiah, MD; Thanh P. Ho, MD; Safia Ahmed, MD; Travis Grotz, MD; Matthew T. Houdek, MD; Andrew Folpe, MD; Scott Okuno, MD; Steven Robinson, MBBS
Mayo Clinic, Rochester, Minnesota, UNITED STATES

Poster #204 #1818852

NEOADJUVANT DENOSUMAB IN GCT. LONG TERM INJECTION CAN DECREASE THE RISK OF LOCAL RECURRENCE

Anastasia Tararykova¹; Alexander Fedenko, PhD²; Elmar Musaev, PhD³; Valerii Burliaev, PhD⁴, ¹Federal State Budgetary Institution «N.N. Blokhin National Medical Research Center of Oncology» of the Ministry of Health of the Russian Federation (N.N. Blokhin NMRCO), Moscow, Russia, Odintcovo, Moskva, RUSSIA, ²National Medical Research Radiological Center of the Ministry of Health of the Russian Federation, Moscow, Russia, Moscow, Moskva, RUSSIA, ³Federal State Budgetary Institution «N.N. Blokhin National Medical Research Center of Oncology» of the Ministry of Health of the Russian Federation (N.N. Blokhin NMRCO), Moscow, Moskva, RUSSIA, ⁴Federal State Budgetary Institution «N.N. Blokhin National Medical Research Center of Oncology» of the Ministry of Health of the Russian Federation (N.N. Blokhin NMRCO), Moscow, Russia, Moscow, Moskva, RUSSIA

Poster #205 #1818867

NEOADJUVANT RADIATION INFLUENCES THE PSEUDOCAPSULE IN SOFT TISSUE SARCOMA: A HISTOPATHOLOGIC AND RADIOGRAPHIC EVALUATION

Nicholas J. Waldvogel, BA¹; Sarah C. Tepper, MD²; Charles A. Gusho, BS³; Ira Miller, MD, PhD²; Gregory M. White, MD²; Michael Ralls, MD²; Dian Wang, MD, PhD²; Steven Gitelis, MD²; Alan T. Blank, MD, MS²; Linus Lee, BE²
¹Rush University Medical College, Chicago, Illinois, UNITED STATES, ²Rush University Medical Center, Chicago, Illinois, UNITED STATES, ³Rush University Medical Center, Milwaukee, Wisconsin, UNITED STATES

Poster #206 #1818974

UNEXPECTED BENEFIT OF CHEMOTHERAPY IN PATIENTS TREATED WITH PULMONARY METASTECTOMY FOR SOFT TISSUE SARCOMA

Samantha Armstrong, MD; Daniel Rushing, MD; Kenneth Kesler, MD; Hao Liu, Ph. D.; Daniel Wurtz, MD; Karen Rieger, MD
Indiana University, Indianapolis, Indiana, UNITED STATES

Poster #207 #1819073

NEOADJUVANT PACLITAXEL IN BREAST ANGIOSARCOMA

Luke V. Selby, MD, MS¹; Emma Clark, MD¹; James L. Chen, MD²; Gabriel Tinoco, MD, FACP¹; Joal Beane, MD³; Raphael Pollock, MD³; David Liebner, MD¹; Valerie Grignol, MD³

¹The Ohio State University, Columbus, Ohio, UNITED STATES, ²Ohio State University, Columbus, Ohio, UNITED STATES,

³James Cancer Hospital, The Ohio State University, Columbus, Ohio, UNITED STATES

Poster #208 #1818928

ANALYSING THE EFFECT OF METASTASECTOMY ON POST-METASTASIS SURVIVAL IN BONE SARCOMA PATIENTS WITH SECONDARY LUNG METASTASES

Maria Anna Smolle, MD¹; Angelika Kogler¹; Joerg Friesenbichler, MD¹; Susanne Scheipl, MD²; Marko Bergovec, MD²; Christoph Castellani, Assoc.-Prof. MD³; Holger Till, Prof. MD³; Freyja-Maria Smolle-Juettner, Prof. MD⁴; Andreas Leithner, Prof. Dr.⁵

¹Department of Orthopaedics and Trauma, Medical University Graz, Graz, Steiermark, AUSTRIA, ²Medical University Graz, Graz, Steiermark, AUSTRIA, ³Department of Paediatric and Adolescent Surgery, Medical University of Graz, Graz, Steiermark, AUSTRIA, ⁴Division of Thoracic and Hyperbaric Surgery, Department of Surgery, Medical University of Graz, Graz, Steiermark, AUSTRIA, ⁵Department of Orthopedics and Trauma, Medical University of Graz, Graz, Steiermark, AUSTRIA

Poster #209 #1818845

WHAT IS THE CLINICAL IMPACT OF SENDING TISSUE FOR HISTOPATHOLOGY DURING SURGERY FOR KNOWN, DIFFUSE METASTATIC DISEASE TO BONE?

Charles A. Gusho, BS¹; Linus Lee, BE²; Alan T. Blank, MD, MS²

¹Rush University Medical Center, Milwaukee, Wisconsin, UNITED STATES, ²Rush University Medical Center, Chicago, Illinois, UNITED STATES

Poster #210 #1819080

THE MANAGEMENT OF HEPATIC METASTASIS FROM SOFT TISSUE SARCOMA: A SYSTEMATIC REVIEW

Aqeel Ashraf, B.Med.Sc., BMBCh; Abdulaziz Al-Mubarak, MD; Simon Gauvin, MD; Neil Kopek, MD;

Jeffrey Barkun, MD, MSc, FRCS(C), FACS; Sinziana Dumitra, MD, MSc (Epi), FRCS(C)

McGill University, Montreal, Province du Québec, CANADA

Poster #211 #1819005

ROLE OF MULTIDISCIPLINARY APPROACH IN A CASE OF SPINE OSTEOSARCOMA WITH OLIGOMETASTATIC HEART DISEASE

Anastasia Tararykova¹; Aslan Valiev, PhD²; Pavel Kononets, PhD²; Ruslan Kabardaev³; Antonio Chekini, PhD³; Nikolay Koslov, PhD³, ¹Federal State Budgetary Institution «N.N. Blokhin National Medical Research Center of Oncology» of the Ministry of Health of the Russian Federation (N.N. Blokhin NMRCO), Moscow, Russia, Odintcovo, Moskva, RUSSIA, ²Federal State Budgetary Institution «N.N. Blokhin National Medical Research Center of Oncology» of the Ministry of Health of the Russian Federation (N.N. Blokhin NMRCO), Moscow, Moskva, RUSSIA, ³Federal State Budgetary Institution «N.N. Blokhin National Medical Research Center of Oncology» of the Ministry of Health, Moscow, Moskva, RUSSIA

Poster #212 #1819031

OUTCOMES FOLLOWING MULTI-DISCIPLINARY MANAGEMENT OF METASTATIC MALIGNANT PHYLLODES TUMOURS

Ru Xin Wong, MBBS¹; Jian Bang Chiang, MBBS¹; Fuh Yong Wong, MBBS¹; Wenshen Looi, MBBS¹; Jason Chan, MBBS¹; Mohamad Farid, MBBS¹; Xuan Rong Thong²

¹National Cancer Centre Singapore, SINGAPORE, ²Lee Kong Chian School of Medicine, Singapore, SINGAPORE

Poster #213 #1819021

MULTIDISCIPLINARY MANAGEMENT OF PLEOMORPHIC DERMAL SARCOMA OF THE SCALP: A SINGLE INSTITUTION EXPERIENCE

Megan L. Sulciner, MD¹; Jiping Wang, MD, PhD¹; Miranda B. Lam, MD, MBA¹; Jason L. Hornick, MD, PhD¹;

Dennis Orgill, MD, PhD¹; Elizabeth H. Baldini, MD, MPH¹; Chandrajit P. Raut, MD, MSc²; Mark Fairweather, MD¹

¹Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES, ²Dana-Farber Cancer Institute, Harvard University, Boston, Massachusetts, UNITED STATES

Poster #214 #1819035

UNDIFFERENTIATED PLEOMORPHIC SARCOMA OF THE EXTREMITIES, FACTORS ASSOCIATED WITH POOR OVERALL SURVIVAL

Dorian Y. Garcia-Ortega, MD, MSc, FACS¹; Alethia Alvarez-Cano, MD, MSc²; Miguel Angel Clara-Altamirano, MD, MSc³; Claudia HS Caro-Sanchez, MD, MSc³; Kuauhyama Luna-Ortiz, MD⁴

¹Instituto Nacional de Cancerología, Mexico, Distrito Federal, MEXICO, ²Christus Muguerza, Monterrey, Nuevo Leon, MEXICO, ³Instituto Nacional de Cancerología, Tlalpan, Distrito Federal, MEXICO, ⁴Instituto Nacional de Cancerología, Tlalpan, Distrito Federal, MEXICO

Poster #215 #1818870

TENOSYNOVIAL GIANT CELL TUMOR OBSERVATIONAL PLATFORM PROJECT (TOPP): 2-YEAR OBSERVATIONAL ANALYSIS OF PATIENT-REPORTED OUTCOMES BASED ON TREATMENT STRATEGIES FROM AN EU/US PROSPECTIVE REGISTRY

Emanuela Palmerini, MD¹; Silvia Stacchiotti, MD²; John H. Healey, MD, FACS³; Sebastian Bauer, MD⁴; Nicholas M. Bernthal, MD⁵; Bart Schreuder, MD, PhD⁶; Andreas Leithner, MD, PhD⁷; Javier Martin-Broto, MD, PhD⁸; Francois Gouin, MD, PhD⁹; Hans Gelderblom, MD, PhD¹⁰; Eric L. Staals, MD¹; Julio Lopez-Bastida, MSc, PhD¹¹; Petra Laeis, PhD¹²; Florence Mercier, MSc¹²; Xin Ye, PhD¹³; Michiel van de Sande, MD PhD¹⁰

¹IRCCS Istituto Ortopedico Rizzoli, Bologna, Emilia-Romagna, ITALY, ²Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY, ³Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES, ⁴West German Cancer Center, University of Duisburg-Essen, Essen, Nordrhein-Westfalen, GERMANY, ⁵David Geffen School of Medicine at UCLA, Santa Monica, California, UNITED STATES, ⁶Radboud University, Nijmegen, Gelderland, NETHERLANDS, ⁷Medical University of Graz, Graz, Steiermark, AUSTRIA, ⁸Fundacion Jimenez Diaz University Hospital, Madrid, Madrid, SPAIN, ⁹Center Leon Berard, Lyon, Rhone-Alpes, FRANCE, ¹⁰Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ¹¹University Castilla-La Mancha, Talavera de la Reina, Castilla-La Mancha, SPAIN, ¹²Daiichi Sankyo Europe GmbH, Munich, Bayern, GERMANY, ¹³Daiichi Sankyo, Inc., Basking Ridge, New Jersey, UNITED STATES

Poster #216 #1836519

OUTPATIENT OPIOID UTILIZATION AMONG PEDIATRIC PATIENTS WITH PRIMARY BONE SARCOMAS AFTER TUMOR RESECTION

Lee M. Zuckerman, MD¹; Omar Ramos, MD²; Alex Mierke, MD²; Ryan Filler, MD²; Nadine Williams, MD²

¹City of Hope National Medical Center, Duarte, California, UNITED STATES, ²Loma Linda University Medical Center, Loma Linda, California, UNITED STATES

Poster #217 #1836512

OUTCOMES INCLUDING LATE AMPUTATION AFTER TREATMENT FOR LOWER EXTREMITY SARCOMA: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY

Erik J. Geiger, MD¹; Wei Liu, PhD²; Kumar Srivastava, PhD²; Nicholas M. Bernthal, MD³; Yutaka Yasui, PhD²; Kirsten Ness, PT, PhD²; Kevin Krull, PhD²; Wendy Leisenring, Sc.D.⁴; Gregory Armstrong, MD, MSCE²; Rosanna Wustrack, MD⁵

¹UCLA, Santa Monica, California, UNITED STATES, ²St. Jude Children's Research Hospital, Memphis, Tennessee, UNITED STATES, ³David Geffen School of Medicine at UCLA, Santa Monica, California, UNITED STATES, ⁴Fred Hutchinson Cancer Research Center, Seattle, Washington, UNITED STATES, ⁵UCSF, San Francisco, California, UNITED STATES

Poster #218 #1836522

THE IMPACT OF DISTANCE FROM TREATMENT CENTER: A PRELIMINARY ANALYSIS SUGGESTING A ROLE FOR TELEMEDICINE IN SARCOMA CARE

Matthew J. Thompson, MD¹; Elizabeth Heath²; Emily Robinson³; Shamele Battan³; Nirnaya Miljacic, MS, PhD⁴; Nayak Polissar, PhD⁴; Jesse Roberts, MD¹; Edward Kim, MD⁵; Stephanie Schaub, MD⁶; Elizabeth T. Loggers, MD, PhD⁷; Michael J. Wagner, MD⁸; Lee D. Cranmer, MD, PhD⁹

¹Seattle Cancer Care Alliance Sarcoma Clinic, Department of Orthopaedics and Sports Medicine, University of Washington School of Medicine, Seattle, Washington, UNITED STATES, ²University of Washington, Seattle, Washington, UNITED STATES, ³University of Washington School of Medicine, Seattle, Washington, UNITED STATES, ⁴The Mountain-Whisper-Light Statistics, Seattle, Washington, UNITED STATES, ⁵Seattle Cancer Care Alliance Sarcoma Clinic, Department of Radiation Oncology, University of Washington School of Medicine, Seattle, Washington, UNITED STATES, ⁶Seattle Cancer Care Alliance Sarcoma Clinic, Department of Radiation Oncology, University of Washington School of Medicine, Seattle, Washington, UNITED STATES, ⁷University of Washington/Fred Hutch/Seattle Cancer Care, Seattle, Washington, UNITED STATES, ⁸University of Washington/Fred Hutch/Seattle Cancer Care Alliance, Seattle, Washington, UNITED STATES, ⁹Univ Washington/Fred Hutchinson Cancer Res Ctr, Seattle, Washington, UNITED STATES

Poster #219 #1836523

THE IMPACT OF DISTANCE ON SARCOMA ONCOLOGIC OUTCOMES: A RETROSPECTIVE COHORT STUDY

Abdulaziz Al-Mubarak, MD¹; Giuseppe Frenda, MD¹; Mireille Dessureault, MSc¹; Ahmed Aoude, .²; Robert Turcotte, MD¹; Sinziana Dumitra, MD, MSc (Epi), FRCS(C)¹, ¹McGill University, Montreal, Province du Québec, CANADA, ²McGill, Montreal, Province du Québec, CANADA

Poster #220 #1836514

THE COSTS OF COVERAGE: EFFECTS OF INSURANCE PROVIDER ON SOFT TISSUE SARCOMA FINANCIAL AND HEALTH OUTCOMES

Hayley Hansen, BSBA; Qiang An, MBBS, MPH; Benjamin J. Miller, MD MS
University of Iowa, Iowa City, Iowa, UNITED STATES

Poster #221 #1836515

VALIDATING THE HEALTH-RELATED QUALITY OF LIFE DATA OF THE PROSA-STUDY BY COMPARISON PATIENT AND TUMOR CHARACTERISTICS OF RPS PATIENTS WITH THE TARPS-WG COHORT

Jens Jakob, MD¹; Leopold Hentschel, Dipl. Psych²; Stephan Richter, MD, PhD²; Peter Hohenberger, MD, PhD³; Bernd Kasper, MD, PhD⁴; Dimosthenis Andreou, MD, PhD⁵; Daniel Pink, MD, PhD⁶; Jochen Schmitt, MD, PhD⁷; Markus K. Schuler, MD, PhD⁸; Martin Eichler, PhD⁹

¹University Medical Center Göttingen, Göttingen, Niedersachsen, GERMANY, ²University Hospital Carl Gustav Carus, University Cancer Center/Medical Department I, Dresden, Dresden, Sachsen, GERMANY, ³Mannheim University Medical Center, University of Heidelberg, Mannheim, Baden-Württemberg, GERMANY, ⁴University of Heidelberg, Mannheim University Medical Center, Mannheim Cancer Center, Sarcoma Unit, Mannheim, Germany, Mannheim, Baden-Württemberg, Germany, ⁵Helios Klinikum Bad Saarow, Bad Saarow, Brandenburg, GERMANY, ⁶Helios Klinikum Bad Saarow, Universitätsmedizin Greifswald, Bad Saarow, Brandenburg, GERMANY, ⁷National Center for Tumor Diseases (NCT/UCC), Dresden, Germany, Dresden, Sachsen, GERMANY, ⁸University Hospital Carl Gustav Carus/ Medical Department I, Dresden, Berlin, Berlin, GERMANY, ⁹University Hospital Carl Gustav Carus/ National Center for Tumor Diseases (NCT/UCC), Dresden, Germany, Dresden, Sachsen, GERMANY

Poster #222 #1836517

PREDICTION OF EARLY POSTOPERATIVE WALKING FUNCTION OF SO-CALLED HIP TRANSPOSITION ARTHROPLASTY AFTER RESECTION OF MALIGNANT PERIACETABULAR TUMORS: A MULTICENTER COHORT ANALYSIS

Liuzhe Zhang, MD¹; Saito Masanori, MD²; Toru Akiyama, MD³; Makoto Nakagawa, MD⁴; Satoshi Tsukushi, MD⁵; Shinichiro Yoshida, MD⁶; Tabu Gokita, MD⁷; Keisuke Ae, MD²; Seiya Nakashima⁸; Munenori Watanuki, MD⁶; Shintaro Iwata, MD⁹

¹The University of Tokyo Hospital, Bunkyo-ku, Tokyo, JAPAN, ²The Cancer Institute Hospital, Tokyo, Tokyo, JAPAN, ³Jichi Medical University Saitama Medical Center, Omiya, Saitama, JAPAN, ⁴National Cancer Center, Chuo-ku, Tokyo, JAPAN, ⁵Aichi Cancer Center, Aichi, Aichi, JAPAN, ⁶Tohoku University Hospital, Miyagi, Miyagi, JAPAN, ⁷Saitama Prefecture Cancer Center, Saitama, Saitama, JAPAN, ⁸Aichi Cancer Center, Tokyo, Tokyo, JAPAN, ⁹National Cancer Center Hospital, Chuo-ku, Tokyo, JAPAN

Poster #223 #1836513

PATIENT REPORTED DATA OF DESMOID TUMORS DURING AND AFTER PREGNANCY FROM AN INTERNATIONAL NATURAL HISTORY STUDY

Amanda L. Lucas¹; Maneesh Kumar, MD, PhD²; Danielle Braggio, PhD, BCMAS³; Lynne Hernandez⁴; Kelly Mercier, PhD⁵
¹Desmoid Tumor Research Foundation, Jacksonville Beach, Florida, UNITED STATES, ²Desmoid Tumor Research Foundation, Cedar Rapids, Iowa, UNITED STATES, ³Desmoid Tumor Research Foundation, Houston, Texas, UNITED STATES, ⁴Desmoid Tumor Research Foundation, Philadelphia, Pennsylvania, UNITED STATES, ⁵Desmoid Tumor Research Foundation, Cary, North Carolina, UNITED STATES

Poster #224 #1836511

A PILOT STUDY OF THE FEASIBILITY AND UTILITY OF A FITNESS TRACKER TO CORRELATE ACTIVITY LEVEL WITH PATIENT REPORTED OUTCOMES IN SARCOMA PATIENTS UNDERGOING SYSTEMIC THERAPY

Elizabeth J. Davis, MD; Gregory D. Ayers, B.S.; Elizabeth Ryan, APRN; Deborah Wallace, APRN; Vicki L. Keedy, MD, MSCI; Rajiv Agarwal, MD
Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES

Poster #225 #1836518

HEALTH-RELATED QUALITY OF LIFE IN YOUNG BONE SARCOMA SURVIVORS

Carolina C. Pereira, MD¹; Diana Pessoa, MD¹; Susana Esteves, MSc Biostatistics¹; Ana Catarina Freitas, MD²; Teresa Alexandre, MD¹; Margarida Ferreira, MD¹

¹Instituto Português de Oncologia de Lisboa Francisco Gentil, E.P.E., Lisbon, Lisboa, PORTUGAL,

²Fundação Champalimaud, Lisbon, Lisboa, PORTUGAL

Poster #226 #1836521

HEALTH-RELATED QUALITY OF LIFE AFTER ISOLATED LIMB PERFUSION COMPARED TO EXTENDED RESECTION, OR AMPUTATION FOR LOCALLY ADVANCED EXTREMITY SARCOMA: IS A LIMB SALVAGE STRATEGY WORTH THE EFFORT?

Sophie JM Reijers, MD¹; Olga Husson, PhD¹; Vicky Soomers, MD, PhD²; Lukas Been, MD, PhD³;

Han Bonekamp, MD, PhD²; Michiel van de Sande, MD, PhD⁴; Cornelis Verhoef, MD, PhD⁵;

Winette T. A. van der Graaf, MD, PhD¹; Winan J. van Houdt, MD, PhD, MSc⁶

¹Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS, ²Radboud University Medical Center, Nijmegen, Gelderland, NETHERLANDS, ³University Medical Center Groningen, Groningen, Groningen, NETHERLANDS,

⁴Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ⁵Erasmus MC Cancer Institute, Rotterdam, Zuid-Holland, NETHERLANDS, ⁶The Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS

Poster #227 #1836520

THE EVALUATION OF HEALTH-RELATED QUALITY OF LIFE ISSUES EXPERIENCED BY PATIENTS WITH DESMOID-TYPE FIBROMATOSIS (THE QUALIFIED STUDY) - A PROTOCOL FOR AN INTERNATIONAL COHORT STUDY

Anne-Rose W. Schut, MD¹; Milea Timbergen, MD, PhD¹; Emma Lidington, MSc²; Dirk J. Grünhagen, MD PhD³;

Winette T. A. van der Graaf, MD PhD⁴; Stefan Sleijfer, MD, PhD¹; Winan J. van Houdt, MD PhD MSc⁵;

Han Bonekamp, MD PhD⁶; Eugenie Younger, MbChB Hons; MRCP²; Alison Dunlop²; Robin L. Jones, BSc, MBBS, MD⁷;

Spyridon Gennatas, BSc, MBChB, PhD, MRCP²; Cornelis Verhoef, MD PhD⁸; Olga Husson, PhD²

¹Erasmus Medical Center, Rotterdam, Zuid-Holland, NETHERLANDS, ²Royal Marsden NHS Foundation Trust, London, England, UNITED KINGDOM, ³Erasmus MC Cancer Institute, Rotterdam, Zuid-Holland, NETHERLANDS, ⁴Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS, ⁵The Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS, ⁶Radboud University Medical Center, Nijmegen, Gelderland, NETHERLANDS,

⁷The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, England, UNITED KINGDOM, ⁸Erasmus MC Cancer Institute, Rotterdam, Zuid-Holland, NETHERLANDS

⁷The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, England, UNITED KINGDOM,

⁸Erasmus MC Cancer Institute, Rotterdam, Zuid-Holland, NETHERLANDS

Poster #228 #1818936

RHABDOMYOBLASTIC DEDIFFERENTIATION IN RETROPERITONEAL LIPOSARCOMAS IS ASSOCIATED WITH REDUCED IMMUNE INFILTRATION

Beatrice Valenti, MSc¹; Sandro Pasquali, MD, PhD²; Monica Brenca, PhD¹; Silvia Brich, PhD³; Davide Baldazzi, MSc¹;

Dominga Racanelli, PhD¹; Ilaria De Benedictis, MSc¹; Chiara Colombo, MD⁴; Marta Sbaraglia, MD⁵; Viviana Vallacchi, PhD⁶;

Chiara Castelli, PhD⁶; Silvia Stacchiotti, MD⁷; Angelo Paolo Dei Tos, MD⁸; Paola Collini, MD⁹; Alessandro Gronchi, MD¹⁰;

Roberta Maestro, PhD¹

¹CRO Aviano IRCCS National Cancer Institute, Aviano, Friuli-Venezia Giulia, ITALY, ²Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ³Fondazione IRCCS Istituto Nazionale dei Tumori (INT), Milano, Lombardia, ITALY, ⁴Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY,

⁵Azienda Ospedaliera Università di Padova (UniPD), Padova, Veneto, ITALY, ⁶Immunotherapy of Human Tumors, Department of Research, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ⁷Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY, ⁸Università di Padova (UniPD), Padova, Veneto, ITALY, ⁹Department of Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori,

Milano, Lombardia, ITALY, ¹⁰Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, Milan, Lombardia, ITALY

Milano, Lombardia, ITALY, ¹⁰Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, Milan, Lombardia, ITALY

Poster #229 #1818950

RETROSPECTIVE EVALUATION OF THE ROLE OF GEMCITABINE- DOCETAXEL IN WELL-DIFFERENTIATED AND DEDIFFERENTIATED LIPOSARCOMA

Prapassorn Thirasastr, MD, MSc.¹; Behrang Amini, MD, PhD²; Heather Lin, PhD²; Christina L. Roland, MD¹; Elise F. Nassif, MD³; Alejandra Zazour²; Anthony P. Conley, MD³; Dejka M. Araujo, MD¹; Emily Z. Keung, MD¹; J Andrew Livingston, MD³; Ravin Ratan, MD⁴; Joseph A. Ludwig, IV, MD⁴; Robert S S. Benjamin, MD⁵; Xiao Zhou, MD, PhD⁵; Shreyaskumar Patel, MD²; Vinod Ravi, MD¹; Barry W. Feig, MD¹; Neeta Somaiah, MD¹

¹The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ²MDACC, Houston, Texas, UNITED STATES, ³MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁴Sarcoma Medical Oncology, University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁵University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES

Poster #230 #1818957

A PHASE I/II TRIAL COMBINING AVELUMAB AND TRABECTEDIN FOR ADVANCED LIPOSARCOMA AND LEIOMYOSARCOMA

Michael J. Wagner, MD¹; Graeme Black, B.S.²; Yuzheng Zhang, M.S.²; Lee D. Cranmer, MD, PhD³; Elizabeth T. Loggers, MD, PhD²; Sabrina McDonnell, B.S.²; Shannon Maxwell, B.S.³; Rylee Johnson, B.S.³; Roxanne Moore, M.S.³; Qianchuan He, PhD²; Robin L Jones, MD, PhD⁴; Seth M. Pollack, MD⁵

¹University of Washington/Fred Hutch/Seattle Cancer Care Alliance, Seattle, Washington, UNITED STATES, ²Fred Hutchinson Cancer Research Center, Seattle, Washington, UNITED STATES, ³University of Washington, Seattle, Washington, UNITED STATES, ⁴Royal Marsden NHS Foundation Trust, London, England, UNITED KINGDOM, ⁵Northwestern University, Chicago, Illinois, UNITED STATES

Poster #231 #1818954

SURGICAL OUTCOMES FOLLOWING TREATMENT WITH PALBOCICLIB IN OF PATIENTS WITH WELL-DIFFERENTIATED AND DEDIFFERENTIATED RETROPERITONEAL LIPOSARCOMAS

Elise F. Nassif, MD¹; Christina L. Roland, MD²; Prapassorn Thirasastr, MD, MSc.²; Christopher P. Scally, MD²; Alejandra Zazour³; Raul F. Valenzuela, MD³; Keila E. Torres, MD, PhD²; Kelly K. Hunt, MD²; Barry W. Feig, MD²; Wei-Lien Wang, MD²; Alexander Lazar, MD, PhD²; Neeta Somaiah, MD²; Emily Z. Keung, MD²

¹MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ²The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ³MDACC, Houston, Texas, UNITED STATES

Poster #232 #1818935

PREDICTIVE VALUE OF NEUTROPHIL TO LYMPHOCYTE RATIO IN SOFT TISSUE SARCOMA: A NORTH AMERICAN PERSPECTIVE

Chloé Thériault, BSc; Dan Moldoveanu, BSc, MDCM, PhD Candidate; Abdulaziz Al-Mubarak, MD; Giuseppe Frenda, MD; Ian Watson, PhD; Sarkis Meterissian, MD; Sinziana Dumitru, MD, MSc (Epi), FRCS(C)
McGill University, Montreal, Province du Québec, CANADA

Poster #233 #1819016

THE COMPREHENSIVE COMPLICATION INDEX REFLECTS THE REAL IMPACT OF POSTOPERATIVE MORBIDITY AND IT IS A NOVEL COST ASSESSMENT TOOL FOR RETROPERITONEAL SOFT TISSUE SARCOMA SURGERY

Laura Ruspi, MD¹; Laura Samà, MD²; Fulvia Aymerito, MD³; Federica Barzaghi, MD³; Sonia Kumar, MD³; Federico Sicoli, MD⁴; Ferdinando Cananzi, MD⁵; Vittorio Lorenzo Quagliuolo, MD⁴

¹Humanitas Clinical and Research Center, Rozzano (MI), Lombardia, ITALY, ²Humanitas Clinical and Research Hospital/ Humanitas University, Milan, Lombardia, ITALY, ³Humanitas University, Milan, Lombardia, ITALY, ⁴Humanitas Clinical and Research Hospital, Milan, Lombardia, ITALY, ⁵Humanitas Clinical and Research Center, Humanitas University, Milan, Lombardia, ITALY

Poster #234 #1818961

POSTOPERATIVE OUTCOMES OF DISTAL PANCREATECTOMY FOR RETROPERITONEAL SARCOMA ABUTTING THE PANCREAS IN THE LEFT UPPER QUADRANT

Kyeong Deok Kim, MD; Kyo Won Lee, MD/Ph.D.; Manuel Lim, MD; Ji Eun Kwon, MD; Eun Sung Jeong, MD; Jaehun Yang, MD; Young Ju Oh, MD; Sunghae Park, MD; Sang Oh Yun, MD; Jae Berm Park, MD/PhD
Samsung Medical Center, Seoul, Seoul-t'ukpyolsi, Republic of Korea

Poster #235 #1818963

COMPARISON OF SURGICAL OUTCOMES BETWEEN LEIOMYOSARCOMA OF INFERIOR VENA CAVA AND OTHER LOCATIONS

Kyeong Deok Kim, MD; Kyo Won Lee, MD/PhD; Manuel Lim, MD; Eun Sung Jeong, MD; Jaehun Yang, MD; Ji Eun Kwon, MD; Young Ju Oh, MD; Sunghae Park, MD; Sang Oh Yun, MD; Jae Berm Park, MD, PhD
Samsung Medical Center, Seoul, Seoul-t'ukpyolsi, REPUBLIC OF KOREA

Poster #236 #1819028

DEDIFFERENTIATED LIPOSARCOMA OF THE RETROPERITONEUM: A TRANSCRIPTOMIC ANALYSIS OF PAIRED WELL DIFFERENTIATED AND DEDIFFERENTIATED TUMOUR COMPONENTS

Sandro Pasquali, MD, PhD¹; Stefano Percio, MSc, PhD²; Silvia Brich, PhD³; Alessia Bertolotti, MSc, PhD²; Marta Barisella, MD⁴; Paola Collini, MD⁵; Andrea Careno, Dr⁶; Edoardo Marchesi, MSc²; Arianna Micali, MSc²; Anna Maria Frezza, MD⁷; Dario Callegaro, MD⁸; Loris De Cecco, PhD⁶; Nadia Zaffaroni, PhD²; Alessandro Gronchi, MD⁹
¹Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ²Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Lombardia, ITALY, ³Fondazione IRCCS Istituto Nazionale dei Tumori (INT), Milano, Lombardia, ITALY, ⁴Department of Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ⁵Department of Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Lombardia, ITALY, ⁶Platform of Integrated Biology, Department of Applied Research and Technology Development, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Lombardia, ITALY, ⁷Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY, ⁸Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ⁹Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, Milan, Lombardia, ITALY

Poster #237 #1819052

CINSARC IS PROGNOSTIC IN PATIENTS WITH RETROPERITONEAL SARCOMA (RPS) BUT DOES NOT ADD TO CLINICAL-BASED NOMOGRAMS

Dario Callegaro, MD¹; Andrea Careno, Dr²; Silvia Brich, PhD³; Alessia Bertolotti, PhD⁴; Gabriele Callegaro, MSc⁴; Marta Barisella, MD⁵; Paola Collini, MD⁶; Arianna Micali, MSc⁷; Edoardo Marchesi, MSc⁷; Anna Maria Frezza, MD⁴; Loris De Cecco, PhD²; Rosalba Miceli, PhD¹; Sandro Pasquali, MD, PhD⁸; Alessandro Gronchi, MD⁹
¹Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ²Platform of Integrated Biology, Department of Applied Research and Technology Development, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Lombardia, ITALY, ³Fondazione IRCCS Istituto Nazionale dei Tumori (INT), Milano, Lombardia, ITALY, ⁴Fondazione IRCCS Istituto Nazionale Tumori Milan, Milan, Lombardia, ITALY, ⁵Department of Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ⁶Department of Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Lombardia, ITALY, ⁷Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Lombardia, ITALY, ⁸Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ⁹Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, Milan, Lombardia, ITALY

Poster #238 #1818879

DISCOVERY OF A POTENT AND SELECTIVE BRD9 DEGRADER FHD-609 FOR THE TREATMENT OF SYNOVIAL SARCOMA AND OTHER CANCERS WITH DYSREGULATION OF CHROMATIN REMODELER COMPLEXES

Qianhe Zhou, PhD; Huawei (Ray) Chen, PhD; Mengni (Christina) Xu, MS; Ammar Adam, PhD; Marissa, Martinez, PhD; Sarah Reilly, MD; Sean Brennan, BS; Salonee Parikh, MS; Ketaki Adhikari, MS; Michael Bocker, PhD; Kimberly Barnash, PhD; Luis Soares, PhD; Jordana Muwanguzi, MS; Zhaoxia (Joyce) Yang, PhD; Jason Lowe, PhD; David Lahr, PhD; Laura Zawadzke, PhD; Johannes Voigt, PhD; Liyue Huang, PhD; Sabine Ruppel, PhD; Murph Hentemann, PhD; Scott Innis, MS; Homan Chan, PhD; Ryan Kruger, PhD; David Millan, PhD; Steve Bellon, PhD; Sam Agresta, MD; Carl Decicco, PhD; Salih Topal, PhD; Hsin-Jung Wu, PhD
Foghorn Therapeutics, Cambridge, Massachusetts, UNITED STATES

Poster #239 #1819049

EXTRASKELETAL MYXOID CHONDROSARCOMA: A RETROSPECTIVE CLINICOPATHOLOGIC STUDY OF 15 CASES

Linus Lee, BE¹; Pavan Kottamasu, MS¹; Michael P. Fice, MD¹; Matthew Cohn, MD¹; Charles A. Gusho, BS²; Steven Gitelis, MD¹; Alan T. Blank, MD, MS¹
¹Rush University Medical Center, Chicago, Illinois, UNITED STATES, ²Rush University Medical Center, Milwaukee, Wisconsin, UNITED STATES

Poster #240 #1818861

THE POTENTIAL LONG-TERM COMPARATIVE EFFECTIVENESS OF LAROTRECTINIB VS. DOXORUBICIN IN COMBINATION WITH IFOSFAMIDE FOR TREATMENT OF METASTATIC TRK FUSION SOFT TISSUE SARCOMA

Kangho Suh, PharmD, PhD¹; Josh J. Carlson, MPH, PhD²; Fang Xia, PhD³; Todd Williamson, PhD³; Sean D. Sullivan, PhD²,
¹University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES, ²Comparative Health Outcomes, Policy, and Economics (CHOICE) Institute, University of Washington, Seattle, Washington, UNITED STATES, ³Bayer U.S. LLC, Whippany, New Jersey, UNITED STATES

Poster #241 #1818904

LAROTRECTINIB IN PEDIATRIC PATIENTS WITH TRK FUSION SARCOMAS: UPDATED EFFICACY AND SAFETY

Catherine M. Albert, MD¹; Stefan Bielack, MD²; Daniel Orbach, MD³; Steven G. DuBois, MD⁴; Noah C. Federman, MD⁵; Birgit Georger, MD, PhD⁶; Leo Mascarenhas, M.D, M.S.⁷; Ramamoorthy Nagasubramanian, MD⁸; Ruihua Xu, MD, PhD⁹; Julia Chisholm, BMBCh, PhD, FRCPC¹⁰; Soledad Gallego Melcon, MD, PhD¹¹; Hiroaki Goto, MD, PhD¹²; Daniel A. Morgenstern, MB BChir, PhD¹³; Cormac Owens, MD¹⁴; Alberto Pappo, MD¹⁵; Sébastien Perreault, MD, FRCPC¹⁶; Johannes Schulte, MD¹⁷; Neerav Shukla, MD¹⁸; Christian Michel Zwaan, MD, PhD¹⁹; Ricarda Norenberg, MS²⁰; Pierre Avis, MD²¹; Esther De La Cuesta, MD, MBA²²; Theodore W. W. Laetsch, MD²³; Cornelis M. van Tilburg, MD, PhD²⁴
¹Seattle Children's Hospital, University of Washington, Fred Hutchinson Cancer Research Center, Seattle, Washington, UNITED STATES, ²Klinikum Stuttgart-Olgahospital, Stuttgart, Baden-Wurtemberg, GERMANY, ³Institut Curie and University of Paris, Paris, Ile-de-France, FRANCE, ⁴Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, Massachusetts, UNITED STATES, ⁵UCLA Medical Center, Los Angeles, California, UNITED STATES, ⁶Gustave Roussy Cancer Center, Université Paris-Saclay, INSERM U1015, Villejuif, Ile-de-France, FRANCE, ⁷Children's Hospital Los Angeles, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES, ⁸Nemours Children's Hospital, Orlando, FL, ⁹Sun Yat-sen University Cancer Center, Guangzhou, Guangdong, CHINA (PEOPLE'S REPUBLIC), ¹⁰Children and Young Peoples Unit, Royal Marsden Hospital, Surrey, England, UNITED KINGDOM, ¹¹Pediatric Oncology and Hematology, Vall d'Hebron Children's Hospital, Barcelona, Catalonia, SPAIN, ¹²Kanagawa Children's Medical Center, Yokohama, Kanagawa, JAPAN, ¹³Hospital for Sick Children, Toronto, Ontario, CANADA, ¹⁴The National Children's Cancer Centre, Children's Health Ireland, Dublin, Dublin, IRELAND, ¹⁵St. Jude Children's Research Hospital, Memphis, TN, ¹⁶Department of Neurosciences, CHU Sainte Justine, Montreal, Province du Québec, CANADA, ¹⁷Charité-Universitätsmedizin Berlin, Berlin, Berlin, GERMANY, ¹⁸Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES, ¹⁹Prinses Maxima Centrum, Utrecht, Utrecht, NETHERLANDS, ²⁰Chrestos Concept GmbH & Co. KG, Essen, Nordrhein-Westfalen, GERMANY, ²¹Bayer Pharmaceuticals, Lille, Nord-Pas-de-Calais, FRANCE, ²²Bayer HealthCare Pharmaceuticals, Inc., Whippany, New Jersey, UNITED STATES, ²³University of Texas Southwestern Medical Center/Children's Health, Dallas, Texas, UNITED STATES, ²⁴Hopp Children's Cancer Center Heidelberg (KiTZ), Heidelberg University Hospital and German Cancer Research Center (DKFZ), Heidelberg, Baden-Wurtemberg, GERMANY

Poster #242 #1818947

SARCOMA AS AN EXTRACOLONIC MALIGNANCY OF LYNCH SYNDROME

Steven Bialick, DO, MS¹; Brianna Valdes²; Philippos Costa, MD³; Priscila Barreto Coelho, MD³; Andrea Espejo-Freire, MD³; Gina D'Amato, MD⁴; Emily Jonczak, MD⁵; Aditi Dhir, MD³; Andrew Rosenberg, MD³; Irman Forghani, MD³; Jonathan C. Trent, MD, PhD⁵

¹University of Miami/Sylvester Comprehensive Cancer Center, Miami, Florida, UNITED STATES, ²University of Miami, Miller School of Medicine, Miami, Florida, UNITED STATES, ³University of Miami, Miami, Florida, UNITED STATES, ⁴Medical Oncology, Sylvester Comprehensive Cancer Center/University of Miami, Miami, Florida, UNITED STATES, ⁵Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES

Poster #243 #1819076

ERCC2 PATHOGENIC VARIANT IDENTIFIED IN EPITHELIOD SARCOMA

Steven Bialick, DO, MS¹; Kurt Statz-Geary²; Emily Jonczak, MD³; Gina D'Amato, MD⁴; Jonathan C. Trent, MD, PhD³; Andrew Rosenberg, MD PhD⁵; Elizabeth Montgomery, MD⁶; Aditi Dhir, MD⁶, ¹University of Miami/Sylvester Comprehensive Cancer Center, Miami, Florida, UNITED STATES, ²University of Miami, Miller School of Medicine, Miami, Florida, UNITED STATES, ³Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES, ⁴Medical Oncology, Sylvester Comprehensive Cancer Center/University of Miami, Miami, Florida, UNITED STATES, ⁵University of Miami, University of Miami, Florida, UNITED STATES, ⁶University of Miami, Miami, Florida, UNITED STATES

Poster #244 #1818905

TRK FUSION SARCOMAS IN LAROTRECTINIB TRIALS: CONCORDANCE OF INDEPENDENT AND LOCAL DIAGNOSIS

Jessica L. Davis, MD¹; Alexander Lazar, MD, PhD²; Ricarda Norenberg, MS³; Marc Fellous, MD⁴; David S. Hong, MD²; Theodore W. W. Laetsch, MD⁵; Alexander Drilon, MD⁶; Angelo Paolo Dei Tos, MD⁷

¹Oregon Health & Science University, Portland, Oregon, UNITED STATES, ²The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ³Chrestos Concept GmbH & Co. KG, Essen, Nordrhein-Westfalen, GERMANY, ⁴Bayer HealthCare Pharmaceuticals, Basel, Basel-Stadt, SWITZERLAND, ⁵University of Texas Southwestern Medical Center/Children's Health, Dallas, Texas, UNITED STATES, ⁶Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES, USA and Weill Cornell Medical College, New York, New York, UNITED STATES, ⁷Università di Padova (UniPD), Padova, Veneto, ITALY

Poster #245 #1818958

ROLE OF PREOPERATIVE RADIOTHERAPY IN THE CURATIVE MANAGEMENT OF ABDOMINAL SOLITARY FIBROUS TUMOUR

Karineh Kazazian, MD, PhD, FRCSC¹; Harini Suraweera, MSc²; Deanna Ng, MD³; Peter Chung, MD⁴; Charles Catton, MD, FRCPC⁴; David Shultz, MD, PhD⁵; Philip Wong, MD, MSc, MDCM, FRCPC⁴; Rebecca A. Gladdy, MD, PhD, FRCSC, FACS²; Savtaj Brar, MD, MSc, FRCSC⁶; Elizabeth G. Demicco, MD, PhD⁷; Carol J. Swallow, MD, PhD, FRCSC, FACS²

¹Department of Surgical Oncology, Princess Margaret Hospital, University Health Network and Mount Sinai Hospital; Lunenfeld Tanenbaum Research Institute, Sinai Health System, Toronto, Toronto, Ontario, CANADA, ²Department of Surgical Oncology, Princess Margaret Hospital, University Health Network and Mount Sinai Hospital, Toronto; Lunenfeld Tanenbaum Research Institute, Sinai Health System, Toronto, Toronto, Ontario, CANADA, ³University of Toronto, Toronto, Ontario, CANADA, ⁴Department of Radiation Oncology, Princess Margaret Hospital, University Health Network, Toronto, Toronto, Ontario, CANADA, ⁵Department of Radiation Oncology, Princess Margaret Hospital, University Health Network, University of Toronto, Toronto, Ontario, CANADA, ⁶Department of Surgical Oncology, Princess Margaret Hospital, University Health Network and Mount Sinai Hospital, Toronto, Toronto, Ontario, CANADA, ⁷Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, Toronto, Ontario, CANADA

Poster #246 #1819048

SURGICAL RESECTION OF BORDERLINE AND MALIGNANT PHYLLODES TUMOURS OF THE BREAST: EXPERIENCE AT A TERTIARY CENTRE

Gausihi Sivarajah, MBBS FRACS¹; Charlotte Benson, BMed Sci, FRCR, MD¹; Robin L Jones, MD, PhD²; Shane Zaidi¹; Gerald Gui¹; Nicola Roche¹; Peter Barry¹; Fiona MacNeill¹; Dirk Strauss, MD³; Andrew J. Hayes, PhD³; Myles Smith, PhD³; Aisha Miah¹

¹The Royal Marsden NHS Foundation Trust, London, England, UNITED KINGDOM, ²Royal Marsden NHS Foundation Trust, London, England, UNITED KINGDOM, ³The Royal Marsden Hospital NHS Foundation Trust, London, England, UNITED KINGDOM

Poster #247 #1818888

VALIDATION OF A NOVEL RISK SCORE TO PREDICT EARLY AND LATE RECURRENCE IN SOLITARY FIBROUS TUMOR

Kjetil Boye, MD, PhD¹; Tatiana Georgiesh, MD¹; Ninna Aggerholm Pedersen, MD, MSc, PhD, Associate professor²; Patrick Schöffski, MD³; Yifan Zhang⁴; Andrea Napolitano, MD, PhD⁵; Judith V.M.G. Bovée, MD PhD⁶; Åse Hjelle, MD⁷; Gordon Tang, MD⁸; Mateusz Spalek, MD, PhD⁹; Margherita Nannini, MD¹⁰; David Swanson, PhD¹; Raf Sciort, MD, PhD¹¹; Asle C. Hesla, MD¹²; Paul Huang, MD, PhD¹³; Desiree Dorleijn, MD⁶; Hans Kristian Haugland, MD, PhD⁷; Maribel Lacambra, MD¹⁴; Jacek Skoczylas, MD⁹; Maria A. A. Pantaleo, MD, PhD¹⁰; Rick L. Haas, MD PhD¹⁵; Anna M. Czarnecka, MD, PhD⁹; Herbert Loong, MBBS, PDipMDPath, MRCP, FRCP Edin, FHKCP, FHKAM(Medicine)¹⁶; Nina L. Jebsen, MD, PhD⁷; Michiel van de Sande, MD PhD⁶; Robin L. Jones, BSc, MBBS, MD¹⁷; Felix Haglund, MD, PhD¹⁸; Iris Timmermans, MD¹⁹; Akmal Safwat, MD, M.Sc., D.M.Sc²⁰; Bodil Bjerkehagen, MD, PhD¹

¹Oslo University Hospital, Oslo, Oslo, NORWAY, ²Aarhus University Hospital, Aarhus, Denmark, Aarhus, Midtjylland, DENMARK, ³General Medical Oncology, University Hospitals Leuven – Campus Gasthuisberg, Leuven, Brabant Wallon, BELGIUM, ⁴Department of Pathology and Cancer Diagnostics, Karolinska University Hospital, Stockholm, Sweden and Department of Oncology-Pathology, Karolinska Institute, Stockholm, Sweden, Solna, Stockholms Lan, SWEDEN, ⁵The Royal Marsden Hospital and The Institute of Cancer Research, London, England, UNITED KINGDOM, ⁶Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ⁷Haukeland University Hospital, Bergen, Hordaland, NORWAY, ⁸Prince of Wales Hospital, Hong Kong SAR, Guangdong, CHINA (PEOPLE'S REPUBLIC), ⁹Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Mazowieckie, POLAND, ¹⁰IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Emilia-Romagna, ITALY, ¹¹Department of Pathology, KU Leuven and University Hospitals Leuven, Leuven, Belgium, Leuven, Vlaams-Brabant, Belgium, ¹²Karolinska University Hospital, Stockholm, Stockholms Lan, SWEDEN, ¹³The Institute of Cancer Research, London, England, UNITED KINGDOM, ¹⁴The Chinese University of Hong Kong, Hong Kong SAR, Guangdong, China (People's Republic), ¹⁵The Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS, ¹⁶The Chinese University of Hong Kong, Hong Kong, HONG KONG, ¹⁷The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, England, UNITED KINGDOM, ¹⁸Department of Pathology and Cancer diagnostics, Karolinska University Hospital, Stockholm, Sweden and Department of Oncology-Pathology, Karolinska Institute, Stockholm, Sweden, Stockholm, Stockholms Lan, SWEDEN, ¹⁹University Hospitals Leuven, Leuven, Vlaams-Brabant, BELGIUM, ²⁰Aarhus University Hospital, Aarhus, Midtjylland, DENMARK

Poster #248 #1818964

ACTIVITY OF STANDARD SOFT TISSUE SARCOMA-TYPE SYSTEMIC THERAPY IN CLEAR CELL SARCOMA (CCS): A RETROSPECTIVE INTERNATIONAL SERIES FROM THE WORLD SARCOMA NETWORK (WSN)

Alannah Smrke, MD¹; Anna Maria Frezza, MD²; Claudia Giani, MD³; Neeta Somaiah, MD⁴; Mehdi Brahmi, MD PhD⁵; Anna M. Czarnecka, MD⁶; Piotr Rutkowski, MD, PhD⁷; Winette T. A. van der Graaf, MD PhD⁸; Giacomo Giulio Baldi, MD⁹; Elizabeth Connolly, MBChB MCRPUK FRACP¹⁰; Florence Duffaud, MD¹¹; Hans Gelderblom, MD, PhD¹²; Vivek Bhadri, MD¹³; Peter Grimison, BSc(Med) MBBS(Hons) MPH PhD FRACP¹⁴; Annabelle Mahar, MD¹³; Silvia Stacchiotti, MD²; Robin L. Jones, BSc, MBBS, MD¹⁵

¹BC Cancer, Vancouver, British Columbia, CANADA, ²Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY, ³Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY, ⁴The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁵Cancer Research Centre of Lyon, Lyon, Auvergne, FRANCE, ⁶Maria Sklodowska-Curie National Research Institute of Oncology, Warszawa, Mazowieckie, POLAND, ⁷Department of Soft Tissue/Bone Sarcoma and Melanoma; Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Mazowieckie, POLAND, ⁸Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS, ⁹Department of Medical Oncology, Hospital of Prato, Prato, Italy, Prato, Toscana, ITALY, ¹⁰ProCan®, Children's Medical Research Institute, Faculty of Medicine and Health, The University of Sydney, Chris O'Brien Lifecare Hospital, Sydney, Camperdown, New South Wales, AUSTRALIA, ¹¹Marseille University Hospital Timone, Marseille, Languedoc-Roussillon, FRANCE, ¹²Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ¹³Chris O'Brien Lifecare, Camperdown, New South Wales, AUSTRALIA, ¹⁴Chris O'Brien Lifecare, Sydney, New South Wales, AUSTRALIA, ¹⁵The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, England, UNITED KINGDOM

Poster #249 #1819024

LURBINECTIDIN INHIBITS THE EWS-WT1 TRANSCRIPTION FACTOR IN DESMOPLASTIC SMALL ROUND CELL TUMOR

Jenna M. Gedminas, MD¹; Rebecca Kaufman, MS²; Elissa Boguslawski¹; Amy Gross³; Marie Adams, MS⁴; Ian Beddows, PhD⁴; Ryan D. Roberts, MD, PhD⁵; Patrick Grohar, MD, PhD⁶

¹Division of Oncology, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, UNITED STATES,

²Childrens Hospital of Philadelphia, Philadelphia, Pennsylvania, UNITED STATES, ³Center for Childhood Cancer, Nationwide Children's Hospital, The Ohio State University James Comprehensive Cancer Center, Columbus, Ohio, UNITED STATES, ⁴Van Andel Research Institute, Grand Rapids, Michigan, UNITED STATES, ⁵Nationwide Children's Hospital, Columbus, Ohio, UNITED STATES, ⁶Division of Oncology, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, UNITED STATES

Poster #250 #1818945

ACTIVITY OF PAN-RAF INHIBITOR DAY101 IN A PEDIATRIC PATIENT WITH A RECURRENT SPINDLE CELL SARCOMA HARBORING A NOVEL SNX8:BRAF GENE FUSION

Katharine Offer, MD¹; Michael McGuire, MD²; Eleni Venetsanakos, PhD³; Samuel C. Blackman, MD, PhD³; Kunchang Song, MD⁴; Michael Goldfischer, MD⁴; Michael C. Cox, PharmD³

¹Joseph M. Sanzari Children's Hospital, Hackensack Meridian Health, Hackensack, New Jersey, UNITED STATES,

²Department of Radiology, Hackensack Meridian School of Medicine, Hackensack, New Jersey, UNITED STATES,

³Day One Biopharmaceuticals, South San Francisco, California, UNITED STATES, ⁴Department of Pathology, Hackensack Meridian Health, Hackensack, New Jersey, UNITED STATES

Poster #251 #1818916

BCOR ALTERED SOFT TISSUE SARCOMAS

Sarah Whittle, MD, MS; Rajkumar Venkatramani, MD

Baylor College of Medicine, Houston, Texas, UNITED STATES

Poster #252 #1818903

LAROTRECTINIB IN ADULT PATIENTS WITH TRK FUSION SARCOMAS: UPDATED EFFICACY AND SAFETY

Shivaani Kummar, MD¹; Lin Shen, MD²; David S. Hong, MD³; Ray McDermott, M.B. B.Ch. B.A.O., PhD, M.B.A., F.R.C.P.I.⁴; Vicki L. Keedy, MD, MSCI⁵; Michela Casanova, MD⁶; George D. Demetri, MD⁷; Afshin Dowlati, MD⁸; Soledad Gallego Melcon, MD, PhD⁹; Ulrik N. Lassen, MD, PhD¹⁰; Serge Levyraz, MD¹¹; Tianshu Liu, MD¹²; Victor Moreno, MD, PhD¹³; Christine Bestvina, MD¹⁴; Tejas Patil, MD¹⁵; Atrayee BasuMallick, MD¹⁶; Nuno Sousa, MD¹⁷; Makoto Tahara, MD, PhD¹⁸; David S. Ziegler, MBBS, BSc (Med), FRACP, MD¹⁹; Ricarda Norenberg, MS²⁰; Pierre Avis, MD²¹; Nicoletta Brega, MD²²; Alexander Drilon, MD²³; Daniel S.W. Tan, MD²⁴

¹Knight Cancer Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES, ²Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Peking University Cancer Hospital & Institute, Beijing, Beijing, CHINA (PEOPLE'S REPUBLIC), ³The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁴St Vincent's University Hospital and Cancer Trials Ireland, Dublin, Dublin, IRELAND,

⁵Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES, ⁶Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ⁷Dana-Farber Cancer Institute and Ludwig Center at Harvard University, Boston,

Massachusetts, UNITED STATES, ⁸University Hospitals Ahuja Medical Center, Beachwood, Ohio, UNITED STATES,

⁹Pediatric Oncology and Hematology, Vall d'Hebron Children's Hospital, Barcelona, Catalonia, SPAIN, ¹⁰Department of

Oncology, Rigshospitalet, Copenhagen, Hovedstaden, DENMARK, ¹¹Charité – Universitätsmedizin, Berlin, Berlin, Berlin, GERMANY, ¹²Zhongshan Hospital-Fudan University, Fudan, Shanghai, CHINA (PEOPLE'S REPUBLIC), ¹³Department of

Medical Oncology, Hospital Fundación Jimenez Diaz, Madrid, Madrid, SPAIN, ¹⁴Northwestern University, Chicago,

Illinois, UNITED STATES, ¹⁵Department of Medicine, Division of Medical Oncology, University of Colorado, Denver,

Aurora, Colorado, UNITED STATES, ¹⁶Sidney Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, Pennsylvania, UNITED STATES, ¹⁷Instituto Portugues de Oncologia do Porto Francisco Gentil, Porto, Porto, PORTUGAL,

¹⁸National Cancer Center Hospital East, Kashiwa, Ibaraki, JAPAN, ¹⁹Sydney Children's Hospital, Randwick, NSW, Australia and School of Women's and Children's Health, University of New South Wales Sydney, Sydney, New South

Wales, AUSTRALIA, ²⁰Chrestos Concept GmbH & Co. KG, Essen, Nordrhein-Westfalen, GERMANY, ²¹Bayer Pharmaceuticals, Lille, Nord-Pas-de-Calais, FRANCE, ²²Bayer Pharmaceuticals, Milan, Lombardia, ITALY, ²³Memorial Sloan Kettering Cancer

Center, New York, NY, USA and Weill Cornell Medical College, New York, New York, UNITED STATES, ²⁴Division of

Medical Oncology, National Cancer Centre Singapore, Duke-NUS Medical School, Singapore, SINGAPORE

Poster #253 #1819054

ULTRA-RARE AND OTHER RARE ADVANCED SARCOMA TREATED WITH TRABECTEDIN: A POST-HOC ANALYSIS OF A NON-INTERVENTIONAL, RETROSPECTIVE, MULTICENTER STUDY OF THE ITALIAN SARCOMA GROUP

Emanuela Palmerini, MD¹; Roberta Sanfilippo, MD²; Giovanni Grignani, MD³; Angela Buonadonna, MD⁴; Antonella Romanini, MD⁵; Giuseppe Badalamenti, MD, PhD⁶; Virginia Ferraresi, MD⁷; Bruno Vincenzi, MD, PhD⁸; Alessandro Comandone, MD⁹; Antonio Pzzolorusso, MD¹⁰; Antonella Brunello, MD¹¹; Fabio Gelsomino, MD¹²; Tommaso De Pas, MD¹³; Toni Ibrhaim, MD, PhD¹; Lorena Guerrieri, MD¹⁴; Federica Grosso, MD¹⁵; Francesca Zanelli, MD¹⁶; Maria A. A. Pantaleo, MD, PhD¹⁷; Laura Milesi, MD¹⁸; Libero Ciuffreda, MD¹⁹; Vittorio Ferrari, MD²⁰; Emanuela Marchesi, PhD²¹; Irene Quattrini, PhD¹; Alberto Righi, MD²²; Elisabetta Setola, MD, PhD²³; Elisa Carretta, PhD¹; Paolo G. Casali, MD²⁴; Pero Picci, MD²¹; Stefano Ferrari, MD¹

¹IRCCS Istituto Ortopedico Rizzoli, Bologna, Emilia-Romagna, ITALY, ²Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ³Department of Medical Oncology-Sarcoma Unit, Candiolo Cancer Institute FPO-IRCCS, Candiolo (TO), Italy, Candiolo, Piemonte, ITALY, ⁴Centro di Riferimento Oncologico di Aviano (CRO Aviano), Aviano, Friuli-Venezia Giulia, ITALY, ⁵Azienda Ospedaliero-Universitaria Pisana, Pisa, Toscana, ITALY, ⁶Department of Medical Oncology, Policlinico "Paolo Giaccone", University of Palermo, Palermo, Italy, Palermo, Sicilia, ITALY, ⁷IRCCS Regina Elena National Cancer Institute – Division of Medical Oncology, Rome, Lazio, ITALY, ⁸Department of Medical Oncology, Università Campus Bio-Medico di Roma, Rome, Italy, Roma, Lazio, ITALY, ⁹SC Oncologia ASL Città di Torino, Torino, Piemonte, ITALY, ¹⁰Istituto Nazionale Tumori IRCCS "Fondazione G. Pascale", Napoli, Campania, ITALY, ¹¹Istituto Oncologico Veneto IOV - IRCCS, Padova, Veneto, ITALY, ¹²Department of Oncology and Hematology, University Hospital of Modena, Modena, Emilia-Romagna, ITALY, ¹³Unit of medical oncology Sarcomas, Thymomas and rare tumors, European Institute of Oncology, IRCCS, Milan, Lombardia, ITALY, ¹⁴IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) "Dino Amadori, Meldola, Emilia-Romagna, ITALY, ¹⁵Mesothelioma and Rare Cancer Unit, Azienda Ospedaliera SS. Antonio e Biagio General Hospital, Alessandria, Piemonte, ITALY, ¹⁶Arcispedale Santa Maria Nuova IRCCS Reggio Emilia, Reggio Emilia, Emilia-Romagna, ITALY, ¹⁷IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Emilia-Romagna, ITALY, ¹⁸Department of Oncology, ASST. Papa Giovanni XXIII Hospital, Bergamo, Lombardia, ITALY, ¹⁹Azienda Ospedaliero Universitaria San Giovanni Battista, Molinette, Torino, Piemonte, ITALY, ²⁰Oncologia Medica, Università degli Studi di Brescia, Brescia, Lombardia, ITALY, ²¹Italian Sarcoma Group, Bologna, Emilia-Romagna, ITALY, ²²Rizzoli Orthopaedic Institute, Bologna, Emilia-Romagna, ITALY, ²³Alma Mater Studiorum, University of Bologna, Bologna, Emilia-Romagna, ITALY, ²⁴Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY

Poster #254 #1819056

ETV4/5 DRIVE SYNOVIAL SARCOMA THROUGH CONTROL OF THE CELL CYCLE AND THE DUX4 EMBRYONIC PATHWAY

Josiane E. Eid, MD¹; Joanna Desalvo, Sr. Research Associate²; Yuguang Ban, PhD²; Luyuan Li, PhD¹; Xiaodian Sun, PhD²; Zhijie Jiang, PhD²; Darcy A. Kerr, MD²; Mahsa Khanlari, MD³; Maria Boulina, PhD²; Mario R. Capocchi, PhD⁴; Juha M. Partanen, PhD⁵; Lin Chen, PhD⁶; Tadashi Kondo, MD, Ph.D⁷; David M. Ornitz, MD, PhD⁸; Jonathan C. Trent, MD, PhD⁹

¹Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES, ²University of Miami, Miller School of Medicine, Miami, Florida, UNITED STATES, ³MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁴University of Utah School of Medicine, Salt Lake City, Utah, UNITED STATES, ⁵University of Helsinki, Helsinki, Kainuu, FINLAND, ⁶Army Medical University, Chongqing, Chongqing, CHINA (PEOPLE'S REPUBLIC), ⁷Division of Rare Cancer Research, National Cancer Center Research Institute, Chuo-ku, Tokyo, JAPAN, ⁸Washington University School of Medicine, St. Louis, Missouri, UNITED STATES, ⁹Sylvester Comprehensive Cancer Center, Miami, Florida, UNITED STATES

Poster #255 #1818860

PRECISION ONCOLOGY IN SARCOMA DRUG DEVELOPMENT: IMPACT OF BIOMARKER MATCHING ON OUTCOMES IN PHASE I CLINICAL TRIALS

Roberto Carmagnani Pestana, MD¹; Justin Moyers, MD²; Nelson Hamerschlag, MD, PhD¹; Jason Roszik, PhD²; Shiraj Sen, MD, PhD³; David S. Hong, MD²; Aung Naing, MD²; Cynthia Herzog, MD²; Siqing Fu, MD, PhD²; Vinod Ravi, MD²; Shreyaskumar Patel, MD⁴; J Andrew Livingston, MD⁵; Neeta Somaiah, MD²; Anthony P. Conley, MD⁵; Funda Meric-Bernstam, MD²; Vivek Subbiah, MD²

¹Hospital Israelita Albert Einstein, São Paulo, Sao Paulo, BRAZIL, ²The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ³Sarah Cannon Research Institute, Denver, Colorado, UNITED STATES, ⁴MDACC, Houston, Texas, UNITED STATES, ⁵MD Anderson Cancer Center, Houston, Texas, UNITED STATES

Poster #256 #1818991

RESULTS OF THE PHASE 1B SOFT TISSUE SARCOMA PORTION OF A GLOBAL RANDOMIZED DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF TAZEMETOSTAT PLUS DOXORUBICIN AS FRONTLINE THERAPY FOR ADVANCED EPITHELIOID SARCOMA

Sant P. Chawla, MD¹; Gerald Falchook, MD²; Melissa Burgess, MD³; James L. Chen, MD⁴; Robin L. Jones, BSc, MBBS, MD⁵; Victoria T. Chua-Alcala, MD¹; Coya Tapia, MD, PhD⁶; Jessica Ainscough, BA⁶; Anthony Hamlett, PhD⁶; Melinda S. Merchant, MD, PhD⁶; Rashmi Chugh, MD⁷

¹Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES, ²Sarah Cannon Research Institute at HealthONE, Denver, Colorado, UNITED STATES, ³University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES, ⁴Ohio State University, Columbus, Ohio, UNITED STATES, ⁵The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, England, UNITED KINGDOM, ⁶Epizyme, Inc., Cambridge, Massachusetts, UNITED STATES, ⁷University of Michigan, Ann Arbor, Michigan, UNITED STATES

Poster #257 #1819000

A MULTICENTER, RETROSPECTIVE ANALYSIS OF CLINICAL CHARACTERISTICS AND TREATMENT PATTERNS FOR SPINDLE CELL AND SCLEROSING RHABDOMYOSARCOMA

Elizabeth J. Davis, MD¹; Sheima Farag, MD²; Hilary Dietz, MD³; Angela C. Hirbe, MD, PhD⁴; Michael J. Wagner, MD⁵; Kristen N. Ganjoo, MD⁶; Robin Jones, MD²; Vicki L. Keedy, MD, MSCI¹; Nam Bui, MD⁷

¹Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES, ²Royal Marsden Hospital, London, England, UNITED KINGDOM, ³Washington University St. Louis, St. Louis, Missouri, UNITED STATES, ⁴Washington University School of Medicine, St. Louis, Missouri, UNITED STATES, ⁵University of Washington/Fred Hutch/Seattle Cancer Care Alliance, Seattle, Washington, UNITED STATES, ⁶Stanford Cancer Center, Stanford, California, UNITED STATES, ⁷Stanford University Department of Oncology, Stanford, California, UNITED STATES

Poster #258 #1819019

PRIMARY SARCOMAS OF THE BREAST-SINGLE INSTITUTION EXPERIENCE

Hanna Koseła-Paterczyk, MD PhD¹; Anna Mariuk-Jarema, MD¹; Paweł Teterycz, MD PhD¹; Michał Kunkiel, MD²; Maria Krotewicz, MD¹; Joanna Placzke, MD¹; Zbigniew Nowecki, MD PhD²; Piotr Rutkowski, MD, PhD³

¹Maria Skłodowska-Curie Institute - Oncology Center; Department of Soft Tissue/Bone Sarcoma and Melanoma, Warsaw, Mazowieckie, POLAND, ²Department of Breast Cancer and Reconstructive Surgery, Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Mazowieckie, POLAND, ³Department of Soft Tissue/Bone Sarcoma and Melanoma; Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Mazowieckie, POLAND

Poster #259 #1818987

INFLAMMATORY MYOFIBROBLASTIC TUMOR- REVISITING A RARE DISEASE IN A REFERENCE CENTER

Inês C. Oliveira, MD¹; Emanuel Gouveia, MD²; Teresa Alexandre, MD²; Isália Miguel, MD²; Hugo Vasques, MD²; Maria Manuel Lemos, MD²; Nuno Abecasis, MD²; Margarida Ferreira, MD²

¹Instituto Português de Oncologia de Lisboa Francisco Gentil, Setúbal, Setubal, PORTUGAL, ²Instituto Português de Oncologia de Lisboa Francisco Gentil, Lisboa, Lisboa, PORTUGAL

Poster #260 #1818992

CHANCES OF LONG-TERM EVENT-FREE SURVIVAL FOR PATIENTS WITH DESMOPLASTIC SMALL ROUND CELL TUMOR (DSRCT)

Claudia Giani, MD¹; Silvia Stacchiotti, MD²; Salvatore Provenzano, MD²; Anna Maria Frezza, MD²; Sandro Pasquali, MD, PhD³; Rossella Maria Bertulli, MD⁴; Michela Casanova, MD⁴; Stefano Chiaravalli, MD⁴; Paola Collini, MD⁵; Gianpaolo Dagrada, MD⁴; Lorenza Gandola, MD⁴; Carlo Morosi, MD⁶; Stefano Radaelli, MD⁴; Claudia Sangalli, MD⁴; Paolo G. Casali, MD²; Andrea Ferrari, MD⁴; Alessandro Gronchi, MD⁷

¹Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY, ²Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY, ³Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ⁴Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ⁵Department of Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Lombardia, ITALY, ⁶Department of Radiology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, Milan, Lombardia, ITALY, ⁷Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, Milan, Lombardia, ITALY

Poster #261 #1818873

WHAT ARE PREOPERATIVE RISK FACTORS FOR FIBROSARCOMATOUS TRANSFORMATION IN DERMATOFIBROSARCOMA PROTUBERANS (DFSP)

Matthew T. Houdek, MD¹; Kim M. Tsoi, MD, PhD²; Sarah Almubarak, BS²; Matthew R. Claxton, BS¹; Katerine Mallett, MD¹; Peter C. Ferguson, MD²; Peter S. Rose, MD¹; Jay S. Wunder, MD²

¹Mayo Clinic, Rochester, Minnesota, UNITED STATES, ²University of Toronto, Mount Sinai Hospital, Toronto, Ontario, CANADA



Rain Therapeutics is proud to sponsor
the 2021 CTOS Annual Meeting

Learn more about Rain Therapeutics at
<https://rainthera.com/>





Poster #001 #1818993

IMMUNE INFILTRATE AND CELL CYCLE / DIFFERENTIATION PROGRAMS ARE INVERSELY CORRELATED IN MYXOID LIPOSARCOMA AND IDENTIFY HIGHER RISK PATIENTS

Andrea Careno, Dr¹; Loris De Cecco, PhD¹; Laura Bergamaschi, Dr²; Marta Barisella, MD³; Paola Collini, MD⁴; Sandro Pasquali, MD, PhD⁵; Chiara Castelli, PhD²; Alessandro Gronchi, MD⁶; Viviana Vallacchi, PhD²

¹Platform of Integrated Biology, Department of Applied Research and Technology Development, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Lombardia, ITALY, ²Immunotherapy of Human Tumors, Department of Research, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Lombardia, ITALY, ³Department of Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ⁴Department of Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Lombardia, ITALY, ⁵Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ⁶Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, Milan, Lombardia, ITALY

Objective: Myxoid liposarcoma (MLS) is characterized by the presence of the FUS-DDIT3 fusion protein, an aberrant transcription factor that by interacting with several chromatin regulatory complexes, induce dysregulation of transcriptional program. Such epigenetic alterations were recently reported to influence immune contexture at tumor level by promoting the escape of tumor cells from immune surveillance and interfering with epigenetic dysregulation restores anti tumor immune response. These data point to a synergism of epigenetic drugs and immunotherapy as a new potential therapeutic strategy, which may be valuable also for MLS patients. The mechanisms linking the immunological landscape and the epigenetic program represent a still largely unexplored field in MLS. The aim of this study is to provide the proof of principle that a deep investigation of molecular mechanisms associated to epigenetic dysregulation in MLS should provide insights about the immune landscape.

Methods: Gene expression profiling data of 52 naïve primary MLS cases, along with patients clinical data, were retrieved from GEO repository (GSE30929, PMID 21335544 and GSE55466, PMID 25115389). MLS were defined by FUS-DDIT3 translocation, and included in the study independently of the degree of cellularity. Expression matrix data was generated by meta-analysis approach. Functional annotation of genes enriched in tumors from patients with shorter disease-free survival was obtained by using Ingenuity Pathway Analysis and Gene Set Enrichment Analysis software. Immune and stromal components were inferred by an in silico approach using the xCell tool.

Results: Transcriptomic profiling of MLS had prognostic value as it categorized patients in two groups characterized by longer disease-free survival (lower risk patients, low Genetic score) or shorter disease-free survival (higher risk patients, high Genetic score). Functional annotation of genes dysregulated in higher risk patients (N=617, FDR <0.05) revealed enrichment in gene modules promoting cell cycle progression and regulating adipocyte differentiation. Analysis of the immune infiltration grouped MLS in clusters displaying different levels and composition of immune infiltrating cells. The following groups were identified: Group A and B, which showed the highest immune scores and resulted enriched both in myeloid and T cells; Group C, which displayed the lower immune score and was characterized by immune 'cold' tumor microenvironment. MLS of group A and B, and MLS of group C are from patients predicted at lower risk and higher risk, respectively, by the transcriptomic signature. Immune score defined two groups of patients with different disease-free survival (DFS) probability. Both Immune score and Genetic score did correlate with DFS at univariate analysis. However, these significant associations did not hold at multivariable analysis, where the transcriptomic signature was the only independent prognostic factor.

Conclusion: These findings suggested that in MLS dysregulation of genes promoting cell cycle progression and dedifferentiation of tumor cells were associated with shorter DFS and is likely the driver regulating anti-tumor immune response. Although the association between MLS genetic profile (Genetic score) and immunity (Immune score), and involvement of program dictated by the oncogenic translocation remain to be investigated, they suggest a therapeutic synergism in co-targeting cell cycle progression and immunity in MLS.



Poster #002 #1819047

DISSECTING DRUG RESISTANCE IN GASTROINTESTINAL STROMAL TUMOURS

Leonardo A. Meza-Zepeda, MSc, PhD¹; Sara K. Sara K., MSc¹; Ksenia Khelik, PhD¹; Saikat Das Sajib, MSc¹; Susanne Lorenz, MSc, PhD¹; César Serrano, MD, PhD²; Heidi M. Namløs, MSc, PhD¹,

¹Oslo University Hospital, Oslo, Oslo, NORWAY, ²Sarcoma Translational Research, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Catalonia, SPAIN

Objective: Imatinib treatment has been extremely successful in gastrointestinal stromal tumours (GIST) and represents a paradigm for the development of precision medicine in cancer. Most of the patients show an initial treatment response, but over time the tumours evolve and develop resistance to the treatment. Thus, despite large improvements in patient outcomes in the imatinib era, patients with high-risk and metastatic GIST still often face an incurable and lethal disease. There is a clear need to expand our knowledge of how GISTs evolve and develop resistance to achieve more durable therapeutic responses. The current treatment approaches are clearly too simple and don't take into account the complexity and heterogeneity that we and others have observed within GIST. The overall objective of the study is to reveal the mechanisms that GIST cells use to escape initial imatinib treatment pressure. We are confident that this can be obtained by deciphering the genomic complexity at a single cell and population level, to reveal the initial dependencies in the early stages of resistance to imatinib.

Methods: The GIST-T1 cell line model, with an in-frame deletion in KIT exon 11 (p.V560_Y578del) that confers imatinib sensitivity, was used to study the transcriptional heterogeneity upon imatinib treatment at single-cell resolution. Cells have been extensively characterised for imatinib sensitivity. We have monitored the cell proliferation under imatinib treatment at different concentrations and the functional activity of the KIT pathway and downstream effectors. GIST-T1 cells were treated with 20 and 40 nM imatinib, and cells were collected for analysis at 4, 24, 72 hrs, as well as at one and two weeks of treatment. At each time, between 4-5,000 individual cells have been analysed using the 10x Genomics Chromium platform and sequenced at high depth. Transcriptional activity has been analysed using the 10x Genomics cell ranger and the Seurat tool kit for single-cell genomics analysis. Functional annotation of genes and pathways have been performed using Ingenuity Pathway Analysis.

Results: GIST-T1 cells showed a drastic decrease in proliferation when treated with 20 nM and 40 nM imatinib. The effect of imatinib was confirmed at the protein level by reduced KIT (p.Y703) phosphorylation, as well as reduced phosphorylation of downstream KIT effectors ERK and AKT after 24 hours of treatment. Phosphorylation of KIT was restored after approximately 14 days of imatinib treatment. Single cells were sequenced at high depth, which allowed the detection of an expression of 6-7,000 genes per cell. Preliminary analysis of single-cell gene expression using 20 nM imatinib showed profound effects in transcription after 24 hrs of treatment compared to untreated cells. Dissection of the transcriptional response showed differential regulation of migration-related pathways in time and across the different cellular subpopulations (cluster). In addition, we observed heterogeneous up- and downregulation of interferon signalling through treatment time when cells are treated with imatinib. Similar results have been recently reported using a GIST mouse model (Liu, et al, Cancer Immunol. Res., 2021) by analysis of bulk tumours.

Conclusion: We have extensively characterised the effect of imatinib on GIST-T1 cells at the phenotypic and signalling level. We have treated cells with imatinib at 20 and 40 nM up to 14 days and used single-cell transcriptome sequencing to characterise the effect at a single-cell level. Our initial analysis of cells treated up to 72 hrs describes a significant transcriptional heterogeneity in response to imatinib, with differential regulation of pathways related to migration and interferon, among others. Further analysis is underway to determine the effects at 7 and 14 days of imatinib treatment.



Poster #003 #1819027

SOFT TISSUE SARCOMAS HARBOR AN INTRATUMORAL MICROBIOME WHICH IS LINKED WITH PROGNOSIS IN PATIENTS UNDERGOING PREOPERATIVE RADIATION AND SURGERY

Lauren M. Perry, MD, MAS¹; Sylvia M. Cruz²; Louis B. Jones, MD³; Ugur N. Basmaci, BS⁴; Sean J. Judge, MD¹; Steven W. Thorpe, MD¹; Nikhil Joshi, PhD⁵; Blythe P. Durbin-Johnson, PhD⁵; Matthew L. Settles, PhD⁵; Jonathon A. Eisen, PhD⁵; Robert J. Canter, MD¹, ¹University of California Davis, Sacramento, California, UNITED STATES, ²Division of Surgical Oncology, Department of Surgery, University of California Davis School of Medicine, Sacramento, California, UNITED STATES, ³Dallas Sarcoma Associates, Dallas, TX, UNITED STATES, ⁴University of California Davis School of Medicine, Sacramento, California, UNITED STATES, ⁵University of California Davis, Davis, California, UNITED STATES

Objective: Groundbreaking studies have linked the gut microbiome with immune homeostasis and anti-tumor immune responses following immunotherapy. Mounting evidence has also demonstrated an intratumoral microbiome, including in soft tissue sarcomas (STS), although a detailed characterization of the STS intratumoral microbiome is limited. Thus, we sought to characterize the intratumoral and gut microbiome in patients with STS undergoing preoperative radiotherapy (RT) and surgery using rigorous prospective sample collection and whole genome shotgun sequencing. We hypothesized that we would identify a distinct intratumoral microbiome and that these microbial signatures would be clinically significant.

Methods: Using a prospective protocol from September 2019 to May 2021, we obtained tumor and stool samples from adult patients with non-metastatic STS. Samples were obtained from each participant at two time points – stool pre-biopsy and pre-definitive surgery and tumor at image-guided biopsy and at definitive surgical resection. All tumor specimens were obtained using a sterile collection protocol to minimize contamination. DNA was isolated using QIAamp PowerFecal Pro kits. Metagenomic classification was used to estimate abundance using the genus and species taxonomic levels across all classified organisms. Analysis of β -diversity was calculated using the Bray-Curtis measure of dissimilarity, while taxonomic comparisons were made with PERMANOVA analyses and ordination plots.

Results: Results: A total of 15 patients were enrolled, with a median follow-up time of 13 (\pm 5) months. Extremity tumors (67%), liposarcoma histology (40%), and tumor grade 3 (73%) were most common. To date, 4 (27%) of patients developed metastases and 3 (20%) died. The intratumoral microbiome was overwhelmingly human DNA (>99%), with a small, consistent proportion of bacterial DNA (0.02-0.03%) present in all samples (Figure 1). The most abundant intratumoral bacterial phyla were Proteobacteria, Bacteroidetes, and Firmicutes. In patients with metastases, *Piscirickettsia* ($P=0.002$) and *Respirovirus* ($P=0.04$) were differentially abundant genera in the pre-RT tumor microbiome (Figure 2). Similarly, intratumoral microbiome β -diversity from the pre-RT biopsy sample demonstrated distinct clustering of the patients who died (Figure 3). There was no significant tumor microbiome clustering based on other clinical-pathologic characteristics. Post-RT at surgery, there was loss of distinct clustering among patients who did and did not develop metastases and those who lived versus died. In contrast, the majority of the gut microbiome was represented by bacterial DNA (>50%), with a small proportion of human DNA (<0.1%). The most abundant gut phyla were Bacteroidetes, Firmicutes, and Actinobacteria. Gut microbiome β -diversity analysis demonstrated no distinct clustering by RT time point or clinical characteristics. Notably, one patient's tumor microbiome exhibited a markedly greater relative abundance of intratumoral viral DNA (0.01%) at both time points compared to all other samples (0%) (Figure 4). Further metagenomic analysis demonstrated exclusivity of human herpesvirus 6B (HHV-6B) in the patient's tumor microbiome with corresponding enrichment of NK cells in the TME (>50% of immune infiltrate). This patient had >90% pathologic necrosis at surgery and remains disease-free over 18 months later.

Conclusion: Conclusion: In this prospective analysis with strict sterile procedures, we demonstrate the presence of a distinct and measurable intratumoral microbiome in STS patients at diagnosis and after RT. Further, our data suggest that the STS tumor microbiome at diagnosis has prognostic significance which normalizes after RT and does not clearly link with the gut microbiome. Additional studies are warranted to assess the impact of our findings, specifically if the STS microbiome predicts clinical outcomes as well as response to systemic therapies.

Figure 1. Relative abundance of human (eukaryotic) and bacterial DNA in tumor and stool samples.

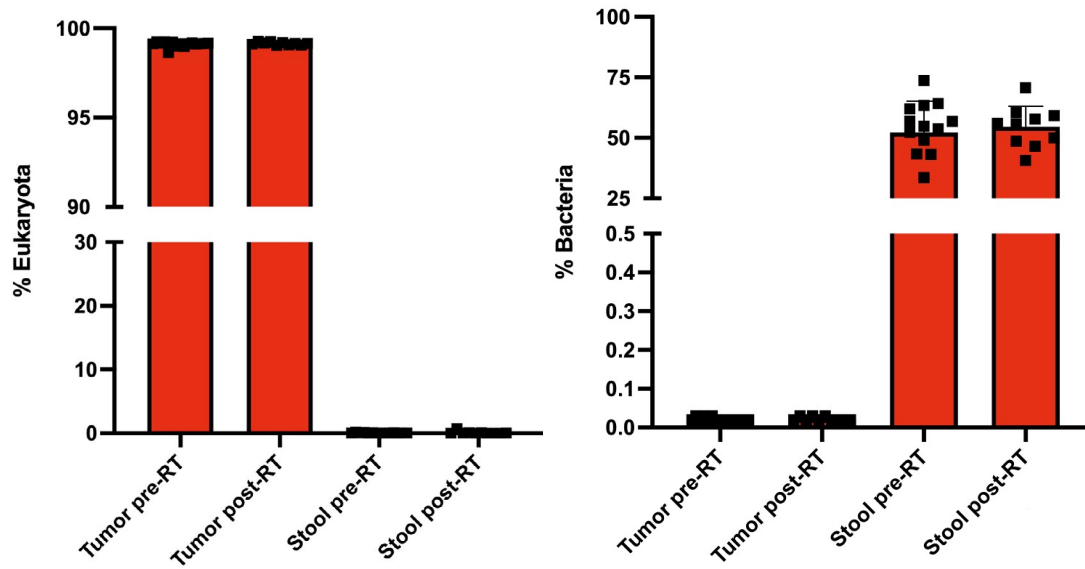


Figure 2. Ordination plot of intratumoral microbiome variability labeled by timepoint and progression to metastases.

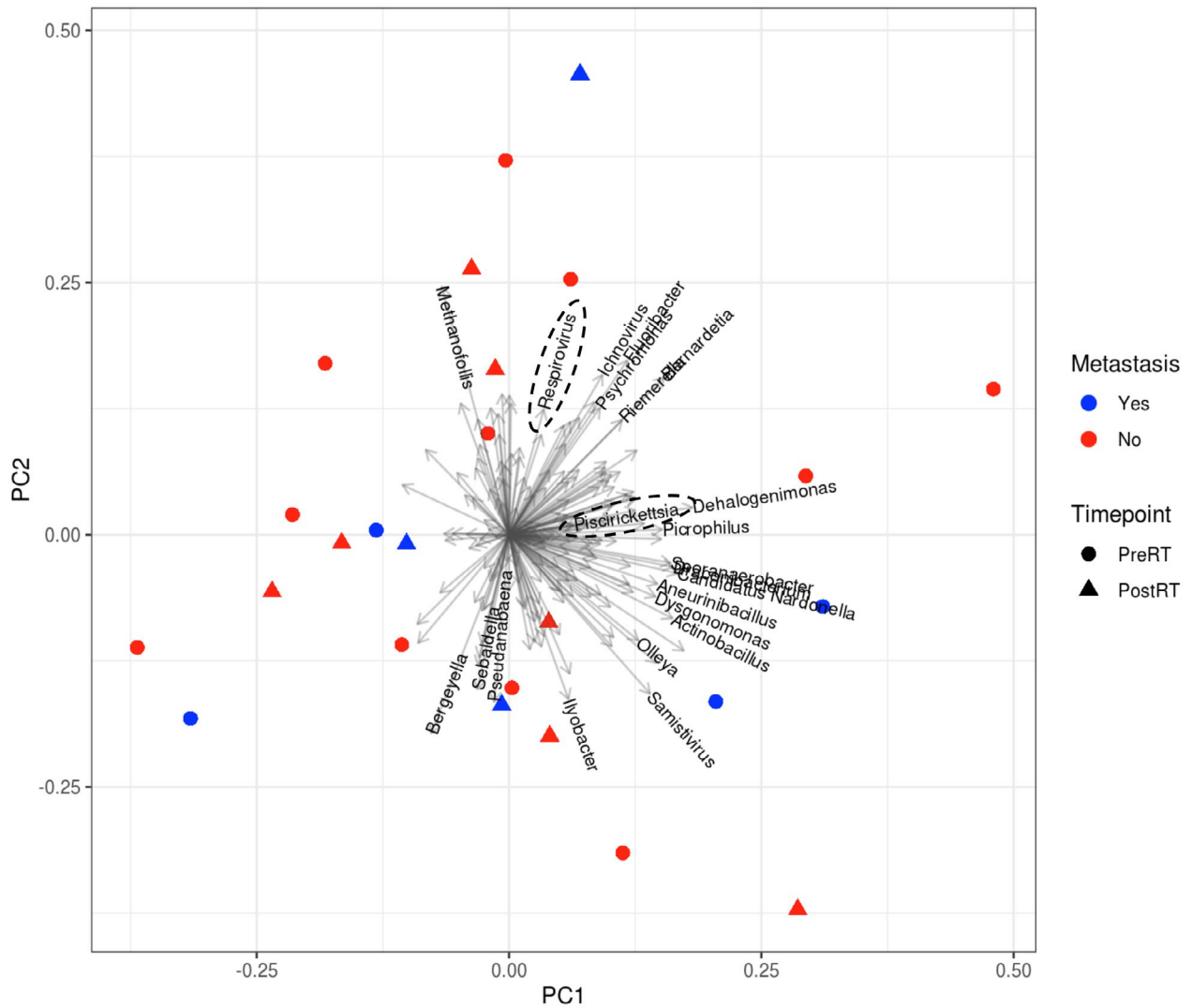


Figure 3. Multidimensional scaling (MDS) plots of the pre-RT intratumoral microbiome β -diversity relating to deaths and metastases.

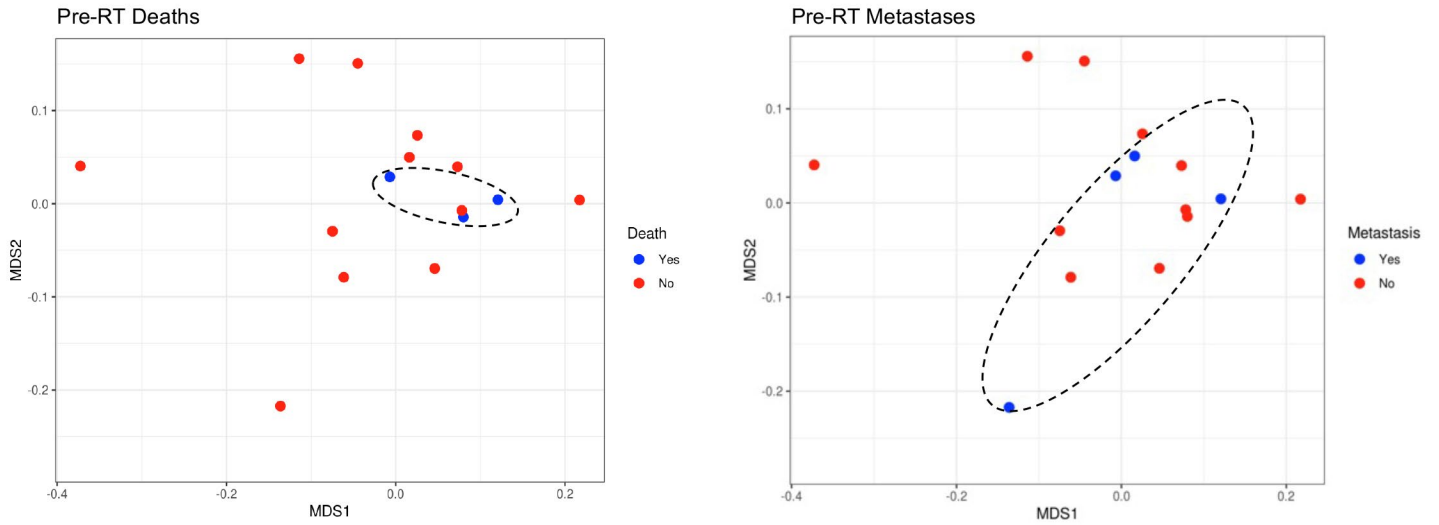
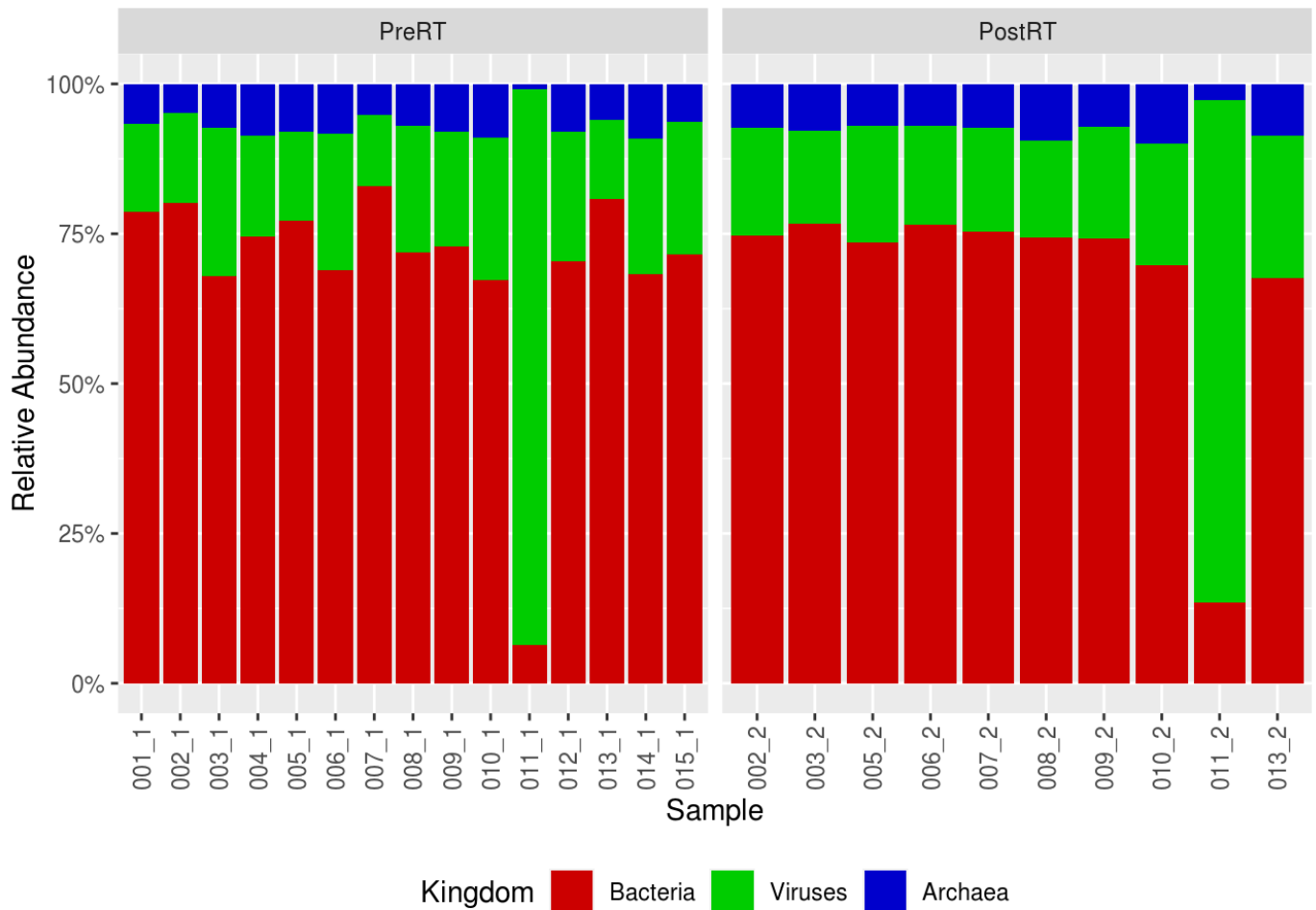


Figure 4. Relative abundance of bacteria, viruses, and archaea in tumor samples by radiation time periods. Notably patient 11 demonstrates a markedly higher relative abundances of viruses across both time periods.





Poster #004 #1819043

SIMILARITY ESTIMATION OF PDX MODEL MULTIOMIC PROFILES WITH CORRESPONDING PATIENT TUMORS

Robin Droit, PhD student¹; Maria Eugénia Marques da costa, PhD²; Anne Gomez-Brouchet, Professor³; Jean-Yves Scoazec, Professor²; Audrey Mohr, PhD²; Pierre Khneisser, Medicine Doctor²; Tiphaine Adam-de-beaumais, PharmD, PhD²; Marlène Pasquet, Professor³; Birgit Geoerger, MD, PhD⁴; Antonin Marchais, PhD²; Nathalie Gaspar, MD, PhD⁵

¹Gustave Roussy, Massy, Ile-de-France, FRANCE, ²Gustave Roussy, Villejuif, Ile-de-France, FRANCE,

³CHU Toulouse, Toulouse, Midi-Pyrenees, FRANCE, ⁴Gustave Roussy Cancer Center, Université Paris-Saclay, INSERM U1015, Villejuif, Ile-de-France, FRANCE, ⁵Gustave Roussy Cancer Campus, Villejuif, Ile-de-France, FRANCE

Objective: Osteosarcoma is the most frequent bone cancer in the adolescent and young adult population. [1] The relapse is the principal cause of mortality. Patient-derived xenograft (PDX) models are used to test treatments on this disease. The purpose of this study is to characterize molecularly the PDX models using a multiOmic approach. We investigate if the genomic and transcriptomic profiles are conserved from relapse to xenograft to identify PDX with promising characteristics as preclinical model.

Methods: Osteosarcoma orthotopic and sub-cutaneous PDX models were generated from 8 different patient samples at relapse; the corresponding diagnosis sample were collected. All tumor samples patient at diagnosis and relapse and orthotopic and subcutaneous PDX models were analyzed by histology, imaging, Whole Exome Sequencing (WES) and RNA-seq. MultiOmics landscape of each samples were defined by somatic mutations, copy number variations, fusions and expression profiles. We estimated molecular similarities/discrepancies through time for each patient and between all samples. PDX samples are composed of a mixture of cells from two species and are grown in immune-depressed mice, two features introducing strong bias in comparison analysis with patient tumors. To minimize those bias, we developed a strategy based on Xenome [2] to identify the host or graft origin of the reads in RNA and WES data. For the RNA-seq, we characterized in an unsupervised manner the genes not expressed in the mice due to immunodepression. Then, we evaluated the genetic and transcriptomic proximity between the PDX and the human samples using unsupervised classification algorithms.

Results: Transcriptome profiles of PDX samples clustered with the corresponding relapse sample. The diagnostics samples are, in most cases, not clustered with the relapse and PDX samples, which suggest a higher transcriptomic modulation between diagnosis and relapse and emphasize the high plasticity of osteosarcoma cells. Strikingly, in each patient tumor, we identified several conserved RNA fusions from diagnosis to PDX models. Despite their patient specificity, those conserved fusions might indicate new early events to explore functionally and topologically. [3]

At genetic level, driver mutations were conserved, diagnostic samples sharing their main genetic characteristic with the relapse and PDX samples. However, several other CNVs and somatic mutations appeared at relapse and were conserved in the PDX models, supporting the clonal evolution model recently proposed by several research groups. [4]

Conclusion: Most of the PDX models conserved alterations driving osteosarcoma oncogenesis and expression profiles similar to the relapse sample they are issued of, when genes implicated in immunity are removed. Osteosarcoma PDX models have a high similarity with the human tumor they are issued of and constitute precious preclinical model to evaluate treatment response.

References

[1] Trama, A. et al. Survival of European adolescents and young adults diagnosed with cancer in 2000–07: population-based data from EURO CARE-5. *Lancet Oncol.* (2016)

[2] Conway T, Wazny J, Bromage A, Tymms M, Sooraj D, Williams ED, Beresford-Smith B. Xenome--a tool for classifying reads from xenograft samples. *Bioinformatics.* (2012)

[3] Riaz Gillani, Bo Kyung A. Seong et al. Gene fusions create partner and collateral dependencies essential to cancer cell survival. *Cancer Res.* (June 7 2021)

[4] Gambera, S., Abarrategi, A., González-Camacho, F. et al. Clonal dynamics in osteosarcoma defined by RGB marking. *Nat Commun* 9, 3994 (2018)

Figure 1.a

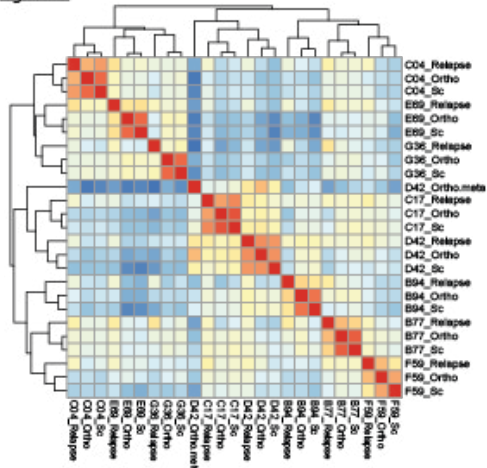


Figure 1.b

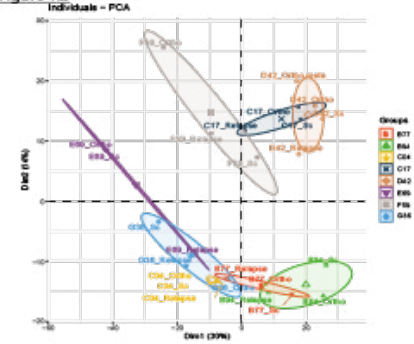


Figure 1.a: correlation on the same list of genes than Figure 1.a, but the Diagnostic samples are removed. The classification is now by sample, the relapse is closer to the PDX than the relapse. Figure 1.b: representation of the two first components of the PCA.

Figure 2

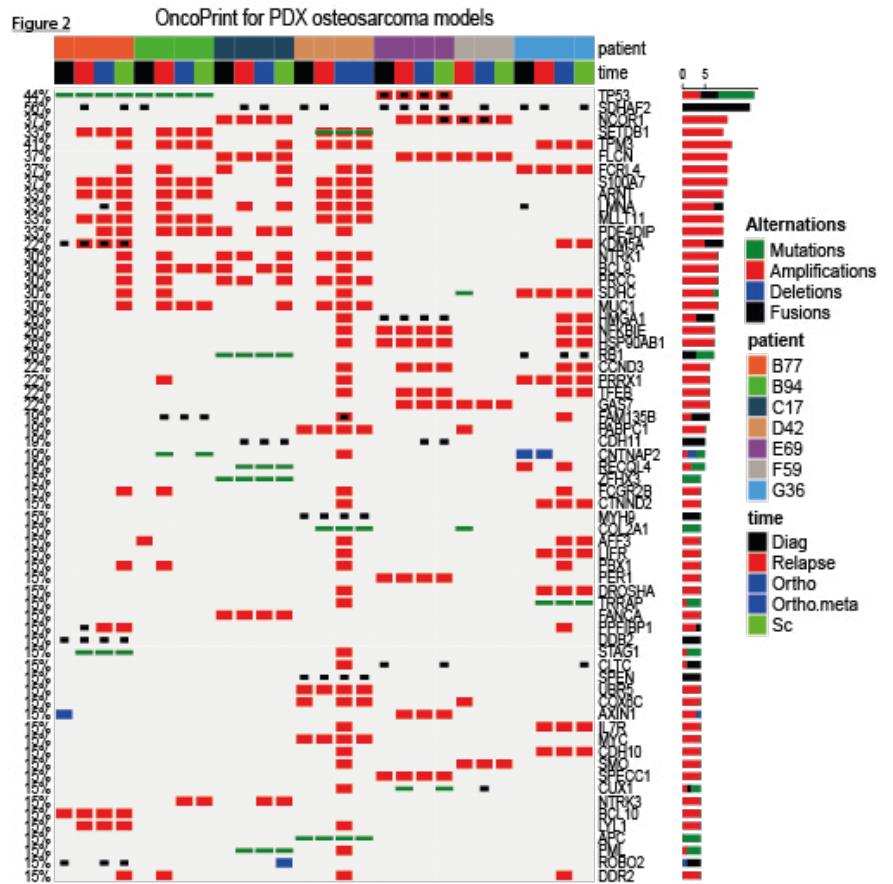


Figure 2: Oncoprint of all the alterations for each sample. the list of alterations is Somatic mutations, amplification, délétion and fusion transcript. The alterations represented are the ones on the genes appearing in the Cancer Gene Census list.



Poster #005 #1819085

**SUPER-ENHANCER RADIO-EPIGENOMIC (SERE) PROFILING OF RHABDOMYOSARCOMA:
A TRANSLATIONAL STUDY CONCEPT**

*Prarthana Bangalore Parthasarathy, MD, FAAP; Andrew Muskara; Berkely Gryder; omar Mian; Stacey Zahler
Cleveland Clinic Children's, Cleveland, Ohio, UNITED STATES*

Objective: To investigate the epigenetic events defined by super-enhancer circuitry in childhood rhabdomyosarcoma; and explore acquired genomic alterations that evolve under therapeutic selection pressures. Specifically, to correlate responses to chemo-radiotherapy in a retrospective patient registry of pre- and post-treatment tumor samples and determine markers of resistance.

Methods: A novel method for the use of archived formalin-fixed paraffin-embedded (FFPE) tissues for super-enhancer analysis by FiTAc-seq (fixed tissue ChIP-seq for H3K27Ac) was adapted. First, optimized using cultured human rhabdomyosarcoma cell lines (RD, SCMC, RH4, RH5 and RH30) and their respective FFPE blocks; was followed by validation with qPCR for known master transcription factors MYOD1, BRD4 and MEST within the regions characterized by acetylated histone marks. A corresponding retrospective review of patient data for the pre- and post-treatment rhabdomyosarcoma tumor samples (n=22), was also conducted.

Results: The cohort of patients with refractory rhabdomyosarcoma treated at Cleveland Clinic over the last 15 years; included ages 1 - 64 years, with only a third being positive for FOXO1 fusion status (Table). Currently undergoing optimization and validation with cell lines, results for FiTAc-seq with FFPE patient samples, initially at diagnosis and subsequently with potentially altered genomics acquired during therapy; will be reported.

Conclusion: Genomic classification is paving the way for risk stratification and designing of clinical trials in rhabdomyosarcoma. With this translational concept of SERE profiling in the evolution of genomic alterations through standard of care treatment, changes in the therapeutic targets could be better characterized.

Table.1 Patient Cohort: Demographics

Patient (n =11)	Diagnosis	Age at Diagnosis (years)	FOXO1 fusion status	Pre-treatment biopsy site	Post-treatment biopsy/resection	Therapy
1	Metastatic Alveolar RMS	17	Negative	Parotid Gland	Right Hip Metastasis	VDC/IE, Olaratumab+Doxorubicin 50.4Gy to R Parotid; 30Gy to femoral head metastasis
2	Metastatic Alveolar RMS	64	Positive	Left forefoot	Right sacral lesion	No adjuvant therapy after initial Chopart amputation; 20Gy to L5-sacral lesion after biopsy
3	Metastatic Embryonal RMS	18	Negative, with anaplastic features	Right perineum	Right femoral canal	VDC/IE (2 cycles), VAC, Doxorubicin+Topotecan, Cyclophosphamide+Irinotecan
4	Alveolar RMS	17	Positive	Prostate	Left lung mass	VAC/VI, 50.4 Gy primary site Cyclophosphamide+Vinorelbine
5	Embryonal RMS	3	Negative	Pelvic mass	Subtotal resection with positive margins	VAC after Ladd's procedure for diagnostic biopsy; RT after subtotal resection
6	Metastatic Alveolar RMS	8	Unknown	Left calf mass	Craniectomy with CP angle tumor excision	VAC/VI,50.4Gy to L calf mass, Vinorelbine+Topotecan
7	Embryonal RMS	6	Negative, with Leigh's syndrome	Right orbital lesion	Right globe exoneration	VAC, Sirolimus, 50.4Gy to primary site, Temozolamide+Irinotecan, Doxil (6 cycles), repeat RT 50.4Gy+ weekly Vincristine
8	Spindle cell/Sclerosing RMS	39	MYOD1 mutation unknown	Right mandible	Right parotid, mandibular and superior facial nerve	VAC-V-V, followed by 36Gy prior to recurrence
9	Alveolar RMS	13	Positive	Right thigh mass	Left breast mastectomy	VDC/IE, 36Gy to thigh mass, Cyclophosphamide+Vinorelbine 50Gy for left breast relapse
10	Metastatic Alveolar RMS	51	Positive	Right cheek mass	Thoracic epidural metastasis	VAC, Head&Neck RT 50.4Gy and 1800cGy for cord compression from relapse
11	Metastatic Alveolar RMS	1	Negative, with Li-Fraumeni syndrome	Left cheek mass	Mandibulectomy with tumor resection and reconstruction	VDC/IE, clinically progressed prior to resection. IMRT after resection.



Poster #006 #1818965

STUDY OF GENE EXPRESSION PROFILE CHANGE AFTER PANOBINOSTAT TREATMENT IN SOFT TISSUE SARCOMA CELL LINESYingjun Zhang, Bsc¹; Connie W.C. HUI, Mphil²; Teresa TSE, MbChB, FRCR(Clinical Oncology), FHKCR(Radiology), FHKAM³; Gordon C.H. TANG, MBBS, MRCP³; Qian TAO, PhD²; Eric C.h. WONG, PhD²;Herbert Loong, MBBS, PDipMDPath, MRCP, FRCP Edin, FHKCP, FHKAM(Medicine)⁴,¹The Chinese University of Hongkong, Hongkong, HONG KONG, ²The Chinese University of Hongkong, HongKong, HONG KONG, ³Prince of Wales Hospital., HongKong, HONG KONG, ⁴The Chinese University of Hong Kong, Hong Kong, HONG KONG

Objective: Soft tissue sarcomas (STS) are rare diseases typically arising from connective tissues in children and adults. Histone deacetylases inhibitors (HDACi) are epigenetic agents which have shown anti-tumour effects as single-agents, as well as synergism with cytotoxics in a variety of solid and hematological malignancies. Panobinostat (LBH589) is a common HDACi approved by the US FDA in several cancer types. We have previously shown synergism of LBH589 when combined with doxorubicin in a group of STS cell lines. The underlying mechanism in the gene expression level of these findings has yet been explored.

Methods: We investigated the potential effects of LBH589 on gene expression profile in four STS cell lines (ISO-HAS-B, SW982, VA-ES-BJ and SK-UT-1). The anti-tumour activities of LBH589 as single agent followed by synergism studies in combination with conventional cytotoxics were studied. RNA samples were extracted from cells after 48 hours treatment with LBH589 at the determined IC50 concentration. RNA sequencing via Illumina platforms were subsequently performed. Ontology (GO) and KEGG (Kyoto Encyclopedia of Genes and Genomes) pathway enrichments were used in bioinformatics analysis.

Results: Synergistic effects with conventional chemo drugs doxorubicin can be observed in ISO-HAS-B, SW982 and VA-ES-BJ but not in SK-UT-1 (Table 1). GO enrichment analysis and KEGG pathway enrichment analysis showed that LBH589 exposure at IC50 can significantly regulate the cell cycle pathway in ISO-HAS-B, SW982 and VA-ES-BJ ($p < 0.00001$, $padj < 0.0005$). Furthermore, the hippo signaling pathway is another important target in SW982 and VA-ES-BJ ($p < 0.00001$, $padj < 0.0005$). Differential gene expression analysis provided some notable examples (Table 2). However, protein processing in endoplasmic reticulum (ER) change is the only remarkable difference in SK-UT-1 after the treatment of LBH589.

Conclusion: Through RNA sequencing, we have identified resultant gene expression profile alterations in four sarcoma cell lines after treatment with LBH589. These changes are associated with multiple functional pathways which may contribute to different magnitude of synergism between different histologies when LBH589 is combined with cytotoxics. Validation of RNA sequencing findings through PCR and protein assays, as well as in-vivo experiments are currently underway.

Table 1. Synergy score of LBH589 + Doxorubicin in four STC cell lines.

	ISO-HAS-B	SW982	VA-ES-BJ	SK-UT-1
LBH589+doxorubicin	14.79	12.95	16.16	10.05

*Synergy score >10 indicates synergism

Table 2. log2 fold value of two notable genes in three STS cell lines. ($p < 0.00001$, $padj < 0.0005$)

	ISO-HAS-B	SW982	VA-ES-BJ
CTGF	-3.2485	-0.67	-2.6028
SERPINE	-2.2577	-2.6421	-2.6509

*log2 fold value < 0 indicates downregulation



Poster #007 #1819075

AXL AS A POTENTIAL THERAPEUTIC TARGET FOR SOFT TISSUE SARCOMA

Daniela d'Empaire, MSc¹; Hester Boven, Pathologist¹; Ji-Ying Song, Pathologist¹; Winan J. van Houdt, MD PhD MSc²; Winette T. A. van der Graaf, MD PhD¹; Daniel Peeper, Prof Dr¹; Julia Boshuizen, MD PhD³,
¹Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS, ²The Netherlands Cancer Institute, Amsterdam, Noord-Holland, Netherlands, ³OLVG West, Amsterdam, Noord-Holland, NETHERLANDS

Objective: Objective: AXL is a Receptor Tyrosine Kinase (RTK) that plays a role in processes like survival and angiogenesis in healthy cells. In several malignancies, aberrant expression of AXL has been linked to worse prognosis, disease progression, EMT and metastasis. Also, this RTK has been associated with therapy resistance; including conventional, targeted and immune therapies^{1,2}.

In the context of sarcomas, often therapy refractory, there are some studies on the role of AXL^{3,4}. Many highlight the connection between AXL increased expression and poorer prognosis. Additionally, some show cell lines with reduced cell proliferation when targeting AXL in vitro. Nevertheless, the definite role of AXL in Soft Tissue Sarcoma (STS) and its targetability remains unclear. Particularly, research in pre-clinical models is needed. Also, the immunomodulatory effects of AXL and its therapeutic potential is largely unknown.

The goal of the present project is to examine the role and potential targeting of AXL in STS. Understanding its effect on both tumor cells and the tumor microenvironment (TME) to generate rational drug combinations for Soft Tissue Sarcoma.

Methods: Methods: Mouse cell lines 17-1 and 17-3 were kindly provided by Paul Krimpenfort. All sarcoma human cell lines were derived from patient samples in-house after informed consent. Melanoma and sarcoma murine cells were maintained in DMEM (GIBCO) and sarcoma primary cell lines in Advanced DMEM/F12 (Gibco); all of them supplemented with 9% fetal bovine serum (Sigma), 100 units per ml of penicillin and 100 µg per ml of streptomycin (GIBCO) and 1% GlutaMAX (Gibco). AXL KO were generated with CRISPR-Cas9. sgRNAs targeting either AXL or non-targeting control were cloned into Lenti-CRISPR-v2 (Addgene) construct with Puromycin resistance cassette. HEK293T transfection and subsequent lentiviral transduction were performed as previously described⁵. Cells were selected using puromycin for 10 days.

For Flow Cytometry cells were stained using a 1:50 dilution of either Mouse AXL antibody (R&D Systems) and analyzed on a Fortessa flow cytometer (BD Bioscience). For measuring AXL molecules on the cell surface, DAKO Qifikit was used. In brief, cells were stained with isotype control IgG1 or AXL antibody (1:100, ab89224, Abcam). Secondary antibody from the Qifi kit was used (Goat-α-mouse FITC). The number of AXL molecules on each cell was calculated using calibration beads from the Qifi kit according to manufacturer's instructions.

For Western Blots cells were lysed using RIPA buffer (50mM TRIS pH 8.0, 150mM NaCl, 1% Nonidet P40, 0.5% sodium deoxycholate, 0.1% SDS) supplemented with Halt™ Protease and Phosphatase Inhibitor Cocktail (Thermo Scientific). Protein concentration was determined using a Bradford Protein Assay (Biorad). Western blotting was performed by conventional techniques using 4%–12% Bis-Tris polyacrylamide-SDS gels (Life Technologies) and nitrocellulose membranes (GE Healthcare). Blots were blocked in 4% milk powder and 0.2% Tween in PBS and then incubated overnight with primary antibodies and 1h in appropriate secondary antibodies. Western blots were then incubated in SuperSignal West Dura Extended Duration Substrate (Thermo Fisher Scientific) and developed using ChemiDoc imaging system.

For in vivo studies 1*10⁶ cells were admixed with Matrigel and injected subcutaneously in either NSG-β2Mnull or FVB. Growth was monitored three times per week with calipers, and tumor size was calculated using the following formula: ½ × length (mm) × width (mm). All experiments ended for individual mice either when the tumor volume exceeded 500 or 1000 mm³, when the tumor showed ulceration, in case of serious clinical illness, when the tumor growth blocked the movement of the mouse, or when tumor growth assessment had been completed.

Treatments with BGB324 was carried out for 72h and readout was performed with Cell Titer Blue according to manufacturers instruction.

Results: We used cell lines derived from sarcoma lesions of CDKN2A KO mice. Of note, CDKN2A deep deletion is a relevant genetic feature in many sarcomas. These cell lines were able to establish successfully after injection in syngeneic mice. Then, we generated AXL KO in cell by CRISPR-Cas9 and confirmed KO efficiency by Flow Cytometry (Fig.1) and Western Blot (Data not shown).

Afterwards, sgControl and sgAxl cell lines were injected in both immune deficient (NSG) and competent (FVB) mice. Despite

successfully establishing in NSG, cell line 17-3 sgRNAs did not grow in an immune competent setting. Interestingly, cell line 17-1 sgAx1 had a statistically significant growth disadvantage in both NSG (Fig. 2A) and FVB (Fig. 2B). This finding suggests a dual role for AXL: on intrinsic tumor growth and an immune-modulatory effect.

Moreover, thorough analysis of these tumors was performed. Firstly, H&E staining and analysis by animal pathologist confirmed the lesions were sarcomatous, encountering spindle cell and undifferentiated pleomorphic regions. Importantly, morphology was found to be representative of human counterparts. Furthermore, we analyzed immune infiltration upon AXL KO. Albeit not significant, there was a trend towards more immune infiltration upon AXL ablation (Fig. 2C). We also checked AXL in human sarcoma cell lines. For this purpose, we included melanoma cell lines with known AXL expression levels as a benchmark¹. Being SkMel28 with very low AXL, SkMel28R (BRAF+MEKi resistant counterpart) very high and A875 a medium-high AXL level. Interestingly, all of the sarcoma cell lines analyzed so far, had a high number of AXL molecules in the surface (Fig. 3).

Afterwards, a well-established AXL inhibitor BGB324 (Bemcentinib) was tested in this panel of cells. BGB324 markedly reduced cell viability and proliferation of most cell lines (Fig. 4). However, when we included cell lines with marginal levels of AXL, such as SkMel28, they were also affected by this AXL inhibitor.

Conclusion: We wanted to use relevant pre-clinical sarcoma models, which constitute an important challenge within the sarcoma field. Thus far, we have successfully transplanted 2 sarcoma murine cell lines with relevant histologies according to our pathologists.

In one of this cell lines, we show that AXL KO cells present a growth disadvantage *in vivo* compared to their WT counterparts. So, AXL not only affects sarcoma growth but affects tumor-immune crosstalk. This finding was further supported by a mild increase in immune infiltration when AXL was absent.

When looking at human cells, we found that our current panel of sarcoma cell lines show considerable levels of AXL. Moreover, we treated our cells with the AXL inhibitor BGB324 or Bemcentinib. This inhibitor is currently in several Phase I and II clinical trials. Surprisingly, in the same set of experiments, we found that some of our melanoma cells with very low AXL expression -SkMel28- was highly sensitive to this AXL selective inhibitor. Which suggested some AXL independent cytotoxicity. In fact, we found some reports of these effects in literature as well⁵. Next steps include the treatment of AXL KO cells with this inhibitor to further understand its specificity and try other AXL inhibitors available.

Importantly, AXL is not only expressed by malignant cells but also by certain immune subsets such as macrophages, NK cells and DCs. In fact, a recent study showed that AXL expression promotes upregulation of PD-L1 in DCs thus dampening anti-tumor immune response. Therefore, targeting AXL with an inhibitor would allow a dual effect in both tumor and immune cells that we find very attractive.

Our future work will focus on additional elucidation of the changes in tumor control and within the immune compartment upon AXL targeting either genetically or pharmacologically in our syngeneic mouse models. Furthermore, studying the potential to combine AXL inhibition with immunotherapy.

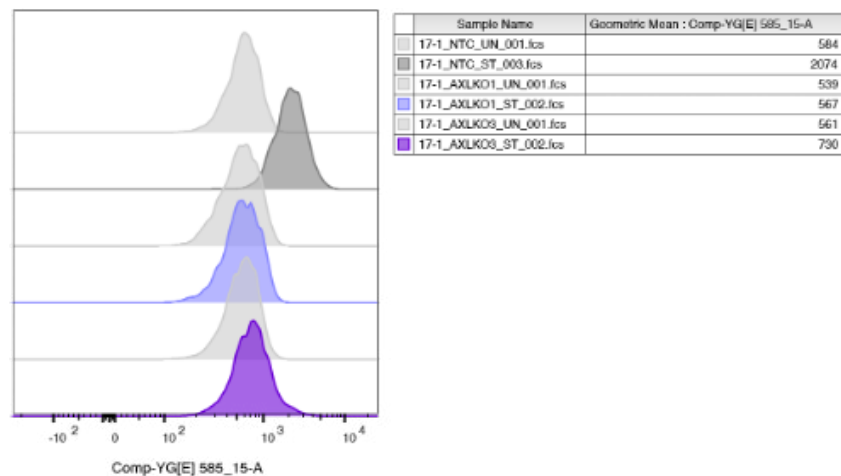


Figure 1. Flow Cytometry plots of mouse AXL. In light grey UN unstained controls, in dark gray NTC/non-targeting control or sgAx1 cells and in purple sgAx1 and 2.

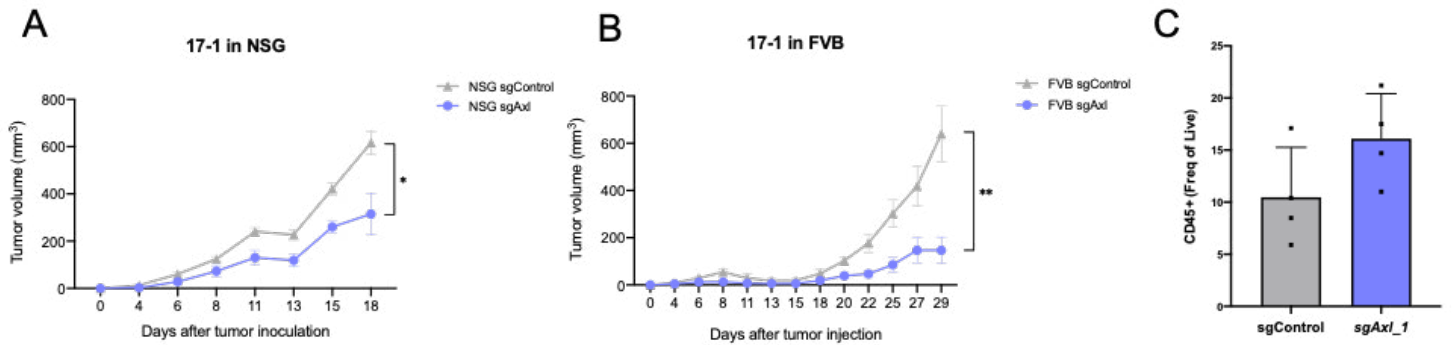


Figure 2. A and B Tumor growth, mice per group n=5, error shown as SEM. C Immune infiltration defined as percentage of CD45+ of gate lived cells by Flow Cytometry of fresh tumor samples of FVB mice at endpoint, error bar is SD, 1 sample per group missing due to technical problems.

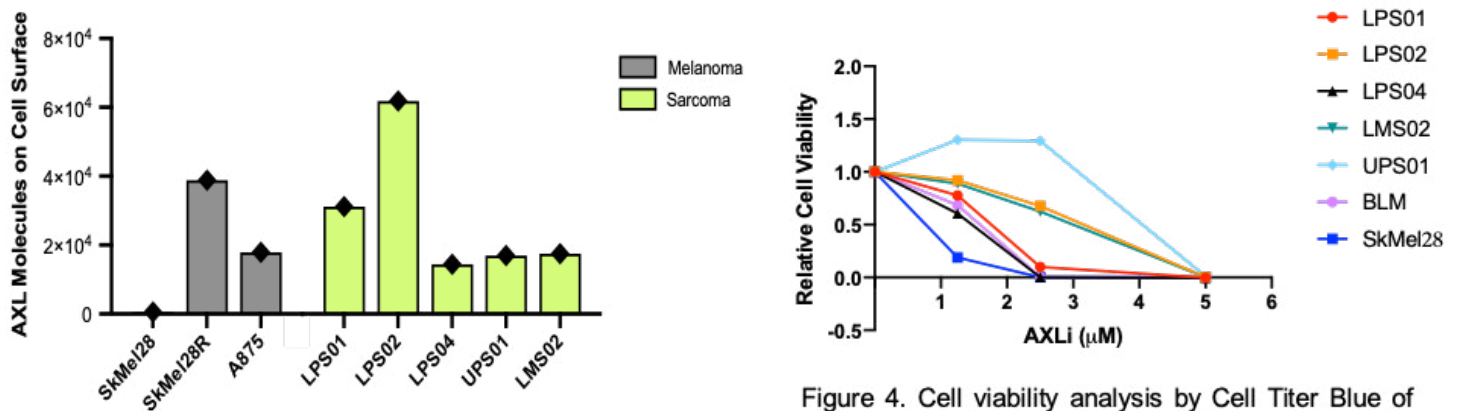


Figure 3. AXL in the surface as measured by DAKO Qifikit LPS are liposarcoma cells 01, 02 and 04, UPS01 is an undifferentiated pleomorphic sarcoma cell line and LMS02 is a leiomyosarcoma cell line.

Figure 4. Cell viability analysis by Cell Titer Blue of cells treated at different concentrations of BGB324. Values shown are the average of technical triplicates.



Poster #008 #1818966

NOVEL CANDIDATE DRUGS FOR THE TREATMENT OF MALIGNANT PERIPHERAL NERVE SHEATH TUMOR REVEALED BY PROTEOMIC ANALYSIS AND A DRUG SCREENING TEST USING PATIENT-DERIVED CELL LINES

Ryuto Tsuchiya, MD¹; Rei Noguchi, MD, Ph.D²; Yuki Yoshimatsu, Ph.D³; Yooksil Sin, Ph.D⁴; Takuya Ono, graduate student¹; Hideaki Kosako, Ph.D⁵; Akihiko Yoshida, MD, Ph.D⁶; Akira Kawai, MD⁷; Tadashi Kondo, MD, Ph.D¹,

¹Division of Rare Cancer Research, National Cancer Center Research Institute, Chuo-ku, Tokyo, JAPAN, ²Division of Rare Cancer Research, National Cancer Center Research Institute, Tokyo, Tokyo, JAPAN, ³Division of Rare Cancer Research, National Cancer Center Research Institute, 5-1-1 Tsukiji, Chuo-ku, Tokyo, JAPAN, ⁴Division of Rare Cancer Research, National Cancer Center Research Institute, chuo-ku, Tokyo, JAPAN, ⁵Division of Cell Signaling, Fujii Memorial Institute of Medical Sciences, Tokushima University, Tokushima-shi, Tokushima, JAPAN, ⁶Department of Diagnostic Pathology, National Cancer Center Hospital, Chuo-ku, Tokyo, JAPAN, ⁷National Cancer Center Hospital, Chuo-ku, Tokyo, JAPAN

Objective: Malignant peripheral nerve sheath tumor (MPNST) is a malignant spindle cell tumor often arising from a peripheral nerve, from a pre-existing benign nerve sheath tumor, or in a patient with neurofibromatosis type 1. Although the incidence of MPNST is approximately 3-5% of all soft tissue sarcomas, the lifetime incidence in patients with neurofibromatosis type 1 is up to 10%. The optimal treatment modality is complete resection. However, MPNST is known for high local recurrence and distant metastasis rate. In addition, MPNST is refractory to conventional chemotherapy and radiotherapy, leading to the poor prognosis. Therefore, the development of novel treatment methods are urgently needed. We tried to identify the new candidate drugs by integrating proteomic analysis on MPNST tumor samples and a drug screening test using patient-derived MPNST cell lines.

Methods: We examined 41 MPNST cases treated in National Cancer Center Hospital, Japan, during June 2004 to March 2019. The proteins expressed in MPNST tumor samples were comprehensively analyzed by liquid chromatography–tandem mass spectrometry (LC-MS/MS), and exponentially modified protein abundance index (emPAI) value of each protein was calculated. By statistically processing the obtained emPAI values, we tried to identify proteins that were overexpressed in the poor prognosis group. We also conducted a drug screening test using 214 drugs including FDA-approved anti-cancer drugs on five MPNST cell lines which we successfully established in our previous studies. Finally, we integrated the proteomic data and the drug screening results to identify the novel candidate drugs for the treatment of MPNST.

Results: We revealed 5292 proteins expressed in MPNST tumor samples by LC-MS/MS. By using the emPAI values of these proteins, we identified 89 proteins that were characteristically overexpressed in the poor prognosis group. The pathway analysis of these proteins revealed that cancer-associated pathways were uniquely enriched. By the drug screening test, multiple drugs demonstrated remarkable anti-proliferative effects on the MPNST cell lines. One of these drugs related to the enriched pathway revealed by the proteomic analysis.

Conclusion: We identified novel candidate drugs for the treatment of MPNST by integrating the proteomic analysis and the drug screening test using original MPNST cell lines. We plan to conduct functional analysis using these cell lines. We hope these candidate drugs will contribute the treatment of MPNST.



Poster #009 #1819069

DLK1 AS A POSSIBLE THERAPEUTIC TARGET FOR SARCOMA

*Ilkyu Han, MD PhD; Han-Soo Kim, MD PhD; Ha Jeong Kim, PhD
Seoul National University Hospital, Seoul, Seoul-t'ukpyolsi, REPUBLIC OF KOREA*

Objective: Cancer stem cells (CSCs) are cells characterized by their self-renewal and tumorigenic potential. The purpose of this study was to discover the role of the delta-like factor 1 (DLK1) in sarcoma.

Methods: mRNA expression of DLK1 from 13 sarcoma cell lines was examined. Isolated CSCs from the tumors were examined using FACS with CD133, the CSC marker, or sphere forming assay. The relationship between DLK1 and CSCs in sarcoma was examined using cell proliferation and cell invasion assays after they were treated with DLK1 siRNA.

Results: A high expression of DLK1 mRNA was observed in all sarcoma cell lines. However, CSCs isolated from sarcomas of DLK1 gene over expression low expressed the DLK1 than wild type. The anti-cancer effects of DLK1 siRNA inhibited cell proliferation and invasion in U2OS, A204, and sw872. In addition, treatment with DLK1 siRNA inhibited cell invasion in sw872 CSCs. DLK1 gene induces tumorigenesis in various sarcoma cells, and regulates the invasiveness of liposarcoma. These results suggest that DLK1 could serve as a possible therapeutic target for sarcoma.

Conclusion: Our study showed that the DLK1 gene induces tumorigenesis in various sarcomas and is associated with invasive mechanism in sarcoma. These results suggest DLK1 could serve as a possible therapeutic target in a variety of sarcomas.



Poster #010 #1818952

TARGETING INHIBITION OF EIF4A AND A HIGH THROUGHPUT SCREENING TO IDENTIFY SYNERGISTIC DRUG COMBINATIONS TO TREAT PEDIATRIC AND ADULT SARCOMAS

Long-Sheng Chang, PhD¹; Janet L. Oblinger, PhD²; Xiaohu Zhang, PhD³; hyndavi Anksapuram, BA¹; Marc Ferrer, PhD³; Ryan D. Roberts, MD, PhD⁴; A Douglas Kinghorn, DSc, PhD⁵

¹Nationwide Children's Hospital and The Ohio State University, Columbus, Ohio, UNITED STATES,

²Center for Childhood Cancer & Blood Diseases, Nationwide Children's Hospital, Columbus, Ohio, UNITED STATES,

³National Center for Advancing Translational Sciences, NIH, Bethesda, Maryland, UNITED STATES, ⁴Nationwide Children's Hospital, Columbus, Ohio, UNITED STATES, ⁵Division of Medicinal Chemistry & Pharmacognosy, The Ohio State University College of Pharmacy, Columbus, Ohio, UNITED STATES

Objective: To sustain uncontrolled growth, cancer cells enhance protein translation by upregulating the translation machinery. We have shown over-expression of the eukaryotic initiation factor 4A (eIF4A) in several types of sarcomas, including malignant peripheral nerve sheath tumors (MPNSTs). Genetic depletion of eIF4A and pharmacological inhibition using the natural eIF4A inhibitor silvestrol reduce multiple oncogenic signaling molecules and effectively suppress tumor growth in vitro and in vivo. We also identified two silvestrol-related eIF4A inhibitors, rocaglamide (Roc) and didesmethylrocaglamide (DDR), with potent growth-inhibitory activities comparable to silvestrol but having better drug-like properties. Both Roc and DDR arrest tumor cells at G2/M and induce DNA damage response and apoptosis, while decreasing the levels of multiple oncogenic kinases including IGF-1R, AKT, and ERK1/2, consistent with translation inhibition. Unlike silvestrol, Roc and DDR are not sensitive to multi-drug resistance 1 (MDR1) efflux, and Roc does not cause pulmonary toxicity in dogs as found with silvestrol. Importantly, Roc has oral bioavailability and, when administered intraperitoneally or orally, potently suppresses the growth of orthotopic MPNST xenografts. Treated tumors have more cleaved caspase 3-positive cells, indicative of increased apoptosis in vivo. These results indicate that these eIF4A inhibitors merit further investigation as sarcoma treatments. The objective of this study is to evaluate the potential of using Roc and DDR to treat multiple types of pediatric and adult sarcomas and to identify other targeted agents that synergize with these eIF4A inhibitors to completely eradicate sarcoma cells.

Methods: Various types of bone and soft-tissue sarcoma cell lines were treated with DDR and Roc, followed by cell proliferation assay, flow cytometry, and immunoblotting. Plasma concentrations of Roc or DDR in blood collected before and after dosing by intravenous or intraperitoneal injection or by oral gavage were analyzed using liquid chromatography coupled with tandem mass spectrometry. Orthotopic cell line-derived xenograft (CDX) and patient-derived xenograft (PDX) models for various pediatric and adult sarcomas were used to assess antitumor efficacy. The matrix high-throughput screening of the Mechanism Interrogation Plates (MIPE) oncology compound library, which contains ~3,000 compounds with diverse mechanisms of action, was used to identify agents that synergized with DDR in killing MPNST cells. Synergistic compound combinations were validated in multiple sarcoma cell lines, and their mechanisms of action were analyzed by Western blot and immunohistochemistry.

Results: We show that like Roc, DDR is also well-tolerated and exhibits oral bioavailability. Both Roc and DDR effectively inhibit tumor growth in multiple PDX models of MPNST, osteosarcoma, Ewing sarcoma, rhabdomyosarcoma, desmoplastic small round cell tumor, as well as the common adult sarcomas liposarcoma and leiomyosarcoma. In addition, these eIF4A inhibitors exhibit potent anti-tumor effects in an orthotopic intra-tibial osteosarcoma CDX model and a canine osteosarcoma PDX model by reducing multiple key growth signaling molecules, including IGF-1R, and inducing apoptosis. These results suggest that inhibition of eIF4A is a potential treatment strategy for multiple types of sarcoma. Based on these promising findings, the NCI Experimental Therapeutics (NExT) Program has approved and selected Roc and DDR for further development as sarcoma treatments. However, while these eIF4A inhibitors profoundly suppress tumor growth, they do not eliminate all sarcoma cells. By conducting a high-throughput screening of the MIPE oncology compound library for agents that synergized with DDR in killing MPNST cells, several targeted agents were identified, including several FDA-approved drugs. The synergistic growth-inhibitory activities of these agents were also found with Roc and were verified in multiple other types of sarcoma cells by enhancing apoptosis.

Conclusion: Collectively, these results suggest that a clinical trial for Roc and DDR to treat sarcomas is warranted. Further, our findings reinforce the notion that simultaneously blocking multiple aberrantly expressed oncogenic signaling molecules

by eIF4A inhibitors and their combination with specific targeted drugs may be effective in completely eliminating pediatric and adult sarcomas. (We sincerely thank Larry W Anderson, Barry R O'Keefe, and Jerry M Collins of the NCI and the NExT program for pharmacokinetic and toxicity analysis and compound synthesis. This study is supported by CancerFree KIDS, Sunbeam Foundation, NF2 Biosolutions, and the US Department of Defense.)



Poster #011 #1819058

DEVELOPING A NOVEL MODEL OF NEUROFIBROMATOSIS TYPE 1 ASSOCIATED MALIGNANT PERIPHERAL NERVE SHEATH TUMORS USING INDUCED PLURIPOTENT STEM CELLS*Garrett M. Draper, B.S.; Mahathi Patchava, B.S.; Wendy Hudson; Kyle B. Williams, PhD; David A. Largaespada, PhD, University of Minnesota, Minneapolis, Minnesota, UNITED STATES*

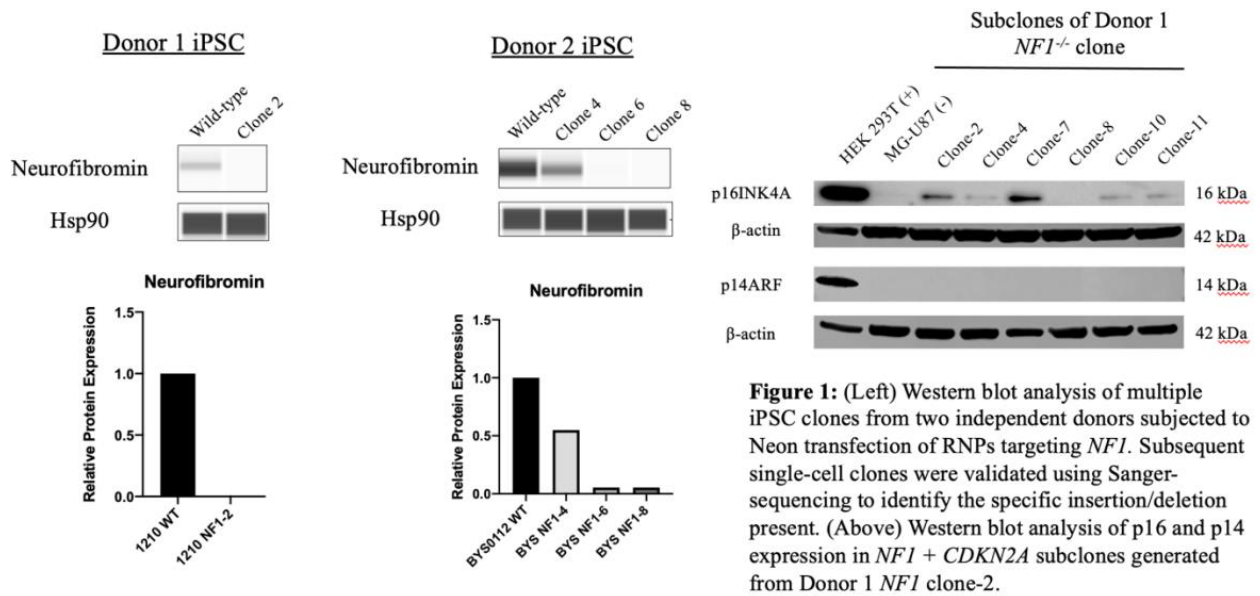
Objective: The genetic tumor predisposition syndrome Neurofibromatosis type 1 (NF1) results from the inheritance of a mutant copy of NF1, a RAS-GAP tumor suppressor gene. Subsequent loss of the remaining wild-type NF1 allele in Schwann cells or Schwann cell precursors of the peripheral nervous system leads to complete functional loss of the encoded protein, neurofibromin. Schwann cells lacking neurofibromin exhibit hyperactive RAS signaling, increased cell proliferation, and contribute to the formation of benign plexiform neurofibromas (PNFs). Through additional mutations in tumor suppressor genes CDKN2A/CDKN2B, these PNFs may escape senescence and progress to atypical neurofibromatous neoplasms of uncertain biological potential (ANNUBP). Furthermore, loss of function mutations in the histone modifying Polycomb Repressive Complex 2 (PRC2) have been strongly implicated in the progression of ANNUBPs to lethal malignant peripheral nerve sheath tumors (MPNSTs). Although these and other genetic alterations have been associated with MPNST formation, their temporal dependence during Schwann cell development and contribution to malignant transformation using a human cell model has not been studied. We hypothesize that sequential loss of NF1, CDKN2A, and finally SUZ12 in Schwann cells transforms them into MPNST, and this process is possible to study using a human induced pluripotent stem cell (iPSC) model system.

Methods: To test our hypothesis, we used published differentiation protocols to generate Schwann lineage cells from commercially available iPSCs. Cells were subjected to targeted mutations using chemically modified short guide RNAs and CRISPR/Cas9 ribonucleoproteins at different stages of development to mimic potential malignant tumorigenesis. This allowed for creation of isogenic wild-type and mutant clones from several independent donors. Cell identity throughout the differentiation process was confirmed through qRT-PCR transcript analysis, flow cytometry, and immunofluorescent staining of Schwann lineage specific markers. 2-D proliferation was measured via MTS proliferation assay, and a Transwell (Boyden Chamber) assay was used to measure migratory ability in vitro. Confirmation of targeted protein knock-out and expression of senescence associated proteins was done by traditional western blotting techniques. Detection of senescence associated b-galactosidase was performed according to manufacturers instructions (Cell Signaling Technologies). All mouse tumor xenograft experiments were conducted according to University of Minnesota Institutional Animal Care and Use Committee (IACUC) approved protocols.

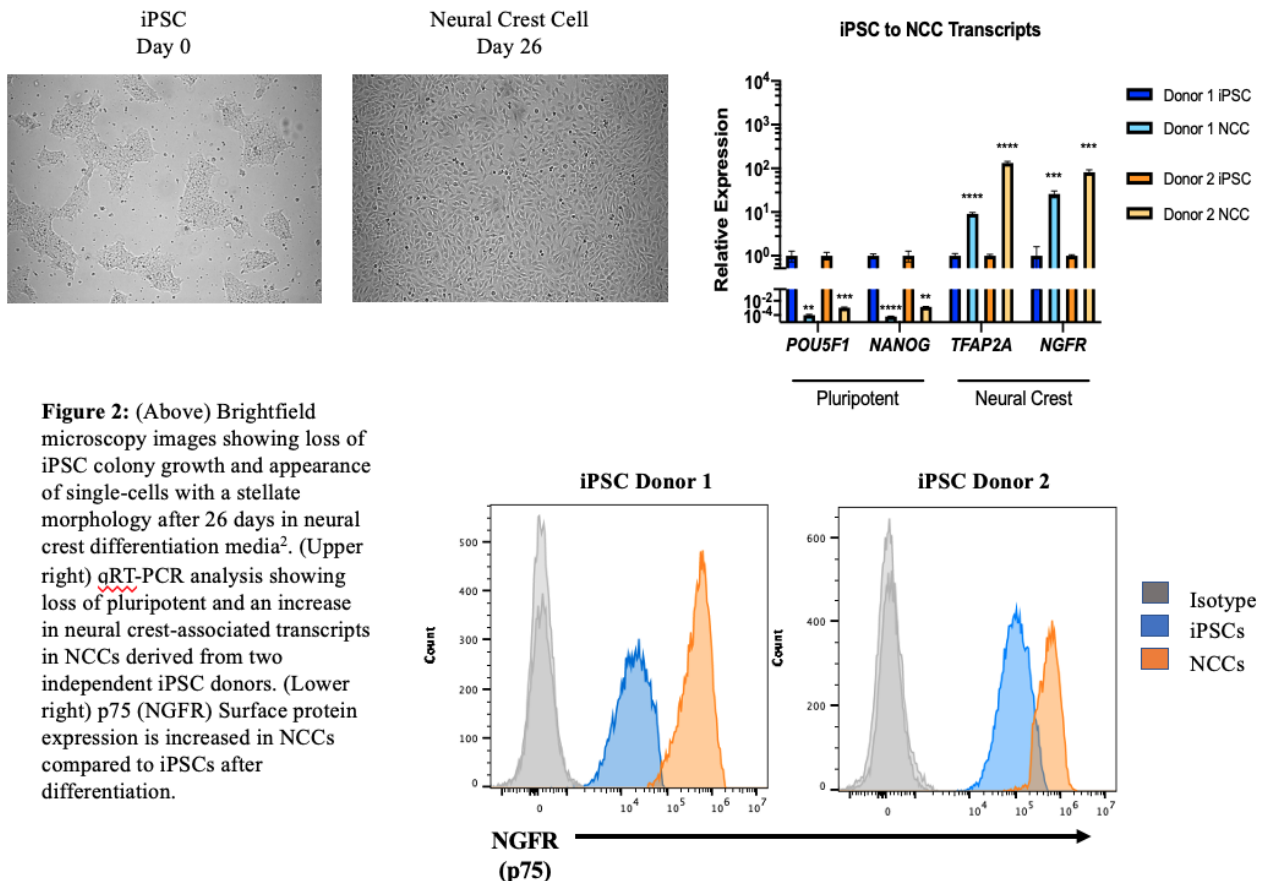
Results: Our preliminary results show that multiple iPSC donor lines can reliably be differentiated to Neural Crest Cells (NCCs), and further to mature Schwann cells. Using CRISPR/Cas9 ribonucleoproteins, we have edited multiple target loci at high levels (>70%) throughout Schwann cell development. NCCs lacking neurofibromin showed an increase in proliferation and migration. While iPSC-derived Schwann cells (iSCs) lacking NF1 and CDKN2A with or without SUZ12 loss became senescent after several passages. These mutant iSCs were unable to form tumors when subcutaneously injected into the flank of NOD-Rag1null IL2rgnull NRG mice, while commonly utilized immortalized human Schwann cell lines lacking NF1 were able to form large subcutaneous tumors.

Conclusion: High levels of gene editing can be achieved throughout the Schwann cell lineage resulting in phenotypic differences in vitro. However, iPSC-derived Schwann cells harboring relevant MPNST-associated mutations fail to escape senescence in vitro. Further refinement of this induced-MPNST (iMPNST) model through targeting of CDKN2B, ATRX, or TP53 may allow for better understanding of the order and timing at which these transforming mutations are sufficient to result in MPNST formation. Additionally, the application of single-cell RNA sequencing technology to this system will uncover potential heterogeneity that could harbor a clone primed for malignant transformation. This model could aid in uncovering novel genetic mutations and pathways which contribute to transformation of benign PNFs to MPNSTs, providing additional targets for future therapeutic intervention.

Generation of *NFI*^{-/-} + *CDKN2A*^{-/-} iPSC clones via CRISPR/Cas9 RNPs



iPSC-derived Neural Crest Cells Express Specific Markers



Targeting of *SUZ12* for loss in iPSC-derived Schwann Lineage Cells

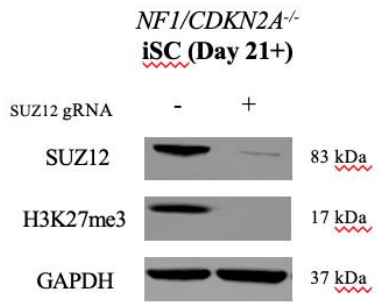
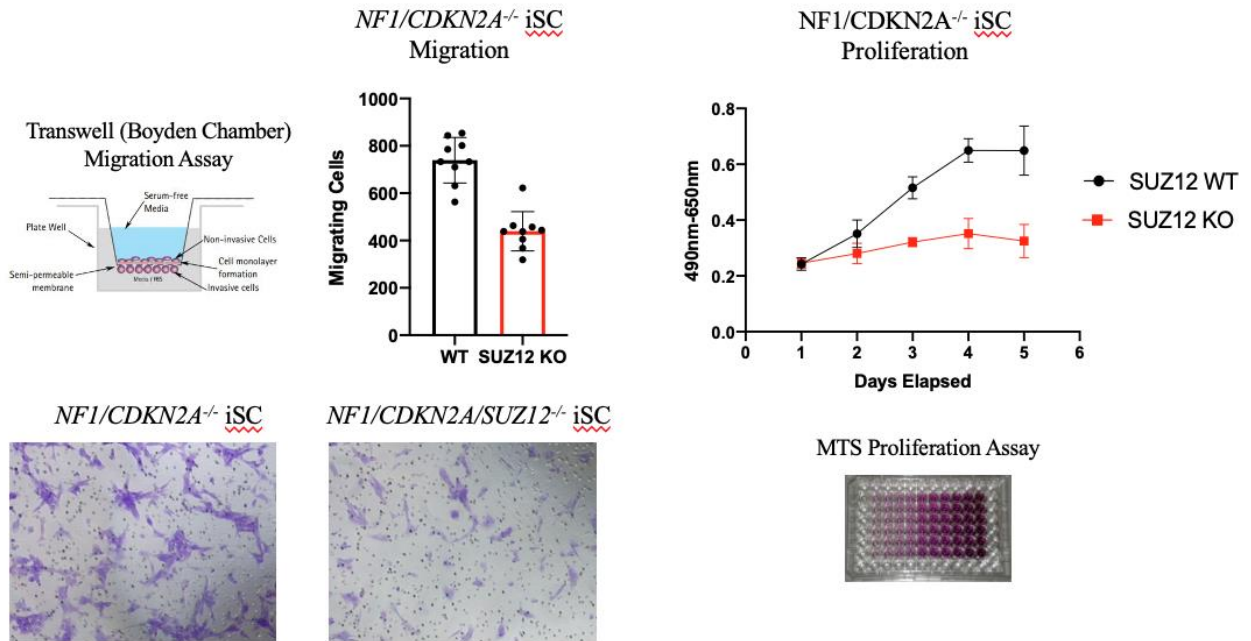


Figure 3: (Left) Western blot of iPSC-derived Schwann cells (iSCs) transfected with a RNP targeting *SUZ12*. Loss of both *SUZ12* and the PRC2-associated H3K27me3 repressive histone mark is achieved at high efficiency. (Bottom Left) Transwell migration assay of *NF1/CDKN2A*^{-/-} iSCs with or without *SUZ12* present shows a decrease in migratory of *SUZ12* knockout iSCs. (Bottom Right) MTS assay shows lack of proliferation in *SUZ12* knockout *NF1/CDKN2A*^{-/-} iSCs.



Detection of senescence associated markers in edited iSCs

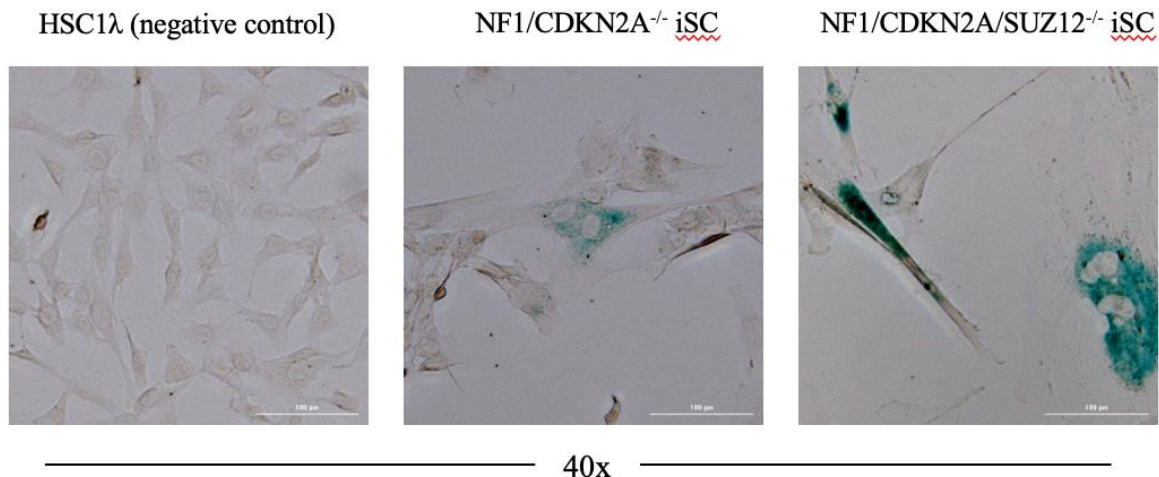
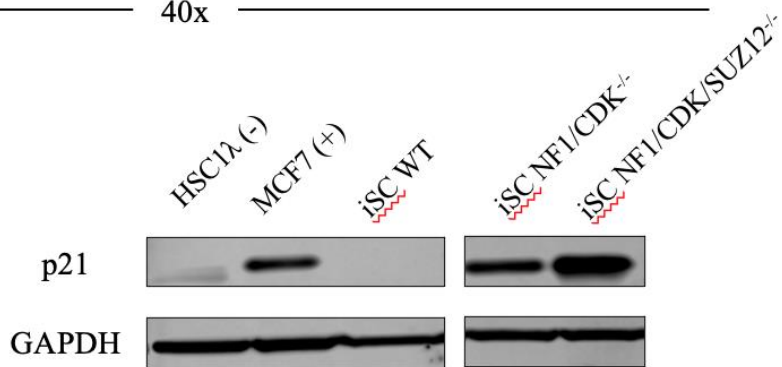


Figure 4: (Above) Detection of senescence-associated β -galactosidase activity in double and triple knockout iSCs. Immortalized human Schwann cells used as a negative control. (Right) Expression of cyclin dependent kinase inhibitor p21 detected in both iSC lines but to a higher degree in SUZ12 knockout cells





Poster #012 #11818919

TARGETING ASPARAGINE METABOLISM INHIBITS TUMOR GROWTH IN LIPOSARCOMA

 Kyle D. Klingbeil, MD MS¹; Blake Wilde, PhD²; Sarah Dry, MD³; Joseph Crompton, MD PhD⁴; Fritz C. Eilber, MD³; David Shackelford, PhD⁵; Heather Christofk, PhD²; Brian Kadera, MD⁶
¹UCLA Health, Department of Surgery, Los Angeles, CA, ²UCLA, Department of Biological Chemistry, Los Angeles, California, UNITED STATES, ³UCLA Medical Center, Los Angeles, California, UNITED STATES, ⁴UCLA Health, Los Angeles, California, UNITED STATES, ⁵UCLA Health, Division of Pulmonary and Critical Care Medicine, Los Angeles, California, UNITED STATES, ⁶UCLA Health, Division of Surgical Oncology, Los Angeles, California, UNITED STATES

Objective: The mTOR complex 1 (mTORC1) senses the presence of nutrients, including asparagine (Asn), to drive cell proliferation and tumor growth in various cancer types. When intracellular Asn is depleted, mTORC1 activity is reduced, thereby limiting tumor proliferation. To restore normal levels, cells import Asn from the microenvironment or synthesize it by converting aspartate (Asp) to Asn via asparagine synthetase (ASNS). Activating transcription factor 4 (ATF4) is a DNA-binding protein that enhances the transcription of ASNS when Asn is low. Asp, as a substrate for ASNS, is generated during mitochondrial respiration. Inhibition of the electron transport chain (ETC) via mitochondrial complex I inhibitors (metformin, rotenone or IACS-010759 (IACS)), depletes Asp-derived Asn. Exogenous Asn can be limited by dietary restriction or by infusion of L-asparaginase. Therefore, we hypothesize ETCi in combination with limiting exogenous Asn will inhibit tumor proliferation in mTORC1-dependent cancers. In this study, we evaluated baseline mTORC1 activity and asparagine metabolism in the two most common subtypes of liposarcoma (LPS): well-differentiated (WD) and de-differentiated (DD). We then assessed the effects of combinatorial therapy on available LPS cell lines, patient-derived tumor organoids (PDTOs), and an in vivo murine xenograft model.

Methods: A 47-patient clinically-annotated WD/DD LPS RNA microarray was used to perform gene set enrichment analysis (GSEA 4.1.0) from 288 validated, metabolism-related gene sets. Normalized enrichment score (NES) was used to rank each gene set and $p < 0.05$ and $FDR (q) < 0.25$ were used as thresholds for significance. These findings were independently validated by immunohistochemistry (IHC) for mTORC1 activation (p4EBP1) and asparagine metabolism (ASNS, ATF4) using a lipomatous tumor tissue microarray (TMA) containing 115 unique patient samples. Positive cell count percentages per core were obtained using automated imaging software (Definiens Tissue Studio). ATF4 staining was correlated to overall survival using Kaplan-Meier analysis. Whole tissue metabolomics was performed on 21 unique patient samples to compare relative abundance of Asn and Asp. Cell viability was measured via luminescent assay (CellTiter Glo) in previously characterized cell lines (DD LPS: LPS1, LPS2, LPS3; WD LPS: 93T449) and freshly resected PDTOs following 48 hours of treatment combinations. Cell lysates were analyzed by standard western blot techniques targeting ASNS, ATF4 and activators of mTORC1: 4EBP1, S6K and S6. The fractional contribution of glucose-derived carbons into Krebs cycle intermediates and nucleotide precursors was determined by [U-13C] glucose metabolite tracing. Propidium iodide staining and flow cytometry assessed for changes in cell cycle progression. A preclinical trial in NOD/SCID IL2y null (NSG) mice utilizing subcutaneous flank xenografts of LPS2 was conducted using IACS 10mg/kg QID and an Asn-controlled diet. Tumor volumes were calculated from serial caliper measurements. IHC staining of xenografts assessed for treatment effects on cell cycle arrest (p21), cell proliferation (ki67), apoptosis (CC3) and asparagine metabolism (ASNS).

Results: The top four gene sets enriched in DD LPS included mTORC1 signaling, pyrimidine metabolism, purine metabolism and Myc targets when compared to WD LPS. TMA histological staining for p4EBP1, ATF4 and ASNS demonstrated higher cell positivity in DD compared to WD LPS (Fig 1A). Patients with ATF4-high WD LPS demonstrated a lower overall survival compared to ATF4-low WD LPS by Mantel-Cox log rank test ($p < 0.0001$) (Fig. 1B). Asn was significantly more abundant in both WD and DD LPS compared to normal white adipose tissue by metabolomic analysis. ETC inhibition using either metformin, rotenone or IACS in combination with 0mM Asn resulted in a significant reduction in cell counts for all cell lines. This effect was partially rescued by 0.1mM Asn (Fig. 2, IACS as representative shown). Similar effects were seen using PDTOs from unique WD and DD LPS samples (Fig. 3). Western blotting demonstrated an increase in ATF4 and ASNS expression with combination treatment and a reduction in phosphorylated activators of mTORC1. Combination treatments resulted in a greater percentage of cells in G0/G1 in both LPS2 and 93T449 compared to controls. [U-13C] glucose metabolite tracing demonstrated an increase in AMP with combination treatments suggesting an imbalance of bioenergetic homeostasis. The xenograft model demonstrated that IACS inhibits tumor growth with no additive effect with dietary restriction (Fig. 4A).

The combination therapy led to an increase in cell cycle arrest and asparagine biosynthesis without significant changes in proliferation and apoptosis by IHC analysis (Fig. 4B).

Conclusion: These findings demonstrate Asn's function as a regulator of anabolic cell signaling via mTORC1 in LPS. Targeting Asn results in energy stress and cell cycle arrest. High ATF4 protein expression in WD LPS is associated with a decreased overall survival, serving as a potential prognostic indicator and biomarker for Asn-targeted therapy. In preclinical models of patient-derived LPS, targeting Asn biosynthesis via mitochondrial complex I inhibits tumor growth.

Figure 1: Lipomatous Tumor TMA

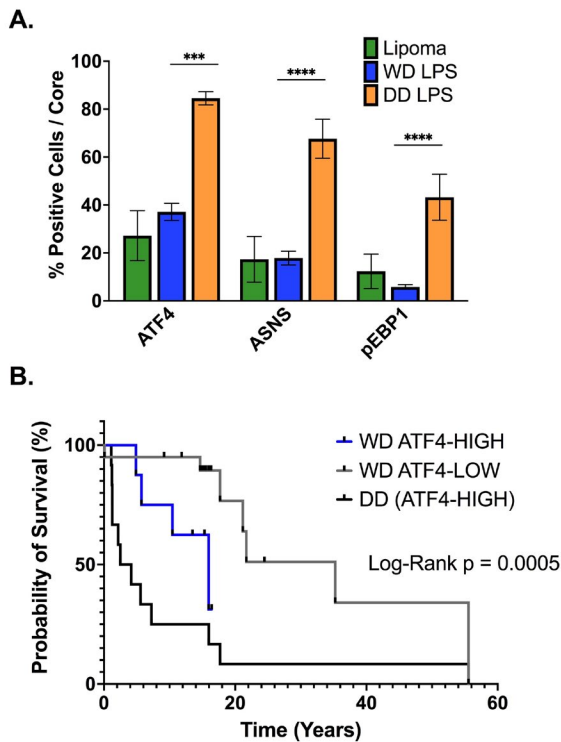


Figure 2: LPS Cell Line Viability

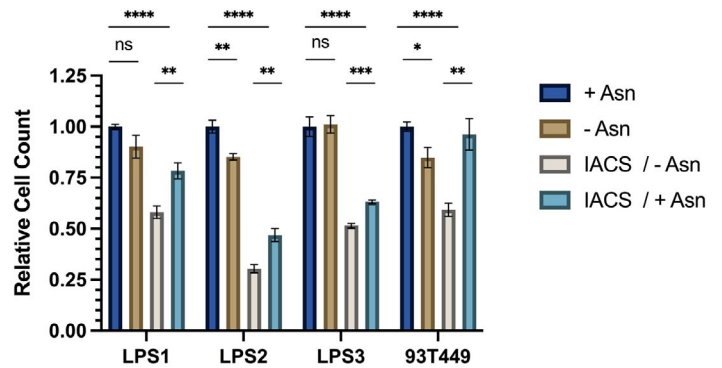


Figure 3: LPS Patient Organoid Viability

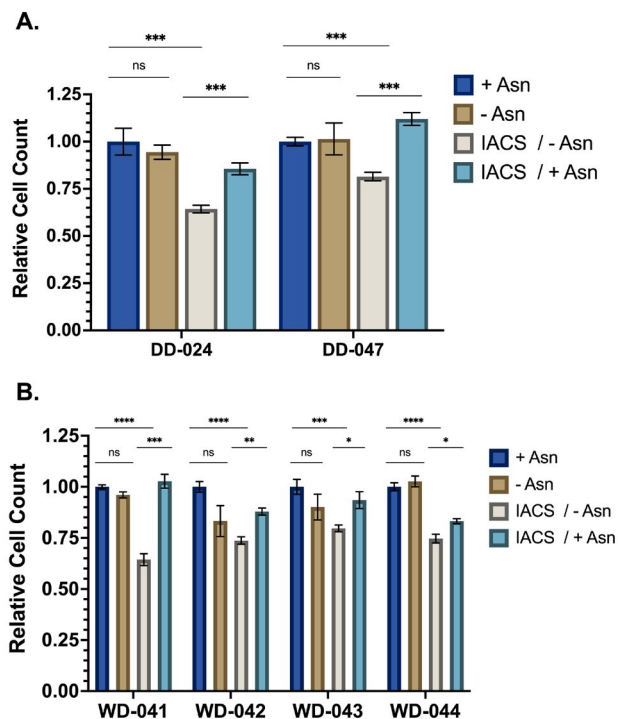
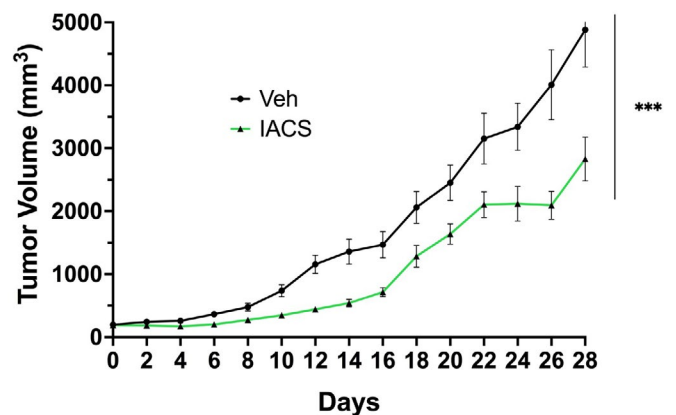


Figure 4: LPS2 Xenograft Trial





Poster #013 #1818996

TARGETING SARCOMA PULMONARY METASTASES WITH ANNAMYCIN

Waldemar Priebe, MSc, PhD¹; Rafal Zielinski, PhD²; Krzysztof Grela, MSc³; Roberto Cardenas-Zuniga, PhD¹; Stanislaw Skora, PhD¹; Izabela Fokt, PhD¹; Radjendirane Venugopal, PhD⁴; Maria Poimenidou, BA¹; Lamhamedi Cherradi Salah-Eddine, PhD¹; Joseph A. Ludwig, IV, MD⁵

¹UT MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ²UT MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ³Moleculin Biotech Inc., Houston, Texas, UNITED STATES, ⁴UT MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁵Sarcoma Medical Oncology, University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES

Objective: The most frequent site of sarcoma metastasis is the lung. While therapeutic options for oligometastatic pulmonary spread include surgical resection and stereotactic radiation, systemic chemotherapy is generally provided for chemo-sensitive sarcoma subtypes. To heighten the efficacy of treatment, we sought a novel approach to enhance drug distribution to the lung using the unique properties of Annamycin (ANN). ANN is a significantly modified analog of doxorubicin (DOX) that possesses novel properties differentiating it from DOX.

This new potent topoisomerase II poison is non-cardiotoxic, demonstrates high activity against multidrug-resistant (MDR) tumors, and an organ distribution noticeably different from DOX, including high lung uptake of ANN.

Our objective was to evaluate ANN activity in preclinical in vitro and in vivo models of sarcoma to assess its clinical potential as a novel drug for the treatment of sarcoma pulmonary metastases.

Methods: In vitro activity of ANN was tested in a panel of cancer cell lines, including the murine fibrosarcoma model (MCA205) and the murine osteosarcoma model (K7M3) using Resazurin Assay. The intracellular uptake of ANN was assessed using FACS and confocal microscopy. The potency of double-strand breaks induction and induction of apoptosis were evaluated by Western Blot using anti H2AX (pS139), cleaved caspase, and cleaved PARP antibody. Pharmacokinetics and tissue-organ distribution of free ANN and ANN formulated for clinical use in multilamellar liposomes (L-ANN) were evaluated in mice and rats and compared with DOX. The animals were dosed with ANN, DOX, or L-ANN, followed by tissue harvesting at indicated timepoints. The levels of ANN, and DOX, in harvested organs were assessed using LC-MS/MS.

Two syngeneic mouse models of lung metastasis for fibrosarcoma (MCA205) and osteosarcoma (K7M3) were used in these in vivo preclinical studies. Briefly, female C57NL/6J and Balb/C mice were injected with 1×10^5 of MCA 205 or 3.0×10^5 K7M3 cells respectively through the lateral tail vein. The mice were randomized into two experimental arms (n=10) receiving a vehicle or intravenous dose of L-ANN at 4 mg/kg. The dosing was repeated on a once-a-week schedule for seven weeks. Survival was a primary output of the study. Additionally, for the K7M3 model, a CT scan of the thoracic cavity was also performed using Bruker SkyScan 1276 micro-CT.

Results: ANN shows low nanomolar level potency (IC₅₀) in tested sarcoma cell lines. Recorded IC₅₀ average values were 49 nM and 33 nM for K7M3 and MCA205, respectively.

FACS and confocal experiments showed time- and dose-dependent uptake of the Annamycin by the cells with nuclear and significant cytosolic localization. Furthermore, Annamycin led to the efficient formation of DNA double-strand breaks and induction of apoptosis.

Tissue-organ distribution studies in mice and rats demonstrated high levels of ANN in lungs after administration as a free drug and incrementally higher for L-ANN. In rats injected with ANN as a free drug, the C_{max} values for ANN were significantly higher than that of DOX and, in the case of L-ANN, were more than 30-fold higher than that of DOX.

In vivo efficacy experiments in established experimental lung metastasis models revealed the remarkable extension of the survival in both K7M3 and MCA205 models. The median survival of the vehicle-treated mice was 21 days in the MCA205 model, while mice receiving L-ANN showed a median survival of 87.5 days (p < 0.0001). In the K7M3 model, the median survival for the control group was 58 days, while median survival was not reached at the study termination on day 222. CT scans performed on mice on days 58 and 71 showed massive lung colonization in vehicle-treated mice, while there were no metastatic changes visible in L-ANN-treated animals.

Conclusion: Annamycin (ANN) is a non-cardiotoxic anthracycline displaying high cytotoxicity against several sarcoma cell lines in vitro. High in vivo activity against lung metastatic sarcomas correlates well with high concentration of ANN in the

lungs. These observations are further supported by the results of additional studies demonstrating excellent therapeutic activity of L-ANN in lung metastasis models of breast (4-T1) and colon (CT26) cancers. These preclinical studies are being expanded using additional sarcoma subtypes.

In summary, the results of our preclinical studies demonstrating high activity of L-ANN in the in vivo sarcoma lung metastasis models warranted detailed preclinical development that led to the initiation of multicenter clinical studies (NCT04887298).

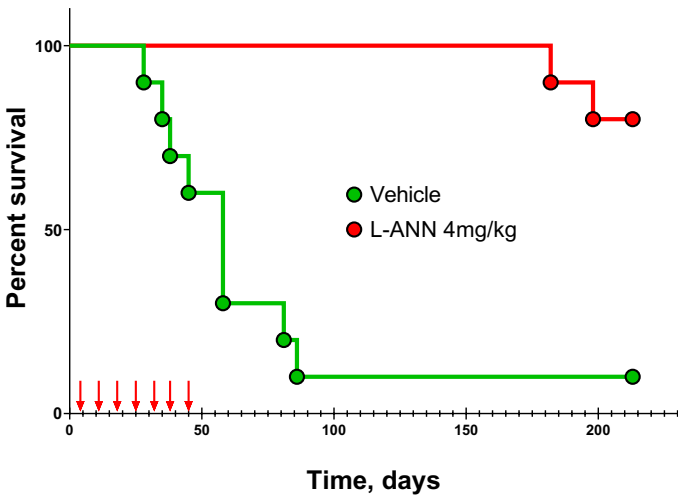


Table 1: Summary of the experimental conditions and survival parameters

Group	Dose	n	M.S.	Survival ratio, %	P*
Vehicle	n/a	10	58	-	-
L-ANN	4 mg/kg	10	>222	>383	<0.0001

*P values calculated using the log-rank (Mantel-Cox) test in GraphPad Prism
M.S. - Median, Survival (days); Study was terminated on day 222.

Figure 1: Kaplan-Meier survival curves for K7M3 osteosarcoma model treated with L-ANN or vehicle. Arrows represent the dose administration.

Twenty, ten-week-old female Balb/c mice were administered intravenously with 3×10^5 K7M3 cells. On day four, animals were randomized into two experimental groups receiving vehicle (n=10) and L-ANN at 4 mg/kg once a week for seven weeks (n=10). Arrows represent the dose administration.

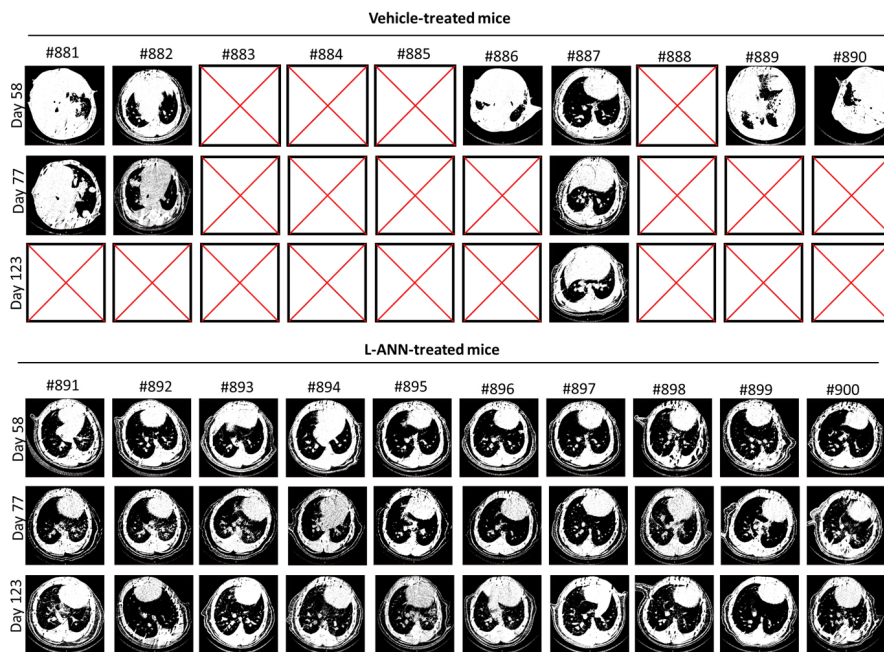


Figure 3. CT images of K7M3 osteosarcoma model treated with vehicle or seven weekly doses of L-Annamycin

Twenty, ten-week-old female Balb/c mice were administered intravenously with 3×10^5 K7M3 cells. On day four, the animals were randomized into two experimental groups receiving vehicle (n=10), and L-ANN at 4 mg/kg once a week for seven weeks (n=10). The CT images were acquired on a Bruker SkyScan 1276 micro-CT at 30 μ m, performed on vehicle or L-ANN treated mice on day 58, 77 and 123.

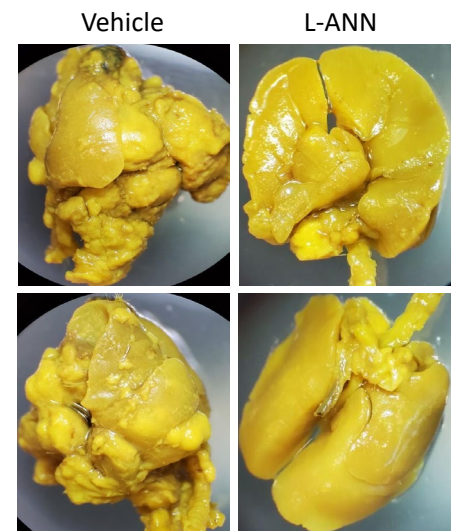


Figure 4. Ex vivo comparison of lungs extracted from vehicle- or L-ANN treated K7M3 osteosarcoma tumor model.

The lungs of vehicle-treated mouse were extracted at the time of mouse euthanasia (left), or L-ANN treated mice (right) at the experiment termination on day 222. The lungs were fixed in Bouin's solution for visualization of the macro metastatic nodules.



Poster #014 #1818876

TYK2 AS A BIOMARKER AND THERAPEUTIC TARGET IN MALIGNANT PERIPHERAL NERVE SHEATH TUMORS

Dana C. Borcharding, PhD¹; Neha Amin¹; Kevin He¹; Carina Dehner, MD/PhD²; Peter Ruminski, MS¹; Sonika Dahiya, MD¹; John S. Chrisinger, MD³; Taylor Sundby, MD⁴; Kai Pollard, B.S., B.A.⁵; Brigitte C. Widemann, MD⁴; Christine Pratilas, MD⁵; Jack F. Shern, MD⁴; Angela C. Hirbe, MD, PhD⁶, ¹Washington University in St. Louis, St. Louis, Missouri, UNITED STATES, ²Washington University Division of Oncology, St. Louis, Missouri, UNITED STATES, ³Washington University Department of Pathology and Immunology, St. Louis, Missouri, UNITED STATES, ⁴NCI, Bethesda, Maryland, UNITED STATES, ⁵Johns Hopkins University, Baltimore, Maryland, UNITED STATES, ⁶Washington University School of Medicine, St. Louis, Missouri, UNITED STATES

Objective: Malignant peripheral nerve sheath tumors (MPNST) are highly aggressive sarcomas with limited treatment options and poor survival rates. About half of MPNST cases are associated with the Neurofibromatosis Type 1 (NF1) cancer predisposition syndrome, while the other half occur sporadically or as a secondary complication of radiation therapy. In individuals with NF1, MPNST develop from benign plexiform neurofibromas (PN), however, there are no predictive biological markers of transformation. Despite therapies including surgery, chemotherapy and/or radiation, these tumors recur in about 50% of patients and most die within 5 years of diagnosis. Our laboratory previously identified TYK2 as a gene mutated in a subset of MPNST. More recently, we have shown that genetic knockdown of TYK2 in MPNST cell lines results in decreased proliferation and increased cell death in vitro. Additionally, Tyk2 knockdown in murine MPNST cells resulted in decreased tumor burden in subcutaneous and metastatic tumor models. Our objectives were to: 1) determine whether TYK2 is a prognostic biomarker for MPNST and can distinguish MPNST from precursor lesions, 2) examine the oncogenic mechanisms of TYK2 in MPNST, and 3) evaluate the utility of targeting TYK2 as a treatment strategy for MPNST.

Methods: Immunohistochemistry (IHC) for TYK2 was performed on 60 MPNST, 40 PN, and 9 atypical neurofibromas (AN) to evaluate TYK2 association with tumor type, overall survival, metastasis and therapeutic response. To evaluate the utility of targeting TYK2 therapeutically, MPNST cell-lines (JW23.3, MPNST-724, JH 2-002, and JH 2-009) were treated with novel TYK2 inhibitors generated at Washington University. Cell confluence and apoptosis were analyzed by IncuCyte live cell imaging assays, and IC50 values were calculated. Protein levels and phosphorylation were examined by WES western blotting system.

Results: Immunostaining revealed elevated TYK2 protein levels in MPNST vs. benign PN. Pharmacologic inhibition of TYK2 dose-dependently decreased the percent cell confluence and induced apoptosis over time in four MPNST cell-lines, as determined by IncuCyte proliferation and apoptosis assays. Additionally, blockade of the downstream targets STAT3 and BCL-2 reduced cell confluence over time, which corresponded with increased cell death. Finally, treatment with TYK2 inhibitors reduced pSTAT3 protein levels, but not pERK1/2 or pS6K.

Conclusion: These findings suggest that TYK2 is a novel therapeutic target that promotes MPNST pathogenesis through STAT3 activation and inhibition of apoptosis. Furthermore, TYK2 expression is associated with MPNST and thus may serve as a biomarker for transformation to MPNST.



Poster #015 #1819037

CHROMOSOME 8 GAIN IS A COMMON EVENT IN MPNST PATHOGENESIS

Carina Dehner, MD/PhD¹; Chang In Moon²; Xiyuan Zhang, PhD³; Zhaohe Zhou⁴; Chris Miller²; Hua Xu²; Xiaodan Wan²; Kuangying Yang²; Jay Mashl²; Sara Gosline⁵; Yuxi Wang²; Xiaochun Zhang²; Abigail Godec⁶; Paul Jones²; Sonika Dahiya, MD⁷; Tina Primeau²; Shunqiang Li²; Kai Pollard, B.S., B.A.⁸; Fausto Rodriguez, MD⁹; Li Ding²; Christine Pratilas, MD⁸; Jack F. Shern, MD³; Angela C. Hirbe, MD, PhD²; Himanshi Bhatia, PhD²,

¹Washington University Division of Oncology, St. Louis, Missouri, UNITED STATES, ²Washington University, St. Louis, Missouri, UNITED STATES, ³NCI, Bethesda, Maryland, UNITED STATES, ⁴Washington U, St. Louis, Missouri, UNITED STATES, ⁵Pnnl, Benton County, Washington, UNITED STATES, ⁶Michigan State, Grand Rapids, Michigan, UNITED STATES, ⁷Washington University in St. Louis, St. Louis, Missouri, UNITED STATES, ⁸Johns Hopkins University, Baltimore, Maryland, UNITED STATES, ⁹Washington University School of Medicine, St. Louis, Missouri, UNITED STATES

Objective: One of the most deadly malignancies affecting adults with Neurofibromatosis type 1 (NF1) is the malignant peripheral nerve sheath tumor (MPNST), an aggressive and often fatal sarcoma which commonly arises from its benign precursor lesion plexiform neurofibromas. Despite the progress in our understanding of MPNST pathobiology, the few effective therapeutic options have shown limited success in clinical trials. To further understand the genomic heterogeneity of MPNST, and to generate a preclinical platform encompassing this heterogeneity, we developed a collection of NF1-MPNST patient derived xenografts (PDX) and compared these to their parental tumors using of whole exome sequencing, copy number analysis and RNA sequencing.

Methods: Human tumor samples were collected at both institutions and implanted subcutaneously into NSG mice. Then, PDX and parental tumors were evaluated histologically. Whole exome and bulk RNA sequencing were performed to identify somatic variant signatures. Copy number variations were used to infer and visualize copy number data from high-throughput WGS sequencing data and to compare to seven plexiform neurofibromas. Fluorescent in situ hybridization was performed to assess for Chromosome 8 gain. Single cell RNA sequencing was used to assess for Chr8q gain on single cell level.

Results: Eight MPNST-PDX lines were established from biopsy-proven NF1-MPNST between 2014 and 2019 at two different institutions. Somatic variant analysis identified an average of 80 high confidence single-nucleotide variants (SNV). Correlation of the VAF in the parental tumor vs the VAF in each PDX demonstrated similarity of the PDX to its parental tumor. Hierarchical clustering highlighted intertumoral heterogeneity between PDX and parental tumor. To characterize the intra-tumoral heterogeneity at single-cell resolution, droplet-based single cell RNA sequencing was performed on 24055 cells from each of the eight MPNST PDX which revealed clustering from different PDX shared transcriptional similarities. CNV analysis found remarkable similarities within the CNV profiles of the PDX compared to the corresponding patient tumors. Notably, 87% of the cases showed a Chr8q gain. CNV analysis on seven plexiform neurofibroma revealed that Chr8q gain was not observed in any of them, supporting this to be an early event in MPNST pathogenesis. Single cell data using the inferCNV method showed that all PDXs exhibited Chr8q gain in all or a high percentage of the tumor cells. Centromeric probe Chr8 fluorescence in situ hybridization (FISH) performed on the eight PDX models, eight corresponding patient tumors, as well as ten additional NF1-MPNST cases that served as a validation cohort showed Chr8 gain in all but one PDX. Of the corresponding parental tumors, Chr8 gain was observed in five cases. However, all of the other cases (both PDX and parental tumors) demonstrated Chr8 gain in at least 10% of cells. These data suggest a selective advantage for cells with Chr8 gain during the engraftment process. Similarly, in the validation cohort, eight out of ten NF1-MPNST had Chr8 gains in >50% of cells, and in the remaining two, Chr8 gains were present in at least 10% of cells. These findings strongly support the notion that Chr8 gain is a nearly universal event in MPNST.

Conclusion: Here we present a deep characterization of a set of eight NF1-MPNST PDX lines. Our analyses included the first use of single cell sequencing in this cancer type and highlight the complex intra- and inter-tumoral heterogeneity of MPNST. Additionally, our data support that gain of Chr8q gain is a common event in MPNST pathogenesis, and an area that warrants further investigation. Future studies, conducted through multi-institutional collaboration, will be aimed at determining the strength of the correlation between CNV and clinical outcomes in a large subset of MPNST, as well as determination of the specific genes at this locus that are critical for MPNST progression.



Poster #016 #1818940

ESTABLISHMENT OF A COMPREHENSIVE CLINICALLY- AND GENOMICALLY ANNOTATED BIOSPECIMEN REPOSITORY FROM PATIENTS WITH NEUROFIBROMATOSIS TYPE 1

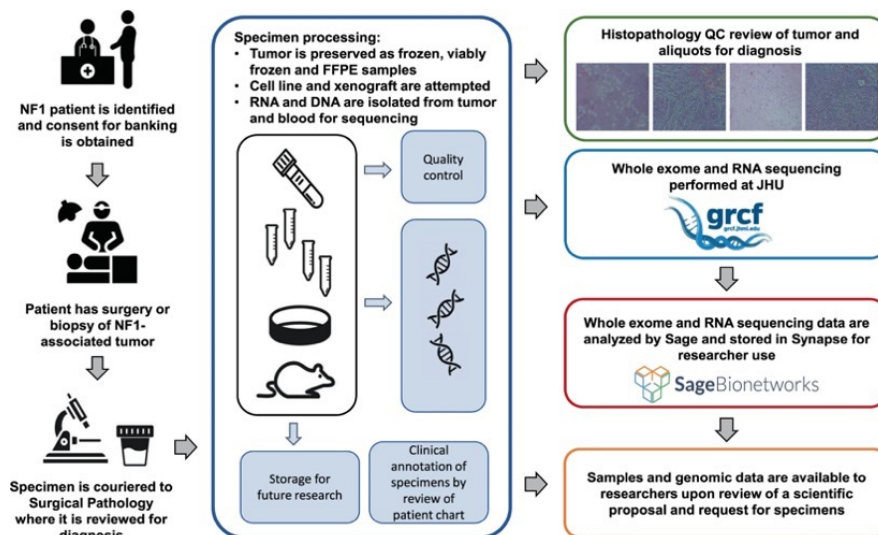
 Kai Pollard, B.S., B.A.¹; Jineta Banerjee, PhD²; Ana Calizo, B.S.¹; Robert Allaway, PhD²; Fausto Rodriguez, MD¹; Christine Pratilas, MD¹
¹Johns Hopkins University, Baltimore, Maryland, UNITED STATES, ²Sage Bionetworks, Seattle, Washington, UNITED STATES

Objective: Neurofibromatosis type 1 (NF1) is a common genetic disorder characterized by a predisposition to the development of nerve sheath tumors, including cutaneous neurofibromas (cNF), plexiform neurofibromas (pNF), and malignant peripheral nerve sheath tumors (MPNST). The development of nonsurgical therapy for pNF has been limited by limited cell culture-based and animal models, and limited access to primary tissue from patients with NF1. Likewise, advancement of therapeutic strategies for patients with MPNST requires discovery efforts based on human tumor specimens and genomically diverse model systems. Comprehensively characterized banked tissue and the creation of new models allows for the most efficient and targeted use of specimens in collaborative NF1 research efforts.

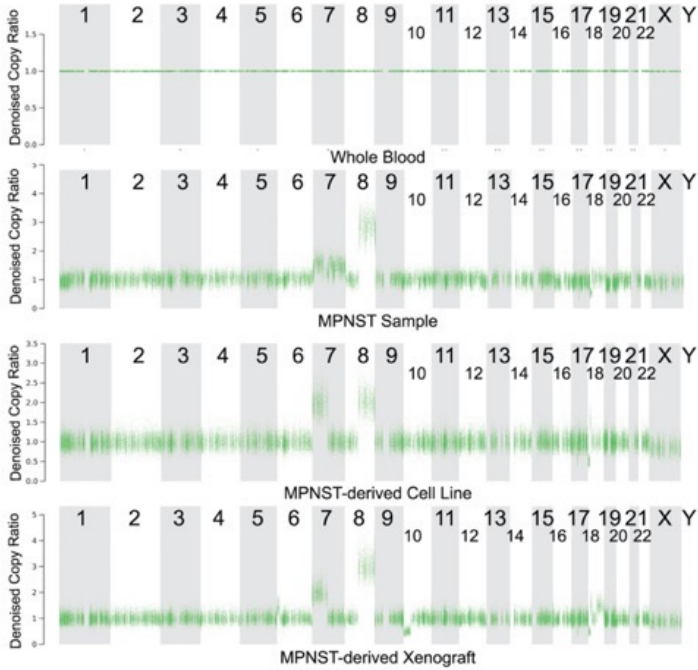
Methods: We have created and expanded a Johns Hopkins University biospecimen repository for the purpose of banking blood fractions and tumor tissue from patients with NF1, and generating cell culture and xenograft models to propagate primary human tissue. Under an IRB-approved research authorization, NF-associated tumor tissue is collected and processed at the time of surgery. H&E slides of each banked sample are reviewed by the study neuropathologist for quality control and accuracy of diagnosis. Banked specimens undergo comprehensive genomic characterization using RNAseq and whole exome sequencing (WES), and data are made publicly available through the NF Data Portal. A clinically -annotated database accompanies the bank, and includes NF1-associated symptoms and findings, tumor characteristics, and outcomes data. We have implemented an internal review process for researchers outside our institution to request access to specimens and accompanying de-identified clinical information.

Results: We have established a Johns Hopkins University NF1 biospecimen repository which includes high-quality, clinically-annotated, and genomically-characterized nerve sheath tumor tissues and blood fractions. Since inception in January 2016, over 209 unique samples have been banked, and include plexiform neurofibroma (n=68), MPNST (n=30), cutaneous neurofibroma (n=59), blood fractions, and xenograft (n=6) specimens, from 110 unique patients. Seventeen researchers from outside institutions have requested access to our specimens. RNAseq data (n=42) and WES data (n=99) are available on the NF Data Portal.

Conclusion: Our NF1 biospecimen repository represents a high-quality, clinically and genomically characterized and valuable resource for ongoing scientific efforts in the NF1 research community.



	Unique participants	Unique Specimens	Paired Blood (normal)	Paired cell line	Paired xenograft	Clinical Data Set Completed
MPNST	19	30	19	5	6	19
ANNUBP	1	1	1	0	0	1
Plexiform or Nodular NF	51	68	42	4	0	51
Cutaneous Neurofibroma	27	59	27	1	0	27
Diffuse infiltrating NF	9	27	9	0	0	9
Diffuse subcutaneous & subcutaneous	15	24	16	0	0	15



2-079 PDX and Cell Line Info Sheet

PI: Christine Pratilas (cpratill@jhmi.edu)
 Research Specialist: Kai Pollard (mkai1@jhmi.edu)
 Laboratory Phone: (443) 287-9370



PDX H&E: 6-7 weeks from fresh implantation to 2cm tumor.	Cell Line Photo (10x):																																												
<p>Tumor Information: Diagnosis: MPNST, FNCLCC Grade 2 High grade, spindle cell neoplasm with areas of skeletal muscle differentiation (malignant triton tumor) and glandular differentiation Creation Date: 08/03/2020 Anatomical Location of Tumor: Left upper popliteal mass</p>																																													
<p>NGS Sequencing:</p> <table border="1"> <thead> <tr> <th></th> <th>Chr:Pos</th> <th>Base Change</th> <th>Reference Database ID</th> <th>AA_change</th> </tr> </thead> <tbody> <tr> <td>NF1 (8/3/2020)</td> <td>chr17:29657517</td> <td>G>A</td> <td>rs876658854; COSM6930737</td> <td>c.5749+1G>A</td> </tr> <tr> <td>NF1</td> <td>chr17:29664863</td> <td>C>A</td> <td>rs1555534918</td> <td>p.C2202*</td> </tr> <tr> <td>EED</td> <td>chr11:85977125</td> <td>G>T</td> <td></td> <td>p.D243Y</td> </tr> </tbody> </table>			Chr:Pos	Base Change	Reference Database ID	AA_change	NF1 (8/3/2020)	chr17:29657517	G>A	rs876658854; COSM6930737	c.5749+1G>A	NF1	chr17:29664863	C>A	rs1555534918	p.C2202*	EED	chr11:85977125	G>T		p.D243Y																								
	Chr:Pos	Base Change	Reference Database ID	AA_change																																									
NF1 (8/3/2020)	chr17:29657517	G>A	rs876658854; COSM6930737	c.5749+1G>A																																									
NF1	chr17:29664863	C>A	rs1555534918	p.C2202*																																									
EED	chr11:85977125	G>T		p.D243Y																																									
<p>STR Profile:</p> <table border="1"> <thead> <tr> <th></th> <th>D5S818</th> <th>D13S317</th> <th>D7S820</th> <th>D16S539</th> <th>vWA</th> <th>TH01</th> <th>AMEL</th> <th>TPOX</th> <th>CSF1PO</th> <th>D21S11</th> </tr> </thead> <tbody> <tr> <td>Tumor</td> <td>11, 12</td> <td>13</td> <td>8, 9</td> <td>9, 12</td> <td>15, 16</td> <td>9</td> <td>X</td> <td>9</td> <td>10, 12</td> <td>34.2</td> </tr> <tr> <td>Cell Line</td> <td>11, 12</td> <td>13</td> <td>8, 9</td> <td>9, 12</td> <td>15, 16</td> <td>9</td> <td>X</td> <td>9</td> <td>10, 12</td> <td>34.2</td> </tr> <tr> <td>Xenograft</td> <td>11, 12</td> <td>13</td> <td>8, 9</td> <td>9, 12</td> <td>15, 16</td> <td>9</td> <td>X</td> <td>9</td> <td>10, 12</td> <td>34.2</td> </tr> </tbody> </table>			D5S818	D13S317	D7S820	D16S539	vWA	TH01	AMEL	TPOX	CSF1PO	D21S11	Tumor	11, 12	13	8, 9	9, 12	15, 16	9	X	9	10, 12	34.2	Cell Line	11, 12	13	8, 9	9, 12	15, 16	9	X	9	10, 12	34.2	Xenograft	11, 12	13	8, 9	9, 12	15, 16	9	X	9	10, 12	34.2
	D5S818	D13S317	D7S820	D16S539	vWA	TH01	AMEL	TPOX	CSF1PO	D21S11																																			
Tumor	11, 12	13	8, 9	9, 12	15, 16	9	X	9	10, 12	34.2																																			
Cell Line	11, 12	13	8, 9	9, 12	15, 16	9	X	9	10, 12	34.2																																			
Xenograft	11, 12	13	8, 9	9, 12	15, 16	9	X	9	10, 12	34.2																																			
<p>Xenograft Testing Results- This Xenograft has tested negative for the following mouse/rat contaminants:</p> <p>HANT (Hantavirus Hantaan), IDIR , K Virus, L CMV, LDV, MAV 1 & 2, MCMV, MHV, Mouse Parvovirus (MPV/MVM) , Mousepox (Ectromelia) , MNV , MRV (EDIM) , MTLV , MuCPV , (MKPV) POLY , PVM , RCMV , RCV/SDAV , REO , Rat Parvovirus (RPV) , RTV , SEND , SEO (Hantavirus) , TMEV/GDVII , Vesivirus, C. bovis , Mycoplasma Genus , and M. pulmonis</p>																																													



Poster #017 #1818949

IDENTIFICATION OF THERAPEUTIC VULNERABILITIES IN NF1-ASSOCIATED MALIGNANT PERIPHERAL NERVE SHEATH TUMORS DEFICIENT FOR POLYCOMB REPRESSIVE COMPLEX 2

Kyle B. Williams, PhD¹; Alex Larsson, BS²; Justin Tibbits, BS, MS²; Tyler Jubenville, BS³; Helena Sverak, BS²; Christopher L. Moertel, MD²; David A. Largaespada, PhD²

¹University of Minnesota, Minneapolis, Minnesota, UNITED STATES, ²University of Minnesota, Minneapolis, Minnesota, UNITED STATES, ³University of Minnesota, Minneapolis, Minnesota, UNITED STATES

Objective: Neurofibromatosis Type 1 (NF1) is a common genetic disorder caused by mutations in the tumor suppressor gene NF1. We constructed models of nerve sheath tumors that arise in NF1 patients and conducted therapeutics discovery using synthetic lethal pharmacogenomic screens. Given both plexiform neurofibromas and malignant peripheral nerve sheath tumors (MPNSTs) arise within the Schwann cell lineage, we developed a drug discovery pipeline to identify targeted therapeutics for treating NF1-related neoplasia.

Methods: Using CRISPR/Cas9, we created immortalized human Schwann cell lines that are deficient for the NF1 gene or NF1 and components of Polycomb Repressive Complex 2 (PRC2), such as SUZ12. ~80% of all MPNST harbor loss of function mutations in PRC2 genes, which is highly suggestive that perturbation of epigenetic homeostasis plays a role in malignant transformation of neurofibromas. Our models closely mimic the genetics of MPNSTs and allowed us to identify drugs by exploiting vulnerabilities specific to their underlying genetics. We describe the identification of these novel drugs, extensive in vivo testing in models of MPNST, and mechanistic studies to explain why they act specifically on MPNSTs.

Results: We successfully identified compounds showing selective lethality towards NF1/SUZ12 double mutant cells. These include drugs affecting epigenetic homeostasis, such as HDAC inhibitors (HDACi). Moreover, many of these drugs showed strong synergy when tested in combination against NF1/SUZ12 deficient human Schwann and MPNST cell lines. This was particularly true when a MEK inhibitor (MEKi) was combined with HDACi. We have explored the mechanism of this synergy using genetics, transcriptome, and proteome analysis. Interestingly, these mechanistic studies have revealed possible emerging avenues of resistance the cells are utilizing in order to compensate for and survive therapeutic intervention. For instance, proteomics analysis, using the PTMScan platform, of PRC2 deficient MPNST cell lines treated with drug candidates (single agent and combination) indicates activation of specific survival pathways. Targeting these pathways in conjunction with the new main-line therapeutics we have identified could prevent emergence of resistance and tumor escape. Clinically interesting drug candidates were advanced and tested as single agents and in combination in multiple in vivo models of MPNST (including patient derived and cell line xenografts). Some have shown dramatic efficacy and top combinations exhibit strong synergy in vivo, giving durable responses. Moreover, combination therapy can dramatically shrink established tumors, with treated tumors showing extensive markers of apoptosis.

Conclusion: The discovery of novel agents effective against several models of MPNST is exciting, as there are currently no approved targeted therapies for MPNST. Results from our studies are forming the basis for clinical trials we hope to propose for the treatment of MPNSTs and aggressive plexiform neurofibromas.



Poster #018 #1819003

PRECLINICAL ASSESSMENT OF PROTEOSTASIS INHIBITION IN RHABDOMYOSARCOMA

Amit J. Sabnis, MD; Jacky Morales, BA; David V. Allegakoen, BS, MS; Leanne Sayles, BS; Alejandro Sweet-Cordero, MD, University of California, San Francisco, San Francisco, California, UNITED STATES

Objective: Poor outcomes for rhabdomyosarcoma (RMS) patients with metastatic or recurrent disease highlight a need for novel therapeutic strategies. Previously, we demonstrated that RMS cell lines are uniquely sensitive to small molecule inhibition of the protein chaperone HSP70, indicating the therapeutic potential of targeting regulators of endoplasmic reticulum (ER) stress and proteostasis. However, as HSP70 inhibitors are not optimized for use in vivo, we searched for alternative means of modulating proteostasis. Here, we sought to use transcriptomic profiling of RMS cell lines to identify other pharmacologic targets by which to enact the same downstream consequences of HSP70 inhibition, and to test their therapeutic effects in patient-derived xenograft (PDX) models. Our data led us to study the therapeutic potential of CB-5083, an inhibitor of the ATPase p97 that promotes ER-associated degradation by extracting misfolded proteins, thus restoring ER homeostasis.

Methods: We carried out transcriptional profiling of RMS cell lines following either chemical or genetic suppression of HSP70, then used informatic tools to identify other targets that might exploit ER quality control dependence. We assessed UPR activation in RMS cell lines after HSP70 and p97 inhibition, and based on these findings, carried out pharmacokinetic and pharmacodynamic dose-finding of CB-5083 in NSG mice implanted with two different RMS PDX. We evaluated the efficacy and toxicity of different dosing schedules, using biomarkers of UPR activation to guide dose selection.

Results: We found that suppression of the protein p97 recreates the downstream effects of HSP70 inhibition. Treatment of RMS cells with the p97 inhibitor CB-5083 led to the accumulation of misfolded proteins in the ER, triggering the apoptotic arm of the unfolded protein response (UPR) at ten-fold higher potency than the HSP70 inhibitor MAL3-101. Given our findings, we advanced testing of CB-5083 into in vivo models. The maximum tolerated dose (MTD) of CB-5083 was 50 mg/kg administered by oral gavage every other day. Continuous dosing was more effective at inducing the unfolded protein response in tumors, but was associated with significant toxicity. At the MTD, CB-5083 had discordant effects in PDX models, allowing us to test UPR activation as a biomarker of response.

Conclusion: Our data highlight pharmacologic strategies that target ER quality control and can induce responses in RMS PDX models. An interrupted dosing strategy is needed to limit toxicity, and correlates with graded levels of UPR activation. Ongoing studies will establish biomarkers to predict the differential responses observed.



Poster #019 #1819014

CLICK ACTIVATED PROTODRUGS AGAINST CANCER (CAPAC) PLATFORM ENHANCES ANTITUMOR EFFICACY, SAFETY AND PHARMACOKINETICS OF CANCER THERAPEUTICS

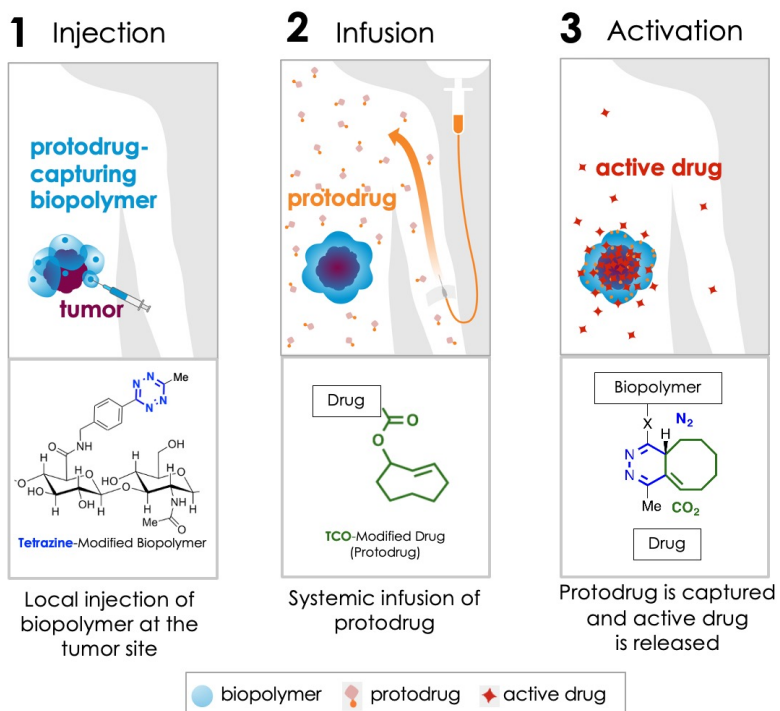
 Sangeetha Srinivasan, PhD¹; Nathan Yee, PhD¹; Amir Mahmoodi, MS²; Michael Zakharian, MS¹; Wayne M. Saville, MD¹; Jose M. Mejia Oneto, MD/PhD¹
¹Shasqi, Inc., San Francisco, California, UNITED STATES, ²Shasqi, Inc., San Francisco, California, UNITED STATES

Objective: The Click Activated Protodrugs Against Cancer (CAPAC) platform is designed to treat cancer without poisoning the body by activating powerful cancer therapies at the tumor site(s). CAPAC's mechanism of activation is based on click chemistry and therefore does not rely on tumor characteristics, biomarker expression, or other biological factors that vary across patients. Thus, the CAPAC platform can be readily applied to various tumor types. The lead candidate of the platform, SQ3370, is being evaluated in a Phase I study in patients with advanced solid tumors (NCT04106492). We describe the therapeutic benefits, safety and pharmacokinetics (PK) of SQ3370 in small and large animals.

Methods: SQ3370, consists of 2 components: SQL70 biopolymer and SQP33 protodrug. First, SQL70, a tetrazine-modified sodium hyaluronate biopolymer, is injected in the tumor. Then, SQP33, a trans-cyclooctene (TCO)-modified protodrug of Doxorubicin (Dox) is given as 5 daily intravenous doses. SQP33 protodrug has attenuated toxicity and is converted to active Dox by SQL70 biopolymer at the tumor through an efficient covalent reaction between the tetrazine and TCO moieties.

Results: SQ3370 elicited dose-dependent anti-tumor responses in multiple syngeneic dual tumor models, and the maximum tolerated dose (MTD) of SQ3370 was nearly 20-times the MTD of Dox in mice. In dogs, the highest non-severely toxic dose (HNSTD) of SQ3370 was found to be 8.95 times higher when compared to the conventional dose of Dox. There were minimal and reversible systemic adverse events, with no evidence of cardiotoxicity. PK analysis in all species showed that SQL70 biopolymer effectively captures SQP33 protodrug from circulation and releases active Dox throughout the treatment period. A single biopolymer dose was capable of activating 5 daily doses of SQP33 protodrug. In the absence of SQL70, SQP33 protodrug was found to be stable and did not spontaneously convert to Dox. In mice, at least 50% of the SQL70 biopolymer remains at the injection site for 2-4 weeks, and plasma levels of SQP33 protodrug and active Dox are similar across different SQL70 injection locations.

Conclusion: The CAPAC Platform represents a new therapeutic modality to treat solid tumors by expanding the pharmacological capabilities of drugs with known efficacy such as Dox. SQ3370, CAPAC's lead candidate, demonstrates enhanced safety and efficacy in vivo, as compared to the conventional Dox, and is being evaluated in a Phase I study in patients with advanced solid tumors (NCT04106492).





Poster #020 #1818953

DEVELOPING AND CHARACTERIZING MODELS OF RESISTANCE TO CYCLIN-DEPENDENT-KINASE 4 (CDK4) INHIBITION IN THE CDK4 AMPLIFIED CANCER, DEDIFFERENTIATED LIPOSARCOMA

 James L. Chen, MD¹; Jocelyn Hsu²; Nathan D. Seligson, PharmD³; Colin Stets, BS²; John Hays, MD, PhD¹
¹Ohio State University, Columbus, Ohio, UNITED STATES, ²The Ohio State University, Columbus, Ohio, UNITED STATES,

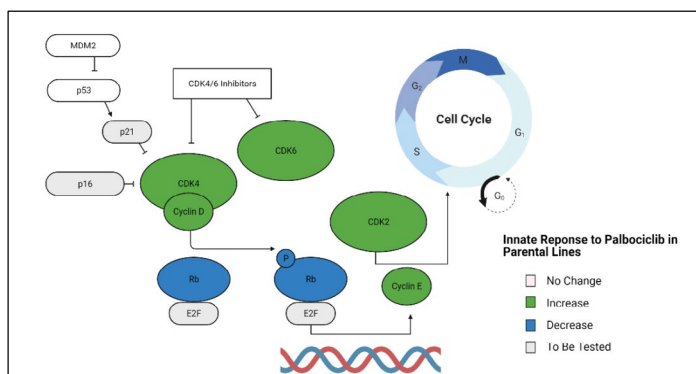
³University of Florida, Gainesville, Florida, UNITED STATES

Objective: Dedifferentiated liposarcomas (DDLPS) are malignant adipocytic cancers characterized by an amplification of the cell cycle regulatory gene, CDK4. Palbociclib, a CDK4/6-inhibitor, is rapidly becoming a standard of care treatment; however, innate and acquired resistance to the drug limits efficacy in patients with DDLPS. Molecular mechanisms and biomarkers of palbociclib resistance have been posited in non-mesenchymal tumors, but are poorly understood in DDLPS. To this end, we developed palbociclib-resistant DDLPS cell lines derived from several patient DDLPS samples to better characterize these phenotypic and genomic differences.

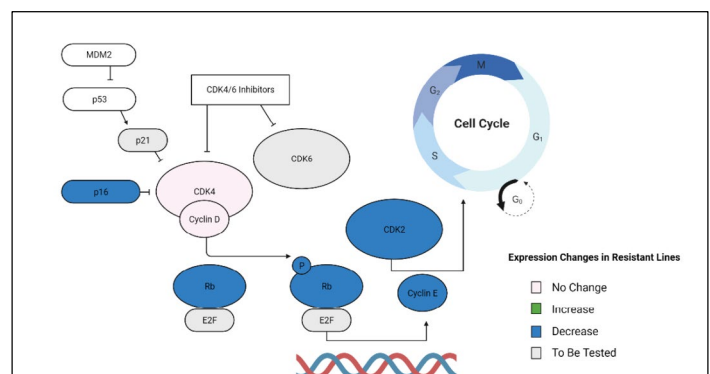
Methods: Three human CDK4 amplified DDLPS cell lines (224A, 246, 863) and one liposarcoma control cell line without CDK4 amplification (LiSa2) were brought into culture. After identifying the IC₅₀ of palbociclib for each cell line, parent cells were intermittently treated at palbociclib's IC₂₅ and surviving cells allowed to recover before retreatment. Parental lines were treated as controls in tandem with the developing resistant lines to compare molecular changes in response to palbociclib. When resistant cell strains were growing at the same rate as their parental strain, cell viability was measured by an XTT assay and protein expression was measured using whole cell lysates for Western blotting. All experiments were performed in triplicate. Descriptive statistics were used to compare differences in drug resistance and protein expression between resistant and parental cell lines.

Results: Parental IC₅₀ of the three CDK4 amplified DDLPS cell lines ranged from 8-12 μ M and the cell line without CDK4 amplification had an IC₅₀ of 12 μ M. Liposarcoma models were incubated with 8 μ M of palbociclib for over six months. Morphologically, resistant cell lines became more mesenchymal and less spherical. Resistant cell strains demonstrated minimal changes in the measured IC₅₀ of 14 μ M (\pm 2.39 μ M) versus 12 μ M (\pm 1.12 μ M) in the parental cell strains. Interestingly, CDK4 protein expression was unchanged between parent and acquired resistant lines ($p > 0.05$). Instead, a statistically significant decrease in the cell cycle inhibitors, pRb, Rb, p16, and CDK2 expression levels were observed in the resistant cell lines (all $p < 0.01$). Conversely, parental cells that remained viable after palbociclib treatment increased expression of cell cycle genes CDK2, CDK4, CDK6, and Cyclin E, and underexpressed pRb. These findings are summarized in Figure 1A&B.

Conclusion: Here we present the development of novel, palbociclib resistant, DDLPS cell lines. Resistant cell lines demonstrated decreased protein expression of Rb, p16, and CDK2. Whereas initial response to palbociclib treatment in parental cell lines was to increase CDK2, CDK6, Cyclin E, and decrease pRb—almost opposite from acquired resistant cells. Nonetheless, clinically, patients with DDLPS that exhibit innate loss of RB1 or CDKN2A may be more likely to demonstrate resistance to palbociclib. Next generation sequencing of DNA and RNA expression in parent and resistant lines are underway.



A. CCND-CDK4-RB pathway: Innate Response to Palbociclib in Parental Lines



B. CCND-CDK4-RB pathway: Expression Changes in Resistant Lines



Poster #021 #1818939

PATIENT-DERIVED SARCOMA MODELS TOWARDS BETTER CLINICAL OUTCOME OF SARCOMAS

Yuki Yoshimatsu, Ph.D¹; Rei Noguchi, MD, Ph.D²; Ryuto Tsuchiya, MD³; Yooksil Sin, Ph.D⁴; Takuya Ono, graduate student³; Mami Takahashi, Ph.D⁵; Hideaki Kosako, Ph.D⁶; Kaoru Hirabayashi, MD⁷; Kazutaka Kikuta, MD, Ph.D⁸; Iwao Ozawa, MD⁹; Akihiko Yoshida, MD, Ph.D¹⁰; Akira Kawai, MD¹¹; Tadashi Kondo, MD, Ph.D³

¹Division of Rare Cancer Research, National Cancer Center Research Institute, 5-1-1 Tsukiji, Chuo-ku, Tokyo, JAPAN, ²Division of Rare Cancer Research, National Cancer Center Research Institute, Tokyo, Tokyo, JAPAN, ³Division of Rare Cancer Research, National Cancer Center Research Institute, Chuo-ku, Tokyo, JAPAN, ⁴Division of Rare Cancer Research, National Cancer Center Research Institute, chuo-ku, Tokyo, JAPAN, ⁵Central Animal Division, National Cancer Center Research Institute, Chuo-ku, Tokyo, JAPAN, ⁶Division of Cell Signaling, Fujii Memorial Institute of Medical Sciences, Tokushima University, Tokushima-shi, Tokushima, JAPAN, ⁷Division of Diagnostic Pathology, Tochigi Cancer Center, Utsunomiya-shi, Tochigi, JAPAN, ⁸Division of Musculoskeletal Oncology and Orthopaedic Surgery, Tochigi Cancer Center, Utsunomiya-shi, Tochigi, JAPAN, ⁹Division of Hepato-Biliary-Pancreatic Surgery, Tochigi Cancer Center, Utsunomiya-shi, Tochigi, JAPAN, ¹⁰Department of Diagnostic Pathology, National Cancer Center Hospital, Chuo-ku, Tokyo, JAPAN, ¹¹National Cancer Center Hospital, Chuo-ku, Tokyo, JAPAN

Objective: Sarcomas are rare mesenchymal malignancies, characterized by the diverse histology and complex molecular backgrounds. It is hard to conduct pre-clinical studies, because the patient-derived cancer models are not available for majority of sarcomas. The genomic profiling combined with the drug sensitivity study have been performed using patient-derived cell lines, resulting in the identification of novel anti-cancer drugs and biomarkers to predict their efficacy. However, these large-scale studies did not include sarcoma cell lines, suggesting that the latest technologies have not benefited research on sarcomas. To address this issue, we established patient-derived sarcoma models, characterized their phenotypes, establish their utility as resources for pre-clinical study, and examined their molecular backgrounds.

Methods: Tumor tissues from the patients with sarcomas were obtained from the National Cancer Center Hospital, and Tochigi Cancer Center Hospital. The tumor tissues were treated with collagenase, and the tumor tissues were seeded onto the tissue culture plates. The cells were maintained under the conventional tissue culture conditions until the tumor cells grow well. The tumor cells were subjected to the authentication study, and their capability of proliferation, spheroid formation, and invasion was assessed in the same tissue culture condition. The anti-proliferative effects of anti-cancer drugs, whose utility was approved in other malignancies, were examined in the established cell lines. The tumor tissues were subcutaneously inoculated in the immune-compromised mice. The molecular backgrounds of established cell lines and xenografts were examined by next-generation sequencing, mass spectrometry, and global kinase activity study. This study was approved by the ethical committees of both National Cancer Center and Tochigi Cancer Center, and the informed consent was obtained from the donor patients.

Results: We have established 40 cell lines and 40 xenografts from the surgically resected tumor tissues. We performed the drug library screening, and identified intriguing anti-cancer drugs, which showed the anti-proliferative effects on the established sarcoma cell lines at the considerably low concentration. While their utility for sarcoma treatments was not expected until our study, they have been used for the treatment of different malignancies. The anti-tumor effects of those drugs were confirmed by in vivo experiments using xenografts. and the predictive biomarkers are currently under investigation using the multi-omics data.

Conclusion: The establishment of novel patient-derived models and the screening of anti-cancer drugs will be an effective approach to sarcomas. The response to anti-cancer drugs are different between the models and patients, and the further investigation should be required to apply the results of our in vitro study. The applications of genome and proteome data are worth challenging, and the development of predictive biomarkers and identification of novel therapeutic targets are the purpose of further omics study.



Poster #022 #1818942

IN VITRO DRUG SCREENING OF CIC-REARRANGED SARCOMAS USING SPHEROID AND MONOLAYER CULTURED PATIENT-DERIVED CANCER CELL LINES

Yu Kuwata, Research Associate¹; Yuki Yoshimatsu, Ph.D¹; Rei Noguchi, MD, Ph.D²; Ryuto Tsuchiya, MD³; Yooksil Sin, Ph.D⁴; Takuya Ono, graduate student³; Hiroyasu Nakatani, Ph.D⁵; Akira Kawai, MD⁶; Tadashi Kondo, MD, Ph.D³

¹Division of Rare Cancer Research, National Cancer Center Research Institute, 5-1-1 Tsukiji, Chuo-ku, Tokyo, JAPAN,

²Division of Rare Cancer Research, National Cancer Center Research Institute, Tokyo, Tokyo, JAPAN, ³Division of Rare

Cancer Research, National Cancer Center Research Institute, Chuo-ku, Tokyo, JAPAN, ⁴Division of Rare Cancer Research, National Cancer Center Research Institute, chuo-ku, Tokyo, JAPAN, ⁵Biospecimen Laboratories, Ota-ku, Tokyo, JAPAN,

⁶National Cancer Center Hospital, Chuo-ku, Tokyo, JAPAN

Objective: CIC-rearranged sarcomas are extremely rare and malignant mesenchymal neoplasms. The effective treatments have not been established probably because of their biological malignancy and rarity of disease.

Methods: We established three cell lines using surgical specimens from three cases of CIC-DUX4 sarcomas. Using these cell lines, we screened the anti-proliferative effects of 214 anti-cancer drugs, which were approved for the treatments of other malignancies. Previous studies reported that spheroid cultures of cancer cells better reflect characteristics of tumors than monolayer cultures, and thus we implemented both culture types.

Results: We treated the cells with the individual anti-cancer drugs at the fixed concentration, and the growth inhibitory rates (%) were used for hierarchical clustering of cell lines and drugs. We found that the cells tended to be grouped according to their origin and culture types, and that the 10 drugs in one cluster inhibited the growth of all cell lines with both culture types.

Conclusion: We concluded that the patient-derived cancer cell line and its application for the drug screening will be an effective approach for the expanded adaptation of existing anti-cancer drugs.



Poster #023 #1819041

SORAFENIB INDUCES FERROPTOSIS AND APOPTOSIS IN DESMOID-TYPE FIBROMATOSIS CELLS

Anne-Rose W. Schut, MD¹; Anne Vriends, MSc¹; Andrea Sacchetti, MSc¹; Milea Timbergen, MD, PhD¹; Benjamin Alman, MD, PhD²; Mushriq al-Jazrawe, MD, PhD³; Dirk J. Grünhagen, MD PhD⁴; Cornelis Verhoef, MD PhD⁵; Stefan Sleijfer, MD, PhD¹; Erik Wiemer, PhD¹, ¹Erasmus Medical Center, Rotterdam, Zuid-Holland, NETHERLANDS, ²Duke University, Durham, NC, ³Broad Institute of MIT and Harvard, Cambridge, Massachusetts, UNITED STATES, ⁴Erasmus MC Cancer Institute, Rotterdam, Zuid-Holland, NETHERLANDS, ⁵Erasmus MC Cancer Institute, Rotterdam, Zuid-Holland, NETHERLANDS

Objective: Desmoid-type fibromatosis (DTF) is a rare, invasive, soft tissue tumour arising in musculoaponeurotic structures, with a highly unpredictable clinical course. Sorafenib, a multikinase inhibitor, has demonstrated anticancer efficacy in DTF patients and is considered the standard systemic agent, but little is known about the underlying molecular mechanisms at a cellular level. In this study we investigated the molecular effects of sorafenib exposure on DTF and stromal primary cell cultures, with an emphasis on cell death mechanisms.

Methods: Four DTF primary cell cultures, with known CTNNB1 status (S45F, T41A), and two primary stromal cell cultures, derived from DTF tissue, were exposed to clinically relevant concentrations of sorafenib (10, 20 μ M) in the presence or absence of inhibitors of ferroptosis- (ferrostatin-1), apoptosis- (Z-VAD-fmk) and autophagy- (hydroxychloroquine) for 24 and 48 hours. Cell viability was determined using in vitro cytotoxicity MTT assays. Annexin V/PI staining, lipid peroxidase analysis and immunoblotting were performed to further assess and quantify apoptosis, ferroptosis and autophagy, respectively.

Results: Exposure to sorafenib resulted in a significant, concentration- and time-dependent decrease in cell viability in all primary DTF and stromal cell cultures. Specific inhibitors of ferroptosis and apoptosis protected against sorafenib-mediated cytotoxicity implicating that both cell death mechanisms are activated. Annexin V/PI stainings confirmed induction of apoptosis with an increase in the percentage of apoptotic cells 24 hours upon sorafenib treatment (10, 20 μ M). Increased lipid peroxidation in sorafenib treated cells was also observed, a hallmark of ferroptosis. Inhibition of autophagy using hydroxychloroquine enhanced the cytotoxic effect of sorafenib and caused a stronger induction of both apoptotic and ferroptotic cell death.

Conclusion: This study identified both ferroptosis and apoptosis as mechanisms for the sorafenib-induced cell death in DTF cells as well as DTF-derived stromal cells. Furthermore, autophagy inhibition enhanced the cytotoxic effects of sorafenib. Knowledge of the mechanisms by which sorafenib affects DTF at a cellular level may help to optimize its clinical efficacy and mitigate toxic effects.



Poster #024 #1818960

PATIENT-DERIVED METASTASIZED ORTHOTOPIC XENOGRAPTS TO GUIDE THERAPEUTIC DECISION MAKING FOR HIGH-GRADE SOFT TISSUE SARCOMA PATIENTS

Suzanne Fischer, MD¹; Elly De Vlieghere, PhD²; David Creytens, MD, PhD³; An Hendrix, PhD, ir.²; Olivier De Wever, PhD, apr.²; Gwen Sys, MD, PhD³; Lore Lapeire, MD, PhD³,

¹Ghent University, Gentbrugge, Oost-Vlaanderen, BELGIUM, ²Ghent University, Gent, Oost-Vlaanderen, BELGIUM,

³Ghent University Hospital, Gent, Oost-Vlaanderen, BELGIUM

Objective: Despite trials with new compounds, survival rates for sarcoma patients have stagnated over the past 20 years. Subcutaneous implanted patient-derived xenografts (PDX) are often used to validate preclinical research, however they do not tend to recapitulate the heterogeneity of the tumour nor have the propensity to metastasize. This discrepancy between preclinical models and the clinical course of sarcoma patients is a possible rationale why clinical translation is still absent. There is a great need for PDX that accurately represents the patient's clinical course, which could be used to predict patient specific treatment response.

Methods: Tumour samples were harvested from 4 high-grade soft-tissue sarcoma patients (2 primary sarcomas and 2 lung metastases) at Ghent University Hospital during tumour resection. Both primary sarcoma patients showed metastasis within 2 years.

Samples were minced into 2mm³ pieces and for every patient implanted in 8 mice: subcutaneously ⁴or orthotopically ⁴on the lower limb of Swiss Nu/Nu and NSG mice (see figure). Animals were followed with MRI. Once the tumour reached a size of > 250 mm³, the limb was amputated. When metachronous metastasis occurred, animals were euthanized. Both primary tumour and metastatic tissue were harvested. Tumour histology was evaluated by a specialised sarcoma pathologist.

In a second experiment, 6 new patient-derived xenografts from 6 patients (4 primary sarcoma patients (2 metastasized < 2 years, 2 not metastasized > 2.5 years) and 2 lung metastasis patients) were developed by implanting tumour tissue pieces orthotopically in 4 NSG mice/every patient. The same follow-up was used as previously described. First and second generations were developed based on both mouse primary tumour and mouse metastasis.

Results: When comparing different PDX development methods, tumour take rate was 100% for all patients in orthotopic NSG models, and drastically lower in all other models. Although all models had negative resection margins at amputation, 50% of orthotopic NSG mice developed spontaneous metastases, and this for all subtypes. None of the other models showed metastasis, except for the lung metastasis derived orthotopic Swiss Nu/Nu models, where the metastasis ratio was 50% for both subtypes (see figure).

The orthotopic implantation method was used to further develop a sarcoma PDX biobank. Five out of 6 models showed metastasis. All primary sarcoma patients that showed metastasis, showed metastasis in corresponding PDX. Second generations have been set-up for both primary and metastasis PDX tissue. Both primary and metastatic tissue show concordance in histopathological characteristics on immunohistochemistry analysis within generations and with both patient primary and metastasis tissue.

Conclusion: We succeeded in developing metastatic PDX that simulate the clinical course of the patient. A PDX clinical trial using both primary as well as metastatic tissue is currently being designed to assess the potential patient treatment prediction.

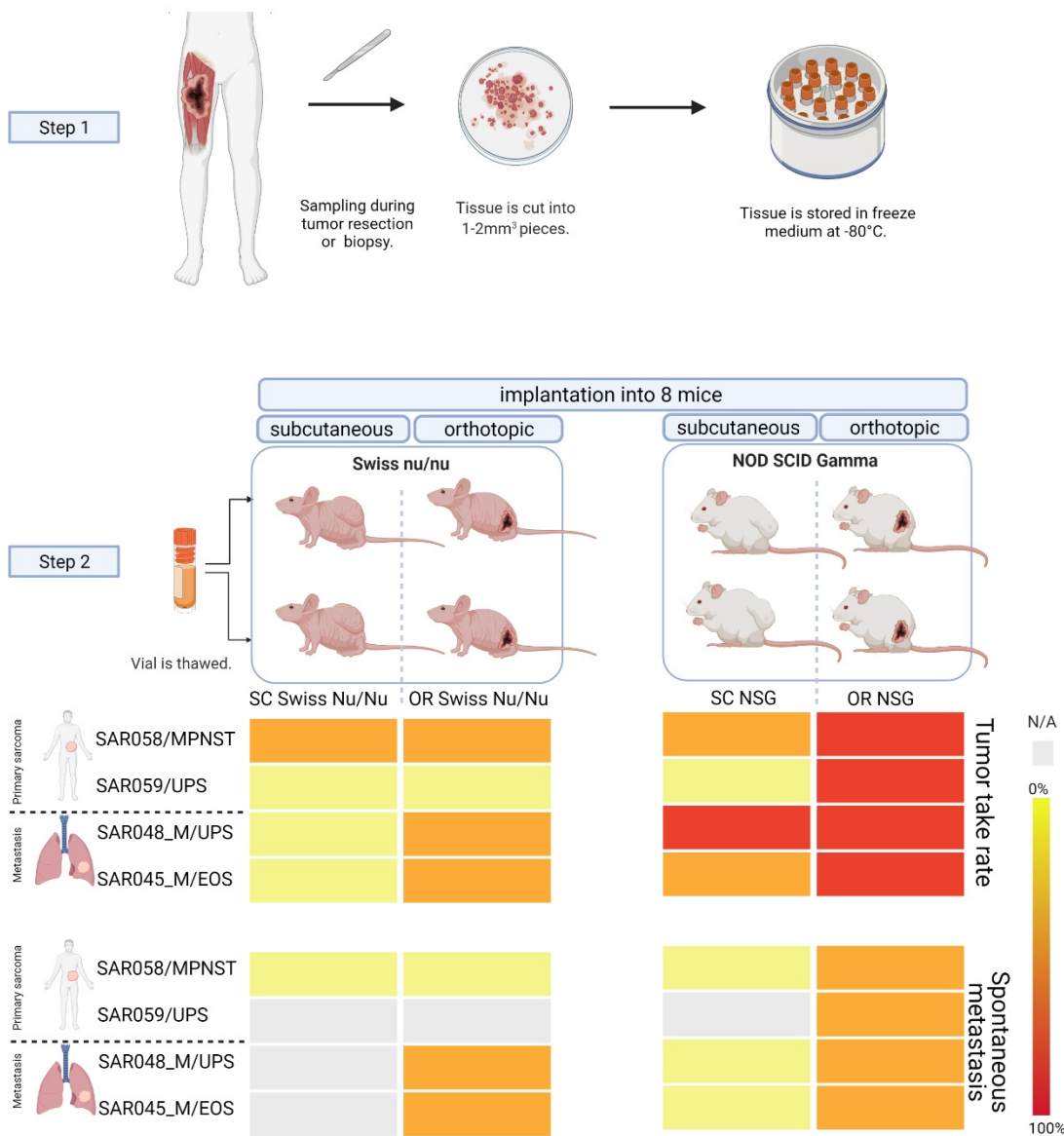


Figure 1: Methods for development of different patient-derived xenografts and individual results for tumour take rate and metastasis.

Development of first generation patient-derived xenografts. Subcutaneous: subcutaneous implantation of a tumour tissue piece. Orthotopic: orthotopic implantation of a tumour tissue piece. Swiss Nu/Nu: atymic swiss nude mice; NSG: NOD SCID gamma mice. MPNST: malignant peripheral nerve sheet tumour. UPS: undifferentiated pleomorphic sarcoma. EOS: extra-skeletal osteosarcoma.

Tumour take rate and spontaneous metastasis rate are displayed in a colour scheme, as indicated by the colour key. N/A: not applicable. Patient tissue is either derived from primary tumour material (SAR058, SAR059) or lung metastasis (SAR048_M, SAR045_M).

Created with Biorender.com



Poster #025 #1819046

XENOSARC: PATIENT-DERIVED XENOGRAFT (PDX) MODELS OF SOFT TISSUE SARCOMA (STS) AND THEIR HISTOPATHOLOGICAL AND MOLECULAR CHARACTERIZATION

Agnieszka Wozniak, PhD¹; Britt Van Renterghem, MSc¹; Luna De Sutter, MD¹; Lore De Cock, MD¹; Che-Jui Lee, MSc¹; Yannick Wang, MD¹; Ulla Vanleeuw, BSc¹; Kimberly Verbeeck, MSc¹; Daphne Hompes, MD, PhD²; Friedl Sinnaeve, MD³; Hazem Wafa, MD³; Baki Topal, MD, PhD⁴; Maria Debiec-Rychter, MD, PhD⁵; Raf Sciot, MD, PhD⁶; Patrick Schöffski, MD⁷

¹Laboratory of Experimental Oncology, Department of Oncology, KU Leuven and Department of General Medical Oncology, University Hospitals Leuven, Leuven Cancer Institute, Leuven, Vlaams-Brabant, BELGIUM,

²Department of Surgical Oncology, University Hospitals Leuven, Leuven, Belgium, Leuven, Vlaams-Brabant, BELGIUM,

³Department of Orthopedic Surgery, University Hospitals Leuven, Leuven, Belgium, Leuven, Vlaams-Brabant, BELGIUM,

⁴Department of Abdominal Surgery, University Hospitals Leuven, Leuven, Belgium, Leuven, Vlaams-Brabant, BELGIUM,

⁵Department of Human Genetics, KU Leuven and University Hospitals Leuven, Leuven, Belgium, Leuven, Vlaams-Brabant, BELGIUM,

⁶Department of Pathology, KU Leuven and University Hospitals Leuven, Leuven, Belgium, Leuven, Vlaams-Brabant, BELGIUM, ⁷General Medical Oncology, University Hospitals Leuven – Campus Gasthuisberg, Leuven, Brabant Wallon, BELGIUM

Objective: STS constitutes a family of rare mesenchymal tumors with more than 70 subtypes described. The limited treatment options available for advanced STS patients underline the need for reliable preclinical models to test new therapies.

Methods: A panel of PDX models (XenoSarc) was established by subcutaneous implantation of fresh tumor specimens in athymic mice. Once tumor growth was observed, pieces of tumor were re-transplanted to next generations of animals. At each passage tumor fragments were collected for histopathological and molecular characterization.

Results: In an ongoing effort 473 STS samples from 375 consenting patients treated at the University Hospitals, Leuven (Belgium) have been transplanted. A total of 64 PDX models have been established, meaning they have stable morphological, immunohistochemical and genetic characteristics over at least 2 passages. The PDX platform includes more common STS subtypes such as myxofibrosarcoma (n=12 models), gastrointestinal stromal tumors (9), dedifferentiated liposarcoma (9), and leiomyosarcoma (8), as well as models from ultra-rare subtypes, e.g. extraskeletal osteosarcoma, mesenchymal chondrosarcoma, myxoinflammatory fibroblastic sarcoma or telangiectatic extraskeletal osteosarcoma, plus many others. All relevant details about the donor patient and tumor characteristics, including sensitivity to the standard treatments, is known for every model. The models are well-characterized, with availability of molecular information on gene copy number changes (by low-coverage whole genome sequencing), and gene expression profile (by RNA sequencing). Xenografts are accompanied by ready to use tissue microarrays (TMA) from the models, which can be used for target identification and model selection for preclinical studies.

Conclusion: The XenoSarc platform offers opportunities for studying the biology of various sarcoma subtypes including ultra-rare entities and was found to be a very reliable tool for early drug screening in STS in preparation of clinical testing of novel compounds. The platform is available for collaborative preclinical projects with academic and industrial partners.



Poster #026 #1818850

SOCIOECONOMIC AND PREOPERATIVE RISK FACTORS ASSOCIATED WITH LIMB SALVAGE VERSUS AMPUTATION FOR ADULT EXTREMITY BONE SARCOMA PATIENTS WITH MEDICAL INSURANCE

Matthew T. Houdek, MD¹; Michael Stuart, MD¹; Elizabeth P. Wellings, MD¹; Eric R. Wagner, MD²; Denis Asante, MS³; Lindsey Sangaralingham, MPH⁴; Peter S. Rose, MD¹; Steven L. Moran, MD¹

¹Mayo Clinic, Rochester, Minnesota, UNITED STATES, ²Emory University, Atlanta, Georgia, UNITED STATES,

³Optum Labs, Cambridge, Massachusetts, UNITED STATES, ⁴Mayo Clinic Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery, Rochester, Minnesota, UNITED STATES

Objective: Limb salvage (LS) has become the preferred treatment for adult patients with bone sarcoma of the extremities. The decision to perform LS versus an amputation is often dictated by tumor characteristics, however socioeconomic and patient factors have been found to be associated with this decision. Previous series have shown that patients from lower socioeconomic status, particularly those with either no insurance or Medicaid coverage, have worse survival and more likely to undergo amputation. Currently there is a paucity of data examining if these socioeconomic factors persist in patient with medical insurance at the time of diagnosis.

Methods: Data from Optum Labs Data Warehouse (OLDW), a national administrative claims database, was analyzed to identify patients with extremity bone sarcomas from 2006 to 2017. The OLDW contains the enrollment records for commercial and Medicare Advantage (MA) enrollees and contains their longitudinal health information. Bivariate regression was used to identify factors associated with LS versus amputation. Of 1,390 (743 males, 647 female) patients, 252 (18%) under amputation while 1,138 (82%) underwent LS.

Results: Adult patients whose families earned less than \$75,000 per year (OR 1.38, (95% CI 1.03-1.85), $p=0.03$), those treated in a public hospital (OR 1.41, 95% CI 1.01-1.97, $p=0.04$) and at a hospital with <200 beds (OR 1.90, 95% CI 1.20-3.02, $p=0.006$) were more likely to be treated with an amputation if they presented with an extremity bone tumor. Household income greater than \$125,000 per year was associated with limb salvage surgery (OR 0.62, 95% CI 0.40-0.98, $p=0.04$).

Patients with a lower extremity sarcoma (OR 4.72, 95% CI 3.37-6.60, $p<0.001$), in addition to a baseline history of congestive heart failure (OR 1.71, 95% CI 1.09-2.69, $p=0.01$), coagulopathy (OR 2.24, 95% CI 1.51-3.33, $p<0.001$), depression (OR 1.50, 95% CI 1.05-2.14, $p=0.02$), and a fluid or electrolyte disorder (OR 1.47, 95% CI 1.08-2.01, $p=0.01$) were more likely to be treated with an amputation. Patients with an upper extremity tumor (OR 0.21, 95% CI 0.15-0.29, $p<0.001$), or a history of diabetes with chronic complications (OR 0.16, 95% CI 0.09-0.27, $p<0.001$), paralysis (OR 0.04, 95% CI 0.002-0.74, $p=0.02$), radiation (OR 0.33, 95% CI 0.22-0.50 $p<0.001$) and less than or equal to 1 Elixhauser risk factor (OR 0.41, 95% CI 0.21-0.81, $p=0.01$) were more likely to be treated with a limb salvage surgery.

Conclusion: In a patient population with preexisting medical insurance, socioeconomic factors such as lower income and being treated at smaller and public hospitals were associated with an amputation for the treatment of an extremity bone sarcoma. Healthier patients, with a higher income, and white race were associated with limb-salvage surgery in adult patients with a bone sarcoma.

Table 1: Demographics of Patients Undergoing Excision of a Bone Sarcoma

Patient Factor	All Patients (n=1,390)	Amputation (n=252)	Limb Salvage (n=1,138)	P Value
Mean Age (SD)	55.2 (14.8) years	53.6 (16.6) years	55.5 (14.3) years	0.06
Age Group				0.01
18-39 Years	219 (16%)	54 (21%)	165 (15%)	
40-64Years	838 (60%)	137 (54%)	701 (62%)	
65+ Years	333 (24%)	61 (24%)	272 (24%)	
Gender				
Female	647 (47%)	104 (41%)	543 (48%)	0.06
Male	743 (53%)	148 (59%)	595 (52%)	
Mean Length of Stay	6.7 (8.4) days	9.6 (12.1)	6.1 (7.2)	<0.001
Race				0.17
Non White	224 (16%)	44 (18%)	180 (16%)	
Unknown	345 (25%)	72 (29%)	273 (24%)	
White	821 (59%)	136 (54%)	685 (60%)	
Insurance Type				0.96
Commercial	1,051 (76%)	191 (76%)	861 (76%)	
Medicare	338 (24%)	61 (24%)	277 (24%)	
Income				0.04
<\$75k	397 (29%)	81 (32%)	316 (28%)	
\$75-\$124K	262 (19%)	41 (16%)	221 (19%)	
>\$125k	216 (16%)	27 (11%)	189 (17%)	
Unknown	515 (37%)	103 (41%)	412 (36%)	
Extremity				<0.001
Lower	743 (53%)	204 (81%)	539 (47%)	
Upper	647 (47%)	48 (19%)	599 (53%)	
AHA				
Bed size				0.03
1-199	98 (7%)	28 (11%)	70 (6%)	
200-399	230 (17%)	37 (15%)	193 (17%)	
400+	896 (64%)	161 (64%)	735 (65%)	
Unknown	166 (12%)	26 (10%)	140 (12%)	
Hospital Ownership				0.14
For Profit	90 (6%)	19 (8%)	71 (6%)	
Private Nonprofit	882 (63%)	150 (60%)	732 (64%)	
Public	252 (18%)	57 (23%)	195 (17%)	
Unknown	166 (12%)	26 (10%)	140 (12%)	
Hospital Teaching Status				0.19
Nonteaching	350 (25%)	55 (22%)	295 (26%)	
Teaching	874 (63%)	171 (68%)	703 (62%)	
Unknown	166 (12%)	26 (11%)	140 (12%)	
Hospital Location				0.42
Division	311 (22%)	51 (20%)	295 (23%)	
Metro	905 (65%)	173 (69%)	703 (64%)	
Micro/Rural/Unknown	174 (13%)	28 (11%)	146 (13%)	

Table 2: Risk Factors for Amputation Compared to Limb Salvage in Adult Patients with Bone Sarcoma

Patient Factor	Odds Ratio (95% CI)	P Value
Age ≥ 65 Years	1.01 (0.73-1.39)	0.91
Male Sex	1.29 (0.98-1.71)	0.06
White Race	0.77 (0.58-1.02)	0.06
Commercial Insurance	1.00 (0.73-1.38)	0.96
Household Income <\$75,000 Per Year	1.38 (1.03-1.85)	0.03
Household Income >\$125,000 Per Year	0.62 (0.40-0.98)	0.04
Lower Extremity	4.72 (3.37-6.60)	<0.001
Upper Extremity	0.21 (0.15-0.29)	<0.001
Hospital Factors	Odds Ratio (95% CI)	P Value
< 200 Bed Hospital	1.90 (1.20-3.02)	0.006
≥400 Bed Hospital	0.97 (0.73-1.28)	0.83
Public Hospital	1.41 (1.01-1.97)	0.04
Non-Teaching Hospital	0.79 (0.57-1.10)	0.17
Teaching Hospital	1.30 (0.97-1.74)	0.07
Rural Hospital	0.84 (0.55-1.30)	0.45
Elixhauser Factors	Odds Ratio (95% CI)	P Value
Alcohol Abuse	0.12 (0.006-1.79)	0.12
Cardiac Arrhythmia	1.04 (0.76-1.44)	0.76
Blood Loss Anemia	0.10 (0.006-1.70)	0.10
Congestive Heart Failure	1.71 (1.09-2.69)	0.01
Chronic Pulmonary Disease	1.10 (0.78-1.55)	0.58
Coagulopathy	2.24 (1.51-3.33)	<0.001
Anemia Deficiency	1.18 (0.72-1.93)	0.49
Depression	1.50 (1.05-2.14)	0.02
Diabetes Without Chronic Complications	1.11 (0.78-1.58)	0.55
Diabetes With Chronic Complications	0.16 (0.09-0.27)	<0.001
Drug Abuse	0.08 (0.005-1.36)	0.08
Fluid and Electrolyte Disorder	1.47 (1.08-2.01)	0.01
AIDS/HIV	4.50 (0.08-227.79)	0.45
Hypertension With Complications	0.86 (0.49-1.49)	0.59
Hypertension Without Complications	1.04 (0.79-1.37)	0.73
Hypothyroidism	0.70 (0.46-1.07)	0.10
Liver Disease	0.62 (0.40-0.97)	0.03
Obesity	0.96 (0.63-1.46)	0.87
Paralysis	0.04 (0.002-0.74)	0.02
Peripheral Vascular Disease	1.43 (0.93-2.18)	0.09
Psychosis	0.11 (0.006-1.88)	0.12
Pulmonary Circulation Disorder	1.41 (0.75-2.68)	0.28
Renal Failure	1.02 (0.63-1.66)	0.91
Rheumatoid Arthritis	1.34 (0.79-2.28)	0.27
Solid Tumor Without Metastases	11.56 (0.70-190.60)	0.08
Valvular Disease	1.09 (0.69-1.72)	0.68
Weight Loss	1.32 (0.82-2.12)	0.25
Chemotherapy	1.07 (0.81-1.40)	0.62
Radiation	0.33 (0.22-0.50)	<0.001
≤ 1 Elixhauser Factor	0.41 (0.21-0.81)	0.01
≥4 Elixhauser Factors	1.29 (0.97-1.71)	0.07



Poster #027 #1818926

PERFORMANCE OF THE 7TH AND 8TH VERSION OF THE AJCC-CLASSIFICATION FOR SOFT TISSUE SARCOMAS REGARDING PROGNOSTIC ACCURACY

Maria Anna Smolle, MD¹; Michiel van de Sande, MD PhD²; Andrew J. Hayes, PhD³; Marko Bergovec, MD⁴; Henry Smith, MD⁵; Bernadette Liegl-Atzwanger, Prof.⁴; Per-Ulf Tunn, MD⁶; Maya Niethard, MD⁷; Reinhard Windhager, Prof. MD⁸; Joanna Szkandera, MD⁹; Andreas Leithner, Prof. Dr.¹⁰

¹Department of Orthopaedics and Trauma, Medical University Graz, Graz, Steiermark, AUSTRIA, ²Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ³The Royal Marsden Hospital NHS Foundation Trust, London, England, UNITED KINGDOM, ⁴Medical University Graz, Graz, Steiermark, AUSTRIA, ⁵Department of Surgery, Royal Marsden Hospital NHS Foundation Trust, London, London, England, UNITED KINGDOM, ⁶HELIOS Klinikum Berlin-Buch, Berlin, Berlin, GERMANY, ⁷Sarcoma Centre, HELIOS-Klinikum Berlin-Buch, Berlin, Berlin, GERMANY, ⁸Department of Orthopaedics and Traumatology, Medical University of Vienna, Vienna, Wien, AUSTRIA, ⁹Medical University of Graz, Graz, Steiermark, AUSTRIA, ¹⁰Department of Orthopedics and Trauma, Medical University of Graz, Graz, Steiermark, AUSTRIA

Objective: The 8th version of the AJCC classification system for soft tissue sarcomas (STS) was released in 2017, aiming at further improving prognosis prediction of STS patients. This study aimed at analysing the prognostic accuracy of the 7th and 8th version of the AJCC classification system for overall survival (OS) in a large dataset of STS patients with high-grade disease treated at tertiary tumour centres.

Methods: In this retrospective study, 1032 patients (54.0% males [n=557], mean age: 60.7±16.3 years), treated at 5 tertiary sarcoma centres with curative intent for G2 or G3 localised STS were included. The median follow-up was 3.1 years (IQR: 1.3-5.9 years). Uni- and multivariate Cox-regression models were used to assess accuracy of the 7th and 8th AJCC-version on OS, with the prognostic power being assessed with Harrell's C-index.

Results: At latest follow-up, 269 and 91 patients had died of disease (26.1%) or unknown causes (8.8%), whilst 531 and 141 were alive without (51.4%) and with (13.7%) disease. Prognostic accuracy of both 7th (c-index: 0.614) and 8th AJCC version (c-index: 0.620) was comparable in the univariate Cox-regression model. In the multivariate analysis including 7th or 8th AJCC version, gender, age, margins, depth, histology, and radiotherapy, a slightly better c-index was observed for the model including the 8th version (c-index: 0.714 vs. 0.705 for 7th version). The stratification into four different T-stages, as used in the 8th version of the AJCC classification system, lead to improvement of prognostic accuracy between each T-stage (c-index: 0.625), whilst T-stages as defined by the 7th version performed worse (c-index: 0.582).

Conclusion: The 7th and 8th version of the AJCC-classification perform comparable regarding prognostic accuracy for overall survival. However, an advantage of the 8th over the 7th version may be seen in omitting tumour depth whilst strengthening tumour size as a T-stage defining parameter.



Poster #028 #1818946

PATTERNS OF CARE AND FACTORS ASSOCIATED WITH OVERALL SURVIVAL IN PATIENTS WITH LIPOSARCOMA AND SYNCHRONOUS PULMONARY METASTASES.

Wasay Nizam, M.B.B.S¹; Richard Nudotor, MD²; Alexandra C. Istl, MD MPH²; Christian Meyer, MD PhD²; Jonathan Greer, MD²; Fabian Johnston, MD MHS²

¹Johns Hopkins University, Silver Spring, Maryland, UNITED STATES, ²Johns Hopkins Hospital, Baltimore, Maryland, UNITED STATES

Objective: Only 6% of liposarcomas (LPS) present with metastatic disease at presentation, most commonly to the lung. While current ESMO guidelines for isolated lung metastases recommend the use of chemotherapy, the role of surgical resection is unclear. However, there is a lack of high quality evidence to guide management as most data are derived from retrospective, single institution series, with small sample sizes and heterogeneous histology. Consequently, practice patterns and treatment outcomes for LPS with isolated lung metastases are largely unknown. This study aims to address this existing gap by utilizing the National Cancer Database (NCDB), with the objective of describing the current patterns of care and factors influencing survival in individuals presenting with LPS and synchronous, isolated pulmonary metastasis.

Methods: The NCDB (2004-2017) was queried for patients with a primary LPS of the extremity, retroperitoneum, pelvis, trunk, chest, or abdominal wall using ICD-10 and ICD-O-3 codes. Patients with metastatic disease to non-pulmonary sites were excluded. Demographic and cancer characteristics were recorded, along with relevant treatment variables including surgical resection of the primary tumor, resection of pulmonary metastases, and use of chemotherapy, immunotherapy, or radiotherapy. 'Curative intent surgery' was defined as resection of both the primary site and metastases. Outcome variables of interest were median overall survival (OS), 1-year OS, and 5-year OS. Multivariate logistic regression models were used to determine factors associated with receipt of chemotherapy, primary tumor resection, or metastasectomy. Survival analyses were conducted using lifetables, Kaplan-Meier curves with log rank test, and multivariate Cox proportional hazards model to determine factors conferring an increased hazard of death.

Results: There were 235 patients with LPS and synchronous isolated lung metastases identified. The mean age of the cohort was 64 years and 30% were women. Primary tumor site was extremity (61.7%), retroperitoneum (24.3%), and trunk/chest/abdominal wall (14%). Most tumors were de-differentiated or pleomorphic LPS (63.4%). Demographic and tumor characteristics are summarized in Table 1. Chemotherapy was administered in 52.7% of patients and resection of the primary tumor was performed in 29.3% of patients; only 5% underwent resection of the primary site and metastasectomy (Figure 1). The median length of stay for patients having surgery was 5 days (IQR 3-8) with a 30-day re-admission rate of 5.9%. Four patients died within 90 days of surgery. Multivariate analysis demonstrated that increased age was a significant predictor for non-utilization of chemotherapy (OR 0.96, 95% CI 0.937- 0.981). Surgical treatment of the primary site was predictive of also undergoing a metastasectomy (OR:3.43, 95% CI: 1.12-10.51). Median OS for the overall population was 7.5 months, but was 6.3 months in patients who did not undergo any surgery compared to 12.8 months for patients having resection of their primary tumor. Select Kaplan-Meier curves are shown in Figure 2. Factors significantly associated with improved survival on multivariate analysis included extremity origin of LPS, RT to the primary site, primary tumor resection, and curative intent surgery. A Charlson comorbidity score of 2 or greater was associated with worse survival (Table 2).

Conclusion: This national series describes treatment patterns and outcomes for primary LPS with isolated lung metastases. These results indicate that primary tumor resection and curative intent surgical therapy may be associated with improved OS in selected patients. Further consideration of these approaches may be warranted for appropriate patients.

Table 1. Demographic and tumor characteristics for patients with primary LPS and synchronous isolated lung metastases

Variable	Overall (N=235)	RPS (N=57)	Extremity (N=145)	Trunk/Chest wall/ Abdominal Wall (N=33)
Age, mean ± SD	64.07 ± 12.61	63.44 ± 10.49	64.23 ± 13.34	64.42 ± 12.95
Female, N (%)	70 (29.79)	20 (35.09)	38 (26.21)	12 (36.36)
Race, N (%)				
White – non-Hispanic	176 (75.21)	44 (77.19)	105 (72.92)	27 (81.82)
Black – non-Hispanic	23 (9.82)	4 (7.02)	17 (11.81)	2 (6.06)
Hispanic	24 (10.26)	6 (10.53)	14 (9.72)	4 (12.12)
Native American	1 (0.43)	0	1 (0.69)	0
Asian	4 (1.71)	2 (3.51)	2 (1.39)	0
Other	6 (2.56)	1 (1.75)	5 (3.47)	0
CCS, N (%)				
0	166 (70.64)	40 (79.18)	102 (70.34)	24 (72.73)
1	44 (18.72)	11 (19.30)	29 (20.00)	4 (12.12)
2+	25 (10.64)	6 (10.53)	14 (9.66)	5 (15.15)
Treatment Site, N (%)				
Academic	153 (67.70)	39 (70.91)	93 (67.39)	21 (63.64)
Community	73 (32.30)	16 (29.09)	45 (32.61)	12 (36.36)
Insurance Status, N (%)				
Uninsured	4 (1.70)	2 (3.51)	1 (0.69)	1 (3.03)
Private	95 (40.43)	20 (35.09)	61 (42.07)	14 (42.42)
Government	127 (54.04)	33 (57.89)	77 (53.10)	17 (51.52)
Unknown	9 (3.83)	2 (3.51)	6 (4.14)	1 (3.03)
Tumor Grade				
I	27 (11.49)	9 (15.79)	14 (9.66)	4 (12.12)
II	15 (6.38)	4 (7.02)	10 (6.90)	1 (3.03)
III	126 (53.62)	31 (54.39)	79 (54.48)	16 (48.48)
Unknown	67 (28.51)	13 (22.81)	42 (29.97)	12 (36.36)
Primary Tumor Size (cm)				
< 10	38 (27.74)	4 (14.29)	24 (26.97)	10 (50.00)
10-20	60 (43.80)	10 (35.71)	40 (44.94)	10 (50.00)
>20	39 (28.47)	14 (50.00)	25 (28.09)	0
Histology				
Well-differentiated				
LPS/ALT	57 (24.26)	15 (26.32)	33 (22.76)	9 (27.27)
De-differentiated	149 (63.40)	39 (68.42)	89 (61.38)	21 (63.64)
LPS/PLPS	25 (10.64)	3 (5.26)	19 (13.10)	3 (9.09)
Myxoid LPS	4 (1.70)	0	4 (2.76)	0
Mixed LPS				

Variable	Univariate analysis			Multivariate analysis		
	Hazard Ratio	95% CI	P value	Hazard Ratio	95% CI	P value
Age	1.01	0.998-1.024	0.109	1.01	0.993-1.024	0.273
Sex						
Male	Ref					
Female	1.01	0.709-1.431	0.970			
Race						
White	Ref					
Non-Hispanic Black	0.57	0.323-1.020	0.058			
Native American	2.27	0.315-16.4	0.416			
Asian	0.63	0.156-2.58	0.523			
Hospital Category						
Academic	Ref					
Community	1.30	0.925-1.83	0.131			
Charlson comorbidity score						
0	Ref					
1	0.92	0.614-1.385	0.699	1.06	0.341-0.804	0.003
2	2.14	1.271-3.604	0.004	2.63	0.608-1.966	0.767
Tumor grade						
1	Ref					
2	0.76	0.314-1.83	0.539			
3	1.43	0.849-2.41	0.178			
Tumor Site						
Retroperitoneal	Ref					
Extremity	0.56	0.383-0.822	0.003	0.52	0.341-0.804	0.003
Trunk/Chest/Abdominal	1.03	0.615-1.738	0.900	1.09	0.608-1.966	0.767
Wall						
Treatment Characteristics						
Resection of primary site	0.49	0.339-0.712	<0.001	0.48	0.317-0.730	0.001
Curative intent surgery*	0.54	0.23-1.249	0.151	0.40	0.165-0.949	0.038
Chemotherapy	1.02	0.733-1.416	0.910			
Primary site radiation	0.60	0.388-0.935	0.024	0.61	0.387-0.958	0.032

*: Curative intent surgery= Resection of primary site and metastasectomy

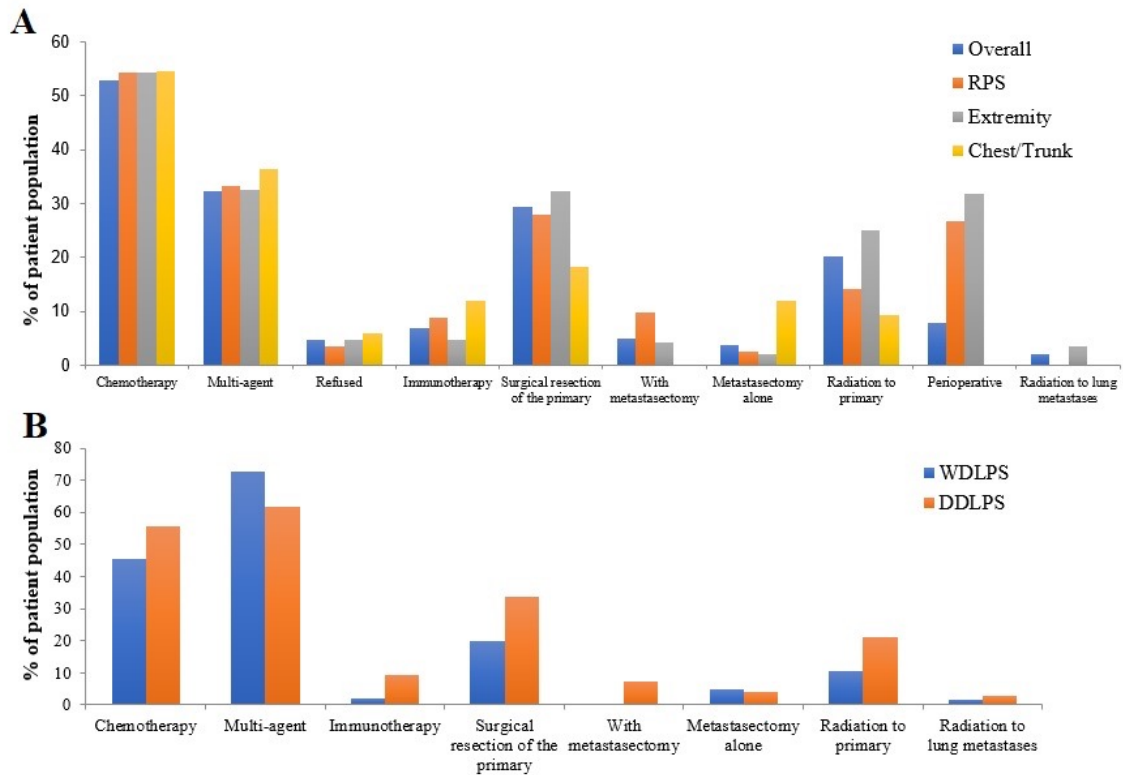


Figure 1: Patterns of multimodality systemic and locoregional therapy for Liposarcoma with single isolated lung metastases A. at different primary sites and B. for well-differentiated and de-differentiated/pleomorphic histologies

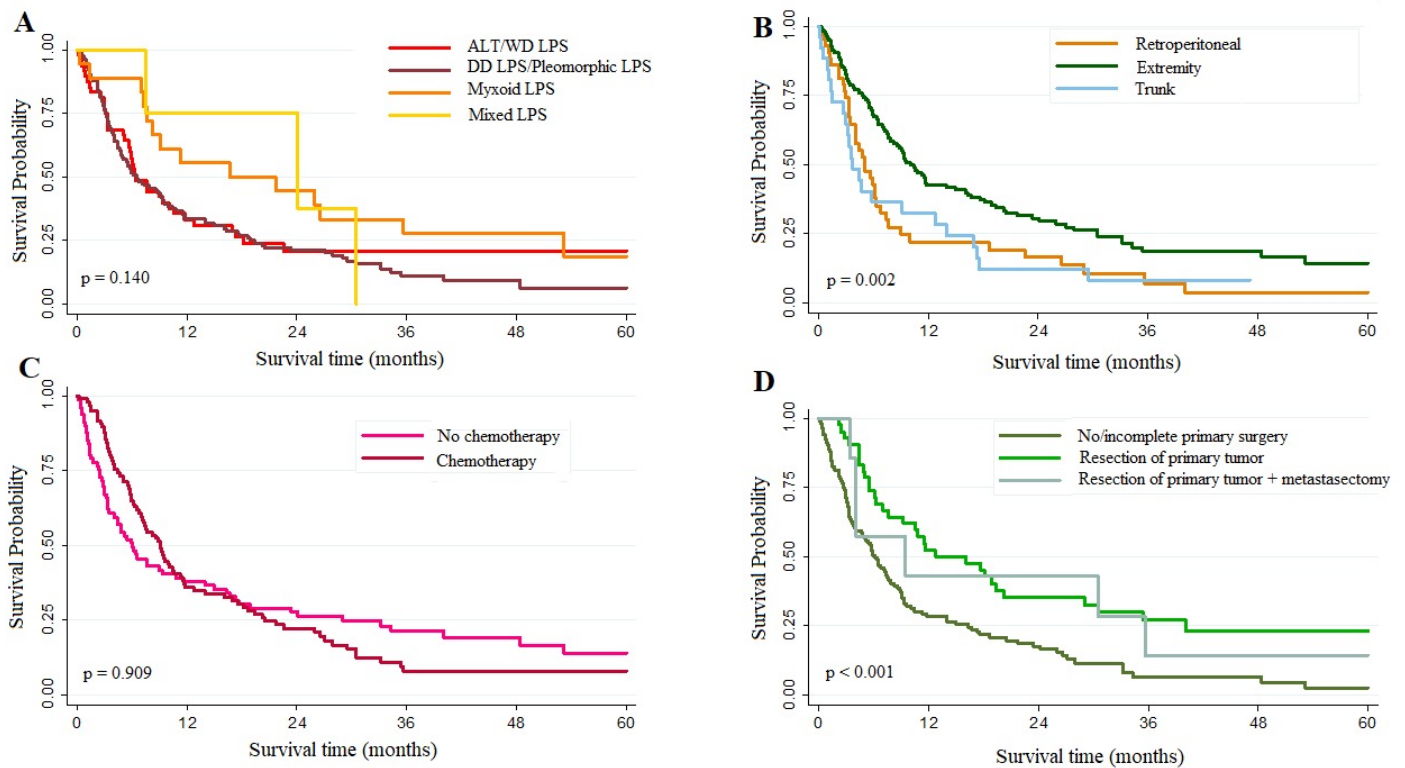


Figure 2: Kaplan Meier curves depicting overall survival by A. Histology; B. Site of Primary tumor; C. Usage of chemotherapy; D. Extent of surgical treatment Abbreviation: ALT/WDLPS: Atypical Lipomatous Tumor/Well-differentiated Liposarcoma; DDLPS: De-differentiated Liposarcoma; LPS: Liposarcoma



Poster #029 #1818857

TREATMENT PATTERNS AND OUTCOMES FOR PRIMARY UTERINE LEIOMYOSARCOMA WITH SYNCHRONOUS ISOLATED LUNG METASTASES: A NATIONAL CANCER DATABASE STUDY OF PRIMARY RESECTION AND METASTASECTOMY

Alexandra C. Istl, MD, MPH; Richard Nudotor, MD; Nerlyne Desravines, MD; Jonathan Greer, MD; Rebecca Stone, MD, MS; Fabian Johnston, MD, MHS
Johns Hopkins Hospital, Baltimore, Maryland, UNITED STATES

Objective: Uterine leiomyosarcomas (uLMS) account for 1% of uterine malignancies and up to 69% of uterine sarcomas. One third of women with uLMS present with distant metastatic disease. Current guidelines recommend resection with debulking in early-stage disease, but there is no established benefit of surgery for metastatic uLMS. However, because women commonly receive primary tumor resection in the metastatic setting for control of symptoms such as vaginal bleeding (34-46%) and bulk symptoms (13-17%), the oncologic benefit of surgical intervention warrants exploration. We aimed to explore oncologic outcomes for women with primary uLMS and synchronous isolated lung metastases (SILM) who underwent either resection of their primary tumor only or primary resection and pulmonary metastasectomy.

Methods: This retrospective analysis of the National Cancer Database (NCDB) identified women with primary FIGO stage IV uLMS and SILM. Cases were defined using ICD-O-3 histologic codes reviewed by a sarcoma pathologist from our institution. Patients with metastases to non-pulmonary sites were excluded. We collected demographic and disease characteristics including age, race, Charlson comorbidity score, treatment facility, tumor grade, and primary tumor size. Treatment data included surgery for either the primary tumor or lung metastases, and receipt of radiotherapy, chemotherapy, hormone therapy, or immunotherapy. Resection of both primary tumor and pulmonary metastases was considered curative intent surgery. We used descriptive statistics to report practice patterns and rates of primary uLMS resection and pulmonary metastasectomy. We assessed clinicopathologic factors associated with the receipt of primary surgery and metastasectomy using univariate and multivariate regression analyses. We calculated median, 1-year, and 5-year overall survival (OS) for patients with different treatment approaches and compared these using Kaplan-Meier curves and log-rank tests. We used multivariate Cox proportional hazard regression to identify factors predictive of survival.

Results: We identified 905 patients with uLMS and SILM between 2004 and 2017. Demographics and cancer characteristic are reported in Table 1. Patterns of systemic therapy administration and rates of surgical resection of the primary tumor or lung metastases are depicted in Figure 1. 600 patients had resection of their primary tumor, of which 63 had curative intent surgery. For those having surgery, median length of stay was 4 days (IQR 2-6) with an 8.5% readmission rate and 1.8% 30-day mortality rate. Patients who did not receive chemotherapy were significantly older (61.5 v. 55.6 years, $p < 0.01$) with a higher comorbidity index ($p < 0.05$) than those who received chemotherapy. Women with private health insurance were more likely to receive chemotherapy ($p < 0.01$) and resection of their primary tumor ($p < 0.01$).

In the survival analysis, patients treated with hormone therapy or chemotherapy had improved OS compared to those who were not, but the addition of hormone therapy to cytotoxic chemotherapy did not add a significant benefit (Figure 3a-c). Patients who had primary tumor resection (hysterectomy or pelvic exenteration) had improved median OS compared to those who did not (Figure 3d). Patients who underwent 'curative intent surgery with resection of both primary tumor and metastases had 1-year OS of 71.2% and 5-year survival of 18%, compared to 1-year survival of 35.6% and 5-year survival of 5.16% for patients who did not have surgery. Cox regression for factors associated with worse OS is presented in Table 2. Black women had worse median OS than the rest of the uLMS population (12.9 v. 14.92 months, $p < 0.05$), with a 5-year OS of 7.9% compared to 12.7% in the rest of the population.

Conclusion: Resection of primary tumor and lung metastases is associated with improved OS in uLMS with SILM. This suggests that curative intent surgery may be a reasonable treatment option in the appropriately selected patient presenting with advanced stage LMS. Prospective studies are needed to better assess this difference.

Table 1. Population characteristics for patients with primary uterine LMS with synchronous isolated lung metastases

Variable	Uterine LMS (N=905)
Age, mean ± SD	57.49 ±10.77
Race, N (%)	
White – non Hispanic	521 (57.77)
Black – non Hispanic	236 (26.08)
Hispanic	86 (9.50)
Native American	3 (0.33)
Asian	33 (3.65)
Other	26 (2.87)
CCS, N (%)	
0	707 (78.12)
1	151 (16.69)
2+	47 (5.19)
Treatment Site, N (%)	
Academic	545 (62.36)
Community	329 (37.64)
Insurance Status, N (%)	
Uninsured	45 (4.97)
Private	510 (56.35)
Government	334 (36.91)
Unknown	16 (1.77)
T Stage, N (%)*	
0	11 (2.44)
I	195 (43.24)
a	11
b	134
II	102 (22.62)
a	23
b	56
III	108 (23.95)
a	26
b	32
IV	35 (7.76)
Primary Tumor Size (cm), N (%)	
<=5	33 (6.56)
>5	470 (93.44)

LMS – leiomyosarcoma, SD – standard deviation, CCS – Charlson Comorbidity Score *N for A and B designations may not add up to total N for numeric stage due to missing data regarding A and B designations

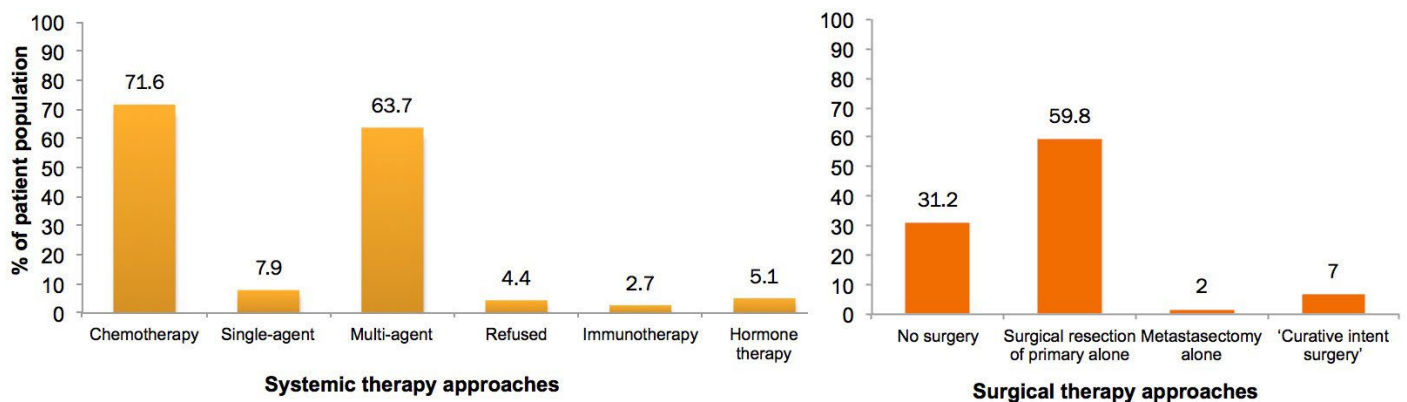


Figure 1. Patterns of treatment utilization by a. systemic and b. surgical therapy

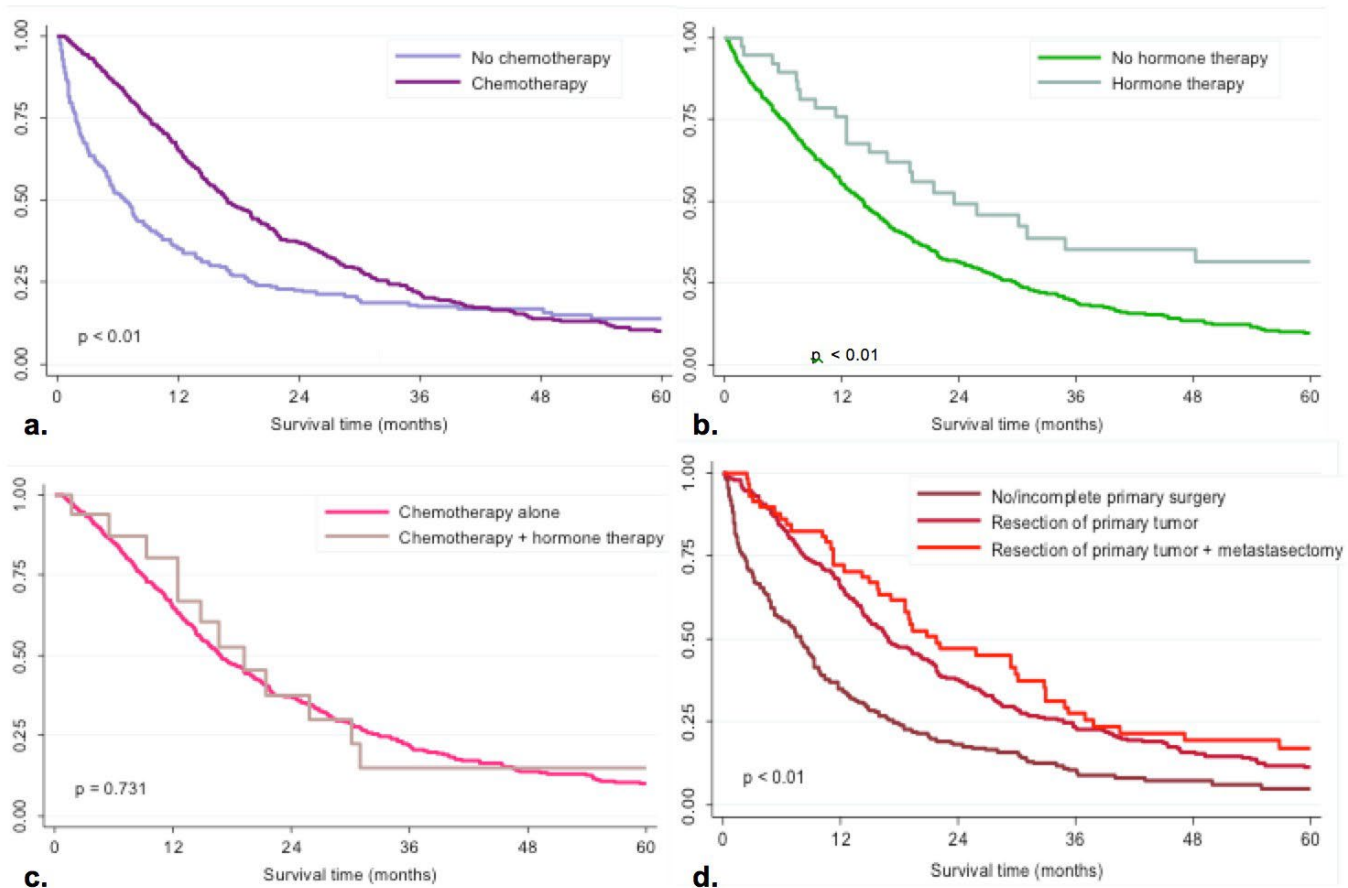


Figure 2. Relative median survival for patients receiving **a.** chemotherapy, **b.** hormone therapy, or **c.** both and **d.** no surgery compared to resection of primary tumor and curative intent surgery.

Table 2. Multivariate Cox proportionate hazards model for patient and treatment factors associated with OS

Variable	HR	95% CI	p value
<i>Patient and tumor characteristics</i>			
Age, mean ± SD	1.01	0.995-1.014	0.198
Black – non Hispanic	1.38	1.140 – 1.685	0.001
CCS, N (%)			
0	ref.		
1	0.85	0.676 – 1.079	0.185
2+	1.00	0.654 – 1.543	0.983
<i>Treatment characteristics</i>			
Resection of primary tumor	0.54	0.443 – 0.647	< 0.001
‘Curative intent surgery’ – resection of primary tumor + metastasectomy	0.44	0.316 – 0.619	< 0.001
Chemotherapy	0.66	0.508 – 0.854	< 0.001
Hormone therapy	0.40	0.246 – 0.634	< 0.001

CI – confidence interval SD – standard deviation, CCS – Charlson Comorbidity score



Poster #030 #1818943

A NATIONAL CANCER DATABASE STUDY OF CURATIVE INTENT SURGERY IN LEIOMYOSARCOMA PATIENTS WITH SYNCHRONOUS ISOLATED LUNG METASTASES

Alexandra C. Isth, MD MPH¹; Richard Nudotor, MD²; Wasay Nizam, M.B.B.S³; Jonathan Greer, MD¹; Christian Meyer, MD PhD¹; Fabian Johnston, MD MHS¹,

¹Johns Hopkins Hospital, Baltimore, Maryland, UNITED STATES, ²Johns Hopkins Hospital, Baltimore, Maryland, UNITED STATES, ³Johns Hopkins University, Silver Spring, Maryland, UNITED STATES

Objective: Forty percent of patients with leiomyosarcoma (LMS) will either present with metastases or develop metastases in their disease course, most commonly in the lungs. For metachronous lung metastases, ESMO guidelines recommend surgical resection of oligometastatic disease if the disease-free interval exceeds one year. For synchronous lung metastases, the standard approach remains doxorubicin-based chemotherapy, even in the absence of extra-pulmonary disease. However, one recent study of pulmonary STS metastases from a high-volume center found that sarcoma patients with synchronous lung metastases – a large proportion of which were LMS – did not have worse survival than those with metachronous metastases (Chudgar 2017). This suggests that consideration of a more aggressive multimodal approach in LMS patients with synchronous isolated lung metastases (SILM) may be warranted. Our histology-specific study explores national management patterns for LMS patients with SILM, describes treatment approaches across disease sites, and reports outcomes for different approaches, including curative intent surgery.

Methods: We used the NCDB to analyze patients with primary LMS of the retroperitoneum, extremity, trunk/chest/abdominal wall, and pelvis. Primary sites and histologies were defined by ICD-10 and ICD-O-3 codes. Patients with metastases to non-pulmonary sites were excluded. We collected demographic and disease characteristics, including tumor size and grade, and treatment variables including receipt of chemotherapy, immunotherapy, radiotherapy, and surgical resection of primary tumor or metastases. Resection of both primary and metastases was termed 'curative intent surgery'. We identified factors associated with primary tumor resection and metastasectomy using multivariate logistic regression. Post-operative outcomes were collected for those having surgery. Outcomes included median overall survival (OS), and 1-year and 5-year OS for various treatment approaches. Survival analysis was performed using log-rank test with Kaplan-Meier curves and multivariate Cox proportional hazard model.

Results: We identified 629 patients presenting with LMS and SILM between 2004-2017. Demographics and cancer characteristic are reported in Table 1. Patterns of systemic therapy administration and rates of surgical resection of the primary tumor or lung metastases are depicted in Figure 1. 11% of patients received radiotherapy for their primary tumor, most of which were in the perioperative setting. Patients who underwent resection of their primary tumor had a median LOS of 5 days (IQR 3-7) with a 6% readmission rate and 2.6% mortality rate within 30 days. Higher comorbidity index and age were associated with failure to receive chemotherapy and 12.5% of patients refused chemotherapy. Having primary tumor resection and metastasectomy were positively associated on multivariate analysis, and patients were more likely to have resection of their primary tumor or lung metastases if treated at an academic center compared to a community cancer center (Figure 2).

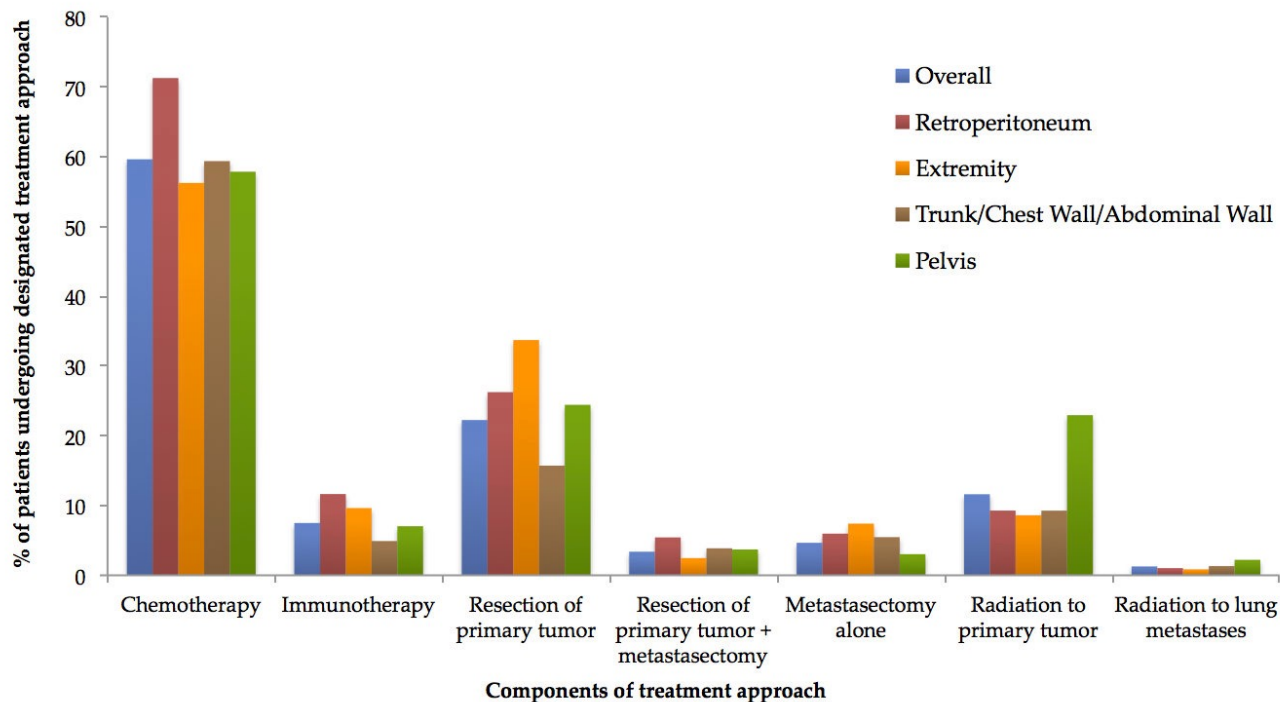
Median overall survival for the study population was 15.5 months (95% CI 14.09 – 17.94). Overall survival was significantly improved with receipt of chemotherapy and with both resection of the primary tumor and, more substantially, with curative intent surgery (Figure 3). 5-year OS for patients undergoing curative intent surgery was 20.9% compared to 9.2% for patients with primary tumor resection alone and 2.6% for patients who did not have surgery. Community treatment site, CCS of 2+, and a larger primary tumor were associated with increased hazard of death, while chemotherapy, primary tumor resection, and curative intent surgery predicted reduced hazard of death on multivariate Cox proportional hazard model.

Conclusion: This large national database studies provides histology-specific data on treatment approaches and outcomes for primary LMS with synchronous isolated lung metastases. Our results suggest that curative intent surgery with primary tumor resection and metastasectomy is associated with improved OS in this patient population and should be considered for suitable patients at high volume centers.

Table 1. Demographic and tumor characteristics for the overall population and specific disease sites presenting with primary LMS and SILM

Variable	Overall (N=629)	RPS	Extremity	Trunk/Chest wall/ Abdominal Wall	Pelvis	Other
Age, mean ± SD	63.76 ± 13.22	61.97 ± 12.94	66.31 ± 13.18	61.98 ± 13.04	64.13 ± 12.58	63.77 ± 15.17
Female, N (%)	366 (58.19)	63 (61.17)	78 (46.99)	93 (56.71)	97 (67.83)	35 (66.04)
Race, N (%)						
White – non-Hispanic	431 (68.52)	68 (66.02)	129 (77.71)	111(67.68)	93 (65.03)	30 (56.60)
Black – non-Hispanic	120 (19.08)	19 (18.45)	27 (16.27)	32 (19.51)	32 (22.38)	10 (18.87)
Hispanic	43 (6.84)	6 (5.83)	5 (3.01)	13 (7.93)	11 (7.69)	8 (15.09)
Native American	2 (0.32)	1 (0.97)	0	0	1 (0.70)	0
Asian	21 (3.34)	5 (4.85)	2 (1.20)	7 (4.27)	4 (2.80)	3 (5.66)
Other	12 (1.91)	4 (3.88)	3 (1.81)	1 (0.61)	2 (1.40)	1 (1.89)
CCS, N (%)						
0	487 (77.42)	75 (72.82)	133 (80.12)	135 (82.32)	102 (71.33)	42 (79.25)
1	102 (16.22)	22 (21.36)	23 (13.86)	22 (13.41)	23 (17.48)	10 (18.87)
2+	40 (6.36)	6 (5.83)	10 (6.02)	7 (4.27)	16 (11.19)	1 (1.89)
Treatment Site, N (%)						
Academic	386 (63.59)	63 (64.95)	113 (70.19)	94 (59.87)	87 (61.70)	29 (56.86)
Community	221 (36.41)	34 (35.05)	48 (29.81)	63 (40.13)	54 (38.30)	22 (43.14)
Insurance Status, N (%)						
Uninsured	31 (4.93)	3 (2.91)	9 (5.42)	5 (3.05)	11 (7.69)	3 (5.66)
Private	251 (39.90)	46 (44.66)	49 (29.52)	78 (47.56)	58 (40.56)	20 (37.74)
Government	330 (52.46)	50 (48.54)	104 (62.65)	75 (45.73)	72 (50.35)	29 (54.72)
Unknown	17 (2.70)	4 (3.88)	4 (2.41)	6 (3.66)	2 (1.40)	1 (1.89)
Tumor Grade						
I	21 (3.34)	6 (5.83)	2 (1.20)	7 (4.27)	4 (2.80)	2 (3.77)
II	60 (9.54)	9 (8.74)	15 (9.04)	19 (11.59)	13 (9.09)	4 (7.55)
III	284 (45.15)	40 (38.83)	107 (64.46)	61 (37.29)	65 (45.45)	11 (20.75)
Unknown	264 (41.97)	48 (46.60)	42 (25.30)	77 (46.95)	61 (42.66)	36 (67.92)
Tumor Size (cm)						
< 10	174 (45.08)	24 (38.71)	55 (48.25)	52 (49.52)	34 (39.53)	9 (47.37)
10-20	165 (42.75)	25 (40.32)	46 (40.35)	43 (40.95)	42 (48.84)	9 (47.37)
>20	47 (12.18)	13 (20.97)	13 (11.40)	10 (9.52)	10 (11.63)	1 (5.26)

LMS – leiomyosarcoma, SILM – synchronous isolated lung metastases, RPS – retroperitoneal sarcoma, SD – standard deviation, CCS – Charlson Comorbidity Score

**Figure 1.** Patterns of multimodality systemic and locoregional therapy for LMS with SILM at different primary disease sites

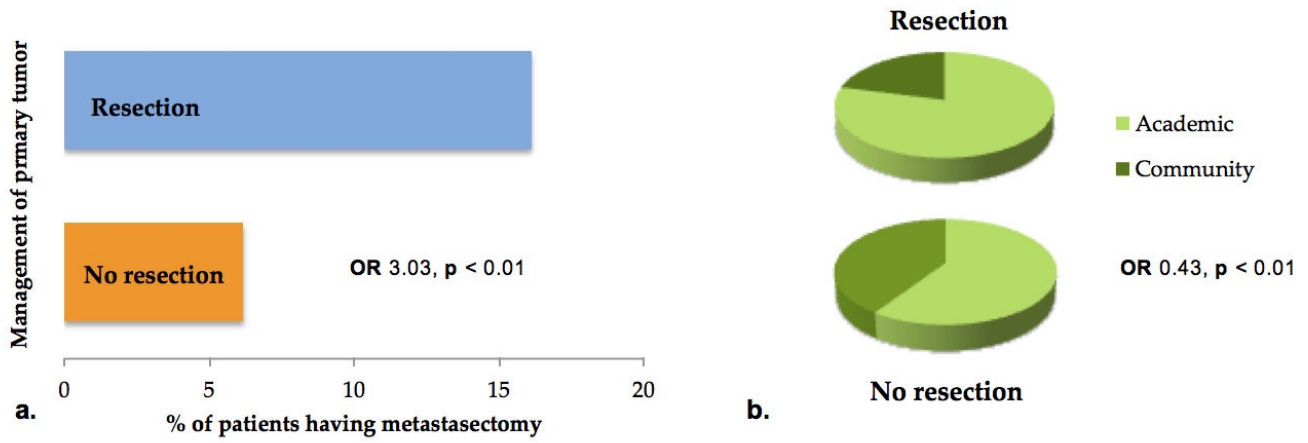


Figure 2. Factors associated with resection of primary tumor: **a.** metastasectomy and **b.** treatment at an academic center (reduced odds if treated at a community cancer center)

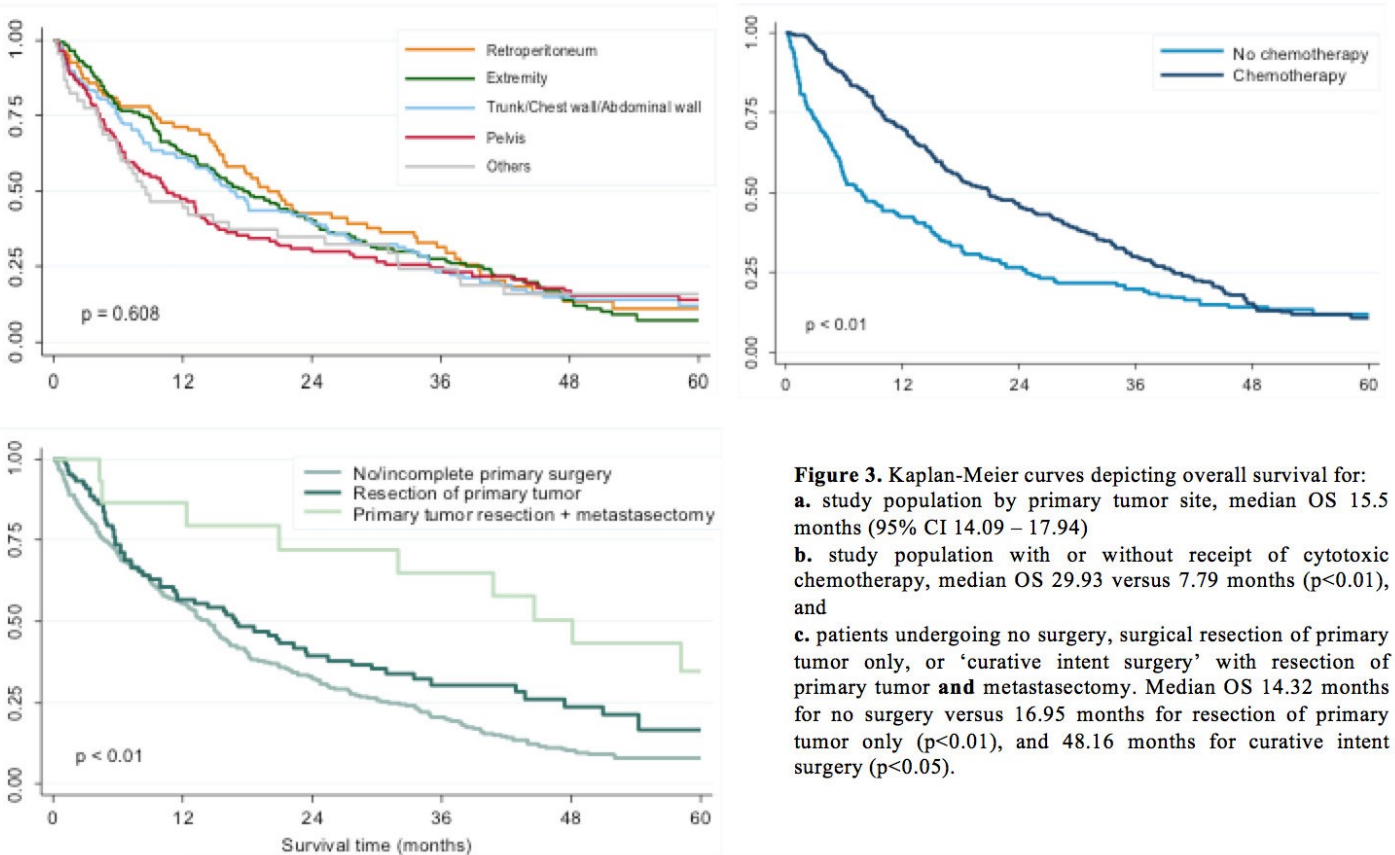


Figure 3. Kaplan-Meier curves depicting overall survival for: **a.** study population by primary tumor site, median OS 15.5 months (95% CI 14.09 – 17.94) **b.** study population with or without receipt of cytotoxic chemotherapy, median OS 29.93 versus 7.79 months ($p < 0.01$), and **c.** patients undergoing no surgery, surgical resection of primary tumor only, or ‘curative intent surgery’ with resection of primary tumor **and** metastasectomy. Median OS 14.32 months for no surgery versus 16.95 months for resection of primary tumor only ($p < 0.01$), and 48.16 months for curative intent surgery ($p < 0.05$).



Poster #031 #1819059

PEDIATRIC RHABDOMYOSARCOMA INCIDENCE AND SURVIVAL - UNITED STATES, 2001-2017

Matthew T. McEvoy, MD¹; M. Fatih Okcu, MD, MPH¹; Shifan Dai, MD, PhD²; David Siegel, MD, MPH²; Philip Lupo, PhD, MPH³,

¹Texas Children's Hospital Cancer Center, Baylor College of Medicine, Houston, Texas, UNITED STATES, ²Division of Cancer Prevention and Control, Centers for Disease Control and Prevention, Atlanta, Georgia, UNITED STATES,

³Texas Children's Cancer Center, Epidemiology Program, Baylor College of Medicine, Houston, Texas, UNITED STATES

Objective: Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma in children. Survival rates depend on clinical factors including age, anatomic site, histology, fusion status, tumor size, and cancer stage. Recent published epidemiological studies investigating RMS incidence and outcomes have largely included patients diagnosed before 2009, focused on tumors within only one anatomic site, and/or used databases that covered <30% of the US population. The objective of this study is to report pediatric (age < 20 years) RMS incidence using data from US Cancer Statistics (USCS) and survival from the National Program of Cancer Registries (NPCR), which cover 100% and 94% of the US population, respectively.

Methods: Incidence and survival of RMS in were assessed for pediatric patients diagnosed during 2003-2017 and 2001-2016, respectively. Variables included sex, race/ethnicity, age, tumor histology, anatomic site, SEER stage, socioeconomic status (SES), urban status, geographic region, and treatment era. Age-adjusted incidence rates, incidence rate ratios, average annual percent change (AAPC), and 5-year relative survival (RS) were calculated, all with corresponding 95% confidence intervals (CI). Cox hazard ratios (HR) were calculated and Kaplan-Meier survival distributions were estimated, with the log-rank test used to evaluate trends. A multivariable Cox regression model was conducted to examine the effect of demographic and clinical variables on survival. Statistical Analysis Software was used to perform all analyses and a p value <0.05 (two-sided) was considered statistically significant.

Results: We identified 5,656 primary RMS cases in USCS during 2003-2017. The age-adjusted incidence rate was 4.58 per 1 million (95% CI: 4.46 – 4.70). For RMS overall, AAPC was 0.3% (95% CI: -0.7 – 1.2%). In contrast to prior studies, AAPC stratified by histology did not show statistically significant changes. Among 5,589 cases identified in the NPCR database, five-year RS for all patients was 68.0% (95% CI: 66.6 – 69.3%) and did not change significantly over the study period. Survival varied by age, histology, anatomic site, and SEER stage, according to well-established clinical prognostic patterns. On multivariable regression, HR for Non-Hispanic (NH) Black children was 1.16 (95% CI: 1.01-1.33, p = 0.04) compared to NH White children.

Conclusion: This study provides the largest, most comprehensive population-based analysis to date for US children with RMS. The incidence of pediatric RMS was stable during the study period, including when stratified by histology. Survival varies by several demographic and clinical characteristics, and unfortunately remains poor for certain sub-populations. On multivariable analysis, a novel finding of worse survival was found for NH Black children compared to NH White children. Further investigation into differences by race/ethnicity and SES for both incidence and survival are warranted.

Table 2: Five-Year Relative Survival (RS) and Cox Hazard Ratios (HR) for Children with Rhabdomyosarcoma in the National Program of Cancer Registries, 2001-2016

Variable	No. (%)	5-year RS (%)	95% CI (%)		HR	95% CI	P-value
Total	5589 (100)	68.0	66.6-69.3				
Sex							
Male	3228 (58)	70.4	68.7-72.1		Ref		
Female	2361 (42)	64.7	62.5-66.7		1.25	1.13-1.38	<0.0001
Age at diagnosis (years)							
1-9	3094 (55)	77.2	75.5-78.7		Ref		
<1	317 (6)	70.6	64.8-75.7		1.45	1.16-1.82	0.001
10-19	2178 (39)	54.4	52.1-56.6		2.30	2.07-2.55	<0.0001
Race/Ethnicity							
NH White	3269 (58)	69.3	67.6-71.0		Ref		
NH Black	941 (17)	64.4	61.0-67.6		1.20	1.05-1.36	0.01
NH API*	196 (4)	64.8	56.7-71.8		~	~	~
NH AI/AN*	53 (1)	69.9	53.3-81.5		~	~	~
Hispanic	1130 (20)	67.5	64.5-70.4		1.09	0.96-1.24	0.18
Histology (ICD-O-3 code)							
Embryonal	2802 (50)	79.2	77.5-80.7		Ref		
Spindle	197 (4)	85.4	79.0-90.0		0.66	0.44-0.99	0.04
Alveolar	1653 (30)	47.9	45.2-50.5		2.96	2.64-3.31	<0.0001
Others^	937 (17)	66.9	63.5-70.0		1.76	1.52-2.04	<0.0001
Primary tumor site							
Favorable							
Orbit	364 (7)	93.4	90.0-95.7		Ref		
Genitourinary system	711 (13)	87.4	84.5-89.8		2.07	1.28-3.34	0.003
Biliary tract/liver	230 (4)	82.8	76.8-87.4		3.05	1.77-5.23	<0.0001
Head/neck	1066 (19)	71.9	68.8-74.7		5.00	3.20-7.80	<0.0001
Unfavorable							
Bladder/prostate	326 (6)	74.4	68.9-79.1		4.44	2.74-7.20	<0.0001
Para-meningeal region	493 (9)	62.8	58.1-67.1		6.93	4.40-10.90	<0.0001
Extremity	744 (13)	54.7	50.7-58.6		8.62	5.54-13.43	<0.0001
Trunk/other	1633 (29)	55.4	52.7-58.0		8.96	5.80-13.84	<0.0001
Unknown	22 (<1)	36.4	17.4-55.7		N/A	~	~
SEER stage							
Localized	1892 (34)	87.9	86.2-89.4		Ref		
Regional	1801 (32)	73.0	70.7-75.1		2.45	2.07-2.90	<0.0001
Distant	1575 (28)	38.5	35.9-41.1		7.55	6.46-8.82	<0.0001
Unknown	321 (6)	66.9	61.0-72.0		N/A	~	~
US Census region							
Northeast	988 (18)	68.6	65.4-71.6		Ref		
Midwest	1060 (19)	69.9	66.9-72.8		0.95	0.81-1.13	0.57
South	2183 (39)	67.6	65.4-69.7		1.03	0.90-1.19	0.66
West	1358 (24)	66.6	63.8-69.2		1.08	0.93-1.26	0.32
Socioeconomic status							

Top 25%	1480 (26)	69.6	66.9-72.1		Ref		
25% - 75%	3283 (59)	67.6	65.8-69.3		1.12	0.99-1.26	0.07
Bottom 25%	716 (13)	65.5	61.6-69.1		1.17	0.99-1.38	0.07
Unknown	110 (2)	74.2	64.1-81.8		0.83	0.56-1.25	0.37
Urban status							
Metro (population)	4884 (87)	67.9	66.4-69.3				
>1,000,000	3299 (59)	68.4	66.7-70.1		Ref		
250,000-1,000,000	1119 (20)	66.9	63.8-69.8		1.08	0.95-1.22	0.26
<250,000	466 (8)	66.1	61.3-70.5		1.13	0.95-1.35	0.17
Non-Metro	704 (13)	68.7	64.9-72.2		1.00	0.86-1.17	0.99
Treatment Era							
2001-2005	1712 (31)	67.4	65.1-69.5		Ref		
2006-2010	1804 (32)	67.9	65.7-70.0		0.96	0.86-1.08	0.53
2011-2016	2073 (37)	68.6	65.7-71.2		0.94	0.83-1.06	0.31

Notes: ~ = unable to calculate due to sample size/missing data. * = Patients with NH API and NH AI/AN race have been combined into a single variable for HR analysis. ^ = Other histologies include: RMS NOS, mixed-type RMS, and embryonal sarcoma. Patients with NH Other race have been excluded from this analysis (n=63). Variables with missing individual cases (n): Urban status (1)

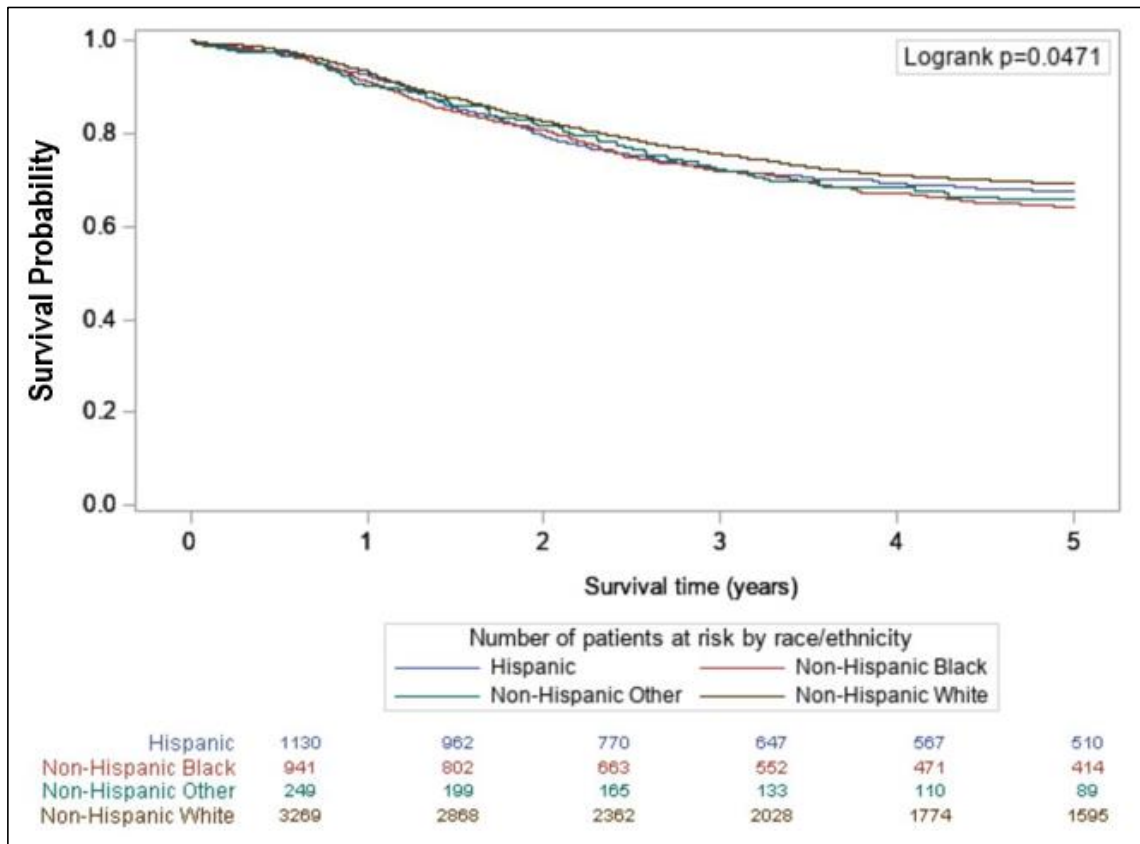
Abbreviations: AI/AN: American Indian/Alaska Native; API: Asian-Pacific Islander; CI: confidence interval; HR: Cox hazard ratio; ICD: International Classification of Diseases; NH: Non-Hispanic; RS: relative survival; SEER: Surveillance, Epidemiology, and End Results; Ref: reference variable

Table 3: Multivariable Cox Regression Analysis with Adjusted Hazard Ratios (aHR) for Children with Rhabdomyosarcoma in the National Program of Cancer Registries, 2001-2016

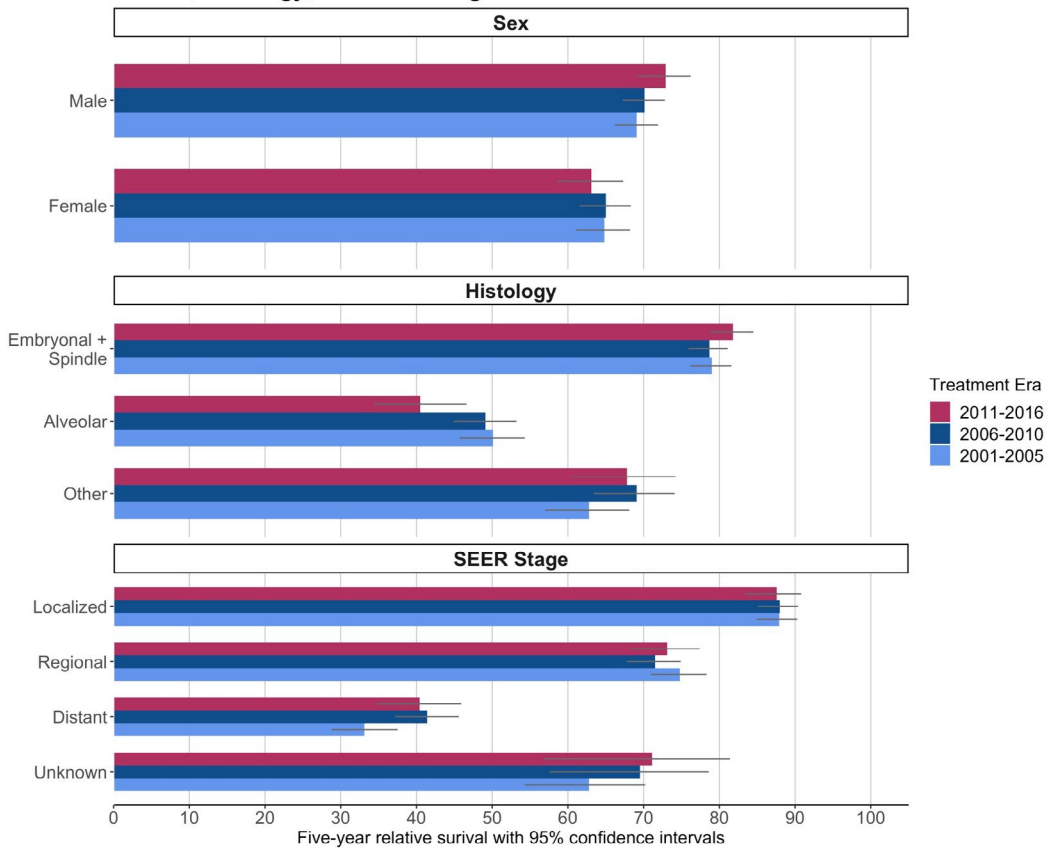
Variable	aHR	95% CI	P value
Sex			
Male	1	Ref	
Female	1.07	0.96-1.18	0.23
Age at diagnosis (years)			
1-9	1	Ref	
<1	1.76	1.39-2.24	<0.0001
10-19	1.74	1.56-1.95	<0.0001
Race/Ethnicity			
NH White	1	Ref	
NH Black	1.16	1.01-1.33	0.04
NH Other*	1.23	0.96-1.58	0.10
Hispanic	1.05	0.92-1.19	0.51
Histology (ICD-O-3 code)			
Embryonal	1	Ref	
Spindle	0.75	0.50-1.12	0.16
Alveolar	1.51	1.32-1.72	<0.0001
Others^	1.48	1.26-1.74	<0.0001
Primary tumor site			
Favorable			
Orbit	1	Ref	
Genitourinary	1.34	0.81-2.20	0.25
Biliary tract/liver	1.66	0.95-2.91	0.08
Head/neck	2.90	1.83-4.59	<0.0001
Unfavorable			
Bladder/prostate	2.61	1.57-4.32	0.0002
Para-meningeal	2.68	1.67-4.30	<0.0001
Extremity	3.20	2.01-5.08	<0.0001
Trunk/other	3.62	2.30-5.69	<0.0001
SEER stage			
Localized	1	Ref	
Regional	2.02	1.70-2.40	<0.0001
Distant	4.95	4.20-5.84	<0.0001
Socioeconomic status			
Top 25%	1	Ref	
25% - 75%	1.09	0.96-1.23	0.19
Bottom 25%	1.19	1.00-1.42	0.052
Unknown	0.88	0.58-1.33	0.54

Notes: * = Patients with NH Asian-Pacific Islander and NH American Indian/Alaska Native race have been combined into a single variable (NH Other). ^ = Other histologies include: RMS NOS, mixed-type RMS, and embryonal sarcoma. Abbreviations: CI: confidence interval; HR: Cox hazard ratio; ICD: International Classification of Diseases; NH: Non-Hispanic; SEER: Surveillance, Epidemiology, and End Results; Ref: reference variable

Figure 3. Kaplan-Meier Survival Estimation Curve for Children with Rhabdomyosarcoma by Race/Ethnicity.



Survival for Children with Rhabdomyosarcoma by Treatment Era for Sex, Histology, and SEER Stage





Poster #032 #1818884

NON-PRIVATE HEALTH INSURANCE PREDICTS ADVANCED STAGE AT PRESENTATION AND AMPUTATION IN LOWER EXTREMITY HIGH GRADE BONE SARCOMA: AN NCDB STUDY

Muhammad U. Jawad, MD¹; Brad Pollock, MD¹; Elysia Alvarez, MD, MPH¹; Janai Carr-Ascher, MD, PhD¹; R. Lor Randall, MD¹; Steven W. Thorpe, MD²

¹University of California, Davis, Sacramento, California, UNITED STATES, ²University of California Davis, Sacramento, California, UNITED STATES

Objective: High-grade bone sarcomas (HGBS) of the lower extremity (LE) are rare but portend a poor prognosis. Advances in the chemotherapy, radiotherapy, non-invasive imaging and surgical techniques over the past four decades have increased the feasibility of limb salvage. Limb salvage procedures are associated with superior functional results, comparable local disease control rate, and improved disease-specific and overall survival. Despite these advances, in some cases achieving local disease control and adequate surgical margins necessitates an amputation. Amputation is associated with an overall lower quality of life.

Factors predicting amputation in high-grade bone sarcoma of the lower extremity have not been well-defined. Recognition of modifiable factors that impact the rate of amputation is critical to strategies designed to increase the rate of limb salvage procedures. There is a paucity of information on the impact of amputation on survival in the literature. Moreover, demographic, socioeconomic and disease-related factors associated with stage at presentation for HGBS of the LE are also missing in the literature. Various sex-related, racial/ethnic and socioeconomic disparities in stage distribution at diagnosis have been implicated for a number of cancer types. Others have demonstrated disparities in amputation rates for lower extremity soft tissue sarcoma (STS) and its negative impact on survival.

For this study, we investigated factors associated with amputation among patients with high grade bone sarcoma of the lower extremities as well as the prognostic significance of amputation and age-related disparities. Using the National Cancer Database (NCDB) we report the socioeconomic and demographic factors associated with stage at presentation for high grade bone sarcoma of the lower extremities.

Methods: Cases were identified using the NCDB from 2004-2017. We selected cases with primary site 'long bones of the lower limb' and 'short bones of lower limb'. Patients with histological diagnoses for osteosarcoma, chondrosarcoma, Ewing sarcoma and malignant giant cell tumor of the bone were included in the analytic cohort. We excluded all grade 1 disease. Information regarding patient demographics including urban/rural origin, facility type and facility location, grade, stage, size, histologic subtypes, year of diagnosis, extent of surgical resection, chemotherapy and radiation treatment, and survival time until death or loss to follow-up was identified. NCDB reports Charlson / Deyo value that is a weighted score Table 1. Median household income, level of education in zip code of residence and insurance status were also extracted. Patients with no insurance and on Medicaid, and patients with medicare and private insurance were grouped together. This was done as patients presenting with no insurance to a healthcare facility are enrolled in Medicaid. Median income and level of education are presented as quartiles; Group 1 representing the lowest group and Group 4 representing the highest group, respectively. Patients with missing data were excluded from analysis.

For actuarial analyses, the log-rank test was used to assess the association between demographic, clinical, pathological, treatment and socioeconomic variables and survival. Multivariate survival analyses were performed to assess the magnitude of association between potential prognostic factors and survival using Cox proportional hazards regression.

Results: A total of 5,781 cases were isolated using the inclusion criteria described above. Demographic and clinical characteristics for the cohort are shown in Table 1. The five- and ten-year overall survival rates for the entire cohort were 0.51 and 0.49, respectively. On multivariate analysis (Table 2), age group 40-65 years, Charlson score of 0 or 1 only, a primary site of short bones of the lower limb, moderately differentiated tumor grade, stage I, II, or III, negative surgical margins, no chemotherapy and limb salvage surgery were independent predictors of improved outcome. We further investigated factors impacting the rate of amputation in this cohort. On multivariate analysis limb salvage was positively associated with patients having primary site of long bones of the lower limb at diagnosis, histology other than osteosarcoma, metropolitan or urban origin and private insurance. We further evaluated the impact of amputation on survival for different age groups. The impact was the highest for pediatric and AYA age groups where 10-year overall survival decreased from 0.65 for LSS to 0.47 for patients undergoing amputation. For age groups '40-65 years' and '> 65 years' 10-year overall survival decreased from 0.39 for LSS to 0.28 for amputation. Figure 1 A and B shows the Kaplan-Meier (KM) curves showing overall survival for

patients undergoing amputation vs. limb salvage surgery in Peds and AYA age group versus the adult age group, respectively. We investigated factors impacting the stage at presentation. On multivariate analysis presentation with metastatic disease was less likely with histology of osteosarcoma or chondrosarcoma, private insurance, year of diagnosis 2004-2010, treating facility type other than community cancer center, and certain facility locations (Table 3). As expected, negative surgical margins were more likely with an earlier stage at presentation (Table 1).

Conclusion: Our analysis showed that amputation is an independent predictor of poor overall survival. The finding is consistent with a previously published report for soft tissue sarcoma (STS) of the lower extremity. The adverse effect of amputation on survival is most pronounced for the pediatric and AYA age group; a finding consistent with STS of the lower extremity. Age related disparities in cancer outcomes are well documented for AYA age group in the literature. Given the high incidence of high-grade bone sarcoma in the pediatric and AYA age group the current finding is highly significant. Lower extremity amputation is associated with poor overall survival in non-neoplastic conditions as well. The current study shows an association of non-private insurance with higher rates of amputation. This finding has also been shown for patients with STS of the lower extremity. The current study also shows an association of non-private insurance with a delayed stage of disease at presentation.

The current study highlights the healthcare disparity between private and non-private insurance for patients with high-grade lower extremity bone sarcoma. The current findings call for healthcare reforms to reduce the disparity and increase the insurance coverage.

Table 1
Demographics and Clinical Characteristics of the Entire Cohort
Cross Tabulation (Pearson's Chi-Square)

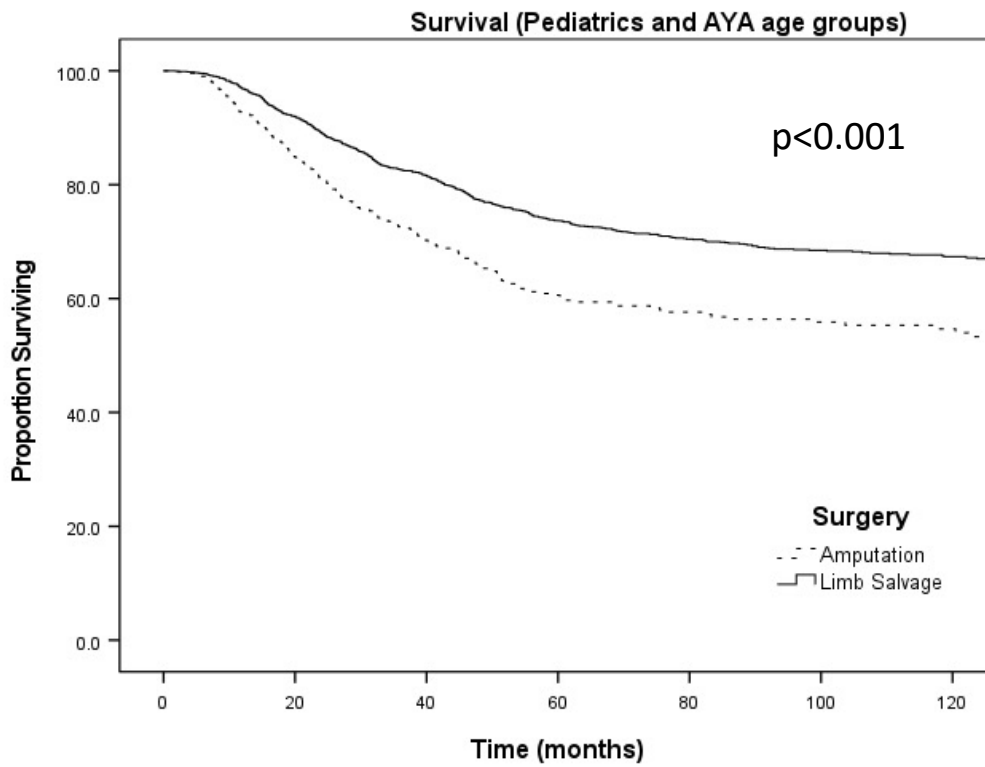
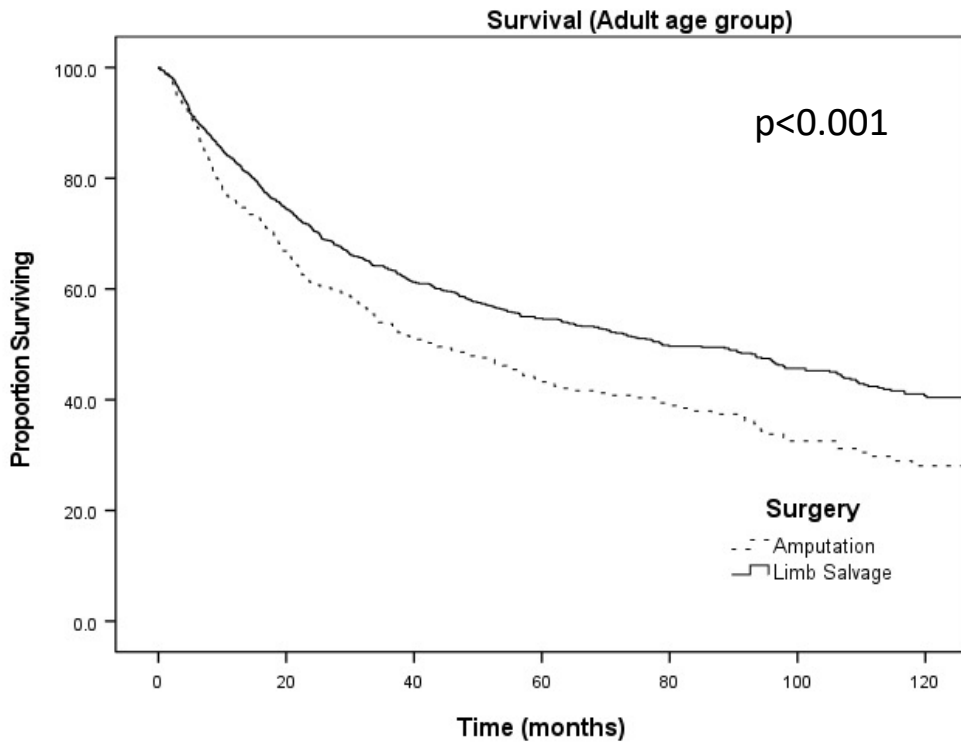
	n	Valid of total	Amputation		p-value	Stage		p-value
			Amputation	Limb Salvage		Non-Metastatic	Metastatic	
Total Patients	5781	100						
Age					<0.001			0.116
00-14 years	1255	21.7	189	935		876	177	
15-39 years	2263	39.1	405	1587		1697	281	
40-64 years	1353	23.4	292	938		1037	160	
≥ 65 years	910	15.7	160	633		687	122	
Sex					<0.001			0.018
Male	3346	57.9	677	2310		2466	459	
Female	2435	42.1	369	1783		1831	281	
Race					0.05			0.322
White	4572	80.5	807	3266		3394	587	
Black	741	13.1	148	509		537	106	
American Indian	41	0.7	12	24		34	4	
Asian/Pacific Islander	218	3.8	45	143		174	21	
Other	105	1.8	14	79		78	12	
Ethnicity					0.032			0.042
Non-Hispanic	4826	87.1	860	3448		3614	600	
Hispanic	714	12.9	145	467		521	109	
Grade					<0.001			<0.001
Moderate	1066	18.4	150	841		885	40	
Poorly	2558	44.2	485	1797		1902	350	
Undifferentiated	2157	37.3	411	1455		1510	350	
Primary Site					<0.001			0.024
Long Bones of Lower Limb	5472	94.7	898	3963		4067	715	
Short Bones of Lower Limb	309	5.3	148	130		230	125	
AJCC Stage					<0.001			
Stage I	1036	20.6	143	830				
Stage II	3131	62.2	602	2322				
Stage III	130	2.6	40	75				
Stage IV	740	14.7	153	384				
Size					0.114			0.312
<8 cm	4986	98.9	951	3626		3974	587	
≥8 cm	57	1.1	6	45		42	9	
Histology					0.012			<0.001
Osteosarcoma	3847	66.5	738	2667		2818	518	
Chondrosarcoma	1531	26.5	254	1163		1223	138	
Malignant Giant Cell Tumor Bone	48	0.8	7	37		32	9	
Ewing Sarcoma	355	6.1	47	226		224	75	
Charlson/Deyo Score					0.052			0.429
0	5106	88.3	895	3627		3778	647	
1	548	9.5	122	386		419	81	
2	86	1.5	20	56		69	7	
≥3	41	0.7	9	24		31	5	
Surgery								
Amputation	1046	20.4						
Limb Salvage	4093	79.6						
Margins					<0.001			<0.001
Negative	4335	92.4	966	3369		3467	417	
Positive	359	7.6	37	322		256	64	
Radiation Therapy								
Radiotherapy	334	5.8						
None	5389	94.2						
Chemotherapy								
Chemotherapy	3835	67.5						
None	1844	32.5						
Insurance					<0.001			<0.001
Private Insurance/ Medicare	4166	72.1	709	3050		3167	484	
No Insurance/ Medicaid	1395	24.1	317	893		985	216	
Facility Type					0.022			0.01
Community Cancer Program	61	2.7	14	25		32	12	
Comprehensive Community Cancer Program	348	15.4	70	213		243	51	
Academic/ Research / NCI Designated	1572	69.5	325	1120		1231	192	
Integrated Network Cancer Center	282	12.5	43	213		218	27	
Facility Location					0.04			0.035
New England	103	4.6	14	77		74	16	
Middle Atlantic	377	16.7	61	284		295	37	
South Atlantic	494	21.8	100	345		379	61	
East North Central	325	14.4	68	215		240	49	
East South Central	148	6.5	26	107		122	13	
West North Central	185	8.2	51	126		150	20	
West South Central	232	10.3	43	155		169	29	
Mountain	155	6.8	32	116		124	14	
Pacific Central	244	10.8	57	146		171	43	
Urban/Rurality Index					<0.001			0.711
Metropolitan	4637	84.9	811	3299		3441	599	
Urban	751	13.7	157	509		555	102	
Rural	76	1.4	26	44		59	8	
Median Income					<0.001			0.175
Group 1 (<30K)	961	18	208	645		704	131	
Group 2 (38-47K)	1266	23.8	247	847		921	179	
Group 3 (48-63K)	1363	25.6	234	992		975	180	
Group 4 (>63K)	1737	32.6	269	1285		1334	207	
Education Level					0.005			<0.001
Group 1 (>21%)	1059	19.9	216	700		753	169	
Group 2 (13-20.9%)	1348	25.3	256	930		980	187	
Group 3 (7-12.9%)	1628	30.5	280	1188		1201	206	
Group 4 (<7%)	1296	24.3	207	954		1003	135	
Year of Diagnosis					0.066			0.002
2004-2010	2772	48	525	1924		1959	293	
2011-2017	3009	52	521	2169		2338	447	

Table 2
Multivariate Analysis

		n	Hazard Ratio	95% CI	p-value
Age	00-14 years	~	~	~	~
	15-39 years	~	~	~	~
	40-64 years	785	0.461	0.388-0.547	<0.001
	≥ 65 years	489		Reference	
Sex	Male	732	1.025	0.872-1.205	0.766
	Female	542		Reference	
Race	White	1110	1.142	0.548-2.381	0.723
	Black	111	0.987	0.452-2.154	0.974
	American Indian	3	1.323	0.263-6.658	0.734
	Asian/Pacific Islander	33	0.822	0.317-2.129	0.687
	Other	17		Reference	
Grade	Moderate	399	0.335	0.240-0.466	<0.001
	Poorly	522	0.944	0.785-1.134	0.535
	Undifferentiated	353		Reference	
Primary Site	Long Bones of Lower Limb	1195	1.722	1.149-2.579	0.008
	Short Bones of Lower Limb	79		Reference	
AJCC Stage	Stage I	412	0.248	0.176-0.351	<0.001
	Stage II	702	0.266	0.210-0.336	<0.001
	Stage III	27	0.359	0.220-0.586	<0.001
	Stage IV	133		Reference	
Histology	Osteosarcoma	494	0.58	0.339-0.994	0.048
	Chondrosarcoma	742	0.63	0.364-1.090	0.099
	Malignant Giant Cell Tumor Bone	16	0.613	0.263-1.428	0.257
	Ewing Sarcoma	22		Reference	
Charlson/Deyo Score	0	994	0.4	0.239-0.670	<0.001
	1	215	0.487	0.284-0.835	0.009
	2	44	0.856	0.456-1.607	0.629
	≥3	21		Reference	
Surgery	Amputation	318	1.516	1.259-1.826	<0.001
	Limb Salvage	956		Reference	
Margins	Negative	1131	0.525	0.417-0.661	<0.001
	Positive	143		Reference	
Radiation Therapy	Radiotherapy	93	1.123	0.853-1.480	0.408
	None	1181		Reference	
Chemotherapy	Chemotherapy	811	1.386	1.120-1.715	0.003
	None	463		Reference	
Facility Type	Community Cancer Program	22	0.616	0.304-1.250	0.18
	Comprehensive Community Cancer Pr	165	0.779	0.553-1.097	0.153
	Academic/ Research / NCI Designat	938	0.878	0.683-1.130	0.313
	Integrated Network Cancer Cente	149		Reference	
Facility Location	New England	44	0.813	0.485-1.363	0.432
	Middle Atlantic	229	0.868	0.625-1.204	0.397
	South Atlantic	290	1.052	0.776-1.426	0.743
	East North Central	187	1.117	0.810-1.541	0.498
	East South Central	88	1.002	0.672-1.496	0.991
	West North Central	112	1.183	0.821-1.706	0.367
	West South Central	102	1.192	0.817-1.738	0.363
	Mountain	87	1.265	0.842-1.9	0.258
	Pacific Central	135		Reference	
Urban/Rurality Index	Metropolitan	1067	1.026	0.589-1.788	0.927
	Urban	185	1.009	0.574-1.775	0.974
	Rural	22		Reference	
Median Income	Group 1 (<30K)	222	1.311	0.956-1.797	0.093
	Group 2 (38-47K)	314	1.105	0.850-1.437	0.456
	Group 3 (48-63K)	307	1.026	0.808-1.302	0.834
	Group 4 (>63K)	431		Reference	
Education Level	Group 1 (>21%)	211	0.778	0.557-1.088	0.142
	Group 2 (13-20.9%)	329	0.881	0.671-1.157	0.363
	Group 3 (7-12.9%)	393	0.966	0.765-1.22	0.771
	Group 4 (<7%)	341		Reference	

Table 3
Cross Tabulation Amputation and Stage with other factors

Logistic Regression		Amputation				Stage			
		n	OR	95% CI	p-value	n	OR	95% CI	p-value
Age									
	00-14 years	~	~	~	~				
	15-39 years	~	~	~	~				
	40-64 years	871	1.029	0.774-1.367	0.845				
	≥ 65 years	571		Reference					
Sex									
	Male	810	0.809	0.620-1.055	0.117	940	1.258	0.943-1.678	0.119
	Female	632		Reference		744		Reference	
Race									
	White	1262	0.587	0.15-2.293	0.444				
	Black	126	0.442	0.106-1.844	0.263				
	American Indian	2	3.3 E+8	0.000~	0.999				
	Asian/Pacific Islander	33	0.489	0.101-2.364	0.374				
	Other	19		Reference					
Ethnicity									
	Non-Hispanic	1337	1.137	0.672-1.922	0.632	1557	1.524	0.85-2.732	0.158
	Hispanic	105		Reference		127		Reference	
Primary Site									
	Long Bones of Lower Limb	1351	5.193	3.268-8.253	<0.001	1584	1.809	0.899-3.639	0.097
	Short Bones of Lower Limb	91		Reference		100		Reference	
Stage									
	Non-Metastatic	1280	1.41	0.956-2.081	0.083				
	Metastatic	162		Reference					
Histology									
	Osteosarcoma	546	0.284	0.086-0.932	0.038	652	0.393	0.18-0.856	0.019
	Chondrosarcoma	853	0.539	0.164-1.774	0.309	976	0.23	0.106-0.502	<0.001
	Malignant Giant Cell Tumor Bone	21	0.777	0.140-4.3	0.773	24	0.428	0.122-1.507	0.186
	Ewing Sarcoma	22		Reference		32		Reference	
Insurance									
	Private Insurance/ Medicare	1258	1.736	1.191-2.531	0.004	1463	0.611	0.414-0.902	0.013
	No Insurance/ Medicaid	184		Reference		221		Reference	
Facility Type									
	Community Cancer Program	26	0.529	0.196-1.425	0.208	38	2.943	1.255-6.902	0.013
	Comprehensive Community Cancer Pro	198	0.66	0.373-1.168	0.154	246	1.635	0.906-2.951	0.102
	Academic/ Research / NCI Designate	1049	0.744	0.472-1.171	0.201	1193	1.243	0.774-1.998	0.368
	Integrated Network Cancer Center	169		References		207			
Facility Location									
	New England	62	1.469	0.671-3.217	0.336	77	0.765	0.366-1.6	0.476
	Middle Atlantic	258	1.568	0.946-2.601	0.081	294	0.495	0.292-0.84	0.009
	South Atlantic	324	1.506	0.929-2.441	0.096	386	0.627	0.387-1.017	0.058
	East North Central	200	1.097	0.653-1.843	0.726	234	0.867	0.521-1.443	0.583
	East South Central	104	1.825	0.942-3.535	0.075	121	0.391	0.189-0.808	0.011
	West North Central	119	0.819	0.459-1.462	0.5	134	0.46	0.236-0.894	0.022
	West South Central	120	1.04	0.584-1.853	0.894	139	0.503	0.267-0.948	0.033
	Mountain	98	1.392	0.721-2.688	0.324	109	0.431	0.206-0.9	0.025
	Pacific Central	157		Reference		190		Reference	
Urban/Rurality Index									
	Metropolitan	1208	4.098	1.634-10.276	0.003				
	Urban	211	4.468	1.736-11.496	0.002				
	Rural	23		Reference					
Median Income									
	Group 1 (<30K)	250	0.738	0.442-1.232	0.245				
	Group 2 (38-47K)	351	0.833	0.545-1.274	0.399				
	Group 3 (48-63K)	355	1.033	0.699-1.527	0.871				
	Group 4 (>63K)	486		References					
Education Level									
	Group 1 (>21%)	242	0.993	0.592-1.668	0.98	284	1.426	0.929-2.189	0.104
	Group 2 (13-20.9%)	346	0.741	0.489-1.122	0.156	401	0.994	0.678-1.457	0.974
	Group 3 (7-12.9%)	321	0.905	0.614-1.332	0.612	368	0.923	0.626-1.361	0.686
	Group 4 (<7%)	533	Ref.		Ref.	631		Reference	
Year of Diagnosis									
	2004-2010					718	0.745	0.557-0.997	0.048
	2011-2017					966		Reference	





Poster #033 #1818841

A POPULATION-BASED ANALYSIS OF LYMPH NODE METASTASIS IN EXTREMITY SOFT TISSUE SARCOMA: AN UPDATE

Charles A. Gusho, BS¹; Linus Lee, BE²; Michael P. Fice, MD²; Cristina M. O'Donoghue, MD, MPH²; Steven Gitelis, MD²; Alan T. Blank, MD, MS²,

¹Rush University Medical Center, Milwaukee, Wisconsin, UNITED STATES, ²Rush University Medical Center, Chicago, Illinois, UNITED STATES

Objective: Soft tissue sarcomas (STS) are mesenchymal tumors that may rarely metastasize to lymph nodes. This investigation sought to evaluate regional lymph node metastasis (RLNM) in extremity STS using a national cohort.

Methods: This study was a retrospective review of the Surveillance, Epidemiology, and End Results database from 1975 to 2016. A Cox proportional hazards model was used to identify prognostic factors associated with disease-specific survival (DSS).

Results: RLNM was present in 3.7% (n = 547) of extremity STS. The rate of RLNM was highest in rhabdomyosarcoma (26.7%), clear cell sarcoma (18.8%), epithelioid sarcoma (14.5%), angiosarcoma (8.1%), spindle cell sarcoma (5.0%), and synovial sarcoma (3.2%). The five-year DSS probability without RLNM was 69% (SE: 1.3%) compared to 26% (SE: 3.6%) with RLNM ($p < 0.001$). For the historically high-risk extremity STS, advanced age (HR, 1.036; 95% CI, 1.0-1.04; $p < 0.001$), higher grade tumors (HR, 1.979; 95% CI, 1.3-3.0; $p < 0.001$), tumor size greater than 10 cm (HR, 1.892; 95% CI, 1.3-2.7; $p < 0.001$), primary site surgery (HR, 0.529; 95% CI, 0.3-0.8; $p = 0.006$), distant metastasis (HR, 4.585; 95% CI, 3.0-6.8; $p < 0.001$), and RLNM (HR, 2.153; 95% CI, 1.3-3.5; $p = 0.003$) were each independent disease-specific prognostic factors.

Conclusion: The prognosis of RLNM in historically high-risk extremity STS is poor with a five-year DSS of 26%. These data support a staging system of STS inclusive of nodal involvement and contribute to the growing body of evidence that characterizes the rates of RLNM in STS.



Poster #034 #1819074

SOFT TISSUE SARCOMAS IN OCTOGENARIAN PATIENTS: ARE TREATMENT OPTIONS AND ONCOLOGICAL OUTCOMES DIFFERENT? - A SEER RETROSPECTIVE STUDY.

Michael P. Guertin, BS¹; Yonghoon Lee, BA²; Jose M. Ramirez, BS²; Alvin Nguyen, BA³; Juan Pretell-Mazzini, MD⁴

¹University of Miami Miller School of Medicine, Miramar, Florida, UNITED STATES, ²University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES, ³University of Illinois College of Medicine, Chicago, IL, ⁴Miller School of Medicine - University of Miami, Miami, Florida, UNITED STATES

Objective: Soft tissue sarcomas (STS) can arise throughout a lifespan. As the US population continues to age, oncological strategies and outcomes for STS should continue to be both examined for varying age groups. This study aims to analyze and compare treatment strategies and oncological outcomes for octogenarian patients with STS.

Methods: Data from patients diagnosed with appendicular STS between 2000-2015 were collected and analyzed using the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database. Demographic variables such as age, gender, race, laterality, location of primary sarcoma were analyzed. Tumor characteristics consisted of type of STS, grade, and stage (both AJCC 6th and 7th edition). Oncological outcomes included metastasis at diagnosis and overall survival (OS). Treatment's strategies included surgery, chemotherapy (QT), and radiotherapy (RT). These variables were analyzed in cohorts of individuals less than 80 years old and those 80 years old or older. SPSS (version 26) was utilized for data analysis. Both Kaplan Meir survival curves, as well as Cox regression analysis were applied to record OS rates and Hazard ratios (HRs), respectively.

Results: A total of 24,666 patients were included. Of which, 3,341 (13.5%) were 80 years old or older. There was no difference in gender and race distribution. The most common STS within the octogenarian cohort was Undifferentiated Pleomorphic Sarcoma (UPS) - previously Malignant fibrous histiocytoma (21.5%). Most STS were located in the lower extremity (62% of cases). The octogenarian group was diagnosed with high grade STS at a higher rate than the younger group (72.8% vs 58.4%, Table 1). 31.3% of octogenarian patient cases were diagnosed at Stage 3 with a similar metastatic rate at diagnosis to the younger group (16.2% vs 15.5%, Table 1). Within the octogenarian group, patients had less surgery of the primary tumor (26.0% vs 13.8%, $p < 0.001$) and received less chemotherapy (3.5% vs 20.7%, $p < 0.001$). There was not a statistical difference in RT administration (39.1%, octogenarian patients vs 41.5%, younger patients).

The OS at 5-years follow up was lower within the octogenarian group (26.5% vs 58.1%, $p < 0.001$). Adjunctive therapy (Table 2 & 3) with RT improved OS of both age groups with Stage 3 or 4. There was not a significant benefit for QT within the octogenarian group. For those that used both RT and QT, only those under 80 years old showed a significant improvement in OS when they were treated in Stages 3 and 4. For both age groups, surgical resection led to more than 5-times lower risk of death ($p < 0.001$). Both cohorts showed a significant decrease in OS when metastasis occurred ($p < 0.001$). More elderly patients died from causes other than their cancer (45.9% vs 11.8%, $p < 0.001$).

Conclusion: As the US population continues to age, STS are seen more within octogenarian patients. The most common type is UPS, and, in most cases, patients are diagnosed in stage 3 with high grade tumors. Metastatic disease at diagnosis is comparable to younger patients. Surgical resection of the primary tumor is beneficial as well as RT; however, QT has not shown many benefits. The octogenarian OS at 5 years is lower than younger patients, but the causes of death unrelated to cancer are also higher within this group of patients.

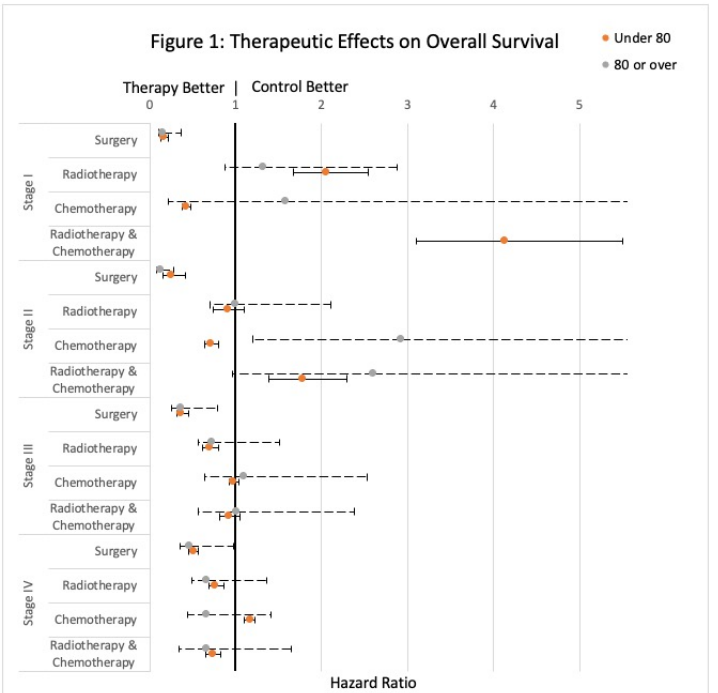
Characteristics	Age		Cramer V	P-value	
	< 80 years old (%)	≥ 80 years old (%)			
Gender	Male	9,580 (44.9)	1,710 (51.2)	0.043	<0.001
	Female	11,745 (55.1)	1,631 (48.8)		
Race & Ethnicity	Hispanic	3,201 (15.0)	195 (5.8)	0.139	<0.001
	NHAI/AN	132 (0.6)	12 (0.4)		
	NHAPI	1,426 (6.7)	190 (5.7)		
	NHB	2,618 (12.3)	183 (5.5)		
	NHU	284 (1.3)	9 (0.3)		
NHW	13,664 (64.1)	2,752 (82.4)			
Primary Site by Location	Upper Limb	6,076 (28.6)	931 (27.9)	0.054	<0.001
	Lower Limb	13,838 (65.2)	2,066 (62.0)		
	Unknown	1,310 (6.2)	336 (10.1)		
Type of STS	Spindle Cell Sarcoma	651 (3.1)	161 (4.8)	0.206	<0.001
	Epithelioid Sarcoma	348 (1.6)	15 (0.4)		
	Leiomyosarcoma	2,514 (11.8)	430 (12.9)		
	Rhabdomyosarcoma	614 (2.9)	53 (1.6)		
	Giant Cell Sarcoma	1,171 (5.5)	314 (9.4)		
	Myxofibrosarcoma	1,197 (5.6)	242 (7.2)		
	Undifferentiated				
	Pleomorphic Sarcoma	2,404 (11.3)	717 (21.5)		
	Liposarcoma	4,175 (19.6)	455 (13.9)		
Synovial Sarcoma	1,429 (6.7)	28 (0.8)			
Other STS	6,822 (32.1)	916 (27.4)			
Grade	1	2,833 (20.9)	293 (12.9)	0.107	<0.001
	2	2,805 (20.7)	325 (14.3)		
	3	3,127 (23.0)	578 (25.5)		
	4	4,813 (35.4)	1,073 (47.3)		
AJCC Stage	I	4,522 (38.5)	487 (25.4)	0.098	<0.001
	II	2,489 (21.2)	519 (27.1)		
	III	2,902 (24.7)	600 (31.3)		
	IV	1,821 (15.5)	311 (16.2)		
Surgery	No	2,675 (13.8)	788 (26.0)	0.115	<0.001
	Yes	16,721 (86.2)	2,245 (74.0)		
Radiotherapy	No	12,279 (58.5)	2,006 (60.9)	0.016	0.010
	Yes	8,704 (41.5)	1,289 (39.1)		
Chemotherapy	No	16,911 (79.3)	3,225 (96.5)	0.152	<0.001
	Yes	4,414 (20.7)	116 (3.5)		

NHAI/AN = Non-Hispanic Alaskan Indian/Alaskan Native
 NHAPI = Non-Hispanic Asian or Pacific Islander
 NHB = Non-Hispanic Black
 NHU = Non-Hispanic Unknown
 NHW = Non-Hispanic White

AJCC Stage	Treatment	5-Year Overall Survival # Patients (%)	Hazard Ratio	95% Confidence Interval		P-value
				Lower CI	Upper CI	
Stage I	Surgery	2,769 (65.5)	0.17	0.13	0.22	<0.001
	Radiotherapy	939 (65.1)	2.06	1.67	2.54	<0.001
	Chemotherapy	161 (46.9)	0.430	0.38	0.48	<0.001
	Radiotherapy & Chemotherapy	108 (52.9)	4.13	3.10	5.50	<0.001
Stage II	Surgery	1,402 (58.0)	0.26	0.16	0.41	<0.001
	Radiotherapy	922 (60.3)	0.91	0.74	1.10	0.323
	Chemotherapy	197 (56.6)	0.71	0.64	0.80	<0.001
	Radiotherapy & Chemotherapy	154 (59.2)	1.78	1.38	2.29	<0.001
Stage III	Surgery	1,166 (43.6)	0.37	0.31	0.45	<0.001
	Radiotherapy	953 (44.3)	0.70	0.61	0.80	<0.001
	Chemotherapy	477 (42.7)	0.98	0.92	1.04	0.424
Stage IV	Radiotherapy & Chemotherapy	391 (45.2)	0.92	0.81	1.05	0.197
	Surgery	143 (17.8)	0.51	0.45	0.56	<0.001
	Radiotherapy	98 (14.3)	0.77	0.69	0.86	<0.001
Stage IV	Chemotherapy	120 (11.2)	1.17	1.10	1.23	<0.001
	Radiotherapy & Chemotherapy	62 (13.7)	0.74	0.65	0.83	<0.001

AJCC Stage	Treatment	5-Year Overall Survival # Patients (%)	Hazard Ratio	95% Confidence Interval		P-value
				Lower CI	Upper CI	
Stage I	Surgery	173 (43.9)	0.16	0.11	0.25	<0.001
	Radiotherapy	45 (34.6)	1.32	0.88	2.00	0.181
	Chemotherapy	1 (33.3)	1.58	0.22	11.32	0.649
	Radiotherapy & Chemotherapy	0 (0)	**	**	**	**
Stage II	Surgery	174 (36.3)	0.13	0.08	0.20	<0.001
	Radiotherapy	109 (41.1)	1.00	0.70	1.41	0.976
	Chemotherapy	2 (22.2)	2.93	1.20	7.18	0.019
	Radiotherapy & Chemotherapy	2 (25.0)	2.61	0.96	7.06	0.06
Stage III	Surgery	112 (20.9)	0.37	0.26	0.53	<0.001
	Radiotherapy	92 (23.7)	0.73	0.56	0.95	0.019
	Chemotherapy	5 (17.9)	1.10	0.64	1.89	0.721
	Radiotherapy & Chemotherapy	5 (20.8)	1.01	0.57	1.81	0.964
Stage IV	Surgery	8 (9)	0.47	0.35	0.63	<0.001
	Radiotherapy	4 (4.3)	0.66	0.49	0.87	0.004
	Chemotherapy	2 (5.7)	0.66	0.44	0.97	0.037
	Radiotherapy & Chemotherapy	1 (9.1)	0.67	0.34	1.31	0.237

** Sample Size too small (n=0)





Poster #035 #1818885

MALIGNANT NEOPLASMS OF THE FOOT: PREDILECTION OF HEMATOLOGICAL MALIGNANCIES AND SEX-RELATED AND ETHNIC DISPARITIES IN AMPUTATION

Muhammad U. Jawad, MD¹; Saif Farhan, MD¹; Max R. Haffner, MD¹; Christopher Kreulen, MD, MS¹; Eric Giza, MD¹; Steven W. Thorpe, MD²; R. Lor Randall, MD¹,

¹University of California, Davis, Sacramento, California, UNITED STATES, ²University of California Davis, Sacramento, California, UNITED STATES

Objective: The human foot has unique anatomical characteristics that facilitate weight bearing, upright posture and bipedal gait. Complex functional structures are packed in close proximity and subjected to immense physical forces. This dynamic medium should enable the early detection of a tumor as a space occupying lesion quickly becomes symptomatic. However, given the rarity, the diagnosis of neoplastic processes affecting the foot is fraught with errors and delays. This has historically resulted in cases of under- or over-treatment with significant morbidity.

It has been estimated that only 3% of osseous neoplasm, 5% of malignant soft tissue neoplasms and 8% of benign soft tissue tumors arise in foot. To date, epidemiological and clinical reports describing foot neoplasms have emanated from single-centers with limited number of patients. Some studies have lumped benign and malignant tumors together while others have limited their analysis to a particular histopathological subtype. Information regarding patient characteristics and prognostic factors is limited due to small patient sample sizes, heterogenous data, and single-center studies that are susceptible to selection bias.

In the current study we used the National Cancer Institute's (NCI) Surveillance, Epidemiology and End Result (SEER) database to extract the data for malignant neoplasms affecting the 'small bones of lower limb and associated joints'. SEER is the only comprehensive source of population-based data in the US and is regarded as a standard of quality among the cancer registries around the world with case completeness of 98%. To our knowledge, this is the first study utilizing the population-based data to investigate the demographics, clinical characteristics and survival data for patients with neoplasms of the foot.

Methods: The cohort of cases for the current study was isolated using the NCI's SEER program. We isolated a total of 514 cases with primary location as 'C40.3 small bones of the lower limb and associated joints'. Information regarding patient demographics, grade, stage, size, histologic subtypes, cause of death, year of diagnosis, surgical and radiation treatment, and survival time until death or loss to follow-up was identified. Histological subtypes were grouped into soft tissue sarcoma (STS), osteosarcoma, chondrosarcoma, Ewing sarcoma and hematological malignancies. Information regarding socioeconomic status (SES) and insurance was extracted using the custom SEER census tract level and rurality database from 2000-2016. Patients with no insurance were grouped together with patients on Medicaid. This was done as patients presenting with no insurance to a healthcare facility are enrolled in Medicaid.

Patient age was converted to a categorical variable (0-14, 15-40, 40-64, ≥65) for the purpose of analysis. Tumor size was also converted into a categorical variable (≤8 cm, >8 cm). Since a majority of the cohort (72.1%) was malignancies originating from bone, size cut off of 8 cm was used as per AJCC recommendation. SEER* Stat software (version 8.3.8, NCI) was used to analyze incidence rates which were age adjusted and normalized using the 2000 US Standard population. Chi-square test was used to make correlations between categorical variables. Log-rank test was utilized for categorical values to gauge the effects of demographic, clinical, pathological, treatment and socioeconomic variables. A multivariate analysis was carried out using the Cox proportional hazards model. Pearson Chi Square test was used to assess correlation between amputation or stage at presentation and other significant prognostic factors. The study was deemed to be exempt from the approval by institutional review board (IRB).

Results: A total of 514 patients were extracted from the SEER database from 1975-2017. The demographics for the cohort are shown in Table 1.

We grouped the histological subtypes into soft tissue sarcoma (13%), osteosarcoma (21%), chondrosarcoma (31.1%), Ewing sarcoma (18.1%), Giant Cell Tumor of Bone (GCTB) (1.9%) and hematological malignancies (14.8%). The incidence of foot neoplasm was 0.024 per 100,000 persons in 2017 and has not changed significantly since 1975; APC 0.76 with $p > 0.05$ (Figure 1 A). The age adjusted incidence shows a bimodal distribution with the first peak at 10-19 years and the second peak at 70-79 years (Figure 1 B). The five- and ten-year disease specific survival rate for the entire cohort was 0.73 and 0.65, respectively (Table 2, Figure 2A). Univariate and multivariate survival analyses are shown in Table 2&3. On multivariate analysis younger age groups, and 'localized' stage, were independent predictors of improved outcomes. 'Amputation' was

found to be an independent predictor of worse outcomes. Size < 8 cm was borderline significant with $p=0.053$ (Figure 2 B through E). Statistical significance was achieved when cross tables were made for 'Surgery' with 'Sex', 'Race/Ethnicity', 'Histology', 'Grade', 'Stage', 'Size' and 'Year of Diagnosis'. For 'Histology' and 'Grade', there was a significant association between patients with 'hematological malignancies and Ewing sarcoma' and 'B/T/NK Cell', respectively with 'no surgery' ($p < 0.001$). There was also a statistically significant association for 'Size > 8cm' and 'Distant stage' with 'no surgery' ($p < 0.001$). Statistically significant association was also observed for 'Ewing sarcoma' and 'hematological malignancies' with 'Distant' stage ($p < 0.001$). Amputation was found to be more likely among 'Male Sex' ($p=0.049$) and 'Hispanic Race/Ethnicity' ($p=0.044$) (Table 4). 'Hispanic Race/Ethnicity' was found to be associated with 'osteosarcoma histology' ($p=0.002$) which may explain a higher rate of amputation. No such correlation was found for 'Male Sex'.

Conclusion: Foot neoplasms are rare but are associated with significant morbidity. The current investigation is the first to utilize a population-based dataset to characterize survival and prognostic factors in patients with foot neoplasms. This is also the first report describing the incidence of foot neoplasm from 1975-2017 and the age adjusted incidence highlighting the bimodal distribution in age groups '10-19 years' and for '>60 years'.

Around 15% of the primary neoplasms of the foot are hematological malignancies. Of note, around 50% (32/68) of the hematological malignancies of the foot in the current series were deemed to be at a distant stage at presentation. Univariate analysis showed older age, poor or undifferentiated grade, distant stage, size ≥ 8 cm, histology other than chondrosarcoma, surgical treatment other than local excision, and an earlier decade of diagnosis were found to be associated with poor outcomes. Younger age group and localized stage, were found to be independent predictors of improved outcomes. Amputation was found to be an independent predictor of poor outcome. Size < 8 cm was borderline significant with $p=0.053$.

Amputation was found to be correlated with a higher grade and an advanced stage of the disease in the current analysis. In addition, the association between amputation with male sex and Hispanic race/ethnicity was found to be statistically significant. Hispanic race/ethnicity was also found to be associated with osteosarcoma histology. This association may explain the higher rate of amputation among Hispanic race/ethnicity.

In our current analysis, there was no association found between SES and amputation. One possible explanation is the compact anatomical structure of the foot, making limb salvage difficult. Further, ray amputation, which is considered a limb salvage procedure, was not distinguished from other non-limb salvage amputations due to the limitations of the SEER database's classification of 'amputation'.

Table 1
Demographics and Clinical Characteristics of the Entire Cohort

	<i>n</i>	Valid 100% of total
Total Patients	514	100
Age		
00-14 years	74	14.4
15-39 years	201	39.1
40-64 years	133	25.9
≥ 65 years	106	20.6
Sex		
Male	296	57.6
Female	218	42.4
Race/Ethnicity		
NH White	349	68.4
NH Black	49	9.6
NHAPI	31	6.1
NHAIAN	5	1
Hispanic	76	14.9
Grade		
Well Differentiated	56	17.6
Moderate	78	24.5
Poorly	62	19.5
Undifferentiated	60	18.9
B/T/NK Cells	62	19.5
Stage		
Localized	215	46.9
Regional	141	30.8
Distant	102	22.3
Size		
<8 cm	203	61.9
≥8 cm	125	38.1
Histology		
Soft Tissue Sarcoma	67	13
Osteosarcoma	108	21
Chondrosarcoma	160	31.1
Ewing Sarcoma	93	18.1
Giant Cell Tumor Bone	10	1.9
Hematological Malignancies	76	14.8
Surgery		
Surgery NOS	52	10.1
Local Excision	210	40.9
Amputation	142	27.6
No Surgery	110	21.4
Radiation Therapy		
Radiotherapy	96	19.7
None/Unknown	392	80.3
Chemotherapy		
Chemotherapy	213	43.6
None/Unknown	275	56.4
Insurance		
Insurance	157	73.7
No Insurance/ Medicaid	56	26.3
SES		
Group 1	50	14.9
Group 2	57	17
Group 3	80	23.9
Group 4	76	22.7
Group 5	72	21.5
Year of Diagnosis		
1975-1984	37	7.2
1985-1994	58	11.3
1995-2004	129	25.1
2005-2017	290	56.4

Table 2
Disease-specific survival according to demographic
and clinical characteristics (proportion surviving)

		5 year Survival	10 year Survival	p-value
Overall		0.73	0.65	n/a
Age				
	00-14 years	0.78	0.74	
	15-39 years	0.76	0.69	
	40-64 years	0.8	0.73	
	≥ 65 years	0.44	0.15	<0.001
Sex				
	Male	0.75	0.67	
	Female	0.7	0.61	0.228
Race/Ethnicity				
	NH White	0.72	0.66	
	NH Black	0.75	0.6	
	NHAPI	0.66	0.28	
	NHAIAN	0.71	0.71	
	Hispanic	0.79	0.72	0.883
Grade				
	Well Differentiated	0.91	0.73	
	Moderate	0.8	0.65	
	Poorly	0.58	0.51	
	Undifferentiated	0.54	0.54	
	B/T/NK Cells	0.76	0.76	<0.001
Stage				
	Localized	0.86	0.78	
	Regional	0.77	0.73	
	Distant	0.46	0.3	<0.001
Size				
	<8 cm	0.8	0.7	
	≥8 cm	0.65	0.56	0.012
Histology				
	Soft Tissue Sarcoma	0.71	0.71	
	Osteosarcoma	0.7	0.59	
	Chondrosarcoma	0.86	0.74	
	Ewing Sarcoma	0.6	0.5	
	Giant Cell Tumor Bone	0.89	0.89	
	Hematological Malignancies	0.73	0.66	<0.001
Surgery				
	Surgery NOS	0.66	0.46	
	Local Excision	0.78	0.74	
	Amputation	0.75	0.64	
	No Surgery	0.64	0.6	0.028
Radiation Therapy				
	Radiotherapy	0.63	0.59	
	None/Unknown	0.75	0.66	0.021
Chemotherapy				
	Chemotherapy	0.66	0.58	
	None/Unknown	0.78	0.69	0.005
Insurance				
	Insurance	0.82	0.82	
	No Insurance/ Medicaid	0.74	0.74	0.163
SES				
	Group 1	0.72	0.72	
	Group 2	0.68	0.6	
	Group 3	0.81	0.81	
	Group 4	0.71	0.65	
	Group 5	0.78	0.7	0.088
Year of Diagnosis				
	1975-1984	0.52	0.37	
	1985-1994	0.69	0.53	
	1995-2004	0.7	0.64	
	2005-2017	0.79	0.76	0.002

Table 3
Multivariate Analysis

		n	Hazard Ratio	95% CI	p-value
Age	00-14 years	13	0.164	0.033-0.823	0.028
	15-39 years	63	0.122	0.034-0.429	0.001
	40-64 years	60	0.194	0.068-0.554	0.002
	≥ 65 years	38		Reference Group	
Grade	Well Differentiated	23	0	0-3.77E+307	0.972
	Moderate	45	0.595	0.037-9.614	0.715
	Poorly	38	1.571	0.109-22.592	0.74
	Undifferentiated	31	0.897	0.078-10.248	0.93
	B/T/NK Cells	37		Reference Group	
Stage	Localized	77	0.248	0.087-0.707	0.009
	Regional	60	0.559	0.185-1.683	0.301
	Distant	37		Reference Group	
Histology	Soft Tissue Sarcoma	11	2.499	0.189-33.023	0.487
	Osteosarcoma	45	1.705	0.114-25.428	0.699
	Chondrosarcoma	69	0.9	0.067-12.099	0.937
	Ewing Sarcoma	10	5.392	0.273-106.526	0.268
	Hematological Malignancies	39		Reference Group	
Size	<8 cm	103	0.414	0.170-1.01	0.053
	≥8 cm	71		Reference Group	
Surgery	Surgery NOS	9	3.659	0.620-21.601	0.152
	Local Excision	65	1.977	0.586-6.674	0.272
	Amputation	66	4.16	1.098-15.755	0.036
	No Surgery	34		Reference Group	
Radiation Therapy	Radiotherapy	32	2.173	0.831-5.687	0.114
	None/Unknown	143		Reference Group	
Chemotherapy	Chemotherapy	74	1.9	0.803-4.494	0.144
	None/Unknown	100		Reference Group	
Year of Diagnosis	1975-1984	1	0	0~	0.995
	1985-1994	15	2.895	0.840-9.978	0.092
	1995-2004	36	2.246	0.951-5.303	0.065
	2005-2017	122		Reference Group	

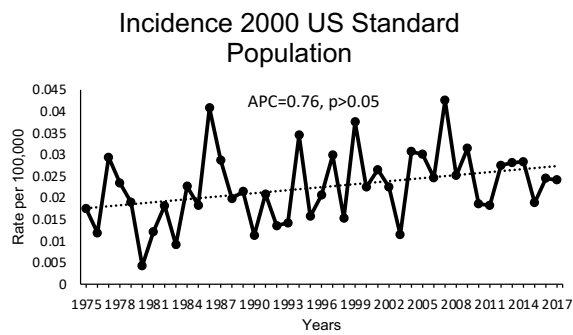
~ Statistic could not be calculated

Table 4

Cross Tabulation of Surgery and other factors

		Surgery				p-value
		Surgery NOS	Local Excision	Amputation	No Surgery	
Sex	Male	31	113	95	57	0.049
	Female	21	97	47	53	
Race/Ethnicity	NH White	40	148	87	74	0.044
	NH Black	7	16	11	15	
	NHAPI	3	13	11	4	
	NHAIAN	0	0	3	2	
	Hispanic	2	31	30	13	

a



b

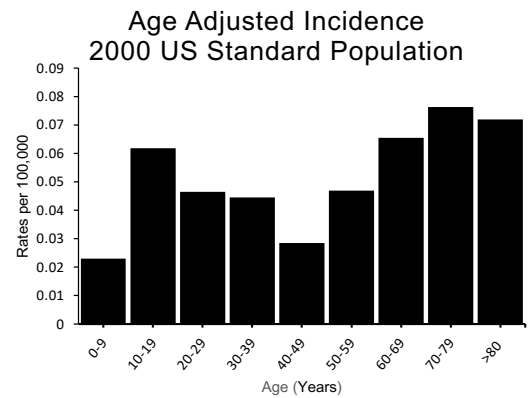


Figure 1

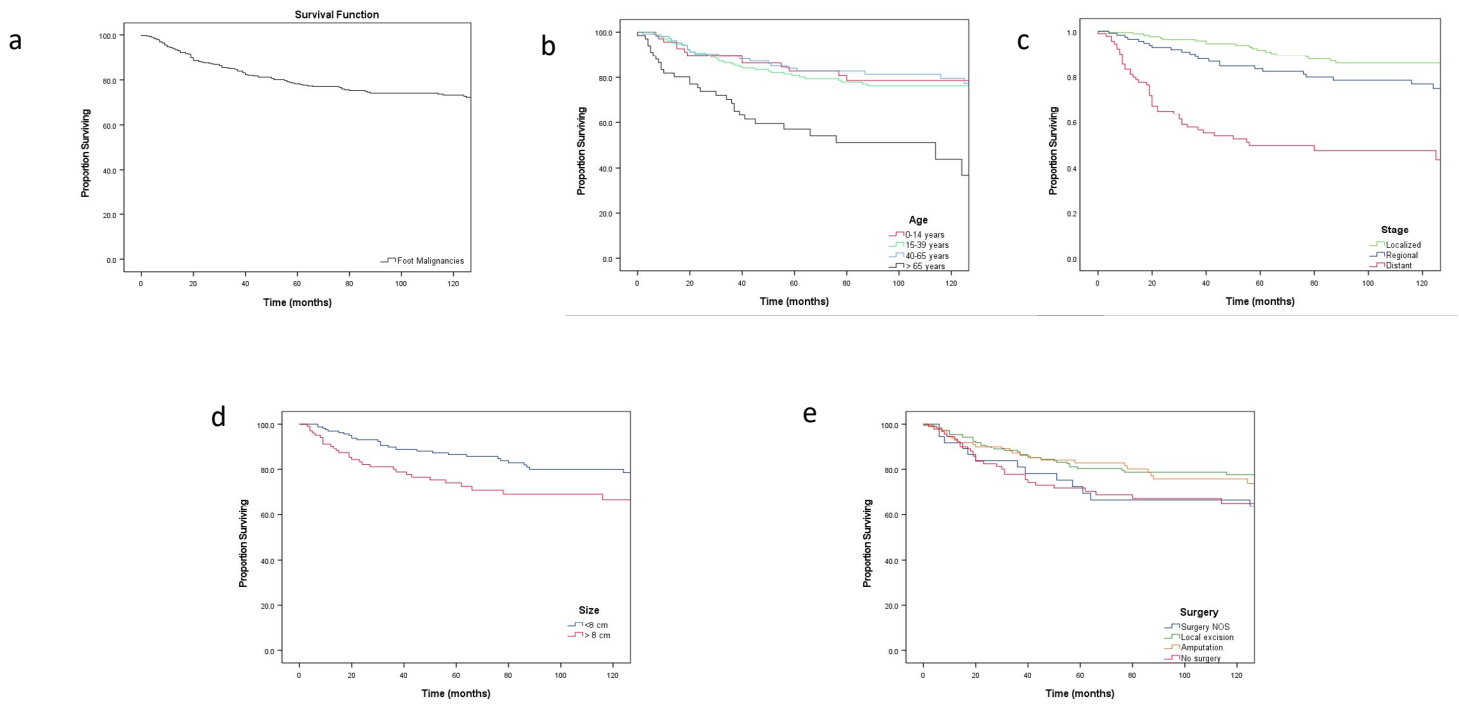


Figure 2

Malignant Neoplasms of the Foot: Predilection of Hematological Malignancies and Sex-Related and Ethnic Disparities in Amputation

Introduction

Information regarding malignant neoplasms of the foot has been limited to case studies from single institutions. Data regarding prognostic factors and survival has been limited.

Methods

In the current study we used the National Cancer Institute (NCI) Surveillance Epidemiology and End Results (SEER) database to extract the data for malignant neoplasms originating from the 'small bones of the lower limb and associated joints'.

A total of 514 cases were extracted. Kaplan Meier and Cox Regression have been used for Univariate and Multivariate Analysis.

Results

Hematological malignancies constituted 15% of the entire cohort. Incidence was 0.024 per 100,000 persons in 2017 and has not significantly changed since 1975 ($p > 0.05$). Disease-specific 5-year survival for the entire cohort was 73%.

On multivariate analysis younger age groups and 'localized' stage were predictors of improved outcomes. 'Amputation' was found to be a predictor of worse outcomes. Cross tabulation of amputation with other significant prognostic factors revealed a significant correlation of amputation with male sex and Hispanic ethnicity.

Discussion

The current study analyzes data from population-based registry reporting incidence and survival data for patients with neoplasms of the foot. Independent prognostic factors include age, stage and extent of surgical resection. Amputation was found to be associated with male sex and Hispanic ethnicity. Burden of morbidity associated with the foot malignancies is not comprehensively reflected by the survival analysis.

Jawad et al. *Ann Surg Oncol*.
Visual Abstract @AnnSurgOnc

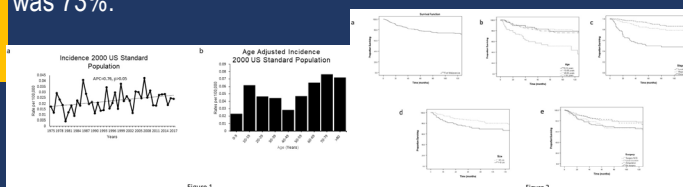


Figure 1

ANNALS OF
SURGICAL
ONCOLOGY



ctos®

2021 *Virtual* Annual Meeting

Poster Presentations

Poster Session 1



Poster #036 #1818917

PRIORITIES AND PROGRESS IN THE FIRST YEAR OF THE MUSCULOSKELETAL TUMOR REGISTRY

Benjamin J. Miller, MD MS¹; Adam Levin, MD MS²; Eric Henderson, MD³

¹University of Iowa, Iowa City, Iowa, UNITED STATES, ²Johns Hopkins, Baltimore, Maryland, UNITED STATES,

³Dartmouth, Lebanon, New Hampshire, UNITED STATES

Objective: The Musculoskeletal Tumor Registry (MsTR), a national prospective sarcoma registry focused on oncologic and functional outcomes, has completed the pilot trial period and was accepted as a full registry into the American Academy of Orthopaedic Surgeons (AAOS) family of registries, joining the American Joint Replacement Registry, the Shoulder and Elbow Registry, and the American Spine Registry (ASR). In the spring of 2020, a steering committee, was formed to lead the registry effort through the first years of maturation. The priorities for 2021 included 1) Publish an Annual Report Preview, 2) Complete existing projects expanding registry utility (Metastatic Disease of Bone [MDB] module, spine tumor module [with ASR], and Giant Cell Tumor [GCT] trial collaboration), and 3) Continue to increase awareness and enrollment of centers. Our goal is to update the membership of CTOS on the current status and future goals of MsTR.

Methods: As of June 1, 2021, 19 sites were fully contracted with 27 additional sites in contracting discussions. The Steering Committee has met on monthly conference calls since its inception with AAOS registry staff, and an additional working group has been formed to create a combined spine tumor module with ASR.

Results: The Steering Committee has approved all data elements to be collected in MsTR for the sarcoma and MDB modules. The AAOS registry team is currently working on development and dissemination to other current and future sites to ensure accuracy and streamline data collection and retrieval. By the end of the calendar year, these will be summarized in an Annual Report Preview and example of provider-facing dashboards. In addition to completing the sarcoma, MDB, and spine tumor modules, we are also collaborating with a prospective, randomized trial funded by the Orthopaedics Research and Education Foundation regarding treatment of GCT to explore the use of MsTR as a data collection instrument for clinical trials. Finally, we are continually focused on highlighting the registry vision and potential benefits to the public and providers to stimulate interest and participation.

Conclusion: The MsTR effort continues to improve and mature. Our future priorities include ensuring data completeness and accuracy, allowing data entered into MsTR to be used easily by individual sites to populate institutional databases, assessing registry performance based on provider feedback, and performing simple hypothesis-driven queries of the registry.



Poster #037 #1818986

ANALYZING THE TEMPORAL TRENDS IN FIVE-YEAR SURVIVAL FOR PATIENTS WITH OSTEOSARCOMA

Daniel R. Evans, MSc¹; Alexander L. Lazarides, MD²; Isabelle Byers, BA¹; Julia D. Visgauss, MD³; Brian E. Brigman, MD, PhD³; William C. Eward, MD³

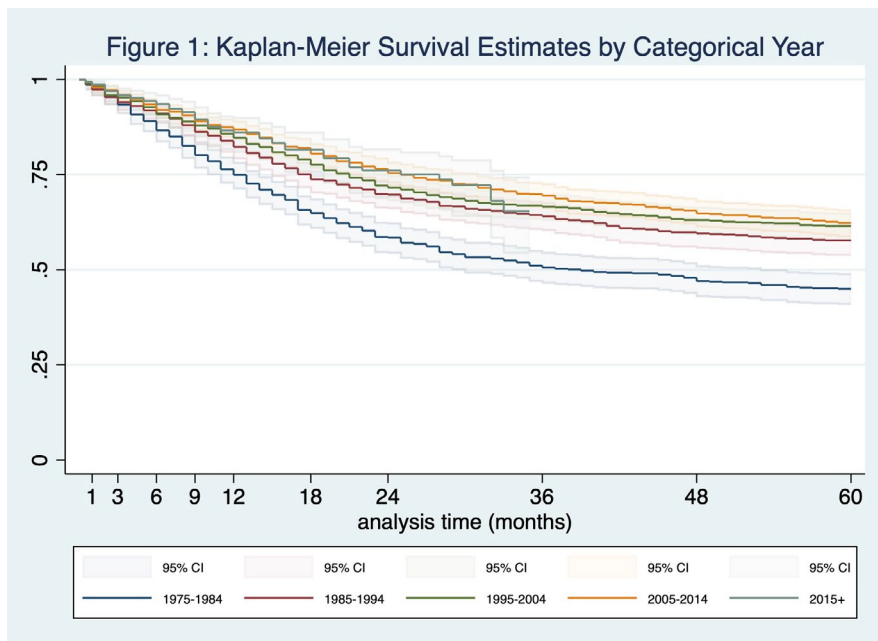
¹Duke University School of Medicine, Durham, North Carolina, UNITED STATES, ²Duke University Hospital, Department of Orthopedic Surgery, Durham, North Carolina, UNITED STATES, ³Duke University Hospital, Department of Orthopaedic Surgery, Durham, North Carolina, UNITED STATES

Objective: Prior the introduction of adjuvant chemotherapy agents in the 1970’s the five-year survival for patients with osteosarcoma was less than 20%. Over the ensuing decade and a half, advancements in chemotherapy treatments and surgical techniques improved five-year survival to greater than 50%. This progress has stagnated though, with studies since showing that there was not a significant improvement in survival between 1984 and 2004. The purpose of this study is to assess whether five-year overall survival (OS) in osteosarcoma has improved over the past four decades.

Methods: We retrospectively reviewed patients (n=3,304) with primary localized osteosarcoma in the National Cancer Institute’s SEER database between 1975 and 2017. Cancer specific five-year survival was available for 2895 patients between 1975-2013. A Kaplan-Meier analysis was used to assess five-year survival by categorical year of diagnosis and univariate cox regression for continuous year of diagnosis. A multivariate cox regression was then used to assess five-year survival while controlling for age, sex, primary site, and spread of cancer.

Results: The overall five-year survival from 1975-2013 was 57.2%. The five-year survival between 1975-1984 was 44.9% (95% CI: 40.1-48.9%), 1985-1994 was 57.7% (53.9-61.3%), 1995-2004 was 61.5% (57.8-64.9%), and 2005-2013 was 62.2% (58.7-65.5%) with no significant changes in survival from 1985-2013 (Log rank test p=0.08). Figure 1 demonstrate a Kaplan-Meier curve of five-year survival by categorical year. Univariate analysis of continuous year of diagnosis demonstrated no significant improvement in survival between 1986-2013. Multivariate analysis controlling for potential confounders demonstrated no significant change in survival since 1995.

Conclusion: Five-year survival for osteosarcoma has not improved appreciably since around the turn of the millennium, consistent with previous reports of the stagnation of survival outcomes for patients with osteosarcoma. As medicinal advancement continues to improve patient outcomes for other patients’ diseases, these findings highlight the dire need for new and innovative treatments for osteosarcoma.





Poster #038 #1818906

**IMPACT OF INSURANCE STATUS ON CHONDROSARCOMA DIAGNOSTIC STAGE:
IMPLICATIONS FOR DETECTION AND OUTCOMES**

Ana C. Belzarena, MD¹; Puja Yatham, BS²; Jacklyn Garcia, BS²; Valeria Fagundo, BS²; Grettel Castro, MPH²;
Pura Rodriguez de la Vega, MPH²; Juan Ruiz-Pelaez, MD MMedSci²

¹Miami Cancer Institute, Miami, Florida, UNITED STATES, ²Herbert Wertheim College of Medicine Florida International University, Miami, Florida, UNITED STATES

Objective: The purpose of this study is to evaluate the association between insurance status and the stage of chondrosarcoma at the time of diagnosis in the United States. Therefore, we asked: is there an independent association between lack of health insurance and diagnosis of advanced stage chondrosarcoma?

Methods: A retrospective comparative (analytical) cross-sectional study was conducted using the Surveillance, Epidemiology and End Results (SEER) database. Patients with a diagnosis of Chondrosarcoma of the limbs and pelvis between 2007 and 2016 were included. A total of 2351 patients matched the search; 164 patients were excluded due to incomplete information. Exposure Variable is insurance status at diagnosis and the outcome is Chondrosarcoma staging at the time of diagnosis. Variables of interest included insurance status, age, gender, race, ethnicity, marital status, place of residence, primary site and stage at diagnosis. Possible associations between the different variables were assessed using the chi-square test. All tests were deemed significant at the 0.05 level.

Results: A total of 2187 patients were included for statistical analysis. The majority were male (58%), between the ages of 31-50 (32%), white (85%), non-Hispanic (85%), married (60%), living in a metropolitan area (90%), Insured (83%). Regarding stage at diagnosis, 1213 (55%) had localized disease while 974 (45%) had a later stage at presentation. The majority of the patients (1883, 86%) had a non-pelvic location as the primary site. Variables with a significant association with a later stage at diagnosis included being older than 65 ($p < 0.001$), male gender ($p < 0.001$) and pelvic location ($p < 0.001$). The unadjusted relative risk (RR) of late stage at diagnoses for the uninsured was 1.25. After adjusting for other variables, the odds of being diagnosed at a later stage of Chondrosarcoma is increased by 77% ($p=0.01$) in uninsured patients compared to insured ones.

Conclusion: Being uninsured increased the chances of a late-stage diagnosis of Chondrosarcoma by 77% when compared to insured patients. Immediate efforts are required to remediate health care access disparities in cancer care. The knowledge gained by exploring the association between insurance status and stage at time of diagnosis will hopefully contribute to improve overall detection and outcomes by emphasizing awareness and promoting early interventions in patients who are at risk for a late diagnosis.



Poster #039 #1818899

SOFT TISSUE SARCOMA INCIDENCES AND CLINICAL CHARACTERISTICS ARE SIGNIFICANTLY DIFFERENT BETWEEN DIFFERENT GEOGRAPHIC AND ETHNIC POPULATIONS

Tom W. Chen, MD¹; Ruru Chang, PhD²; Axel Le Cesne, MD³; Yuchun Hsieh, MSc⁴; Antonine Italiano, MD⁵; Ya-Wen Yang, MSc⁶; Nicolas Penel, MD⁷; Wen-Chung Lee, MD, PhD⁶; Emmauelle Bompas, MD⁸; Thibaud Valentin, MD⁹; Philippe Anract, MD¹⁰; Nelly Firmin, MD¹¹; Florence Duffaud, MD¹²; K. Arnold Chan, MD PhD¹³; Jean-Yves Blay, MD, PhD¹⁴

¹National Taiwan University Hospital, Taipei, Taipei, TAIWAN (REPUBLIC OF CHINA), ²Institute of Epidemiology and Preventive Medicine, College of Public Health, National Taiwan University, Taipei, Taipei, TAIWAN (REPUBLIC OF CHINA), ³Institut Gustave Roussy-Gustave Roussy Cancer Center-DITEP, Villejuif, Ile-de-France, FRANCE, ⁴Health Data Research Center, National Taiwan University College of Public Health, Taipei, Taipei, TAIWAN (REPUBLIC OF CHINA), ⁵Institute Bergonié, Bordeaux, Aquitaine, FRANCE, ⁶Taiwan Cancer Registry Center, Institute of Epidemiology and Preventive Medicine, National Taiwan University College of Public Health, Taipei, Taipei, TAIWAN (REPUBLIC OF CHINA), ⁷Oscar Lambret Cancer Center, Lille, Nord-Pas-de-Calais, FRANCE, ⁸Institut de Cancérologie de l'Ouest, Saint-Herblain, Pays de la Loire, FRANCE, ⁹IUCT Oncopole, Toulouse, Languedoc-Roussillon, FRANCE, ¹⁰Assistance Publique – Hôpitaux de Paris, Paris, Ile-de-France, FRANCE, ¹¹ICM, Institut du Cancer de Montpellier, Montpellier, Languedoc-Roussillon, FRANCE, ¹²Marseille University Hospital Timone, Marseille, Languedoc-Roussillon, FRANCE, ¹³Graduate Institute of Oncology, National Taiwan University College of Medicine, Taipei, Taipei, TAIWAN (REPUBLIC OF CHINA), ¹⁴Centre Léon Bérard, Lyon, Auvergne, FRANCE

Objective: Geographical and ethnic differences in cancer incidences may be a harbinger for different underlying molecular mechanisms and biology, as exemplified in lung adenocarcinoma. Although STSs are rare, the incidences among different geographic and ethnical populations have not been investigated thoroughly.

Methods: STS patients from 2013 to 2016 were obtained from National Cancer Registry Databases from France and Taiwan. We selected five most common lineage-specific STS histologies (liposarcoma (LPS), leiomyosarcoma (LMS), angiosarcoma (AS), synovial sarcoma (SS), and malignant peripheral nerve sheath tumor(MPNST)) to estimate the age-standardized incidence rates (ASR, as in per one-million person years). Taiwan ASR was standardized using the French population. The histology and body parts criteria were based on International Classification of Disease for Oncology 3rd edition (ICD-O-3).

Results: A total of 9398 (France 7148, Taiwan 2250) patients are included in the analysis. The ASR of all 5 histologies are significantly different (non-overlapping of the 95% confidence intervals (CI)) (Table 1). The ASRs of angiosarcoma (5.4 vs 2.8) and MPNST (2.0 vs 1.0) are significantly higher in Taiwan; France has significantly higher LPS (12.0 vs 10.0), LMS (9.7 vs 7.6), and SS (1.7 vs 1.2) ASRs. Age distribution patterns demonstrate that LMS ($p < 0.001$) and LPS ($p < 0.001$) patients in Taiwan have a younger age peak than those in France. The body part distributions are also significantly different. French patients are more likely to have extremity and truncal LMS (odds ratio (OR) 2.84, $p < 0.001$), AS (OR 2.67, $p < 0.001$), MPNST (OR 1.55, $p = 0.01$), LPS (OR 1.37, $p < 0.001$), and breast AS (OR 10.6, $p < 0.001$). Taiwanese patients have higher odds for liver AS (OR 10.7, $p < 0.001$) and uterine LMS (OR 3.21, $p < 0.001$). SS age distribution and body parts are not significantly different between the two countries.

Conclusion: The significant differences in incidence and clinical characteristics of common types of STS suggest that geographic (environmental) and ethnicity factors likely play an important role in the pathogenesis of STS.

Table 1 The ASR and 95% CI between France and Taiwan, 2013-2016

	ASR per million person years (95% CI)	
	France	Taiwan
Angiosarcoma	2.8 (2.56-2.96)	5.4 (4.95-5.93)
Leiomyosarcoma	9.7 (9.29-10.05)	7.6 (6.98-8.13)
Liposarcoma	12.0 (11.54-12.37)	10.0 (9.37-10.70)
MPNST	1.0 (0.88-1.13)	2.0 (1.70-2.29)
Synovial sarcoma	1.7 (1.52-1.84)	1.2 (0.94-1.40)



Poster #040 #1818932

IMPACT OF OSTEOARTHRITIS ON SURGICAL TREATMENT PATTERNS AMONG PATIENTS WITH TENOSYNOVIAL GIANT CELL TUMORS

Feng Lin, PhD¹; Kathleen Wilson, MPH²; Matthew Brouillette, MPH²; Winghan J. Kwong, Pharm.D., PhD³; John A. Abraham, MD, FACS⁴

¹Daiichi Sankyo Inc., Basking Ridge, New Jersey, UNITED STATES, ²Custom Data Analytics, Life Sciences, IBM Watson Health, Cambridge, Massachusetts, UNITED STATES, ³Daiichi Sankyo, Inc., Basking Ridge, New Jersey, UNITED STATES, ⁴Rothman Institute and Fox Chase Cancer Center, Philadelphia, Pennsylvania, UNITED STATES

Objective: Tenosynovial giant cell tumors (TGCT) are rare, locally aggressive neoplasms that can cause pain, stiffness, and joint destruction. Given its rarity and similarity in symptoms, TGCT may be misdiagnosed as osteoarthritis (OA). Moreover, the chronic course of TGCT might lead to development of secondary OA. Little is known about the impact of comorbid OA on surgical pattern among patients with TGCT.

Methods: A retrospective study was conducted using IBM® MarketScan® Commercial and Medicare Supplemental administrative claims data. The study included adults who had at least one medical claim for TGCT from 01/01/2014 to 06/30/2019, ≥ 3 years of continuous enrollment before and after the first (index) TGCT diagnosis, and no additional cancer diagnosis during the study period. Patients were stratified by presence of OA diagnosis in relation to the index date. Pattern of surgery (arthroplasty, arthrodesis, arthroscopic excision, open excision, and amputation) were described. Cox regression was used to assess the effect of having OA medical claims before and after index TGCT diagnosis on the risk of first surgery and reoperation post-index while controlling for baseline characteristics and pre-index surgery.

Results: A total of 2856 patients with TCGT were included (mean age 51.6 years; 61.7% female): 1153 (40.4%) had no OA claims before or after index, 207 (7.2%) had OA claims before index but not after, 644 (22.5%) had OA claims after index but not before and 852 (29.8%) had OA claims before and after index (Table 1). Rate of surgery during the post-index period was higher for patients with OA claims post-index compared to those without OA claims post-index (55.7% vs 33.2%). Among patients undergoing surgery post-index, patients with OA claims post-index also had higher rates of reoperation than patients without OA claims post-index (35.6% vs 18.0%). Arthroscopic and open excisions were the most common surgical procedures performed in TGCT patients. More patients with post-index OA had arthroplasty than those without OA post-index (18.7% vs 0.2%).

After controlling for baseline characteristics, adjusted post-index surgery risk in patients with OA claims before and after index was more than twice of patients without OA claims before or after index [adjusted hazard ratio (HR) (95% confidence interval) = 2.48 (2.13, 2.88)] (Figure 1a). Adjusted post-index surgery risk in patients with OA claims after but not before index was almost twice of those without OA claims before or after index [adjusted HR = 1.74 (1.49, 2.03)] (Figure 1a). Compared to patients without any OA diagnosis, the risk of reoperation was higher in patients with OA claims before and after index [adjusted HR (95% CI) = 2.28 (1.68, 3.11)] and in patients with OA claims after but not before index [adjusted HR = 2.18 (1.60, 2.97)] (Figure 1b).

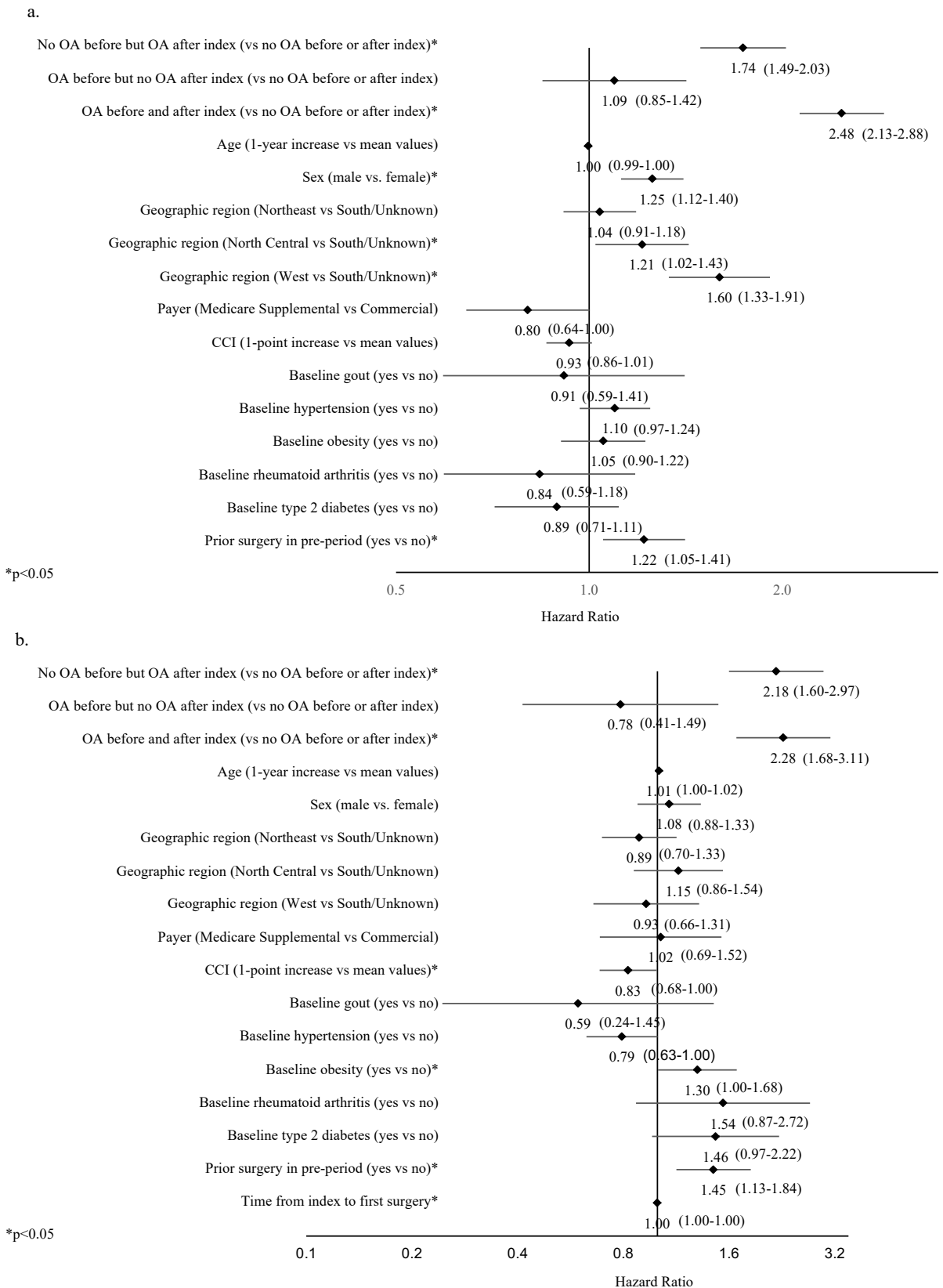
Conclusion: Symptoms of TGCT can resemble the symptoms of osteoarthritis. This study found a small group of TGCT patients with medical claims of OA before but not after TGCT diagnosis whose TGCT condition might have been misdiagnosed as OA. A third of patients maintained OA diagnosis even after confirmation of TGCT diagnosis, suggesting these patients were not initially misdiagnosed as OA. Post-index OA claims were associated with an increased risk of joint surgery, suggesting this group may be more symptomatic. The high rates of surgery and reoperation on TGCT patients with post-index OA reinforces the need for effective treatment options to reduce joint damage, and the difficulty of controlling the disease with surgery alone, particularly in patients with comorbid OA.

Table 1. Surgical patterns of patients with TGCT assessed by presence of OA pre- or post-index

	All Patients N=2,856	Without OA post-index		With OA post-index	
		No OA before or after N=1,153	OA before but no OA after N=207	No OA before N=644	OA before N=852
Patients with pre-index surgery (N, %)	419 (14.7)	69 (6.0)	50 (24.2)	57 (8.9)	57 (8.9)
Patients undergoing surgery post-index (N, %)	1,285 (45.0)	380 (33.0)	71 (34.3)	318 (49.4)	516 (60.6)
Type of all surgeries post-index					
Arthroscopic excision	594 (20.8)	130 (11.3)	27 (13.0)	188 (29.2)	249 (29.2)
Open excision	506 (17.7)	253 (21.9)	40 (19.3)	104 (16.1)	109 (12.8)
Arthrodesis	81 (2.8)	5 (0.4)	5 (2.4)	23 (3.6)	48 (5.6)
Arthroplasty	283 (9.9)	2 (0.2)	1 (0.5)	52 (8.1)	228 (26.8)
Amputation	4 (0.1)	1 (0.1)	0 (0.0)	1 (0.2)	2 (0.2)
Time from index to first surgery post-index among patients having surgery (days): mean (SD), median	170.6 (274.9) 41.0	126.3 (220.2) 41.0	169.9 (288.2) 40.0	210.7 (305.5) 56.0	178.7 (285.4) 30.0
Type of first surgery post-index					
Arthroscopic excision	564 (43.9)	126 (33.2)	26 (36.6)	177 (55.7)	235 (45.5)
Open excision	472 (36.7)	248 (65.3)	39 (54.9)	96 (30.2)	89 (17.2)
Arthrodesis	50 (3.9)	4 (1.1)	5 (7.0)	14 (4.4)	27 (5.2)
Arthroplasty	197 (15.3)	2 (0.5)	1 (1.4)	30 (9.4)	164 (31.8)
Amputation	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.2)
Patients receiving at least 2 surgeries post-index among patients undergoing surgery (N, %)	378 (29.4)	70 (18.4)	11 (15.5)	104 (32.7)	193 (37.4)
Time from first surgery to second surgery post index (days) among patients having ≥ 2 surgeries: mean (SD), median	414.2 (277.6) 363.0	437.2 (298.2) 385.0	485.5 (338.2) 394.0	445.9 (283.1) 360.5	384.6 (261.7) 331.0
Type of second surgery post-index					
Arthroscopic excision	160 (12.5)	32 (8.4)	4 (5.6)	53 (16.7)	71 (13.8)
Open excision	98 (7.6)	37 (9.7)	7 (9.9)	25 (7.9)	29 (5.6)
Arthrodesis	26 (2.0)	1 (0.3)	0 (0.0)	8 (2.5)	17 (3.3)
Arthroplasty	94 (7.3)	0 (0.0)	0 (0.0)	18 (5.7)	76 (14.7)
Amputation	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

OA = osteoarthritis; SD = standard deviation.

Figure 1. Adjusted risk ratio (95% confidence interval) of first surgery and reoperation post index TGCT diagnosis. a. Risk of first surgery post-index. b. Risk of reoperation among patients who had at least one surgery post-index



CCI = Charlson comorbidity index; OA = osteoarthritis.



Poster #041 #1818894

THE EPIDEMIOLOGY OF DESMOID TUMORS IN DENMARK

Naushin Hooda, PharmD¹; Marie Anneberg Brahe, MD²; Helene M.L. Svane, PhD, MS³; Jon Fryzek, MPH, PhD⁴; Gina Nicholson, MPH⁴; Jessica White, MS⁵; Badreddin Edris, MS, PhD⁵; Mary Smith, PhD⁵; Michael M. Petersen, MD, PhD⁶; Thomas Baad-Hansen, MD, PhD⁷; Johnny Ø Keller, MD, PhD⁷; Peter H. Jørgensen, MD, PhD⁷; Alma B. Pedersen, DMsc, PhD³

¹EpidStrategies, Vancouver, British Columbia, CANADA, ²Department of Clinical Epidemiology, Aarhus University, Aarhus, Hovedstaden, DENMARK, ³Department of Clinical Epidemiology, Department of Clinical Medicine, Aarhus University and Aarhus University Hospital, Aarhus, Midtjylland, DENMARK, ⁴EpidStrategies, Rockville, Maryland, UNITED STATES, ⁵SpringWorks Therapeutics, Inc., Stamford, Connecticut, UNITED STATES, ⁶Musculoskeletal Tumor Section, Department of Orthopedic Surgery, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Hovedstaden, Denmark, ⁷Department of Orthopedic Surgery, Aarhus University Hospital, Aarhus, Midtjylland, DENMARK

Objective: Due to the rarity and complex clinical heterogeneity of desmoid tumors (DTs), high-quality evidence regarding their etiology, treatment, and prognosis is limited. Herein, we described the epidemiology, demographic, clinical, and treatment characteristics of DT patients treated at two sarcoma centers in Denmark.

Methods: Using Danish medical databases, we identified DT patients treated between 2009 and 2018. Data on patients, tumors, treatments, inpatient and outpatient hospital visits, and pharmacy dispensing activities were obtained. For each patient, ten persons from the general population were randomly matched on birth year, sex, and region of residence.

Results: A total of 179 DT patients, with a mean age of 38 and 76% of whom were female, were identified. Incidence of DTs ranged from 2.2 (2011) to 4.1 (2015) per 1,000,000 individuals and exhibited no notable time trend. Anatomical DT sites included extra-abdominal (49%), abdominal wall (40%), and intra-abdominal or retroperitoneal areas (8%). The percent of patients treated with an initial surgical intervention fell from 73% in 2009-2014 to 34% in 2015-2018. A total of 56% of patients utilized chemotherapeutic agents, tyrosine kinase inhibitors, NSAIDs, opioids, antidepressants, or steroids at some point during the three years before their DT diagnoses, and 70% of surgically treated and 63% of non-surgically treated patients utilized at least one of the same drugs in the subsequent three years. The average number of inpatient and outpatient visits, days of hospitalization, and additional surgical procedures were higher among DT patients than the comparison cohort.

Conclusion: DTs are rare, but have a significant impact on patients' health and healthcare resource utilization for at least three years after diagnosis. Insight into current epidemiologic and treatment-related trends continues to remain imperative to optimize diagnosis and treatment for this rare but debilitating disease.



Poster #042 #1818877

A SEER-BASED ANALYSIS OF ALVEOLAR SOFT PART SARCOMA FROM 1975-2018: INCIDENCE, PATTERNS OF PRESENTATION, AND TRENDS IN SURVIVAL

Hari Sankaran, MD MSc¹; Geraldine O'Sullivan Coyne, MD²; Alice P. Chen, MD³; Ana Best, PhD⁴

¹National Institute of Health - NCI, Bethesda, Maryland, UNITED STATES, ²NCI, Bethesda, Maryland, UNITED STATES,

³NCI/NIH, Bethesda, Maryland, UNITED STATES, ⁴NCI, Bethesda, Maryland, UNITED STATES

Objective: Alveolar soft part sarcoma (ASPS) is a rare, histologically distinct, aggressive soft tissue sarcoma that consists of 0.5% to 1% of all soft tissue sarcomas and is characterized by expression of an ASPL-TFE3 chimeric fusion protein postulated to act as an aberrant transcription factor. The median age of presentation is 25 years of age. Patients usually present with an asymptomatic, slow-growing mass, but metastatic disease is associated with a poor prognosis. As conventional chemotherapy and radiation treatment has resulted in limited clinical activity, novel therapies such as targeted agents have been piloted in clinical trials since the early 2000s. However the impact of these newer therapies on the overall survival of patients with ASPS in the targeted therapy era has not been well documented from a global perspective.

The objective of this study was to examine the incidence of ASPS, compare the demographic and treatment modalities of ASPS, and evaluate the difference in outcomes after the introduction of targeted therapies using 2 SEER databases (SEER9 and SEER18,).

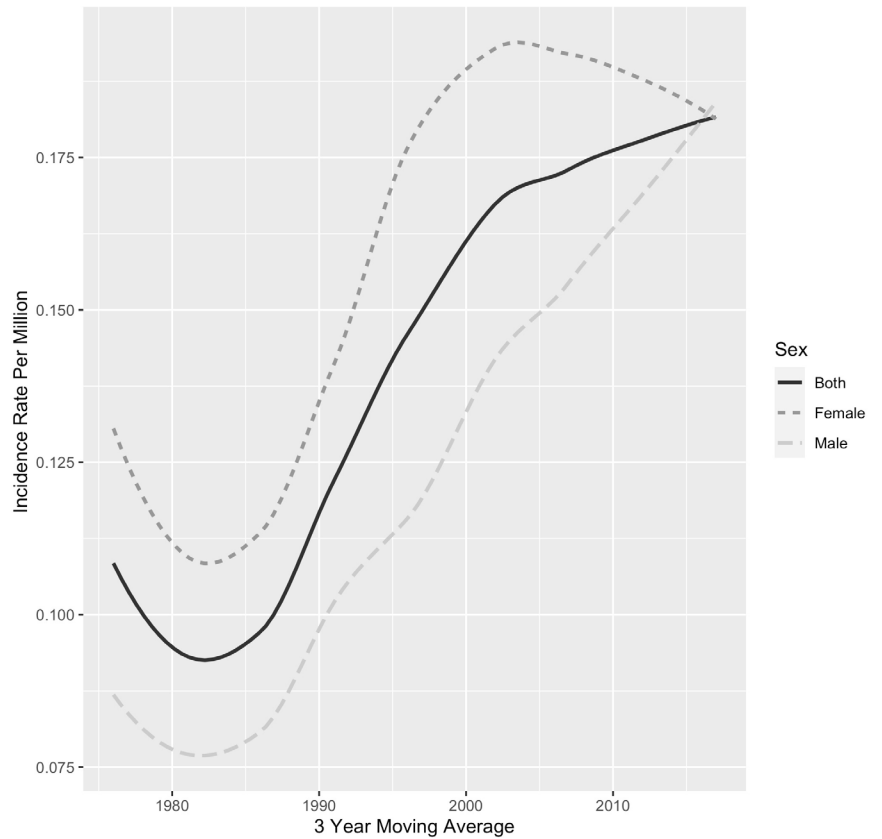
Methods: ASPS cases were identified using the International Classification of Diseases for Oncology, 3rd edition (ICD-O-3) histology code 9581, behavior 3 from the SEER9 (1975-2018) and SEER18 (2000-2018) databases (n=413). Duplicate patients were filtered (n=93) using the patient ID variable leaving a total of 320 analyzable patients. The variables extracted for this analysis included year of diagnosis, sex, age at diagnosis, race, age recoded into 10-year groupings, vital status, stage, location, and treatment information (surgery, radiation, and chemotherapy). All variables are stratified by decade groupings using the year of diagnosis and are displayed as numbers and percentages (Table 1). Incidence rate data were extracted from the SEER9 registry (1975-2018) using incidence rate session in SEER*Stat version 8.3.8. Incidence rates adjusted per million population were calculated by year and as a 3-year moving average for all patients, and by sex separately. Using overall survival data, Kaplan-Meier curves were generated for metastatic and non-metastatic (regional and localized) disease using the SEER historic staging variable and if unavailable, using the Summary stage variable. Kaplan-Meier curves were also generated for overall survival before and after 2010. Cox regression was used to evaluate the association of selected variables of interest.

Results: The incidence of ASPS in female patients is higher than in male patients based on SEER9 (0.17 cases per million population vs. 0.12 cases per million population, respectively) for the overall time period (Figure 1). Of the 320 evaluable patients, the female:male ratio was 1.16, with a median age of diagnosis of 25 years (range: 1- 78 years). The most common locations (in order) included extremities (n=190, 59.4%), abdomen and pelvis (n=45, 14.1%), chest (n=33, 10.3%), head and neck (n=29, 9.1%), and the female reproductive tract (n=16, 5.0%) as well as other patient characteristics are provided in Table 1. A higher proportion of head and neck tumors were seen in the pediatric age group (n=19, 65.5%) compared to the adolescent and young adult population (n=9, 31.0%) and adult (n=1, 3.4%). Examining stage by race, a significantly higher (p=0.02) proportion of black patients (n=77) presented with metastatic disease versus non-metastatic (58.9% vs 41.1%) compared to all other races (44.1% vs. 55.9%). For patients with recorded sites of metastases (n=58), the most common sites included lung (n=55, 94.8%), bone (n=12, 20.7%), brain (n=7, 12.0%), and liver (n=4, 6.9%). All patients with brain metastatic lesions occurred with concurrent lung metastases. When examining staged patients (n= 295) by location, non-metastatic compared to metastatic presentation at diagnosis was seen more commonly in head and neck (n=24, 88.9% vs. n=3, 11.1%) and female reproductive tract tumors (n= 12, 92.3% vs. n=1, 7.7%). There were no significant differences in upfront treatment modalities before and after 2010 (Table 2). The average follow-up for the whole group was 7.2 years. All univariate results are presented in Table 3 of which stage, surgery, and age at diagnosis were significant (p < 0.001). Though not statistically significant (p=0.14), there was a trend towards improved overall survival after 2010 (HR: 0.72, 95%CI: 0.47-1.11) seen in Figure 2.

Conclusion: Though no agent has been approved for the treatment of ASPS in the decade after 2010, our findings during this period were consistent with known literature and included head and neck location tumors occurring in younger age groups, lung metastases being the most common site of distant spread, and brain metastases occurring in the presence of

other metastatic sites. Our analysis also found previously not reported findings including a higher metastatic presentation at diagnosis in the black population and localized disease at presentation in head and neck and female reproductive tract tumors. There is a non-statistically significant trend for improved overall survival though this is limited by follow-up. Our findings highlight the need for more analyses to explore the advanced presentation of disease in black patients, and need for more mature follow-up to see the impact of newer therapies on overall survival in this rare disease.

SEER9 incidence of ASPS overall and by Sex: 1975-2018



ASPS Overall Survival Before and After 2010

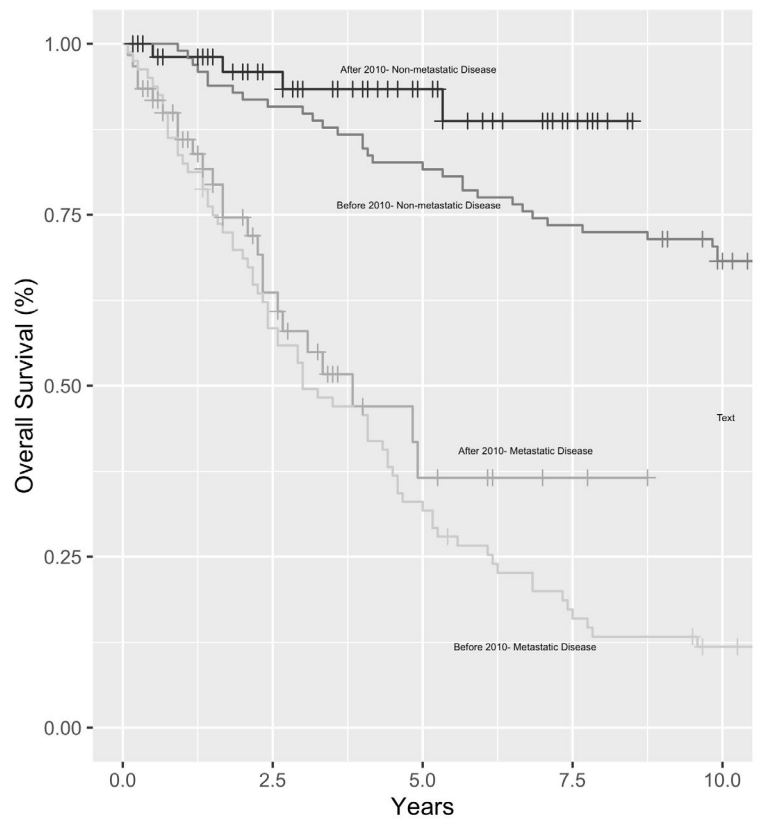


Table: All ASPS patients in all SEER databases from 1975-2018

Sex	1970s	1980s	1990s	2000s	2010s	Total
Male	8 (53.3%)	9 (39.1%)	11 (32.4%)	57 (46.3%)	63 (50.4%)	148 (46.2%)
Female	7 (46.7%)	14 (60.9%)	23 (67.6%)	66 (53.7%)	62 (49.6%)	172 (53.8%)
Race						
Black	3 (20.0%)	5 (21.7%)	5 (14.7%)	32 (26.0%)	31 (24.8%)	76 (23.8%)
Other (American Indian/AK Native, Asian/Pacific Islander)	2 (13.3%)	3 (13.0%)	5 (14.7%)	21 (17.1%)	23 (18.4%)	54 (16.9%)
White	10 (66.7%)	15 (65.2%)	24 (70.6%)	68 (55.3%)	68 (54.4%)	185 (57.8%)
Unknown	NA (-)	NA (-)	NA (-)	2 (1.6%)	3 (2.4%)	5 (1.6%)
Vital Status						
Alive	5 (33.3%)	8 (34.8%)	13 (38.2%)	50 (40.7%)	93 (74.4%)	169 (52.8%)
Dead	10 (66.7%)	15 (65.2%)	21 (61.8%)	73 (59.3%)	32 (25.6%)	151 (47.2%)
Stage						
Metastatic	4 (26.7%)	9 (39.1%)	12 (35.3%)	55 (44.7%)	61 (48.8%)	141 (44.1%)

Non-Metastatic	9 (60.0%)	13 (56.5%)	14 (41.2%)	62 (50.4%)	56 (44.8%)	154 (48.1%)
Unstaged	2 (13.3%)	1 (4.3%)	8 (23.5%)	6 (4.9%)	8 (6.4%)	25 (7.8%)
Follow-up years	19.61667	15.63768	11.54657	7.552168	3.213333	37.94975
Age						
0-9 years	1 (6.7%)	4 (17.4%)	2 (5.9%)	3 (2.4%)	7 (5.6%)	17 (5.3%)
10-19 years	4 (26.7%)	6 (26.1%)	5 (14.7%)	33 (26.8%)	34 (27.2%)	82 (25.6%)
20-29 years	7 (46.7%)	6 (26.1%)	17 (50.0%)	44 (35.8%)	39 (31.2%)	113 (35.3%)
30-39 years	NA (-)	6 (26.1%)	6 (17.6%)	20 (16.3%)	22 (17.6%)	54 (16.9%)
40-49 years	NA (-)	1 (4.3%)	1 (2.9%)	15 (12.2%)	13 (10.4%)	30 (9.4%)
50-59 years	1 (6.7%)	NA (-)	2 (5.9%)	6 (4.9%)	7 (5.6%)	16 (5.0%)
60-69 years	1 (6.7%)	NA (-)	1 (2.9%)	NA (-)	NA (-)	2 (0.6%)
70-79 years	1 (6.7%)	NA (-)	NA (-)	2 (1.6%)	3 (2.4%)	6 (1.9%)
Site						

Abdomen and Pelvis	2 (13.3%)	1 (4.3%)	5 (14.7%)	17 (13.8%)	20 (16.0%)	45 (14.1%)
Chest	2 (13.3%)	1 (4.3%)	2 (5.9%)	17 (13.8%)	11 (8.8%)	33 (10.3%)
Extremities	7 (46.7%)	15 (65.2%)	20 (58.8%)	75 (61.0%)	73 (58.4%)	190 (59.4%)
Head and Neck	4 (26.7%)	4 (17.4%)	2 (5.9%)	7 (5.7%)	12 (9.6%)	29 (9.1%)
Female Reproductive Tract	NA (-)	2 (8.7%)	4 (11.8%)	5 (4.1%)	5 (4.0%)	16 (5.0%)
Other	NA (-)	NA (-)	1 (2.9%)	2 (1.6%)	2 (1.6%)	5 (1.6%)
CNS	NA (-)	NA (-)	NA (-)	NA (-)	2 (1.6%)	2 (0.6%)

Table 2: Treatment modality trends before and after 2010

		After 2010	Before 2010	Total
Surgery	No	40 (32.0%)	44 (22.6%)	84 (26.2%)
	Yes	85 (68.0%)	151 (77.4%)	236 (73.8%)
Chemotherapy	No/Unknown	78 (62.4%)	118 (60.5%)	196 (61.3%)
	Yes	47 (37.6%)	77 (39.5%)	124 (38.8%)
Radiation	No	68 (54.4%)	100 (51.3%)	168 (52.5%)
	Yes	57 (45.6%)	95 (48.7%)	152 (47.5%)

Table 3: Univariate Cox regression analysis of selected variables

		Hazard Ratio	95% CI	P value
Stage	Non-Metastatic	Ref		
	Metastatic	6.36	4.34-9.43	<0.001
Before 2010	Before 2010	Ref		
	After 2010	0.72	0.47-1.11	0.14
Surgery	No	Ref		
	Yes	0.19	0.13-0.28	<0.001
Age (yrs)		1.03	1.02-1.04	<0.001



Poster #043 #1819067

NUCLEAR ORGANIZATION OF MYOGENIC TRANSCRIPTION FACTORS IN PEDIATRIC RHABDOMYOSARCOMAKyle L. MacQuarrie, MD/PhD¹; Steven Kosak, PhD²,¹Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, Illinois, UNITED STATES, ²Northwestern University, Chicago, Illinois, UNITED STATES

Objective: Skeletal muscle cells undergo gene expression, genomic organization, and morphologic changes when proceeding from a proliferative myoblast state to that of terminally differentiated myotube. The pediatric tumor of skeletal muscle, rhabdomyosarcoma (RMS), expresses the regulatory factors that should cause terminal differentiation, yet fails to undergo that process. A subset of RMS possess a characteristic gene fusion, while other RMS are fusion-negative. The tumor cells express myogenic factors and can be induced to undergo myogenic differentiation. Despite this, the cells continue to proliferate. Since normal skeletal muscle cells exhibit a relationship between nuclear organization and gene regulation during differentiation, this implies both that RMS cells have some degree of nuclear disorganization, and that there is a mechanistic relationship between nuclear organization and the differentiation defect in these cells. We hypothesize that the nuclear organization of RMS cells possesses similarities to normal myocytes, but with gene fusion-dependent differences in positioning and epigenetic modifications at a subset of gene loci, including those critical to myogenesis.

Methods: 3D-FISH (fluorescent in situ hybridization) was performed to determine the nuclear positioning of the gene loci for the early myogenic transcription factor MyoD, the late myogenic transcription factor myogenin, and the non-myogenic immunoglobulin heavy chain (IgH) gene in the gene fusion-negative RMS tumor RD cell line, the gene fusion-positive RH30 cell line, and commercially available human myocytes. Myocytes were examined at two stages: undifferentiated (myoblasts/MBs) and terminally differentiated (myotubes/MTs). After acquisition, microscope images were analyzed using a custom imaging pipeline to identify cell nuclei and FISH signals in a non-biased fashion, partition nuclei into concentric nuclear rings, and assign FISH signals to the rings.

Results: In both undifferentiated MBs and differentiated MTs, the early myogenic factor MyoD shows a relatively consistent distribution of FISH signal across all nuclear rings (except for the innermost rings where occupancy is low for all tested genes), as well as a similar average of FISH signal at a given distance when comparing inner to outer nuclear rings. The non-myogenic gene IgH shows a similar consistent distribution of signal in the normal skeletal muscle cells. In contrast, the myogenin locus shows markedly increased occupancy and average signal in outer rings in MBs. This difference is then diminished in MTs, concomitant with an increase of occupancy in the inner nuclear rings, suggesting a shift of the myogenin gene locus to a more internal localization with differentiation. As in normal myocytes, RMS cell lines demonstrate relatively consistent FISH occupancy between inner and outer nuclear rings for MyoD in both fusion-negative and fusion-positive tumor cells. Interestingly, myogenin signal occupancy in the tumor cells shows a similar pattern to that of differentiated myotubes, with comparable values for inner and outer nuclear rings. Unexpectedly, IgH signal occupancy exhibits differences between fusion-negative and fusion-positive RMS cells, with differences both when considering inner versus outer rings and when considering occupancy fraction for individual rings.

Conclusion: In contrast to the differentiation-dependent positioning of the late myogenic factor myogenin seen in normal skeletal muscle cells, RMS cells show a more consistent distribution of myogenin positioning between inner and outer nuclear rings, suggesting a disconnect between positioning and gene activity in the tumor cells. RMS cells also demonstrate a gene fusion-related difference in positioning of the non-myogenic IgH gene locus, supporting the hypothesis that the gene fusion broadly impacts the organization of the nucleus, leading to changes in positioning of even non-myogenic genes. These findings support a model in which the organization and physical positioning of genes in the nucleus of pediatric rhabdomyosarcoma cells can differ depending on gene-fusion status and play a role in the continued proliferation of the tumor cells.

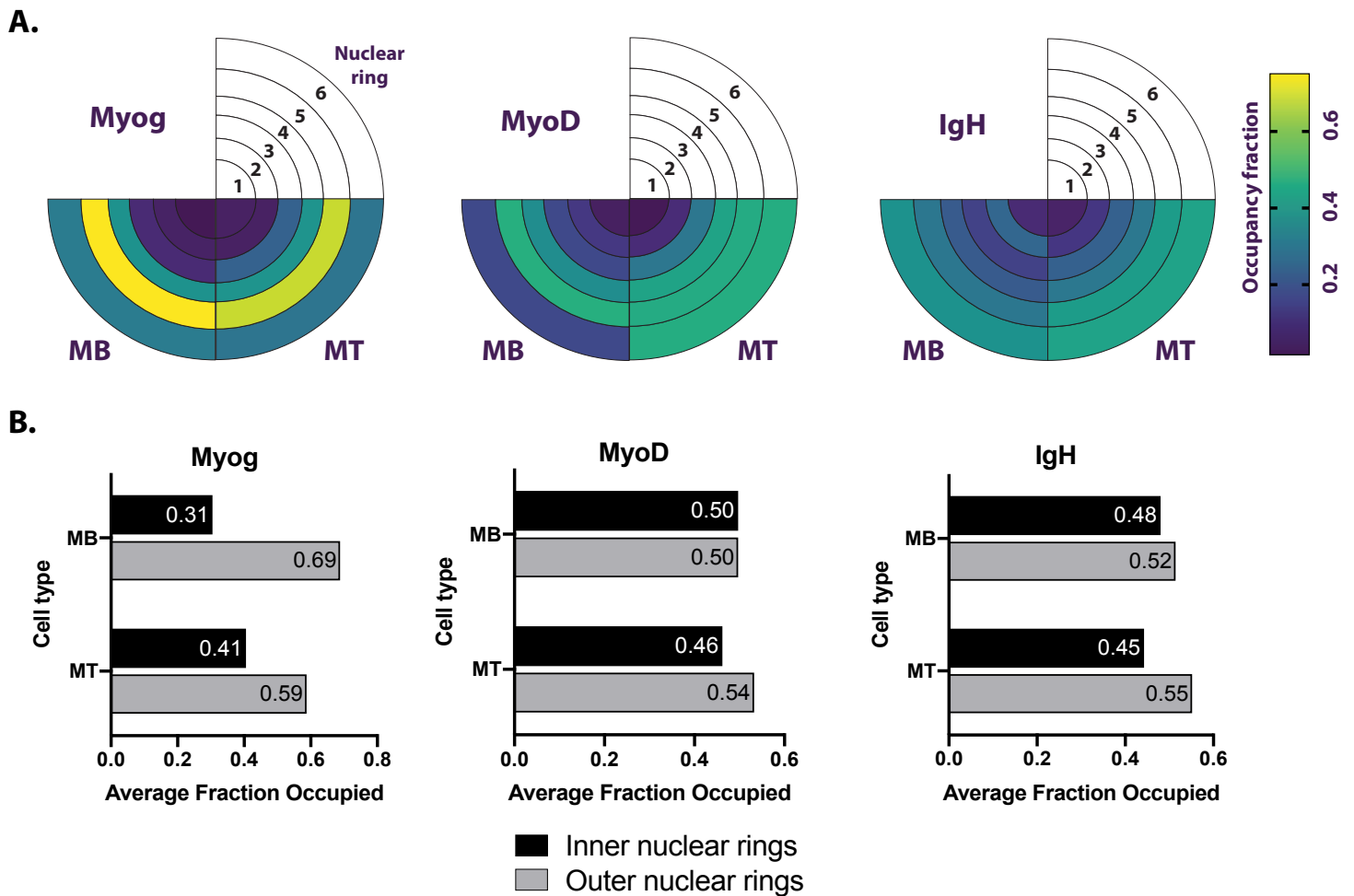


Figure 1. The late myogenic factor myogenin exhibits increased internal localization in differentiated myotubes compared to an early myogenic factor and a control locus. 3D-FISH was performed in myoblasts (MB) and myotubes (MT) using probes containing either the MyoD gene locus (MyoD), the myogenin gene locus (Myog) or the immunoglobulin heavy chain gene locus (IgH). Localization of FISH signal was quantified in all cell types relative to six concentric nuclear rings to account for differences in cell size and shape. A) Heat maps demonstrating the proportion of nuclear rings that demonstrate any FISH signal occupancy by either Myog, MyoD, or IgH (lef, middle, and right as indicated). B) Graphs indicating the average FISH signal occupancy in each cell type and for each FISH probe as indicated, for both inner nuclear rings (black bars, rings 1-4) and outer nuclear rings (light grey bars, rings 5-6). $n > 60$ cells per condition.

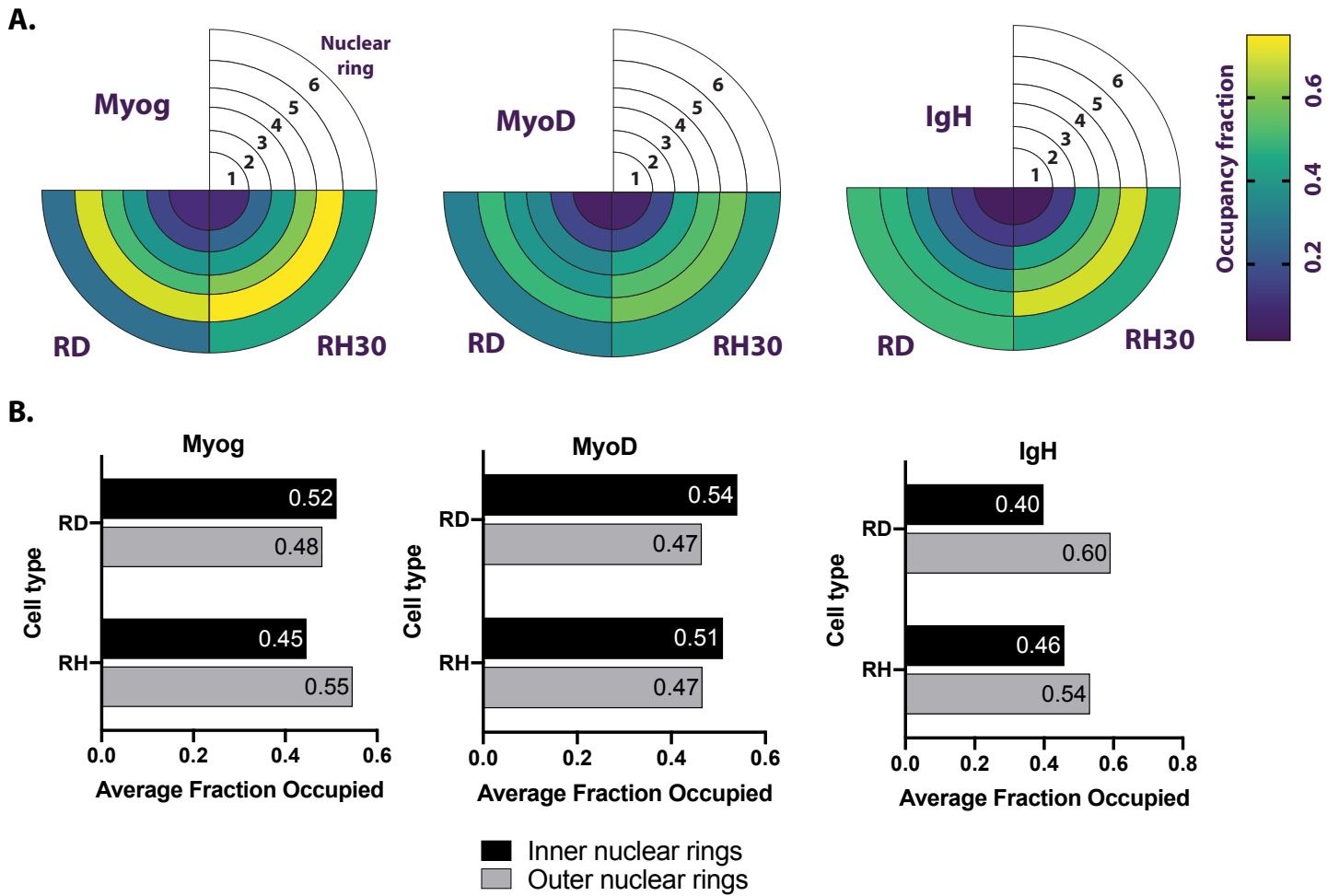


Figure 2. Nuclear positioning in rhabdomyosarcoma tumor cell lines. 3D-FISH was performed in a gene fusion-negative rhabdomyosarcoma (RMS) tumor cell lines (RD) and a gene fusion-positive RMS cell line (RH30) using probes containing the same genes as in Figure 1. As in normal skeletal cells, localization of FISH signal was quantified in all cell types relative to six concentric nuclear rings to account for differences in cell size and shape. A) Heat maps demonstrating the proportion of nuclear rings that demonstrate any FISH signal occupancy by either Myog, MyoD, or IgH (left, middle, and right as indicated). B) Graphs indicating the average FISH signal occupancy in each cell type and for each FISH probe as indicated, for both inner nuclear rings (black bars, rings 1-4) and outer nuclear rings (light grey bars, rings 5-6). $n > 60$ cells per condition.



Poster #044 #11818901

RADIOMICS AND MACHINE LEARNING PREDICT DIAGNOSIS IN MUSCULOSKELETAL MYXOID SOFT TISSUE TUMORS

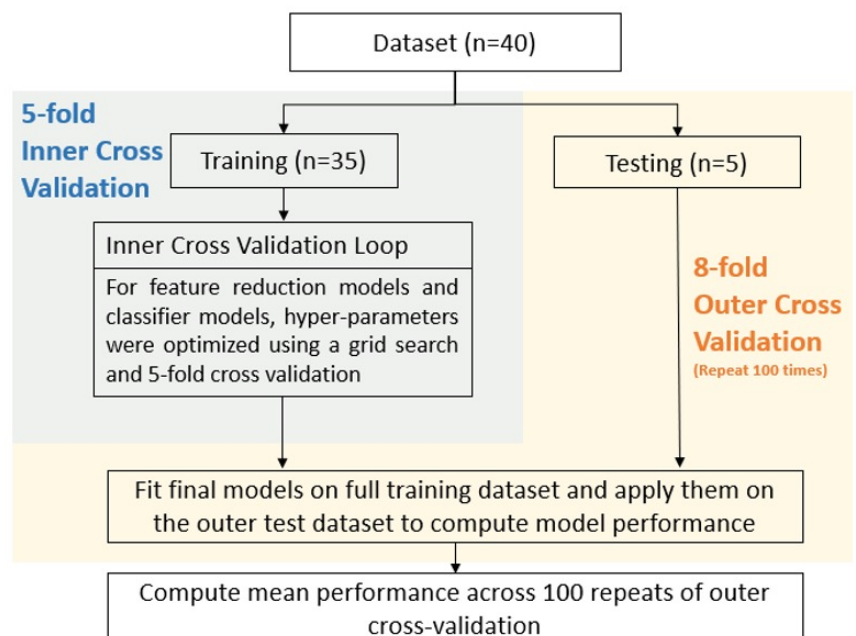
Joshua M. Lawrenz, MD; Can Cui, MS; Samuel R. Johnson, BS; Cullen P. Moran, BS; Katherine S. Hajdu, BS; Andrew B. Rees, MD; Benjamin L. Coiner, BS; Brian Bingham, MD; Joanna L. Shechtel, MD; David S. Smith, PhD; John J. Block, MD; Leo Luo, MD; Hakmook Kang, PhD; Jennifer L. Halpern, MD; Herbert S. Schwartz, MD; Benoit Dawant, PhD; Ginger E. Holt, MD
 Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES

Objective: Differentiating benign and malignant musculoskeletal myxoid soft tissue tumors is challenging due to their shared clinical, imaging, and histologic features. Our recent institutional experience of two hundred patients with myxoid tumors revealed 40% with preoperative needle biopsies were indeterminate in distinguishing a benign or malignant diagnosis, commonly resulting as “low grade myxoid neoplasm not otherwise specified”. As treatment strategy (resection type +/- adjuvant therapy) often differs between myxomas and myxofibrosarcomas, accurate preoperative diagnosis is preferred. Radiomics, a method of machine learning that consists of large data extraction from medical images, has shown early potential in predicting diagnosis and prognosis of musculoskeletal tumors. In this study, we asked: Can a machine learning based predictive model consisting of clinical and radiomics features reliably differentiate benign and malignant musculoskeletal soft tissue myxoid tumors?

Methods: A retrospective review of 40 patients with a pre-treatment MRI and a histologically confirmed myxoid soft tissue tumor (20 myxomas and 20 myxofibrosarcomas) on final resection pathology was performed. Baseline clinical features were determined a priori and consisted of patient age, sex, tumor size, tumor depth, tumor location, pain, and tumor as an incidental finding. Manual image segmentation of the tumor was performed on T1 and T2 images by attending clinicians who were blinded to clinical information and final histologic diagnosis. A LASSO model was used for qualitative and quantitative MRI feature reduction. With the selected features, five machine learning models (random forest, ridge logistic regression, multi-layer perceptron, XGBoost and SVM) were separately implemented to classify benign and malignant myxoid soft tissue tumors using cross validation (Figure 1). Predictive models based on clinical and radiomics features were compared for diagnostic performance based on mean area under the ROC curves (AUC).

Results: The five classification models using T1 and T2 radiomics features + clinical features achieved mean AUC of 0.729 to 0.780 and accuracy of 0.696 to 0.757 (Table 1). The highest AUC achieved was 0.780 using a support vector machine (SVM) model (Figure 2). All combined radiomics + clinical feature models outperformed the classification models using clinical features alone (AUC = 0.359 to 0.627; accuracy = 0.514 to 0.640). The radiomics features ‘Gray Level Variance’ and ‘Gray Level Non-Uniformity Normalized’ extracted from the Gray Level Run Length Matrix on T2 images were the top two features associated with diagnostic discrimination. Malignant tumors on average had greater non-uniformity, suggesting a more heterogeneous intensity pattern on T2 images.

Conclusion: Classification models using T1 and T2 radiomics features + clinical features perform better in differentiating benign and malignant myxoid soft tissue tumors than

Figure 1. Model construction and validation.


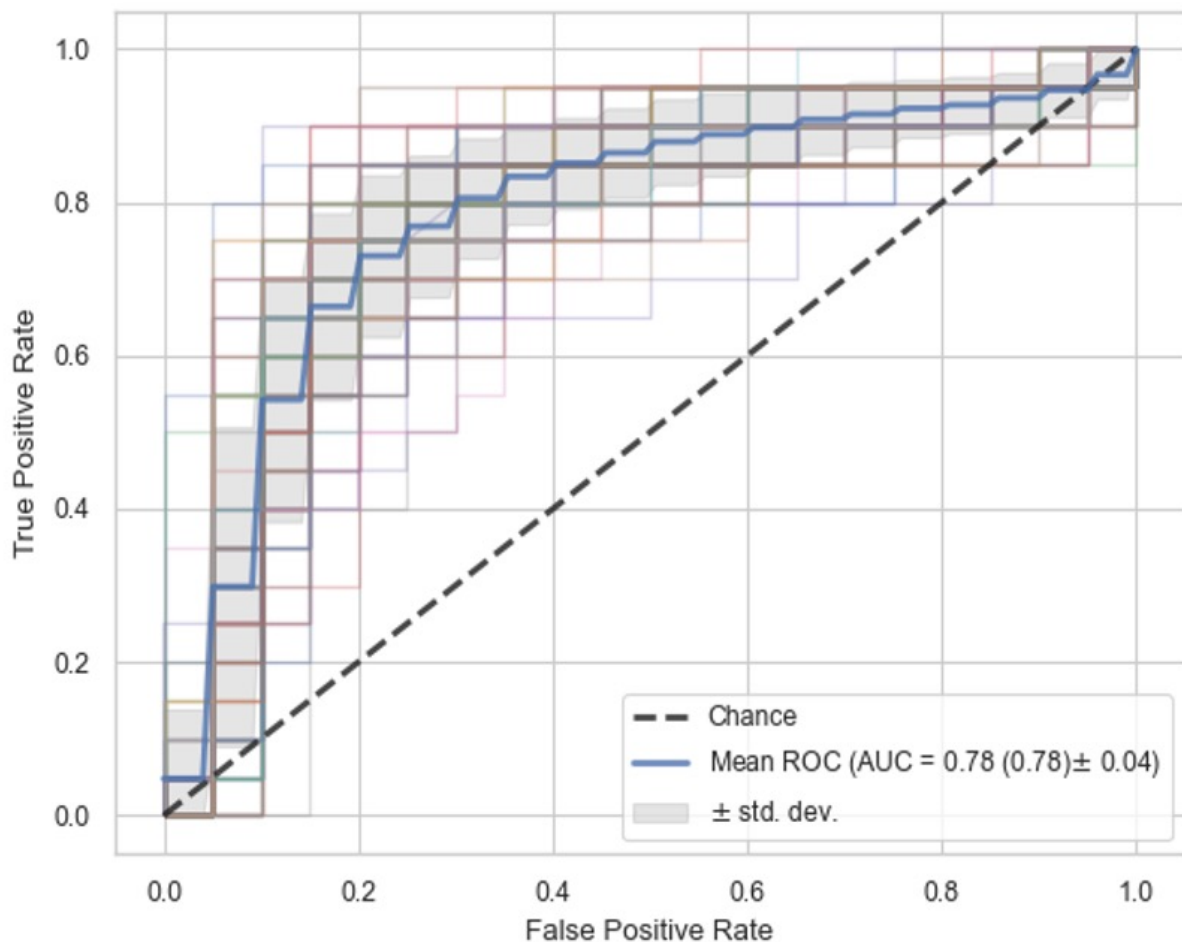
models using clinical features alone. Future studies include validation of these preliminary findings in a larger and separate data set, and comparison of the diagnostic performance of radiomics to manual review of images by clinicians.

Table 1. Classification accuracy and AUC of machine learning models.

Classifier	Radiomics + Clinical Features		Clinical Features Only	
	Accuracy	AUC	Accuracy	AUC
Random Forest	0.716 +/- 0.045	0.765 +/- 0.038	0.599 +/- 0.041	0.589 +/- 0.038
Ridge Logistic Regression	0.751 +/- 0.049	0.772 +/- 0.053	0.640 +/- 0.034	0.627 +/- 0.039
Neural Network	0.718 +/- 0.057	0.729 +/- 0.058	0.514 +/- 0.051	0.540 +/- 0.056
XGBoost	0.696 +/- 0.046	0.738 +/- 0.039	0.597 +/- 0.041	0.569 +/- 0.037
SVM	0.757 +/- 0.052	0.780 +/- 0.042*	0.548 +/- 0.054	0.359 +/- 0.071

*This represents the highest achieved AUC from the data set. All values represent mean value +/- standard deviation computed from 100 times of nested cross-validation.

Figure 2. Receiver Operating Characteristic for Classification Model to Predict Malignancy.



The highest AUC achieved was 0.780 using a support vector machine (SVM) model.



Poster #045 #1818914

GENOMIC LOSS OF HETEROZYGOSITY REVEALS RARE, CLINICALLY MEANINGFUL SUBTYPES OF LEIOMYOSARCOMA

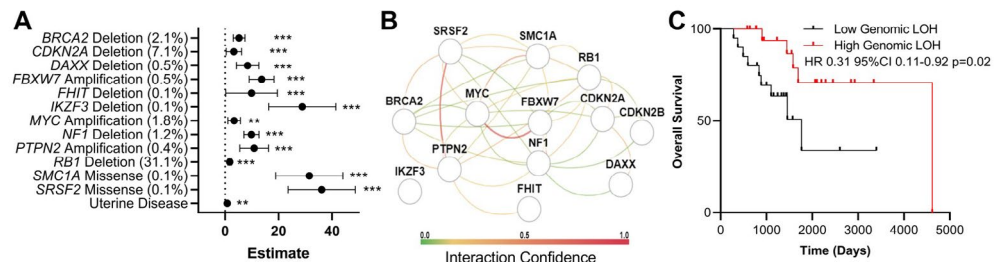
Nathan D. Seligson, PharmD¹; Joy Tang, MD²; Dexter Jin, PhD³; Monica Bennett, BS⁴; Julia Elvin, MD, PhD³; Kiley Graim, PhD⁵; John Hays, MD, PhD²; Sherri Millis, PhD³; Wayne Miles, PhD²; James L. Chen, MD²,
¹University of Florida, Jacksonville, Florida, UNITED STATES, ²Ohio State University, Columbus, Ohio, UNITED STATES, ³Foundation Medicine Inc, Cambridge, Massachusetts, UNITED STATES, ⁴University of Florida, Jacksonville, Florida, UNITED STATES, ⁵University of Florida, Gainesville, Florida, UNITED STATES

Objective: Leiomyosarcoma (LMS) is a rare, aggressive subtype of soft-tissue sarcomas. Previous studies have noted deficiencies in the homologous recombination (HR) pathway (HRD) in LMS and suggested that these deficiencies may be targetable by PARP inhibition. Genomic loss of heterozygosity (LOH) has been used as a surrogate marker of HRD in other solid tumors. Moreover, an extensive list of gene have been associated with elevated genomic LOH in ovarian, breast, and prostate cancers among others. Here, we present the largest assessment of the association of genomic LOH with single genomic alterations and assess whether genomic LOH in LMS is distinct from that of tumors of carcinomatous origin.

Methods: Genomic profiling data from 2,478 unique LMS tumors was collected from the Foundation Medicine Incorporated (FMI). Of these 1,658 met the criteria for calculation of genomic LOH and were included in this study. Only pathogenic genomic alterations were included in the study. Clinical data was available for 40 of the LMS tumors profiled by FMI from The Ohio State (OSU IRB: 2021E0149).

Results: In 1,658 LMS samples, the mean genomic LOH was 12.9% with a SD of 6.9%. Uterine LMS was correlated with an elevated genomic LOH (13.8±7.0% vs 12.4±6.8%, p<0.0001). Genomic alterations in the HR pathway were identified in 12.5% of tumors; however, only homozygous loss of BRCA2 was associated with an elevated genomic LOH. Multivariate analysis identified alterations in cell cycle regulation (RB1, CDKN2A/B, MYC, FBXW7, NF1) and DNA repair (BRCA2) genes correlated with elevated genomic LOH (Figure 1A). Biological process enrichment identified patterns of cell proliferation, DNA replication, and protein phosphorylation regulation as most significantly enriched in this gene set (Figure 1B). Clinical data was available for 40 early stage LMS tumors all treated with curative-intent surgical resection. In this cohort, genomic LOH scores above the group median (9.9%) were associated with an improved prognosis (HR 0.31, 95%CI 0.11-0.94, p=0.02).

Conclusion: LMS demonstrates genomic alterations driving genomic LOH distinct from other cancers. While the data here does not suggest that genomic LOH is a predictive biomarker to any single therapy, it points to specific genomic subtypes of LMS which are clinically meaningful and not yet described. In early stage LMS elevated genomic LOH was associated with improved survival. Further study is necessary to determine the meaning and clinical value of genomic LOH in LMS.



A) Multivariate analysis identified twelve genomic alterations to be associate with increased genomic loss of heterozygosity (LOH) independent of uterine disease status. **B)** Tissue specific network analysis identified common signaling connections between twelve genomic alterations associate with increased genomic LOH. Biological process enrichment identified patterns of cell proliferation, DNA replication, and protein phosphorylation regulation in this gene set. **C)** In 40 T>1 LMS non-metastatic at diagnosis, genomic LOH scores above the group median (9.9%) was associated win an improved prognosis (HR 0.31, 95%CI 0.11-0.94, p=0.02).

College of Pharmacy
Department of Pharmacotherapy and Translational Research

1225 Center Drive
PO Box 100486
Gainesville, FL 32610-0486
352-273-6236
352-273-6270 Fax

June 14, 2021

Board of Directors
Connective Tissue Oncology Society(CTOS)

To Whom It May Concern:

It is my pleasure to provide this letter in support of the application of Dr. Nathan Seligson for the 2021 CTOS Young Investigator Award. We were fortunate to recruit Dr. Seligson to join our faculty in the Department of Pharmacotherapy and Translational Research at the University of Florida; Dr. Seligson began his faculty appointment in July 2019. Dr. Seligson is currently a Clinical Assistant Professor in our department; his responsibilities include teaching, clinical practice, research, and service.

Sincerely,



Reginald Frye
Chair and Professor
Department of Pharmacotherapy and Translational Research
UF College of Pharmacy

The Foundation for The Gator Nation

An Equal Opportunity Institution



Poster #047 #1818853

COMPARISON OF CLINICOPATHOLOGICAL FEATURES AND OUTCOMES IN PATIENTS WITH PRIMARY LEIOMYOSARCOMA OF BONE AND SOFT TISSUE

Charles A. Gusho, BS¹; Linus Lee, BE²; Alan T. Blank, MD, MS²; Steven Gitelis, MD²

¹Rush University Medical Center, Milwaukee, Wisconsin, UNITED STATES, ²Rush University Medical Center, Chicago, Illinois, UNITED STATES

Objective: This investigation sought to describe the outcomes of primary leiomyosarcoma of bone (PLB) compared to soft tissue leiomyosarcoma (SLMS).

Methods: This was a review of the Surveillance, Epidemiology, and End Results database from 1975 to 2016. Kaplan-Meier methods were used to estimate disease-specific survival (DSS), and a Cox regression model was used to identify prognostic factors.

Results: Of the 7502 identifiable cases, 1% (n = 74) were PLB and 99% (n = 7428) were SLMS. Survival was the same between PLB and SLMS (p = .209). On multivariable analysis for high-grade SLMS, radiation (neoadjuvant: hazard ratio [HR], 0.56; 95% confidence interval [CI], 0.4-0.8; p = .003; adjuvant: HR, 0.75; 95% CI, 0.6-0.9; p = .008) and surgery (procedure specific) improved DSS. For PLB, wide resection/limb salvage (HR, 0.40; 95% CI, 0.3-0.5; p = .018) and amputation (HR, 0.69; 95% CI, 0.5-0.9; p < .001) were positive prognostic factors. Neither radiation nor chemotherapy were prognostic factors for survival in PLB.

Conclusion: For SLMS, radiation portends a survival advantage. For PLB, however, neither chemotherapy nor radiation were significant prognostic factors, which suggests the optimal treatment for PLB, similar to other primary soft tissue sarcomas originating in bone, remains an unmet medical need.



Poster #048 #1819004

COMPLICATIONS AND POSTOPERATIVE MORTALITY RATE AFTER SURGERY FOR METASTASIS TO FEMUR: ANALYSIS OF A NATIONWIDE DATABASE

Yusuke Tsuda, MD, PhD¹; Liuzhe Zhang, MD²; Sakae Tanaka, MD, PhD²; Hiroshi Kobayashi, MD, PhD²

¹The University of Tokyo Hospital, Tokyo, Tokyo, JAPAN, ²The University of Tokyo Hospital, Bunkyo-ku, Tokyo, JAPAN

Objective: Currently, there are few reports regarding predictors of postoperative complications and short-term mortality after surgery for pathological femur fracture related to bone metastasis.

Methods: Using data from the Japanese Diagnosis Procedure Combination Database from 2007 to 2012, we retrospectively identified 1497 patients who underwent internal fixation (n = 1073) or proximal femur resection and endoprosthetic reconstruction of the proximal femur (n = 424) for pathological femur fracture related to bone metastasis. Multivariable logistic regression analysis was performed to examine the relationship of various factors with postoperative complications and 30-day mortality.

Results: The overall 30-day mortality after surgery was 2.6%, and the proportion of postoperative complications was 12.1%. Multivariable logistic regression analysis showed that postoperative complications overall were significantly associated with older age [odds ratio (OR), 2.15; 95% confidence interval (CI) 1.23-3.74 for age ≥ 80 vs. ≤ 59 years]; lung carcinoma (OR 2.05; 95% CI 1.47-2.86); esophageal carcinoma (OR 4.41; 95% CI 1.57-12.43); higher Charlson Comorbidity Index (OR 1.50; 95% CI 1.03-2.18 for ≥ 9 vs. 8); and blood transfusion (OR 1.57; 95% CI 1.14-2.15). Thirty-day mortality also was significantly higher in patients with rapid-growth tumors, visceral metastasis, internal fixation, and no postoperative chemotherapy in the univariate analysis.

Conclusion: Older age, type of primary tumor, higher Charlson Comorbidity Index, and blood transfusion were associated with higher morbidity. These findings can provide important information to assess perioperative risk in patients with pathological femur fracture related to bone metastasis.



Poster #049 #1818844

PULMONARY METASTASECTOMY IN BONE AND SOFT TISSUE SARCOMA WITH METASTASIS TO THE LUNGS

Charles A. Gusho, BS¹; Christopher W. Seder, MD²; Nicolas Lopez-Hisijos, DO²; Linus Lee, BE²; Alan T. Blank, MD, MS²; Marta Batus, MD²

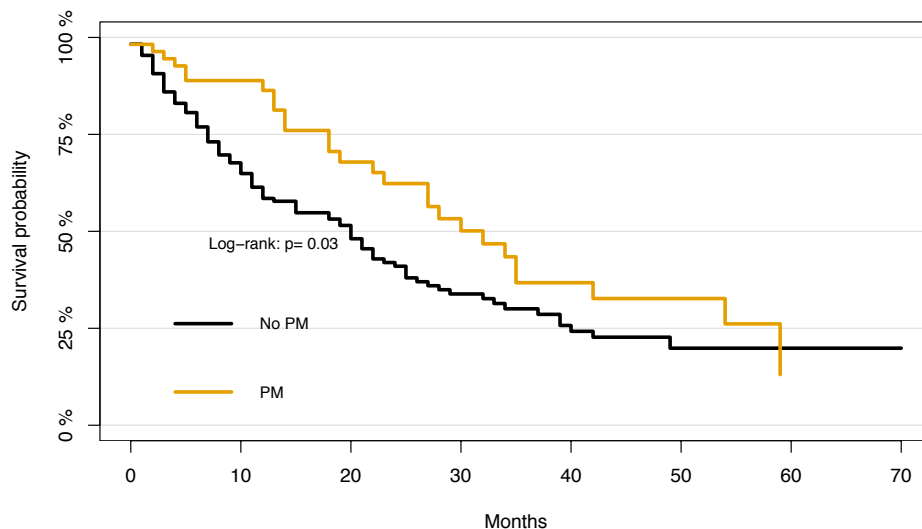
¹Rush University Medical Center, Milwaukee, Wisconsin, UNITED STATES, ²Rush University Medical Center, Chicago, Illinois, UNITED STATES

Objective: This study investigated the outcomes of sarcoma patients with lung metastases who underwent pulmonary metastasectomy (PM), compared to patients who underwent medical management alone. The secondary objective was to compare survival after PM between variables of interest.

Methods: This was a retrospective review of 565 sarcoma patients with confirmed, isolated pulmonary metastasis identified from the Surveillance, Epidemiology, and End Results database between 2010 to 2015. 1:4 propensity score matching was used to select PM and non-PM groups. Multivariable Cox proportional hazards model was used to analyze prognostic factors of disease-free survival (DFS).

Results: Of the eligible 565 patients, 59 PM patients were matched to 202 non-PM patients in a final ratio of 3.4. After propensity-matching, there were no significant differences in baseline characteristics between PM and non-PM patients. The median DFS after PM was 32 months (IQR, 18;59), compared to 20 months (IQR, 7;40) in patients without PM (p=0.032). Using a multivariable Cox proportional hazards model, metastasectomy (HR, 0.536; 95% CI, 0.33 to 0.85; p=0.008) was associated with improved DFS. In a subset analysis of patients who underwent PM only, the median DFS was longer in males compared to females (p=0.021), as well as in bone sarcoma compared to soft tissue sarcoma (p=0.014).

Conclusion: For sarcoma patients with metastatic lung disease, PM appears to improve the prognosis compared to medical management. Furthermore, there may be a survival association with gender and tumor origin in patients who underwent PM. These data may be used to inform the surgical indications and eligibility criteria for metastasectomy in this setting.



Intervention: No PM :	174	120	79	56	35	21	16	8	5	4	2
Intervention: PM :	56	45	31	25	18	13	9	5	3	0	0



Poster #051 #1819057

CHARACTERIZATION OF TWO NOVEL PATIENT-DERIVED SPONTANEOUSLY IMMORTALIZED MYXOFIBROSARCOMA CELL LINES FOR DRUGS AND INNOVATIVE TREATMENTS SCREENING

Ania Naila Guerrieri, MSc, PhD¹; Chiara Bellotti, MSc¹; Roberta Laranga, MSc, PhD¹; Barbara Dozza, MSc, PhD¹; Enrico Lucarelli, MSc, PhD¹; Claudia Cocchi, MSc²; Alessandro De Vita, PhD, Pharm D²; Laura Mercatali, MSc, PhD²; Marco Gambarotti, MD³; Tommaso Frisoni, MD, PhD¹; Davide M. Donati, MD, PhD¹; Toni Ibrahim, MSc, MD, PhD¹, ¹IRCCS Istituto Ortopedico Rizzoli, Bologna, Emilia-Romagna, ITALY, ²IRCCS Istituto Romagnolo Per Lo Studio Dei Tumori (IRST) "Dino Amadori", Meldola, Emilia-Romagna, ITALY, ³Istituto Ortopedico Rizzoli, Bologna, Emilia-Romagna, ITALY

Objective: Myxofibrosarcoma (MFS) is a malignant soft tissue sarcoma (STS) that affects patients after the 5th decade of age. Though MFS patients have a lower risk to develop distant metastasis respect to other STS, they can be subjected to several surgeries and frequently to amputation, due to multiple recurrence. When tumor recurs generally has a higher grade, decreased response to radio- and chemotherapy and increased metastatic potential. Considering that the age of global population is rising, the incidence of MFS is likely to increase in the future. Primary cell cultures have been a basic tool to investigate molecular pathogenesis, to identify specific markers and to study the effect of anticancer drugs at cellular and subcellular level. However, few MFS models are currently available. Considering the extreme heterogeneity, both at cellular and molecular levels, there is a need to find new tools to deepen the knowledge on MFS.

Methods: MFS samples were obtained from a 79 male and a 41-year-old female patients that underwent surgery at the Rizzoli Orthopedic Institute. The first patient was diagnosed with local recurrence and metastasis, while the second presented a primary lesion. Tumor specimens were mechanically and enzymatically digested; derived cell lines named MF-R 3C and MF-R 7C respectively, were cultured in DMEM-HG+10% FBS. When the number of cumulative population doublings (CPD) surpassed the Hayflick limit (around 50 CPD) we hypothesized that spontaneous immortalization had occurred. We performed phenotypical characterization of both cell lines through multiple assays (proliferation, clonogenic potential, anchorage-independent growth and colony formation, migration, cytoskeletal organization) to analyze cells' morphology and behavior. 143B cells were used as reference of aggressive sarcoma cell line.

Results: MF-R 3C and MF-R 7C were grown for more than 200 days in culture (> 150 PD) (Fig.1A). Both lines mostly consist of small spindle-shaped cells; in early passages, some giant cells were detectable but slowly lost during days; some multinucleated cells are still present at late passages probably due to atypical cellular division. MFS cells have multiple nucleoli, indicating a surge in protein synthesis to sustain the major protein demand typical of aggressive tumors. MF-R 3C cells show weak adherence, with several semi-floating cells that are also detectable in MF-R 7C, although to a smaller extent (Fig.1D). We evaluated cells proliferation, finding a similar doubling time (DT) in MFS cells that is slightly lower than 143B cells' DT (Fig.1E). Both MFS cell lines are able to grow in colonies when seeded at very low density, similarly to 143B cells (Fig.1F). When challenged to grow in ultra-low attachment conditions both MF-R 3C and MF-R 7C show sustained growth in 3D aggregates that can be propagated in culture, indicating a similar stemness potential to 143B (Fig.2A). Moreover, we studied the anchorage-independent colony formation ability, index of aggressiveness, by the soft agar colony formation (SACF) assay. MF-R 3C has higher SACF efficiency than MF-R 7C even if inferior to that of 143B cells (Fig.2B). In addition, given MFS ability to infiltrate adjacent tissues, we demonstrated through a wound healing assay that these cells are able to close the gap in 48 hours, with an inferior wound closure rate compared to 143B cells (Fig.3). Finally, we analyzed vinculin and F-actin expression through IF as markers of cytoskeletal organization and adhesion plaques formation. Preliminary results show a less intense vinculin signal in MF-R 3C respect to MF-R 7C cells, supporting the hypothesis of a less adhesive phenotype in line with clinical tumors' diagnoses (Fig.4).

Conclusion: In conclusion, we established two novel patients-derived MFS cell lines showing phenotypical characteristic resembling the original tumor. Therefore, both cell lines could serve as models for studying molecular pathogenesis of MFS and potentially test drugs and innovative treatments.

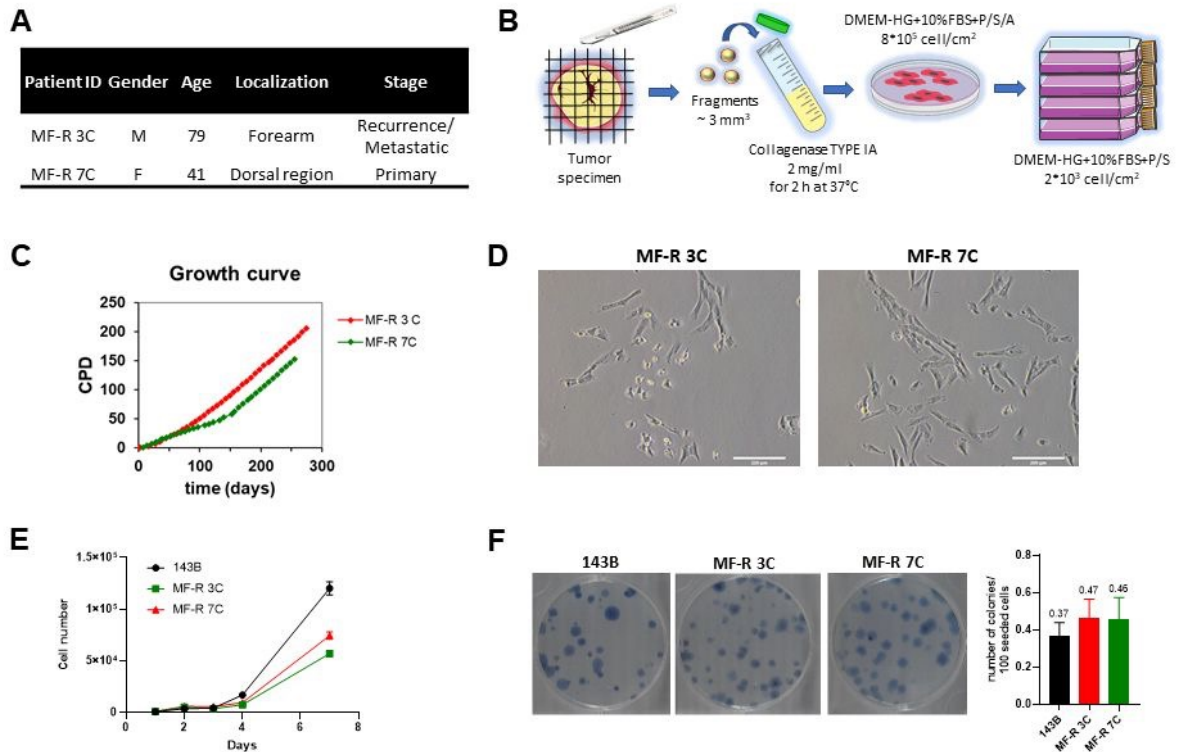


Figure 1.

A) Clinical data of patients. B) Schematic representation of isolation and in-vitro culture protocols. C) Growth curve of MF-R 3C and MF-R 7C, population doublings were calculated at each passage as $\log_2(N_1/N_0)$, where N_0 is the number of cells seeded and N_1 is the number of cells harvested at the end of the passage. D) Representative images of morphological aspect of the cells after spontaneous immortalization. E) Proliferation assay: 2×10^3 cell/well were seeded and Methylene blue staining was used to calculate cell number at indicated time point. F) Colony forming potential in 2D: 100 cells/well were seeded in a 6-well plate and Methylene blue stained colonies were counted after 7 (143B) or 14 days (MF-R 3C and MF-R 7C). Mean and SD of three independent experiment.

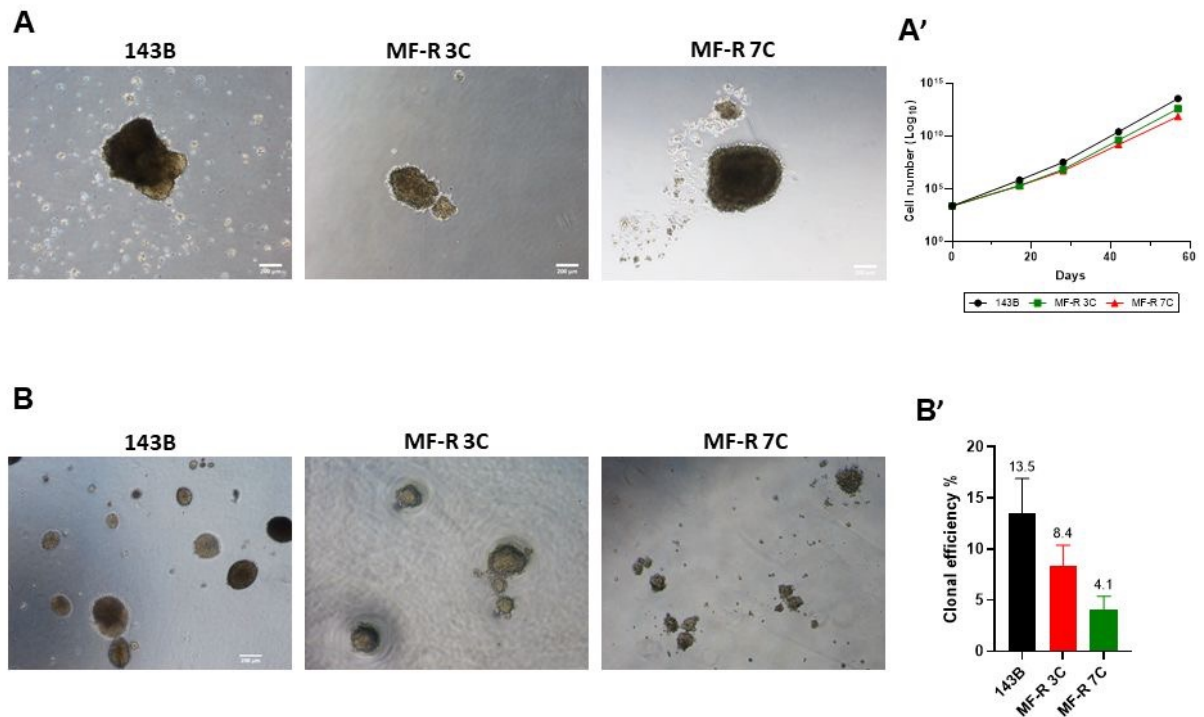


Figure 2

A) Anchorage-independent propagation of MF-R 3C, MF-R 7C and 143B: representative images of cell aggregates formed in ultra-low attachment plates. A') Cell proliferation of cells maintained in non-adherent culture with initial seeding of 1200 cell in 2ml of culture medium. B) Soft agar colony formation assay: representative images of colonies formed by single cells embedded in 0,33% low-melting agar after 2 weeks of culture. B') Clonal efficiency measured as the percentage of the colony counted at the end over the number of cell seeded in each well. Mean and SD of three independent experiment.

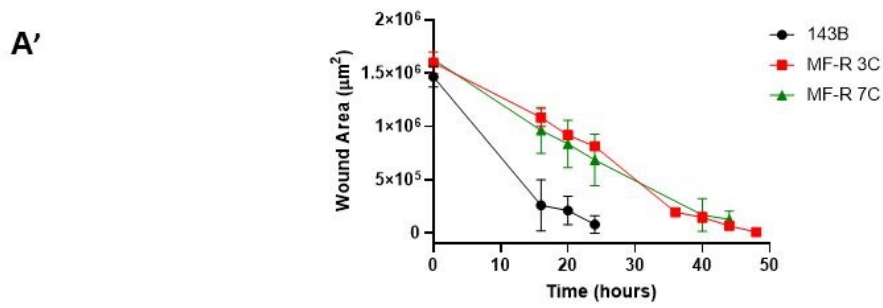
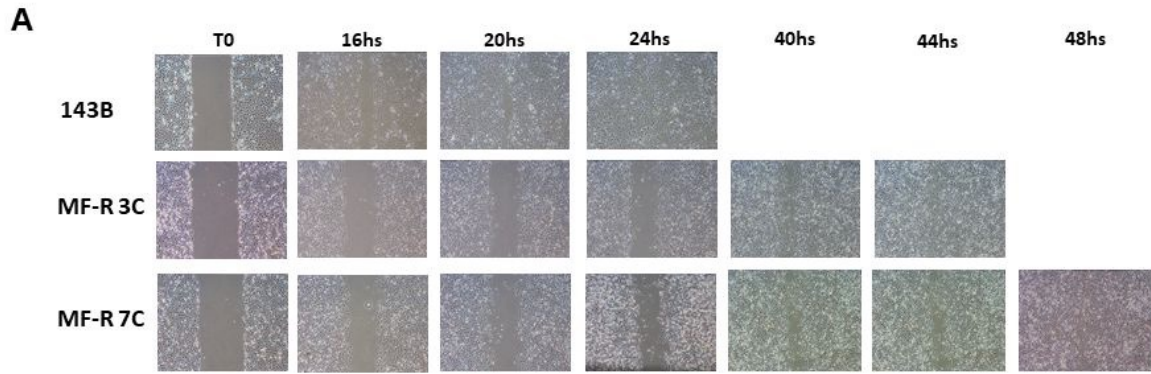


Figure 3.

A) Wound healing assay: representative images of cells closing the scratch produced mechanically with a pipette tip on a confluent monolayer. A') Graph reporting the area of the plate not covered by cells (wound area) at the different timepoints. Area measures were calculated with Area auto-detection tool of NIS Elements D software on microscopic images captured with a calibrated camera. Mean and SD of three independent experiment.

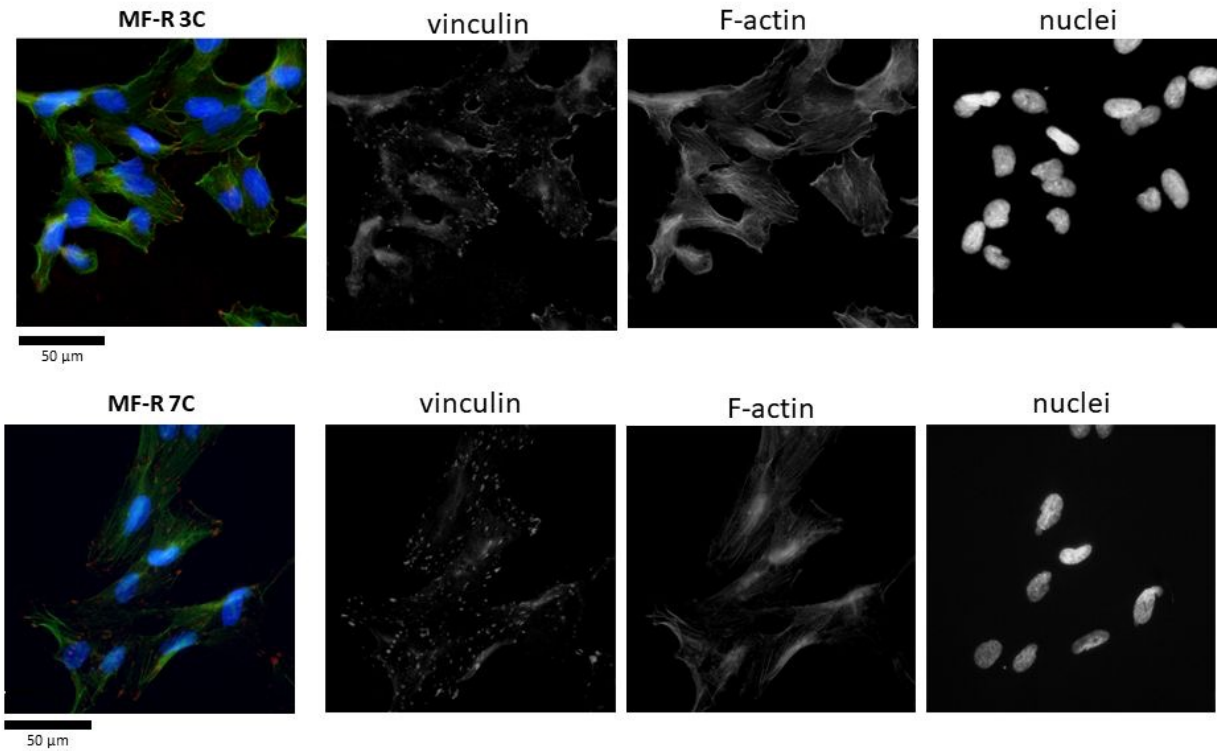


Figure 4

Cytoskeletal organization of MFS cell lines: vinculin staining show the contact point between Actin filament and cell membrane.



Poster #052 #1819045

THERAPEUTIC IMPLICATIONS OF PROSPECTIVE WHOLE GENOME SEQUENCING IN SARCOMA PATIENTS

Luuk J. Schipper, MD¹; Kim Monkhorst, MD, PhD¹; Pia van der Laan, MD¹; Kris G. Samsom, MD¹; Linda J. W. Bosch, PhD¹; Petur Snaebjornsson, MD PhD¹; Hester van Boven, MD PhD¹; Paul Roepman, PhD²; Lizet E. van der kolk, MD PhD¹; Gerrit A. Meijer, MD PhD¹; Emile E. Voest, MD PhD¹; Winan J. van Houdt, MD PhD MSc³; Winette T. A. van der Graaf, MD PhD¹,

¹Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS, ²Hartwig Medical Foundation, Amsterdam, Noord-Holland, NETHERLANDS, ³The Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS

Objective: The prognosis of patients with advanced sarcomas remains unfavorable, and there is need for improved patient stratification and discovery of predictive biomarkers to optimize therapy decisions. Comprehensive genomic characterization of patient and tumor can guide patient-specific therapy decisions for sarcoma patients by detecting diagnostic biomarkers, actionable and germline variants. Here, we report the therapeutic implications of prospective WGS in 80 patients with advanced sarcomas.

Methods: Patients received a prospective WGS analysis of tumor and germline DNA in a tertiary referral center after (repeated) previous histopathological assessment by expert pathologists. WGS results were reported back to oncologists to be incorporated in further therapy decisions. Actionability of variants was retrospectively scored using the ESMO scale for clinical actionability of molecular targets (ESCAT).

Results: With detection of diagnostic biomarkers, five regular therapy decisions were adjusted after diagnostic revision of sarcoma subtype. Actionable variants were present in 31 patients, and consisted of 39 different therapeutic opportunities. Notably, a large KIT deletion had remained undetected with previous NGS-based panel sequencing diagnostics. Germline variants had therapeutic implications in three patients, including two pathogenic TP53 mutations (one previously detected), and a CHEK2 germline mutation with somatic loss. Eight patients started biomarker-based experimental therapy, and 11 patients have additional experimental therapy options after progression on last-line regular treatment.

Conclusion: Comprehensive patient and tumor characterization identifies relevant genetic alterations in a substantial proportion of sarcoma patients. Furthermore, international large-scale genomic characterization of sarcoma patients can aid discovery of new relevant biomarkers and enhance future precision oncology.



Poster #053 #1819083

THE PERCEPTIONS OF TELEMEDICINE SATISFACTION IN IMMUNOCOMPROMISED PEDIATRIC PATIENTS DURING THE COVID-19 PANDEMIC

Molly M. Aguina¹; Alexandra Arca¹; Ariel Gliksberg, MD²; Paul M. Kent, MD³,

¹Rush University Hospital, Chicago, Illinois, UNITED STATES, ²University of Illinois Hospital, Chicago, Illinois, UNITED STATES, ³Rush University Medical Center, River Forest, Illinois, UNITED STATES

Objective: Initially in the COVID-19 pandemic, not much was known about the SARS-CoV-2 virus, so the perceived threat of nosocomial infection was high. For immunocompromised pediatric patients such as cancer patients, there is an increased risk for severe infection. Therefore, the pandemic put physicians caring for this vulnerable population in the hard position of deciding to either delay care or to have the patient risk a hospital visit. Hospitals tried to prevent unnecessary visits for most patients and introduced the concept of using telehealth as a safe and effective alternative to in-person-care during extreme circumstances. However, the majority of these immunocompromised pediatric patients required multiple hospital visits per month, some even weekly. As a result, telemedicine was used to avoid the delay or cancellation of these appointments and treatments. Furthermore, for our pediatric and AYA clinic, we sought to determine if telemedicine was satisfactory from the patient's point of view.

Methods: Chart review was performed for all patients that entered the pediatric and AYA oncology clinic between March 2020 - March 2021. All patients that received telemedicine care were recorded (n=49). Each patient was contacted for a phone interview. If the patients partook in the interview, they responded to a standardized survey using a likert scale. As most of the patients were minors, we spoke with the parent or legal guardian of many patients instead. Statistical analyses using t-tests were performed to analyze the data and determine if results were significantly different.

Results: Multiple t-tests of two samples assuming unequal variances were performed on stratified data to determine if patient satisfaction varied on the basis of insurance type (Medicaid vs. private), race, or years of parental education. The results indicated no statistical difference in each of these stratified groups. The overall mean of the satisfaction score (how satisfied the patients were with telehealth visits) indicated that patients liked the telemedicine alternative.

Conclusion: Based on our sample, when it is possible for immunocompromised pediatric patients to receive care through telemedicine, the patients or their caretakers evaluated the services to be useful and were satisfied with the experience. Therefore, we conclude that telehealth can still provide the face-to-face interaction most patients desire in times where it is not ideal or convenient to meet in person and can also provide a lower-cost alternative to patients when a physical exam is not necessary.



Poster #054 #1818923

HOW COVID-19 AFFECTED THOSE CONTACTING THE SARCOMA UK SUPPORT LINE.

*Helen Stradling, MSc, BNurs (Hons); Sam Hackett, BSc (Hons) Oncology Nursing, PgD in Nursing;
Carly McDonald, BSc (Hons)
Midwifery, PgC Obstetric Ultrasound, Sarcoma UK, London, England, UNITED KINGDOM*

Objective: Introduction: In February 2016 Sarcoma UK, the only UK based charity focusing on all types of sarcoma, launched the Sarcoma UK support line, a free, confidential, health care professional run support line for anyone affected by sarcoma. In the last 5 years the team have had more than 10,500 contacts with over 2,500 individuals. The team would like to share their experiences and learnings from the COVID-19 pandemic and how it has impacted the people who have been in contact with them.

Methods: The start of lockdown: In March 2020 the UK went into the first national lockdown due to the COVID-19 pandemic. Information and guidance was changing on a daily basis and people were not sure what the news meant for them. In the 2 weeks prior to the lockdown the support line team saw an increase of 81% in the number of individuals contacting them and quickly doubled the staffing of the support line to ensure those needing support and advice were able to get it. The earlier contacts were mostly people asking about whether a sarcoma diagnosis made them more vulnerable and should they or their family members be shielding because of it. As the lockdown began to affect the NHS services and clinical teams were starting to adapt how they worked the support line team observed a shift in the reasons for people contacting them.

Results: What we heard and learnt: As the pandemic really started to take hold it affected the patients receiving or about to start palliative chemotherapy. It was felt that the risk of administering the treatments and therefore making people less likely to be able to fight COVID-19 should they get it outweighed the benefit. Tough conversations were being had between clinicians and patients, since patients and families felt as though their only option for a longer life was being taken away from them, hence there was a lot of anger and upset. As time went on the team heard how actually, not having to go through with the palliative chemotherapy led to some people having a more positive experience of end of life care, in that they were able to enjoy real quality time with their families, making memories that would not have been possible pre-COVID. Families were all at home, no visitors were allowed and so it really was seen as time that previously would have been spent making hospital trips for treatment, feeling unwell between each cycle and not seeing immediate family. The way clinic appointments were being undertaken changed, with many teams moving to teleconferencing for follow up appointments and some people had follow up scans delayed or cancelled. The support line team saw an increase in contacts relating to the fear of recurrence of 40% over the 2020/21 year. Some people preferred the new teleconferencing follow-up appointments and actually felt it was an improvement, even when receiving bad news, as they were in their own homes with family and did not have to travel home on public transport or for many hours having to take in what had just been relayed to them. Getting access to a GP when people had worrying symptoms was an issue. The team heard from 3 times as many people with worrying symptoms than they had in the previous year and spent time giving people the actual words to be using when trying to access primary care.

Conclusion: The COVID-19 pandemic was completely unprecedented. The support line team spoke to many patients, family members and friends who all had different experiences of how it affected them or their loved one. Not all of the experiences were positive, but some definitely were and these were life changing for many. We know that there have been less referrals into the specialist sarcoma teams during the pandemic and a tsunami of diagnoses are currently waiting to get into primary care. The effect that these possible late diagnoses will have on future patients is not yet known, but we know that the outcomes for sarcoma patients are improved when found early, which means these late diagnoses are concerning. The support line team heard about what was happening in the clinical setting from patients, family and friends in real time and so really were able to be a beacon of what was happening. This allowed them to share the experiences with NHS England and other governing bodies to ensure any concerns about delays or service impacts were escalated as soon as possible. The team continue to hear about and understand the impact COVID-19 is having and believes, unfortunately, the the effects will be felt for years to come.



Poster #055 #1818862

TREATMENT OF OSTEOSARCOMA PATIENTS IN THE PHILIPPINE GENERAL HOSPITAL DURING THE COVID-19 OUTBREAK

Czar Louie Gaston, MD

University of the Philippines Manila - Philippine General Hospital, Manila, National Capital Region, PHILIPPINES

Objective: The ongoing Coronavirus disease 2019 (COVID-19) pandemic has disrupted healthcare systems worldwide. This study aimed to document the effect of COVID-19 on osteosarcoma treatment pathways in the Philippine General Hospital (PGH) and determine if there were any delays.

Methods: A retrospective review of osteosarcoma patients treated at the PGH from January 1, 2019 – January 1, 2020 (pre-COVID-19) was compared to those treated during the COVID-19 pandemic from March 1, 2020 – September 1, 2020. Rates of diagnosed osteosarcoma, admission for chemotherapy, admission for surgery, treatment abandonment, metastatic disease on presentation, 1-year mortality, and amputation were calculated and compared between the two groups.

Results: From March to September 2020, 11 newly diagnosed osteosarcoma patients sought consult at the PGH. Only one patient sought consult during the initial 3-4 months of the study, suggesting that patients delayed seeking healthcare during the period of enhanced community quarantine. Patients seen during the pandemic had a higher rate of metastatic disease on presentation, reflecting the delay in diagnosis. Due to COVID-19 restrictions early in the pandemic, osteosarcoma patients were coordinated and referred to outside hospitals for intravenous chemotherapy and surgery. Normalization of services (hospital admissions, limb salvage surgeries) were seen at the later stages of the study, corresponding to the loosening of the quarantine.

Conclusion: Osteosarcoma patients experienced delays in seeking consult, diagnosis, and treatment at the PGH due to the COVID-19 pandemic. Early indicators suggest worse outcomes for these patients due to the delays. Strategies employed during the pandemic, such as networking of care and telemedicine, may help in future outbreaks.



Poster #056 #1818856

DISPARITIES IN TYROSINE KINASE INHIBITOR USE IN OLDER PATIENTS WITH GASTROINTESTINAL STROMAL TUMOR

Thanh P. Ho, MD¹; Hayley Dykhoff¹; Lindsey Sangaralingham, MPH²; Brittany L. Siontis, MD¹; Travis Grotz, MD¹; Scott Okuno, MD¹; Steven I. Robinson, MD¹

¹Mayo Clinic, Rochester, Minnesota, UNITED STATES, ²Mayo Clinic Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery, Rochester, Minnesota, UNITED STATES

Objective: Gastrointestinal stromal tumor (GIST) is a common sarcoma for which survival can be significantly impacted by tyrosine kinase inhibitors (TKI). Prior review of patients (pts) at our tertiary academic center demonstrated lower use of TKI in older pts, age 65 years and above (≥ 65). We conducted a review of a larger cohort to determine if this trend persisted.

Methods: We used OptumLabs Data Warehouse[®] which contains de-identified medical/pharmacy claims and enrollment records for commercial and Medicare Advantage enrollees who represent diverse mix of ages, ethnicities, and regions across the United States (US). We focused on TKI (imatinib, sunitinib, regorafenib) patterns of use in pts with GIST from 2012-2019, which corresponds to the 3-year adjuvant therapy recommended for imatinib in high-risk pts, as well as approval of later-line sunitinib and regorafenib for advanced disease.

Results: Total of 922 adults with GIST were included (median age 63 years). Over half were men (53%). Most were White (66%); remainder were Black (15%), Hispanic (8%), Asian (4%) or unknown (7%). Pts lived mainly in the South (50%) or Midwest (24%). For pts with reported income, 54% had an annual household income less than \$75,000 (Table 1).

Few pts (11%) received more than 1 TKI therapy. Median duration of filled prescriptions for imatinib was 10.6 months (range 0.2-98.1), compared to 4 months (0.7-69.1) for sunitinib and 3.2 months (0.7-15.2) for regorafenib. The number of filled prescriptions for imatinib, sunitinib or regorafenib were similar for pts ≥ 65 years compared to younger pts. Older pts received a shorter duration of any TKI (9.1 months, 0.2-98.1), and specifically, received fewer months of imatinib (9.1 months, 0.2-98.1) and sunitinib (3.2 months, 0.7-27.2). By comparison, pts under age 65 years (< 65) received 11.9 months (0.2-98.1) for any TKI, 11.4 months (0.2-98.1) for imatinib, and 5.0 (0.9-69.1) for sunitinib (all $p < 0.05$). Duration of regorafenib was similar (3.5 months for pts < 65 years compared to 2.3 months for older pts, $p=0.15$). Pts < 65 years had a lower Charlson index (median 3 versus 4, $p < 0.0001$).

For 30-day TKI pharmacy costs, health plans paid 95% (mean US \$7349, based on 2019 inflation). Pts covered 5% out-of-pocket on average (mean \$314) with cost varying by TKI; specifically, imatinib (\$304), sunitinib (\$445), and regorafenib (\$621). Most pts < 65 years had commercial plan (93%), compared to older pts who were more likely to have Medicare advantage (90%). Pts with commercial plan paid lower out-of-pocket (\$111) than pts with Medicare Advantage (\$592) ($p < 0.0001$).

Conclusion: In an insured population, the duration of therapy for any approved TKI for GIST was lower than expected from their respective phase 3 trials. The shorter duration for pts ≥ 65 years, compared with their younger counterparts, may be due to higher out-of-pocket costs, co-comorbidities, disease biology, or a combination. Future research will aim to characterize this discrepancy, as well as explore the impact of recently approved TKIs on prescription patterns for pts with GIST.

Table 1: Patient Characteristics by Age Group

	Number of patients (%)			p value
	Age <65 years (N=507)	Age ≥65 years (N=415)	Total (N=922)	
Sex				<0.01
Female	218 (43.0%)	216 (52.0%)	434 (47.1%)	
Male	289 (57.0%)	199 (48.0%)	488 (52.9%)	
Race/Ethnicity				0.01
White	346 (68.2%)	264 (63.6%)	610 (66.2%)	
Black	63 (12.4%)	73 (17.6%)	136 (14.8%)	
Hispanic	50 (9.9%)	27 (6.5%)	77 (8.4%)	
Other/Unknown	26 (5.1%)	36 (8.7%)	62 (6.7%)	
Asian	22 (4.3%)	15 (3.6%)	37 (4.0%)	
Region				0.02
South	249 (49.1%)	209 (50.4%)	458 (49.7%)	
Midwest	119 (23.5%)	103 (24.8%)	222 (24.1%)	
West	89 (17.6%)	46 (11.1%)	135 (14.6%)	
Northeast	50 (9.9%)	57 (13.7%)	107 (11.6%)	
Annual Household Income				<0.0001
<\$40K	66 (13.0%)	127 (30.6%)	193 (20.9%)	
\$40K-\$74,999	111 (21.9%)	95 (22.9%)	206 (22.3%)	
\$75K-\$124,999	119 (23.5%)	67 (16.1%)	186 (20.2%)	
\$125K-\$199,999	66 (13.0%)	26 (6.3%)	92 (10.0%)	
\$200K+	55 (10.8%)	11 (2.7%)	66 (7.2%)	
Other/Unknown	90 (17.8%)	89 (21.4%)	179 (19.4%)	
Health Plan				<0.0001
Commercial	470 (92.7%)	40 (9.6%)	510 (55.3%)	
Medicare Advantage	37 (7.3%)	375 (90.4%)	412 (44.7%)	
Treated with Imatinib				0.99
No	28 (5.5%)	23 (5.5%)	51 (5.5%)	
Yes	479 (94.5%)	392 (94.5%)	871 (94.5%)	
Treated with Sunitinib				0.62
No	434 (85.6%)	360 (86.7%)	794 (86.1%)	
Yes	73 (14.4%)	55 (13.3%)	128 (13.9%)	
Treated with Regorafenib				0.42
No	471 (92.9%)	391 (94.2%)	862 (93.5%)	
Yes	36 (7.1%)	24 (5.8%)	60 (6.5%)	
Received more than 1 TKI				0.91
No	452 (89.2%)	369 (88.9%)	821 (89.0%)	
Yes	55 (10.8%)	46 (11.1%)	101 (11.0%)	



Poster #057 #1818976

A RANDOMIZED PHASE 2 STUDY OF NIVOLUMAB MONOTHERAPY OR NIVOLUMAB COMBINED WITH IPILIMUMAB IN ADVANCED GASTROINTESTINAL STROMAL TUMORS

 Arun Singh, MD¹; Joel Hecht²; Lee Rosen, MD²; Xiaoyan Wang, PhD²; Sandra Brackert, NP²; Warren Chow, MD³; Fritz C. Eilber, MD⁴; John Glaspy, MD²; Bartosz Chmielowski, MD PhD²
¹University of California, Los Angeles, Santa Monica, California, UNITED STATES, ²University of California, Los Angeles, Santa Monica, California, UNITED STATES, ³City of Hope Comprehensive Cancer Center, Duarte, California, UNITED STATES, ⁴UCLA Medical Center, Los Angeles, California, UNITED STATES

Objective: Most GISTs are driven by KIT/PDGFRa mutations and secondary mutations in these genes confer resistance to TKIs. TKI benefit is progressively less after imatinib failure. This phase II trial analyzed the efficacy of nivolumab (N) or nivolumab + ipilimumab (N + I) in refractors GIST patients.

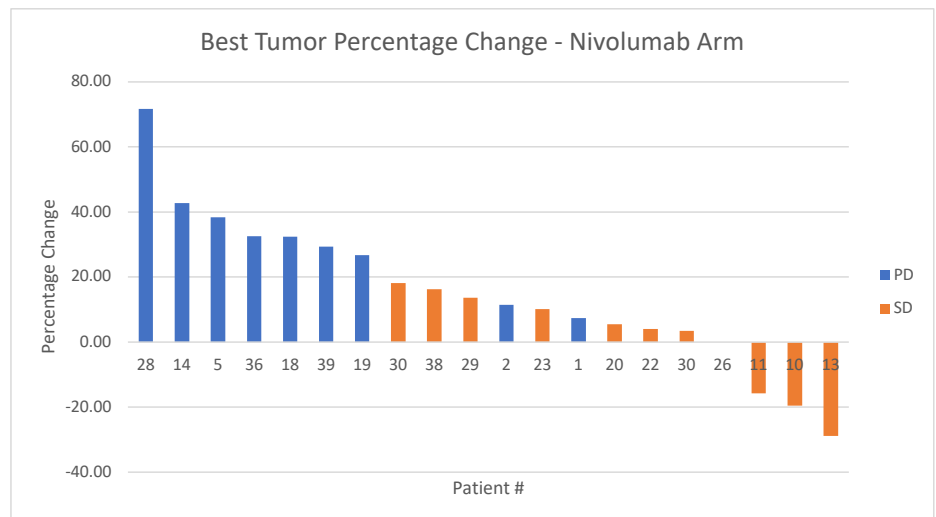
Methods: Advanced/metastatic GIST patients refractory to at least imatinib were enrolled on a randomized, parallel group, unblinded Phase 2 trial of nivolumab(N) (240mg Q2wks) or N(240 mg Q2wks) with ipilimumab(N+I) (1mg/kg Q6wks). The primary endpoint was the ORR of N alone or N+I by RECIST 1.1 criteria. Secondary objectives are to ascertain the PFS, CBR, RR by Choi criteria and safety.

Results: 36 of a planned 40 patients were enrolled. The entire cohort had a median of 3 prior lines of therapy (Range: 1-6). In the N arm, 10/19(52.6%) patients had SD for a CBR of 52.6 %; the median PFS was 11.7 wks (95% CI, 7.0, 17.4). In the N+I arm, 1/16(6.7%) patients had a CR and 4/16(25.0%) had SD for a CBR of 31.3% and a median PFS of 8.3wks (95% CI, 5.6, 22.2). The 4 and 6 month PFS were 42.1% and 26.3%, respectively for N and 31.3% and 18.8%, respectively for N+I. The most common adverse events (AEs) attributed to N and N+I were fatigue: 13.9% and 22.2%, respectively. There were 9 total attributable grade 3-4 AEs.

Conclusion: The primary endpoint of RR>15% was not observed for N or N + I. In a heavily pretreated GIST population, responses and long term disease control with both N and N+I were observed. No new safety signals have been observed.

Figure 1: Waterfall Plots of Tumor Response (RECIST 1.1) of (A) Nivolumab Arm and (B) Nivo + Ipi Arm

A.



B.

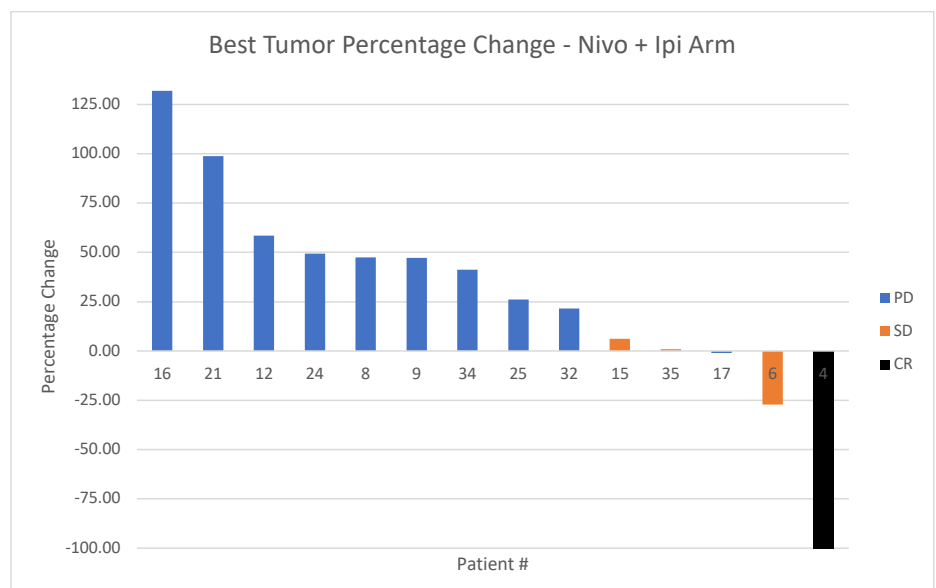
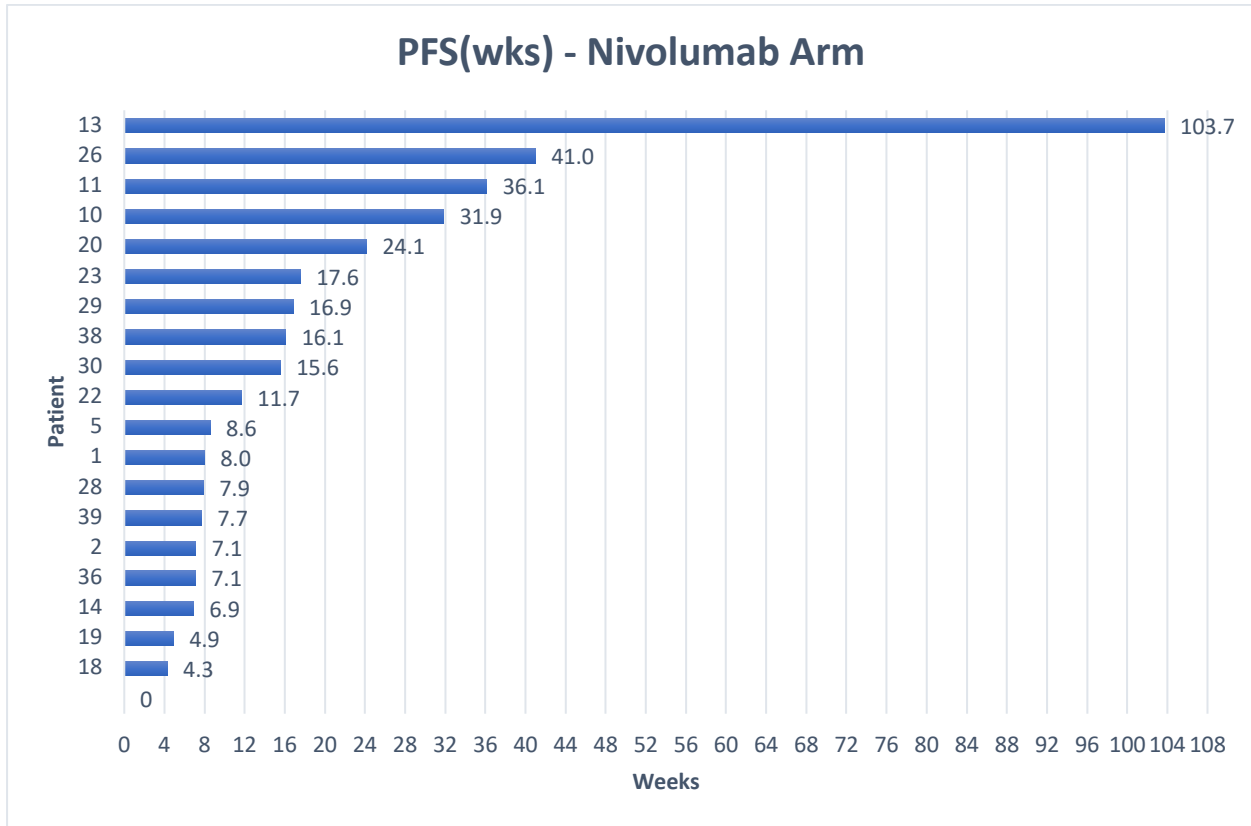


Figure 2: Swimmer’s Plot of PFS for (A) Nivolumab arm and (B) Nivo + Ipi Arm

A.



B.

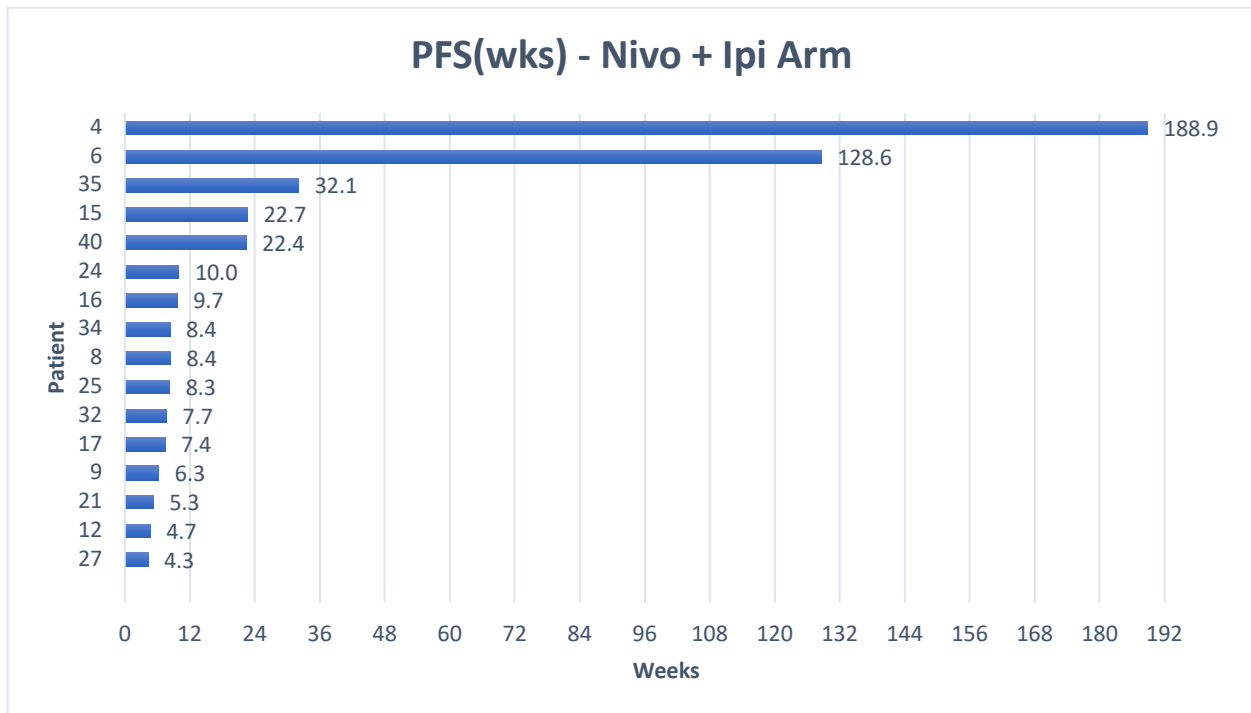


Table 1: Patient Characteristics

Characteristic	Finding (N=36)
Mean age at Consent (Range)	61 (21-80)
Sex	
Male	19 (53)
Female	17 (47)
Race	
White	20 (56)
Asian	7 (19)
Hispanic	3 (8)
African American	1 (3)
Other	2 (6)
Unknown	3 (8)
ECOG Performance at Consent	
0	20 (56)
1	16 (44)
Prior therapy for advanced or metastatic disease	
Imatinib	36 (100)
Sunitinib	32 (89)
Regorafenib	22 (61)
All Other Treatments	
Sorafenib	7 (19)
Nilotinib	3 (8)
Ponatinib	1 (3)
Cabozantinib	2 (6)
Pazopanib	4 (11)
Other	7 (19)
Surgery	28 (78)
Lines of prior therapy	
1	4 (11)
2	9 (25)
3	8 (22)
4	9 (25)
5+	6 (17)
Data are presented as number (percentage) of patients unless otherwise indicated.	

Table 2: Tumor Characteristics

Characteristic	Finding (N=36)
Location of primary tumor	
Stomach	14 (28)
Small bowel	19 (53)
Other/Unknown	3 (8)
Presented with metastatic Disease	
	26 (72)
Mitoses, /50 HPF (Original Diagnosis, Untreated)	
≥5	19 (53)
<5	7 (19)
Not available/Not Done	10 (28)
GIST Subtype	
<i>KIT</i> exon 9	3 (8)
<i>KIT</i> exon 11	13 (36)
<i>KIT</i> exon 13	1 (3)
<i>KIT</i> exon 17	1 (3)
<i>KIT</i> exons 9, 17	1 (3)
<i>KIT</i> exons 11, 13	3 (8)
<i>KIT</i> exons 11, 17	10 (28)
<i>KIT</i> exons 11, 18	1 (3)
"Wild Type"	2 (6)
Unknown/Not Done	2 (6)



Poster #058 #1818969

THE ROLE OF NEOADJUVANT IMATINIB IN GIST PATIENTS: A RETROSPECTIVE COHORT STUDY

Sara Renberg, MD¹; Yifan Zhang²; Fredrik Karlsson, MD, PhD³; Robert Bränström, MD, PhD³; Jan Åhlen, MD, PhD³; Li Jalmzell, MD, PhD⁴; Elisabet Lidbrink, MD, PhD⁴; Christina Linder Stragliotto, MD, PhD⁴; Felix Haglund, MD, PhD⁵; Andri Papakonstantinou, MD, PhD⁶

¹Department of Head, Neck, Lung and Skin Tumors, Karolinska University Hospital, Stockholm, Sweden, Stockholm, Stockholms Lan, SWEDEN, ²Department of Pathology and Cancer diagnostics, Karolinska University Hospital, Stockholm, Sweden and Department of Oncology-Pathology, Karolinska Institute, Stockholm, Sweden, Solna, Stockholms Lan, SWEDEN, ³Department of Breast cancer, Endocrine tumors and Sarcoma, Karolinska University Hospital, Stockholm, Sweden and Department of Molecular Medicine and Surgery (MMK), Karolinska Institute, Stockholm, Sweden, Stockholm, Stockholms Lan, SWEDEN, ⁴Department of Breast cancer, Endocrine tumors and Sarcoma, Karolinska University Hospital, Stockholm, Sweden, Stockholm, Stockholms Lan, SWEDEN, ⁵Department of Pathology and Cancer diagnostics, Karolinska University Hospital, Stockholm, Sweden and Department of Oncology-Pathology, Karolinska Institute, Stockholm, Sweden, Stockholm, Stockholms Lan, SWEDEN, ⁶Department of Breast cancer, Endocrine tumors and Sarcoma, Karolinska University Hospital, Stockholm, Sweden and Department of Oncology-Pathology, Karolinska Institute, Stockholm, Sweden, Stockholm, Stockholms Lan, SWEDEN

Objective: Gastrointestinal stromal tumor, or GIST, originates from the interstitial cells of Cajal and can arise anywhere along the gastrointestinal tract. Surgery remains first line therapy, but complementary adjuvant treatment with the tyrosine kinase inhibitor imatinib has significantly improved the outcome for GIST patients. Neoadjuvant imatinib has been applied in tumors with large size or with difficult anatomical locations but has not been formally investigated to the same extent.

Methods: This is a retrospective review of all patients diagnosed with GIST at Karolinska University Hospital in Stockholm, Sweden, between January 2000 and December 2019. Patients treated with neoadjuvant imatinib were selected and a descriptive analysis was performed in terms of response to treatment and survival outcomes.

Results: A total of 455 patients were included and out of those 84 received neoadjuvant treatment with imatinib for a primary non-metastatic GIST. The patients who received neoadjuvant imatinib had tumors located throughout the whole gastrointestinal tract but foremost close to the gastroesophageal junction (10 (12%)) or elsewhere in the stomach (29 (35%)), or in the small intestine (30 (36%)) or rectum (12 (14%)). The tumors were generally large in size (mean 10.5 cm, range 2-27 cm) and located near vulnerable anatomical structures such as the gastroesophageal junction, pancreas or the hepato-duodenal ligament, Treitz ligament or the lower part of the rectum. Size or anatomical location were the main indications for neoadjuvant imatinib, and the tumors did in general shrink after neoadjuvant treatment (mean 7.6 cm, range 1,3-30 cm). None of the patients with tumors located in the stomach (0 out of 29) and four out of the ten patients with tumors located near the gastroesophageal junction underwent gastrectomy. A minor part of the patients with tumors in the small intestine, including duodenum, (3 out of 30) underwent more extensive surgery, whereas seven out of the twelve patients with tumors in rectum had to undergo rectal amputation. After surgery 94% of the neoadjuvant treated tumors accomplished R0-resection. About one-fourth experienced local relapse or distant metastasis.

Conclusion: Imatinib is feasible as neoadjuvant therapy for GIST, and it can lead to tumor size reduction and prevent high morbidity due to more extensive surgery or at least reduce the extent of the surgery, especially for tumors located in the stomach or small intestine.



Poster #059 #1818937

REAL-WORLD EVIDENCE FROM ONLINE PATIENT FORUMS COMPLEMENTING CURRENT MEDICAL PERSPECTIVES: THE EXAMPLE OF GASTROINTESTINAL STROMAL TUMOUR PATIENTS

Anne Dirkson, MSc¹; Suzan Verberne, PhD¹; Gerard van Oortmerssen, PhD²; Wessel Kraaij, PhD¹; Hans Gelderblom, MD, PhD³

¹Leiden Institute of Advanced Computer Science, Leiden University, Leiden, Zuid-Holland, NETHERLANDS, ²Patient Platform Sarcomas & Leiden Institute of Advanced Computer Science, Leiden University, Leiden, Zuid-Holland, NETHERLANDS, ³Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS

Objective: Four years ago we gave an oral presentation at CTOS about the value of harvesting previously unexplored patient-generated information from internet discussion forums [1]. Now we can present concrete results of side effects and coping strategies for these side effects that patients share online. Without burdening patients, internet discussion forums have the potential to complement current pharmacovigilance practices and medical knowledge by providing real-time, uncensored and unsolicited information. We pioneer work into discovering such strategies automatically.

Methods: We have developed machine learning algorithms to automatically extract and aggregate side effects from messages on open online forums. These techniques are based on natural language processing, a research field that deals with how computers can be used to understand text. Major challenges are the use of laymen's terms and the large variation in how patients describe the same side effect. Similarly, we have developed algorithms to automatically extract and aggregate coping strategies and to determine which side effect patients recommend these strategies for. Our work is a unique collaboration between computational linguistics, oncologists and patient organizations.

Results: We will present results for an international discussion forum of Gastrointestinal Stromal Tumor (GIST) patients and show how our approach can indicate which side effects most strongly impact quality of life. For instance, alopecia and impaired cognition were reported far more often by patients using avapritinib than one would expect based on the registration trial and thus are likely to either be more prevalent than previously thought or have a strong negative impact on a patient's quality of life. We will also give examples of how a patient forum can provide real-world evidence for both long-term and novel side effects. For example, some long-term side effects for imatinib that patients discuss online are problems with their teeth, osteoporosis, muscle atrophy and tremors. Patients also discuss side effects resulting from imatinib that were not previously reported in registration trials, including muscle cramping, insomnia and dry eyes. Finally, we will present which coping strategies GIST patients recommend to each other online for dealing with their side effects.

Conclusion: Automated analysis of patient discussion forums can unlock novel insights into how the quality of life of patients can be improved. Our approach can provide a complementary perspective to that of the health professional and thereby novel hypotheses which can and should be tested in further rigorous medical research. 1. Gelderblom, A.J. and van Oortmerssen, G. (2017). Harvesting patient-generated information from internet discussion forums. Oral presentation at CTOS 2017.



Poster #060 #1818912

REAL-WORLD ASSESSMENT OF CLINICAL OUTCOMES IN GIST PATIENTS TREATED WITH SUNITINIB AFTER IMATINIB FAILURE

Virginia Martínez-Marín, MD, PhD¹; Gloria Marquina, MD PHD²; Claudia Maria Valverde Morales, MD³; Mar Galera, MD⁴; Isabel Pajares, MD⁵; Pilar Solis, MD⁶; Nadia Hindi, MD⁷; Maria Angeles Vaz, MD⁸; Eduardo Pujol, MD⁹; Inmaculada Ballester, MD¹⁰; Oscar Reig, MD¹¹; Juana Cano, MD¹²; Alberto Moreno, MD¹³; Rebeca Mondejar, MD¹⁴; Jose Andres Meana, MD¹⁵; Amelia López-Ladrón, MD¹⁶; Roberto Diaz Diaz-Beveridge, MD¹⁷; David Vicente, MD¹⁸; Ana Leon, MD¹⁹; Antonio Fernández-Serra, MD²⁰; César Serrano, MD, PhD²¹

¹H. U. La Paz, Madrid, Madrid, SPAIN, ²H. U. Clínico San Carlos, Madrid, Madrid, SPAIN, ³Vall D'Hebron University Hospital, Barcelona, Catalonia, SPAIN, ⁴H. U. Gregorio Marañón, Madrid, Madrid, SPAIN, ⁵H. U. Miguel Servet, Zaragoza, Aragon, SPAIN, ⁶H. U. Central de Asturias, Oviedo, Asturias, SPAIN, ⁷Fundacion Jimenez Diaz University Hospital, Madrid, Madrid, SPAIN, ⁸H. U. Ramón y Cajal, Madrid, Madrid, SPAIN, ⁹H. U. Lozano Blesa, Zaragoza, Aragon, SPAIN, ¹⁰H. U. Morales Meseguer, Murcia, Murcia, SPAIN, ¹¹H. U. Clinic, Barcelona, Catalonia, SPAIN, ¹²H. General Ciudad Real, Ciudad Real, Castilla-La Mancha, SPAIN, ¹³H. U. Reina Sofía, Cordoba, Andalusia, SPAIN, ¹⁴H. U. La Princesa, Madrid, Madrid, SPAIN, ¹⁵H. U. Alicante, Alicante, Comunidad Valenciana, SPAIN, ¹⁶H. de Valme, Sevilla, Andalusia, SPAIN, ¹⁷H. U. La Fe, Valencia, Comunidad Valenciana, SPAIN, ¹⁸H. U. Virgen Macarena, Sevilla, Andalusia, SPAIN, ¹⁹H. U. Fundación Jiménez Díaz, Madrid, Madrid, SPAIN, ²⁰Fundación Instituto Valenciano de Oncología, Valencia, Comunidad Valenciana, SPAIN, ²¹Sarcoma Translational Research, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Catalonia, SPAIN

Objective: Approved globally, sunitinib is established as the standard-of-care second line for the treatment of advanced and/or metastatic gastrointestinal stromal tumor (GIST) patients after failure or intolerance to imatinib. Although prognostic and predictive factors for sunitinib activity and toxicity are relatively known, there are still unexplained disparities in GIST patients treated with sunitinib, particularly in the community. Likewise, management of GIST patients have changed significantly since sunitinib approval in 2006. Therefore, the objective of this study was to undertake a real-world assessment of sunitinib use in the treatment of GIST patients as well as contemporary outcomes.

Methods: An observational and retrospective analysis was performed from data collected from adult GIST patients treated with sunitinib across 20 Spanish institutions between February 2018 and June 2019. From a total of 123 patients included, 109 had enough data to be analyzed. Patients' demographic, clinicopathological and molecular data was collected and correlated with outcomes. Toxicity data was recorded as well. Logistic regression models were used to identify predictive factors for progression free survival (PFS) and overall survival (OS). Statistically significant variables in the univariate analysis were further studied in the multivariate Cox proportional hazards model.

Results: With a median age of 62 years, 109 patients received sunitinib at schedule according to treating physician's choice: 37.5 mg QD (45%), 50 mg QD 4/2 (36%), other (19%). Nearly half of the patients (43%) had been treated previously with high-dose imatinib previously (600-800mg/day). Mutational status was available in 75 patients (69%). For the entire cohort, the median progression free survival (mPFS) was 12.2 months, and the median overall survival (mOS) was 105 months. PFS was seemingly increased in KIT exon 9 mutations and wild-type vs exon 11 (25.1 months, 12.2 months v. 10.4 months respectively, $p=0.760$). There were no differences in outcomes regarding on the type of institution (referral center v. community-based). The best response during the treatment was stable disease (46%) followed by partial response (32%). Most common toxicities were asthenia, hand-foot-skin reaction and hypertension, mostly grade 1-2. Two groups of patients could be clearly identified: refractory (progression ≤ 3 months) and long-term responders (progression > 8 months). PFS in the latter group was significantly superior, 25.3 months ($p < 0.001$). In the univariate analysis, the following factors predicted a longer PFS in GIST patients treated with sunitinib: peritoneal metastases, low number of metastases, hypothyroidism, decreased neutrophil count, sunitinib dose reduction and partial/complete response. In the multivariate analysis, the following factors predicted better PFS: partial/complete response, decreased neutrophil count and sunitinib dose reduction.

Conclusion: Our retrospective real-world study confirms that sunitinib is an effective and safe option for the treatment of imatinib-resistant, advanced GIST patients. Our results highlight that alternative sunitinib schedules are widely used and dosage adaptation impacts positively on the duration and the prolonged activity of the treatment. GIST patients in this

study displayed a more durable PFS compared to prior studies and the pivotal trial, underscoring a group of long-term responders that particularly benefit from sunitinib therapy. This will be further characterized in the future. Finally, this analysis offers a contemporary benchmark for PFS and outcomes among metastatic GIST patients treated in the second line for metastatic disease.



Poster #061 #1818927

IMPACT OF ADJUVANT IMATINIB ON BONE AND MUSCLE DENSITY IN PATIENTS WITH RESECTED GASTRO-INTESTINAL STROMAL TUMORS

 Claudia Angela Maria Fulgenzi, MD¹; Andrea Napolitano, MD, PhD¹; Eliodoro Faiella, MD²; Laura Messina, MD²; Gennaro Castiello, MD²; Flavia Paternostro, MD²; Marianna Silletta, MD, PhD²; Francesco Pantano, MD, PhD²; Giuseppe Tonini, MD, PhD²; Daniele Santini, MD, PhD²; Bruno Vincenzi, MD, PhD³
¹Campus Bio-Medico, Roma, Lazio, ITALY, ²Campus Bio Medico, Roma, Lazio, ITALY, ³Department of Medical Oncology, Università Campus Bio-Medico di Roma, Rome, Italy, Roma, Lazio, ITALY

Objective: Gastrointestinal stromal tumors (GISTs) are mesenchymal tumors with an estimated incidence of 10–15 cases per million every year. The treatment for non-metastatic GISTs is surgical resection. Three years of adjuvant treatment with Imatinib (400 mg/die) is recommended for tumors with high-risk features and c-KIT mutations.

Imatinib is an orally available tyrosine kinase inhibitor (TKI) that targets c-abl, c-KIT and PDGFR; at therapeutic concentration it can also inhibit the macrophage-colony stimulating factor (M-CSF) receptor. There is evidence that Imatinib can influence bone metabolism. In *in vitro* and *in vivo* murine models, Imatinib can promote osteoclasts apoptosis and can inhibit their differentiation, contextually stimulating osteoblast differentiation mainly through PDGFR inhibition.

The effect of Imatinib on bone composition in patients receiving treatment for GISTs has not been investigated. There is a weak evidence that Imatinib, in patients affected by GISTs, can have a role in influencing muscle composition, which is closely related to bone health.

Bone and muscle composition have recently been correlated with drug-related toxicities, quality of life, performance status and prognosis in patients affected by solid cancer. The prevention, diagnosis and treatment of alterations in these tissues are of particular interest in patients with long life expectancy, as those receiving adjuvant treatment. Here, we hypothesized that Imatinib treatment could have an effect on bone mineral density (BMD) and muscle composition. We also assessed the role of these anthropometric parameters on Imatinib-related toxicities.

Methods: We retrospectively selected patients with surgically resected high-risk GIST that completed 3 years of adjuvant therapy with Imatinib (starting dose 400 mg/die). Patients electronic charts were reviewed. To confirm the potential effect of Imatinib on bone density, we subsequently selected a control group from patients with low risk surgically resected GIST. Age at diagnosis, sex, height, weight, date of surgery, prognostic features according to Joensuu's classification, Imatinib toxicities and dose reduction were recorded by two investigators in a predefined data form. Toxicities were assessed at each visit by Common Terminology Criteria for Adverse Events (CTCAE) v.4. Disease progression was defined per Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 criteria.

Muscle and bone density were evaluated on CT scan at baseline and after 6, 12 and 18 months. BMD was evaluated at third lumbar vertebra in axial slice. A density ≥ 120 mg/cm³ was considered normal, osteopenia was defined as a density between 80 and 120 mg/cm³ and osteoporosis if density was < 80 mg/cm³. Muscle density was assessed evaluating two consecutive images at 3 lumbar vertebra (L3) through Oxiris software. Patients were defined sarcopenic if their SMI was < 39 cm²/m² for women and < 55 cm²/m² for men (16). Total lean body mass (LBM) was extracted using Mourtzakis formula (LBM (kg) = $(0.30 \times (\text{skeletal muscle area at L3 using (cm}^2)) + 6.06)$ (17).

Patient characteristics at baseline were compared using Fisher's exact test for categorical variables and Mann-Whitney-Wilcoxon for continuous variables. Pearson's r and r^2 coefficients were reported. Changes of BMD over the different time points were analyzed using a one-way repeated measures analysis of variance by ranks (Friedman test). All reported p values were two-sided. A p value < 0.05 was considered statistically significant. Statistical analyses were performed using GraphPad Prism version 8.2 (GraphPad Software, La Jolla CA, USA).

Results: Overall 14 patients were eligible for the final analysis (6 women and 8 men). (Table 1). At baseline, men had a significantly higher BMD, SMI and LBM (median BMD: 142.5 vs 83.0; $p=0.013$; median SMI: 45.0 vs 37.3; $p=0.018$; median LBM: 46.5 vs 32.3; $p=0.001$) (Fig. 1).

BMD was positive associated with SMI ($p=0.039$, $r=0.556$, $r^2=0.309$) and LBM ($p=0.005$, $r=0.746$, $r^2=0.556$). We also observed a significant association between BMI and SMI ($p=0.041$, $r=0.550$, $r^2=0.303$).

BMD showed an overall significant increase over time ($p=0.021$). A significant inverse correlation between baseline and delta BMD was found ($p=0.021$, $r=-0.653$, $r^2=0.426$).

We separately analyzed BMD changes in patients with basal level <120 mg/cm³ (Table 2). In this subset of patients, BMD showed a significant increase over the different time points (p=0.002), whereas there was no significant change in the remaining patients with higher BMD (p=0.993). We also selected a control group made up by patients with low basal BMD, affected by low risk resected GIST who did not receive Imatinib therapy.

In total we selected 8 patients (4 women and 4 men). Controls did not significantly differ from cases in terms of baseline characteristics (Table 3). In this group, the BMD did not significantly change over the course of 18 months of follow-up (p=0.918).

Overall, 8 (57.1%) patients experienced at least one Imatinib-related toxicity; 2 (14.3%) had grade 1 toxicity; 2 (14.3%) had grade 2 and 4 (28.6%) reported grade 3 events; diarrhea was the most common toxicity of any grade. No correlation between any grade toxicities and BMI, BMD, SMI and LBM was found. However, patients who suffered from grade 3 AEs had a significantly lower baseline BMI (median: 22.5 vs 25.8: p=0.014) and LBM (median: 34.2 vs 44.3: p=0.024) (Fig. 2). There also was a non-significant trend between basal BMD and grade 3 toxicities (p=0.060).

Conclusion: This is the first paper to investigate the impact of Imatinib on BMD, SMI and LBM in GIST patients treated in the adjuvant setting. In our cohort, men reported higher BMD, SMI and LBM at baseline. We found a positive correlation between BMD and both SMI and LBM. On the contrary, BMI, age and site of the primary tumor did not influence BMD, SMI and LBM. The therapy with Imatinib led to a significant increase in BMD in patients with low basal value and it did not influence other anthropometric parameters. The effect of Imatinib in bone metabolism has been previously reported and it is thought to be mainly caused by Imatinib-mediated inhibition of PDGFR. Pre-clinical models confirmed the modulatory activity of Imatinib on bone cells. The increase in BMD that we observed is in keeping with the above findings. The fact that only patients with low basal BMD experienced an increase in bone density could be related to the prominent activity of osteoclast typical of osteoporosis and osteopenia. As a consequence of the above evidence, we could infer that the Imatinib-mediated inhibition of bone resorption is more evident in case of predominant osteoclast activity as osteoporosis and osteopenia. We have described an association between BMI, LBM and drug-related adverse events. In particular, we found that development of grade 3 toxicities was more common in patients with low BMI and low LBM. Low LBM and low BMI could result in impaired distribution with higher drug exposure. This effect is more evident for molecules with high albumin binding as Imatinib, which is about 95% bound to plasma protein.

In conclusion, we demonstrated for the first time that Imatinib increases BMD in GIST patients with low baseline values treated in the adjuvant setting. Furthermore, we confirmed the role of body composition in influencing drug-related toxicities.

Table 1. Basal characteristics of case group

Number	14
Age (Median; Range)	69.1 years; 35.9–82.5
Gender: N (%)	6 women (42.9%) 8 men (57.1%)
Site of primary tumor: N (%)	6 small bowel (42.9%) 5 stomach (35.7%) 2 rectum (14.3%) 1 retroperitoneum (7.1%)
BMI (Median; Range)	24.6 kg/m ² ; 17.8–30.1
BMD (Median; Range)	110.5 mg/cm ³ ; 52–175
LBM (Median; Range)	41.3 kg; 26.8–58.1
SMI (Median; Range)	42.6 cm/m ² ; 30.8–56.1

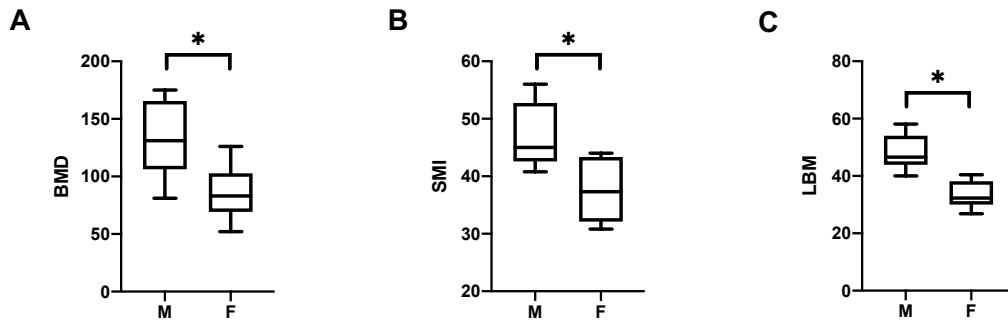
Table 2. Baseline characteristics in patients with low and high BMD

	All patients	Patients with basal BMD <120 mg/cm³	Patients with basal BMD ≥120 mg/cm³	Differences
Number	14	8	6	p >0.05
Age (Median; Range)	69.1; 35.9-82.5	69.2; 35.9-77.4	70.5; 48.0-82.5	p >0.05
Gender (N (%))	6 F (42.9%), 8 M (57.1%)	5 F (62.5%), 3M (37.5%)	1 F (16.6%), 5M (83.4%)	p >0.05
BMI (Median; Range)	24.6; 17.8-30.1	23.9; 17.8-27.7	25.9; 20.6-30.1	p >0.05
BMD (Median; Range)	110.5; 52-175	83.5; 52-110	143.5; 126-175	p <0.001
SMI (Median; Range)	42.6; 30.8-56.1	42.9; 30.8-46.2	43.5; 40.8-56.0	p >0.05
LBM (Median; Range)	41.3; 26.8-58.1	34.9; 26.8-46.1	46.0; 40.4-58.1	p =0.029

Table 2. Baseline characteristics in patients with low BMD and control group

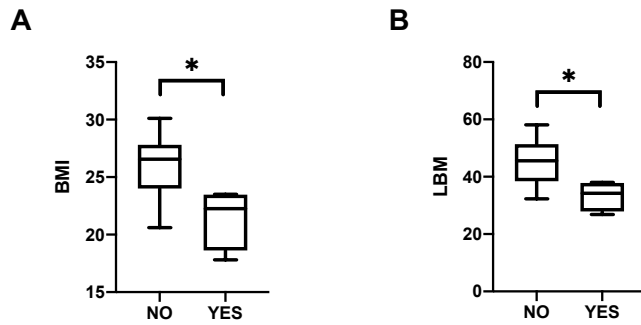
	Patients with basal BMD <120 mg/cm³	Control group with basal BMD <120 mg/cm³	Differences
Number	8	8	N/A
Age (Median; Range)	69.2; 35.9-77.4	70.4; 61.9-75.6	p>0.05
Gender (N (%))	5 F (62.5%), 3M (37.5%)	4 F (50%), 4 M (50%)	p>0.05
BMI (Median; Range)	23.9; 17.8-27.7	24.6; 17.3-31.8	p>0.05
BMD (Median; Range)	83.5; 52-110	83; 59-119	p>0.05
SMI (Median; Range)	42.9; 30.8-46.2	38.2; 32.7-64	p>0.05
LBM (Median; Range)	34.9; 26.8-46.1	34.4; 31.5-68.3	p>0.05

FIGURE 1



(A) Differences in BMD according to gender in cases ($p=0.013$)
(B) Differences in SMI according to gender in cases ($p=0.018$)
(C) Differences in LBM according to gender in cases ($p=0.001$)

FIGURE 2



(A) Differences in basal BMI between patients who did not and who did experience grade 3 adverse events ($p=0.014$)
(B) Differences in basal LBM between patients who did not and who did experience grade 3 adverse events ($p=0.024$)



Poster #062 #1818973

PSOAS MUSCLE INDEX HAS NO PROGNOSTIC VALUE IN PATIENTS WITH PRIMARY GASTROINTESTINAL STROMAL TUMOR

Steven Hopkins, BA¹; Leah Stockton, MD²; Weier Li, MD²; Elizabeth Handorf, PhD²; Elaine Vo, MD²; Stephanie Greco, MD²,
¹Temple Lewis Katz School of Medicine, Philadelphia, Pennsylvania, UNITED STATES, ²Fox Chase Cancer Center, Philadelphia, Pennsylvania, UNITED STATES

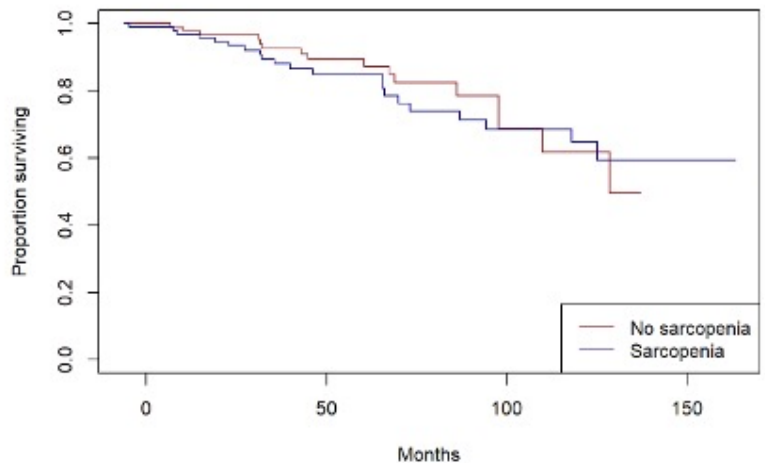
Objective: Pre-treatment Psoas Muscle Index (PMI) has been implicated to have predictive value in a variety of solid body tumors. Presently, there is a lack of evidence on the association between PMI and outcomes of patients diagnosed with primary gastrointestinal stromal tumor (GIST). This study was performed to evaluate the prognostic significance of pre-treatment PMI depletion on overall survival (OS) and recurrence free survival (RFS) in GIST patients.

Methods: We conducted a retrospective analysis of 209 patients who underwent curative resection for GIST between 2004-2019. Pre-treatment PMI was measured by computer tomography (CT) at the L3 vertebral level. Median PMI values were calculated as 42.2 cm²/m² and 29.5 cm²/m² for males and females, respectively. Patients who fell below these median values of PMI were classified as sarcopenic. An adjusted Cox Proportional-Hazards model was carried out to assess the impact sarcopenic status had on OS and RFS.

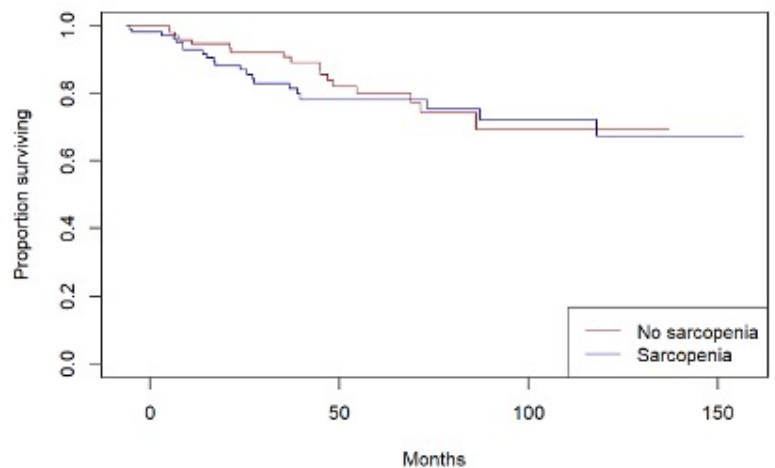
Results: 104 patients (49.8%) were classified as sarcopenic. Patients with sarcopenia were significantly older than the non-sarcopenic cohort (p=0.04, 61.4 and 56.4, respectively) and had larger mean post-operative final tumor size (p=0.019, 8.8 and 6.7 cm, respectively). There were no statistically significant differences between groups comparing sex, race, BMI, pathological stage, or mitotic count. There additionally was no significant difference in post-operative complications (p=0.828). Sarcopenia status was not prognostic of OS (HR 0.81, 95% CI: 0.38-1.75, p=0.598) or RFS (HR 0.90, CI: 0.43-1.86, p=0.767).

Conclusion: Sarcopenic status was associated with older age and larger post-op GIST tumor size. Pre-treatment PMI depletion had no prognostic value on OS or RFS.

Overall survival



Recurrence-free survival





Poster #063 #1819063

**NEOADJUVANT IMATINIB IN LOCALLY ADVANCED GASTROINTESTINAL STROMAL TUMOURS (GIST):
A SINGLE CENTRE RETROSPECTIVE COHORT ANALYSIS**

Georgina E. Wood, MBBS MRCP BSc MSc PhD; Thomas Carter, MBChB MRCP BSc PhD; Michael Luong, BMedMD; Emma Jones, BMBS BSc; Beatrice Seddon, MBBS MRCP FRCR PhD; Palma Dileo, MD; Arjun Shankar, MBBS FRCS MD(Res); Vasilios Karavasilis, MD
London Sarcoma Service, Department of Oncology, University College London Hospitals, London, England, UNITED KINGDOM

Background: The majority of gastrointestinal stromal tumours (GISTs) are sensitive to treatment with the tyrosine kinase inhibitor imatinib. Patients with locally advanced disease require morbid surgery such as total gastrectomy or Whipple's procedure. Local London Sarcoma Service policy is for these patients to receive neoadjuvant imatinib, to reduce the tumour size and hence the need for multi-visceral resection. The optimal duration of therapy and the impact on surgical morbidity/feasibility needs to be elucidated.

Methods: We retrospectively analysed clinical data and multidisciplinary team (MDT) outcomes from adult GIST patients with locally advanced disease treated with neoadjuvant imatinib at our centre to identify response rates, duration of treatment and the impact of treatment on surgery.

Results: 42 patients with locally advanced disease that received imatinib with neoadjuvant intent were analysed, 21 (50%) of whom were male, with an age range of 32-93 years at diagnosis. Sites of disease included stomach 24 (57%), small bowel 4 (10%), large bowel 7 (17%) abdominal 4 (10%) oesophagus 2 (4%) and pelvic 1 (2%). KIT gene mutational analysis was available for 39 patients, with the majority possessing variants in exon 11 of c-KIT (35; 83%). 38 patients (90%) had a partial response to neoadjuvant imatinib.

Of these 42 patients, 25 patients proceeded to surgery, all except 2 of which had a partial response (one stable disease; one proceeded to surgery after 1 month of treatment). Reasons for not proceeding to surgery included patient choice, co-morbidities or a low likelihood of curative resection.

In 18 of the 25 (72%) patients who proceeded to surgery the tumour was downsized, most likely enabling a less extensive operation. Of these 18 patients, 7 patients had reduction in a gastric tumour that enabled sleeve or partial gastrectomy where initially total gastrectomy was judged to be required. Resection of other organs (spleen and/or pancreas) was avoided in 2 of these patients. For one rectal GIST patient, imatinib facilitated abdominoperineal (AP) resection where pelvic exenteration was judged necessary at diagnosis. One other rectal GIST patient avoided AP resection with an anterior resection. 2 patients were deemed inoperable at diagnosis and neoadjuvant imatinib meant that a resection was able to be undertaken. 2 patients remain on neoadjuvant imatinib.

Median duration of neoadjuvant imatinib for patients who proceeded to surgery was 11 months (range 1 – 38 months).

Conclusions: We have shown that for patients with locally advanced GIST, neoadjuvant imatinib has a positive impact on surgical outcomes with less morbid surgery in up to 40% of patients, after a median duration of 11 months of treatment. Recent ESMO guidelines support standard use of neoadjuvant imatinib if R0 surgery is not feasible, provided there is histological confirmation of a genotype that is sensitive to imatinib.



Poster #064 #1818875

RIPRETINIB DOSE ESCALATION IN ADVANCED GASTROINTESTINAL STROMAL TUMOR: A REAL-WORLD DATA

Philippos A. Costa, MD¹; Brianna Valdes²; Priscila Barreto Coelho, MD¹; Caroline Hana, MD¹; Steven Bialick, DO, MS³; Andrea Espejo-Freire, MD¹; Luyuan Li, PhD⁴; Jillian Lykon, PharmD, BCOP¹; Emily Jonczak, MD⁴; Gina D'Amato, MD⁵; Ty K. Subhawong, MD¹; Jonathan C. Trent, MD, PhD⁴

¹University of Miami, Miami, Florida, UNITED STATES, ²University of Miami, Miller School of Medicine, Miami, Florida, UNITED STATES, ³University of Miami/Sylvester Comprehensive Cancer Center, Miami, Florida, UNITED STATES, ⁴Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES, ⁵Medical Oncology, Sylvester Comprehensive Cancer Center/University of Miami, Miami, Florida, UNITED STATES

Objective: Despite an initial response, most patients with metastatic gastrointestinal stromal tumor (GIST) will ultimately be refractory to all current therapies, including imatinib, sunitinib, and regorafenib. After the results of the INVICTUS phase III trial (NCT03353753), ripretinib, a switch-control tyrosine kinase inhibitor (TKI) that broadly inhibits KIT and PDGFRA kinase, at 150 mg daily (QD) was approved by the Food and Drug Administration (FDA) for patients with advanced GIST refractory to at least three tyrosine kinase inhibitors (TKIs). Both in the INVICTUS trial and the phase I trial (NCT02571036), allowed patients receiving ripretinib at 150 mg QD with progressive disease (PD) were allowed to dose escalate to 150 mg twice a day (BID). Sub-analysis of the phase I trial and the INVICTUS trial showed that patients which ultimately received ripretinib at 150 mg BID achieved an additional progression-free survival (PFS) of 8.3 months when BID dosing was used as second- or third-line therapy (phase I trial), and 3.7-5.5 months when used as the fourth-line (INVICTUS and phase I). The safety profile was comparable to QD dosing.

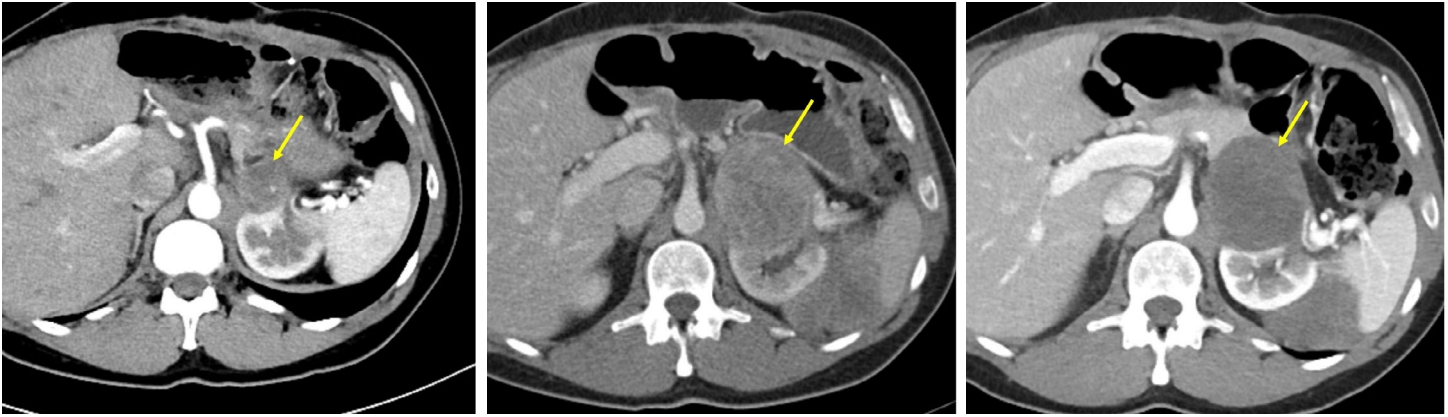
Randomized clinical trials (RCTs) focus on producing internally valid results with stringent adherence to protocol, but this may compromise external validity. Compared with RCTs, real world-data better reflects the clinical environments in which medical interventions are used, including demographics, comorbidities, adherence, and concurrent treatments. In this scenario, retrospective real-world data can complement the evidence generated by RCTs. Here we evaluate the tolerability and response of patients with GIST treated outside clinical trials with ripretinib dose escalation.

Methods: By searching the institution's clinical pharmacy database, we identified patients with locally advanced or metastatic GIST, which received ripretinib at 150 mg QD and 150 mg BID at a single center between 2019 and 2021. Clinicopathologic features were retrospectively reviewed. Treatment adverse effects were recorded according to the Common Terminology Criteria for Adverse Events, and treatment responses were documented according to Choi's criteria. Duration of response was calculated from the initiation of therapy until disease progression. PFS was estimated by the Kaplan-Meier method.

Results: A total of 8 patients with a median age of 59 at diagnosis (range 25-72) were identified. Three patients were male, and 5, female. The primary location was the stomach in 4 cases, small intestine in 3 cases, and unknown in 1 case. The median initial size at diagnosis was 15 cm (range 5.5 - 22), with a median mitotic index of 12.5 by HPF (0-50). Mutation analysis revealed kit exon 9 mutations in two patients and kit exon 11 in 6 patients. The median number of treatment lines before initiation of ripretinib 150mg QD was 3 (range 2-4), and ECOG status was 0 in 5 patients and 1 in 3.

While on ripretinib 150mg QD, the reported grade 1 adverse effects(G1) were: alopecia (n=4), hand-foot syndrome (n=2), fatigue (n=2), abdominal distention (n=1), allergic reaction (n=1), anemia (n=1), anorexia (n=1), arthralgia (n=1), cramping (n=1), and papulopustular rash (n=1). The grade 2 adverse effects(G2) were: anorexia (n=1), constipation (n=1), diarrhea (n=1), and weight loss (n=1). While on ripretinib 150mg BID, the reported G1 were: abdominal pain (n=1), alopecia (n=1), chills (n=1), fatigue(n=1), and skin hyperpigmentation (n=1). G2: arthralgia (n=1). Adverse effects were responsible for discontinuation of ripretinib in two patients. One while on QD (diarrhea) dosing and another while on BID (fatigue). Seven patients had scans available to assess response. Four (58%) patients achieved partial response by Choi criteria, two (28%) had progressive disease, and one maintains stable disease (14%). The mean PFS while on ripretinib BID was 4.3 months (95%CI 2.6-5.9).

Conclusion: Similar to the sub-analysis of the INVICTUS and phase I clinical trial, real-world data shows that dose escalation of ripretinib leads to objective responses in patients whose tumors progressed after standard dose. In our cohort, dose escalation also was also well tolerated with similar toxicity profile than then daily dose. Future studies are needed to assess when dose escalation would be most appropriate: after progression on the standard dose, as a ripretinib re-challenge after a different agent, or even initially in a subset of patients harboring specific mutations or clinical characteristics.



Mitotic index	Mutation Analysis	ECOG at Initiation of Ripretinib 150mg BID	Previous Number of Lines of Therapy In the Metastatic Setting Before Ripretinib (No surgery, radiation or interventional)	Side Effects while on QD	Side Effects, Grade, QD/BID:	Any Drug Interruption, Reduction or AE leading to discontinuation QD/BID?	Imaging best response	Duration of response (months)	Survival
5	KIT exon 9	0	0	Constipation G2, Anemia G1, Anorexia G2, 3 Weight Loss G2	None	No	PR	6	Alive
2	KIT exon 9	0	0	Hearing Loss G1, Alopecia G1, Hand-Foot G1, 3 Cramping G1	Fatigue G1	No	PD	2	Alive
20	Kit exon 11, kit exon 13 and kit exon 17	1	1	3 Diarrhea G2, Alopecia G1, Fatigue G1	None	Yes, diarrhea, QD	PR	3	Alive
0	Kit exon 11	0	0	3 Fatigue G1	Allopecia G1	No	PR	5	Alive
50	Kit exon 11 and exon 13	1	1	4 Alopecia G1, Allergic Reaction G1	None	Yes, fatigue, BID	No scans available	1	Dead
22	Kit exon 11 and 13	0	0	2 None	None	No	PD	0	Alive
0	Kit exon 11	1	1	Abdominal distention G1, Arthralgia G1, 3 Papulopustular rash G1	Skin Hyperpigmentation G1, Chills G1, Arthralgia G2	No	PR	2 (ongoing)	Alive
33	Kit exon 11	0	0	3 Alopecia G1, Loss of Appetite G1	Palmar-plantar G1, Abdominal Pain G1	No	SD	3 (ongoing)	Alive



Poster #066 #1819082

HETEROGENOUS INTERTUMORAL KIT MUTATIONS FOUND IN LONG-TERM STAGE 4 GASTROINTESTINAL STROMAL TUMOR SURVIVOR

Seiya Liu¹; Ty K. Subhawong, MD²; Andrew Rosenberg, MD³; Jonathan Trent, MD⁴; Emily Jonczak, MD⁵; Elizabeth Montgomery, MD²; Alan Livingstone, MD⁶; Gina D'Amato, MD⁷

¹University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES, ²University of Miami, Miami, Florida, UNITED STATES, ³Department of Pathology, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES, ⁴Sylvester Comprehensive Cancer Center, Miami, Florida, UNITED STATES, ⁵Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES, ⁶Department of Surgery, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES, ⁷Medical Oncology, Sylvester Comprehensive Cancer Center/University of Miami, Miami, Florida, UNITED STATES

Objective: Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal neoplasm of the gastrointestinal tract. Immunohistochemistry has identified KIT or PDGFRA as targets of primary activating mutations in 85% of reported GISTs. As such, CD117 (c-Kit) arises as a reliable immunohistochemical diagnostic tool. The development of next-generation sequencing (NGS) technology has also improved the detection of gene alterations in tumor-specific gene sequences, identifying new gene variations in KIT-expressing GISTs. These identifiable and targetable mutations have led to the successful deployment of tyrosine kinase inhibitors (TKIs) such as imatinib, sunitinib, regorafenib, and ripretinib for treatment of KIT-positive, KIT-exon-mutant, or PDGFRA-positive GISTs. In terms of clinical management, it is of utmost importance to assess patient-specific and local tumor-specific GIST mutations for risk of resistance to existing therapies due to variations in molecular subsets.

Methods: A 54-year old male with a past medical history of large intraabdominal GIST presented to the emergency room with anemia and computed tomography (CT) work-up revealing a large mass adherent to the small bowel with associated pelvic ascites and carcinomatosis. The mass measured 22 cm and was found to be c-Kit and exon 9 mutation positive with extensive necrosis and a mitotic rate of 17 per 50 high-power field (hpf). With a diagnosis of GIST from the omentum, the patient underwent surgical resection of the abdominal wall mass and partial omentectomy, which revealed metastatic disease. With metastatic disease, he was initially started on imatinib. Due to progression of disease after 6 months, he was transitioned to sunitinib, initially 50 mg regimen daily for four weeks on and 2 weeks off, then to 37.5 mg continuous regimen due to side effects. With sunitinib he had chronic hand-foot skin reaction and diarrhea, for which he took a three-day break per month to alleviate his symptoms. He additionally used urea cream for his hands and feet, as well as Imodium and loperamide for diarrhea relief. He was followed with elevated transaminases, elevated ferritin, and iron saturation, but with no full diagnosis of hemochromatosis due to history of fatty liver and improved iron levels after ceasing alcohol intake. He received phlebotomies for symptom relief. After eight years of use with stable disease, a PET-CT scan revealed three enlarging omental peritoneal implants on the right side of the abdomen, with the largest measuring 3.4 x 2.3 cm compared to 1.4 x 1.2 cm previously, alongside a SUV uptake value of 11.7, increased from 5.0. The patient underwent metastasectomy, excising residual metastatic GIST in the space of the retropubic space (retzius), omentum, as well as removal of a left upper quadrant implant and Trucut biopsy of the left liver lobe.

Results: Of note, molecular profiling (Caris Life Sciences TM) was conducted for each excised tumor rather than the standardized practice of only assessing one site. Two omental implants demonstrated different kit exon variations on exon 17, exon 9, and exon 1, that would both benefit from regorafenib but have resistance to imatinib and sunitinib. One pelvic peritoneum implant demonstrated kit exon 9 and 13 variance, while another retroperitoneal implant showed kit exon 9 variance. Both peritoneal implants were recommended positive benefit potential with use of imatinib, sunitinib if imatinib-refractory, or regorafenib if imatinib/sunitinib-refractory. Guardant 360® CDx liquid biopsy testing for comprehensive tumor mutation profiling revealed 0.2% cfDNA of TP53 R248W alteration with no microsatellite detection and no associated effective therapies and did not show the presence of any kit mutations. Ascending colon implants and left liver lobes were deemed negative for malignancy, while the other excised tumors were consistent with GIST. Four months after surgery, he developed ulcerative skin lesions outside the heels of both feet, as well as elevated liver function test (LFT) values and testicular swelling. As such, sunitinib administration was put on hold and other treatment modalities were considered. Due to progression and worsening symptoms, the patient was switched to third-line treatment, regorafenib, at 160mg daily. However, poor tolerance in the

first week of treatment led to the dose decreasing to 120 mg for one week before returning to the original dose. In the 18 days of regorafenib treatment, patient reported complete loss of appetite and associated weight loss of five pounds, severe fatigue, skin sensitivity and redness in the upper extremities bilaterally, pain and swelling in the left knee, skin blisters in the heel bilaterally, chills and shivering, and a fever of 104.8 Fahrenheit. Symptoms were resolved after withholding treatment.

Conclusion: This 54-year old male GIST patient demonstrates the importance of conducting NGS on multiple metastatic sites. Given the heterogenous exon mutations at each local tumor location, clinical management would be dramatically different without the relevant knowledge of exon-specific resistances. The development of disease progression and metastatic implants despite multiple years of stable disease with sunitinib demonstrates the importance of follow-up, imaging, and NGS of resected tumors. If metastatic implants have heterogenous exon mutations, as is the case of this patient, the clinical approach must change appropriately to effectively control further disease progression. Of particular interest, the omental implants with KIT exon 17, exon 9, and exon 1 mutations, respectively, grew the most aggressively compared to the other pelvic peritoneum and retroperitoneal implants with KIT exon 9 and 13 mutations. Exon 17 mutations are most associated with small intestine GIST with no difference in clinical prognosis compared to non-KIT-mutated GISTs. However, the largest implant with KIT exon 17 and 9 mutations is consistent with previous studies that outlined the aggressiveness of non-gastric exon 9 mutated tumors. KIT exon 13 mutations are more common in secondary imatinib resistance, presenting more aggressively in gastric locations, but no different than other small intestinal GISTs when in the small intestines. The KIT exon mutations present in the implants are consistent with expected growth patterns, with non-gastric, omental exon 9 expression demonstrating the most explosive growth and the non-gastric retroperitoneal and pelvic peritoneum implants with KIT exon 9 and 13 mutations demonstrated lower levels of growth and smaller size compared to the omental implants. Improved understanding of kit mutations will lead to improved outcomes. Discovering agents that will target the current TKI resistance mutations is therefore of utmost importance.



Poster #067 #1818898

A DANISH EXPLORATIVE STUDY OF CIRCULATING TUMOUR DNA PRE- AND POSTOPERATIVE SAMPLES FROM PATIENTS WITH GASTROINTESTINAL STROMAL TUMOUR

Charlotte Margareta Brinch, MD¹; Estrid Høgdall, Prof., PhD, DMSc²; Ninna Aggerholm Pedersen, MD, MSc, PhD³; Pieter de Heer, PhD⁴; Anders Krarup-Hansen, PhD⁵,

¹Department of Oncology, Copenhagen University Hospital, Herlev and Gentofte Hospital, Herlev, Denmark, Copenhagen, Hovedstaden, DENMARK, ²Department of Pathology, Copenhagen University Hospital, Herlev and Gentofte Hospital, Herlev, Denmark, Copenhagen, Hovedstaden, DENMARK, ³Aarhus University Hospital, Aarhus, Denmark, Aarhus, Midtjylland, DENMARK, ⁴Rigshospitalet, Copenhagen, Denmark., Copenhagen, Hovedstaden, DENMARK, ⁵Department of Oncology, Copenhagen University Hospital, Herlev and Gentofte Hospital, Herlev, Denmark, Copenhagen, Hovedstaden, DENMARK

Objective: Circulating tumour DNA (ctDNA) has shown promising results within several cancer types, such as lung and colorectal cancer. A phase III GRID trial by Georg Demetri et al. (2013) showed 84% concordance between KIT mutations in tissue and plasma in patients with Gastrointestinal Stromal Tumour (GIST) (1). Other studies on GIST have described a correlation between the amount of ctDNA and clinical response (2).

In a study by Frank Diehl et al. (2010), ctDNA was analyzed in blood from patients with colorectal cancer taken during surgery. The study found that the total amount of DNA in plasma (normal- and tumour) increased immediately after resection in all patients, most likely due to surgically induced tissue damage. The relapse rate was significantly higher for patients with sustained measurable ctDNA at the first follow-up visit after surgery (3).

The objectives of this study are to investigate

- the correlation between gene mutation analyses of corresponding ctDNA and tissue samples.
- if ctDNA is detectable postoperative compared to pre-operative.
- if the amount of ctDNA decrease during neoadjuvant treatment with imatinib.

Methods: This explorative study includes patients with GIST ≥ 4 cm evaluated on CT-imaging or by pathologist, planned for primary surgery or patients planned for surgery after neoadjuvant treatment with the tyrosine kinase inhibitor, imatinib, Rigshospitalet, Copenhagen.

EDTA blood samples, 36 ml, are collected before surgery and one day after surgery. Extraction of circulating free DNA (cfDNA) will be performed by QIASymphony. C-KIT and PDGFR α mutated sequences of ctDNA will be analyzed using Next Generation Sequencing (NGS).

DNA from the patients' tissue samples will be used for exome sequencing of all coding sequences in eleven genes, including c-KIT and PDGFR α with NGS.

Results: From July 2019 to June 2021, nine patients were included. The inclusion period ends in July 2021. We have not yet analyzed ctDNA, but we aim to have the results at CTOS 2021.

Patient and tumour characteristics of the included patients are showed in table II. Two of the patients have undergone surgery after neoadjuvant treatment with imatinib, where we collected blood samples during the neoadjuvant treatment.

Conclusion: In this explorative study, we aim to investigate the value of measuring ctDNA pre-and postoperatively. ctDNA can aid in the selection of patients to offer neoadjuvant treatment to as well as helping in evaluation of response to the neoadjuvant treatment and thereby the optimal timing of surgery.

Table I
References

1	Demetri GD JM, Reichardt P, Kang Y, Blay JY, Rutkowski P et.al. . Mutational analysis of plasma DNA from patients (pts) in the phase III GRID study of regorafenib (REG) versus placebo (PL) in tyrosine kinase inhibitor (TKI)-refractory GIST: Correlating genotype with clinical outcomes [abstract 10503]. J of Clin Oncol. 2013;31(15_suppl).
2	Maier J, Lange T, Kerle I, Specht K, Bruegel M, Wickenhauser C, et al. Detection of mutant free circulating tumor DNA in the plasma of patients with gastrointestinal stromal tumor harboring activating mutations of CKIT or PDGFRA. Clinical cancer research: an official journal of the American Association for Cancer Research. 2013;19(17):4854-67.
3	Diehl F, Schmidt K, Choti MA, Romans K, Goodman S, Li M, et al. Circulating mutant DNA to assess tumor dynamics. Nat Med. 2008;14(9):985-90.

Table II
Patient- and Tumor Characteristics

Characteristics	No. of Patients (%), n=9
Sex	
Male	3 (33)
Female	6 (67)
Age, years	
Median	76
Range	52-81
Primary tumor site	
Ventricle	8 (89)
Small intestine	1 (11)
Size of primary tumor, cm ^(a)	
≤5	4 (44)
>5, ≤10	4 (44)
>10	1 (11)
Mitotic count per 50 HPF ^(b)	
≤5	6 (67)
>5	3 (33)
Treatment	
Surgery alone	7 (78)
Neoadjuvant treatment	2 (22)
Mutations in c-KIT and PDGFR α in tissue	
c-KIT exon 11	7 (78)
c-KIT exon 13	1 (11)
PDGFR α exon 14	1 (11)

^(a) The longest tumor diameter measured on CT imaging

^(b) High power fields (HPF)



Poster #068 #1819053

INTRAOPERATIVE NEAR-INFRARED FLUORESCENCE IMAGING WITH INDOCYANINE GREEN FOR IDENTIFICATION OF GASTROINTESTINAL STROMAL TUMOURS; PRELIMINARY RESULTS OF A CLINICAL TRIAL

Gijsbert M. Kalisvaart, MD¹; Ruben P. Meijer, MD²; Okker D. Bijlstra, MD²; Hidde A. Galema, MD³; Wobbe O. de Steur, MD²; Henk H. Hartgrink, MD PhD²; Yvonne M. Schrage, MD PhD²; Dirk J. Grünhagen, MD PhD³; Lioe-Fee de Geus-Oei, MD PhD²; Alexander L. Vahrmeijer, MD PhD²; Jos A. van der Hage, MD PhD²
¹LUMC, Leiden, Zuid-Holland, NETHERLANDS, ²Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ³Erasmus MC Cancer Institute, Rotterdam, Zuid-Holland, NETHERLANDS

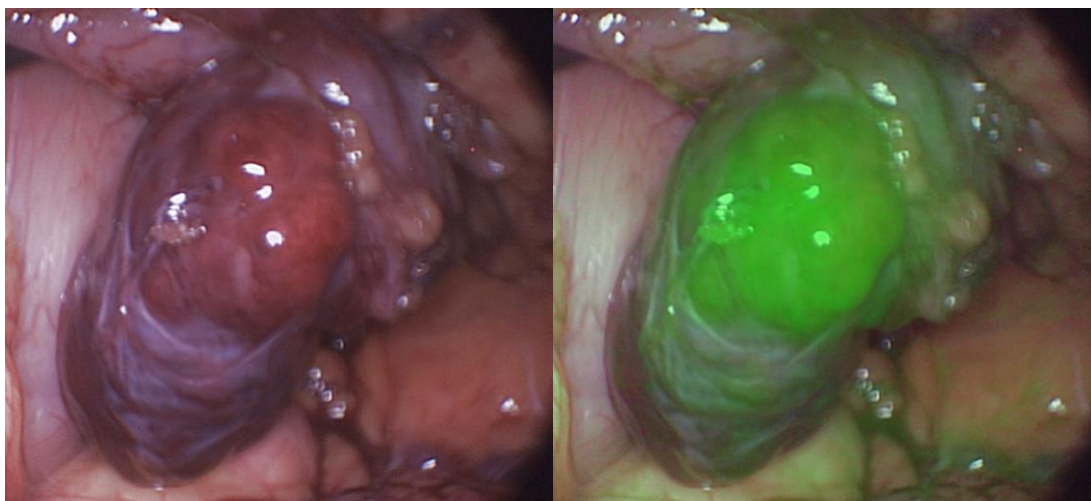
Objective: Surgical resection is pivotal in treatment of most gastrointestinal stromal tumors (GISTs). Accurate intraoperative tumor identification can be challenging, especially during minimally invasive procedures and in the case of endoluminal tumor growth. This study aims to explore the use of indocyanine green (ICG) guided near-infrared (NIR) fluorescence imaging for the intraoperative identification of GISTs.

Methods: Ten GIST patients planned for open or laparoscopic resection will be included. During surgery 10 mg of ICG is intravenously administered and NIR fluorescence imaging is performed according to a step-up step-down protocol allowing experience-based shifts in imaging timepoints. Tumor enhancement is primarily scored on visual assessment. Tumor-to-background ratios (TBRs) are calculated by dividing the mean pixel intensities of the tumor annotation by the background on the corresponding fluorescence image.

Results: Nine patients have been treated in this study. Tumor enhancement is visually scored as more intense than the background in 3 patients. In 4 patients tumor enhancement was similar as the background. In 2 patients no tumor enhancement was observed. The mean TBR in all GIST lesions was 1.29 (range = 1.10–1.87) and was highest at 10 minutes after ICG administration.

Conclusion: GISTs show enhancement in intraoperative NIR imaging using ICG. However, intertumoral TBRs are varying and overall enhancement is not specific for tumor tissue. Therefore, intraoperatively administered ICG is currently not applicable for adequate tumor identification and further research should focus on development of tumor specific fluorescent tracers for GISTs.

Figure 1 | Intraoperative laparoscopic images of an exophytic gastric GIST in bright light (left) and ICG-fluorescence imaging (right).





Poster #069 #1819022

ENGINEERED BONE MARROW: A NOVEL MODEL TO INVESTIGATE EARLY OSTEOSARCOMA PROGRESSION

Steven W. Thorpe, MD¹; Katherine Griffin, BS²; R. Lor Randall, MD³; Kent Leach, PhD³, ¹University of California Davis, Sacramento, California, UNITED STATES, ²University of California, Davis, Davis, California, UNITED STATES, ³University of California, Davis, Sacramento, California, UNITED STATES

Objective: Osteosarcoma (OS) is the most common primary malignant bone cancer in children and adolescents. Despite its prevalence, the standard treatment has remained unchanged for 4 decades and offers less than a 25% 5-year survival rate for those with metastatic disease. This mandates a critical need to develop novel therapeutic targets for OS. This will only be possible once we have a better grasp of the initial progression and metastagenesis of this still poorly understood disease. Current OS in vitro models fail to account for important components of the bone marrow environment, including the three-dimensional (3D) nature of sarcomas, the physiological oxygen tension of bone marrow (5%), and the spatial and cellular heterogeneity of bone marrow. This complexity of OS and lack of improvement in treatment outcome necessitate the study of this disease in a novel system.

Here, we aim to adapt and further develop a previously described engineered bone marrow (eBM) construct for use as an improved in vitro model for the study of OS. eBM recapitulates the heterogeneous cell population found in native bone marrow, therefore addressing many of the current in vitro model shortcomings. However, we hypothesize that altering the anatomical implantation site for eBM formation will improve the quality of generated tissue. We also describe early OS loading studies that demonstrate how these constructs will provide a novel 3D platform to study OS tumor progression in future experiments.

Methods: Bone-inducing constructs were assembled by filling polydimethylsiloxane (PDMS) molds with demineralized bone matrix, Type I collagen, and BMP-2 and BMP-4. Constructs were implanted subcutaneously (SQ) or subfascially (SF) in C57BL/6 or CD-1 mice as shown (Figure 1). Constructs were harvested after 8 weeks, and eBM was removed from the PDMS molds. eBM was evaluated immediately or maintained under dynamic culture conditions with SFEM basal medium. Tissue quality was evaluated histologically with H&E and immunohistochemical (IHC) staining for OCN and CD31. Due to improved tissue quality, further studies proceeded with SF constructs only. Flow cytometric analysis was performed for hematopoietic stem cells and progenitors. A highly metastatic OS cell line, K7M2, was loaded into samples and cultured under 21% and 5% O₂ for 1 to 8 days. Metabolic activity and flow cytometry for macrophage populations, indicative of the immune microenvironment, were evaluated.

Results: Gross differences in eBM formed within different anatomical locations were appreciated. Generally, SF constructs appeared more vascularized, whereas SQ constructs appeared to contain more adipose tissue and less vascularization (Figure 1). IHC revealed increased OCN expression in subcutaneous constructs of both mouse species, and vascularization indicated by CD31 staining was most evident in SF constructs in CD-1 mice (Figure 2A and 2B). Further flow cytometric characterization revealed that eBM progenitor cell populations were analogous with native mouse bone marrow and that maintenance in ex vivo culture was most stable under normoxic (5% O₂) conditions (Figure 2C). eBM loaded with K7M2s exhibited decreased metabolic activity over time only when cultured under 21% O₂ (Figure 3), and macrophages of M1 polarization decreased over time under all conditions whereas M2 populations did not change (Figure 4).

Conclusion: These data demonstrate that we can alter eBM formation to more closely resemble native bone marrow compared to previously published methods. This model provides a tunable biomaterial that can be applied to any disease process involving the bone marrow with comparable cell populations and 3D tissue structure. Moreover, this model facilitates the enhanced study and understanding of OS pathophysiologic progression that leads to metastagenesis, and will thus advance the treatment of human and canine patients afflicted by OS.

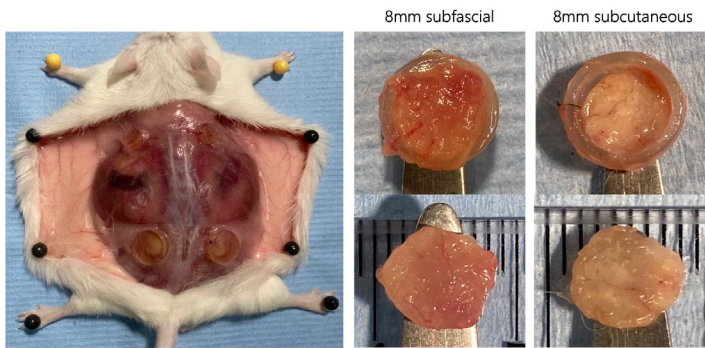


Figure 1. Gross images of 8-week eBM explants in CD-1 mouse. Whole animal (left), and 8mm explants (right). Constructs within PDMS molds (above), eBM removed from PDMS molds (below).

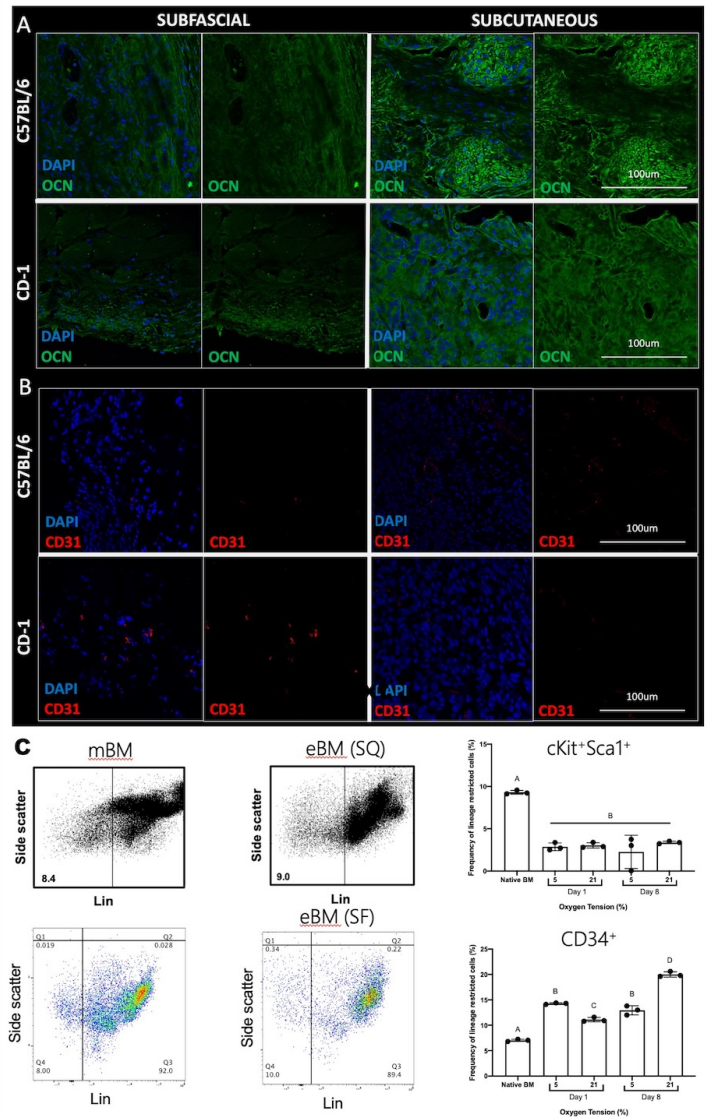


Figure 2. Representative images of (A) OCN (green) and (B) CD31 (red) staining with DAPI (blue) counterstaining of eBM immediately after explantation. Scale bar is 100 μ m. (C) Representative flow plots and quantification of eBM progenitor cell populations after 1 and 8 days in culture under ambient air (21% O₂) and normoxic (5% O₂) conditions compared to native mouse bone marrow. Data presented as mean \pm SD. Letters denote statistical significance between groups.

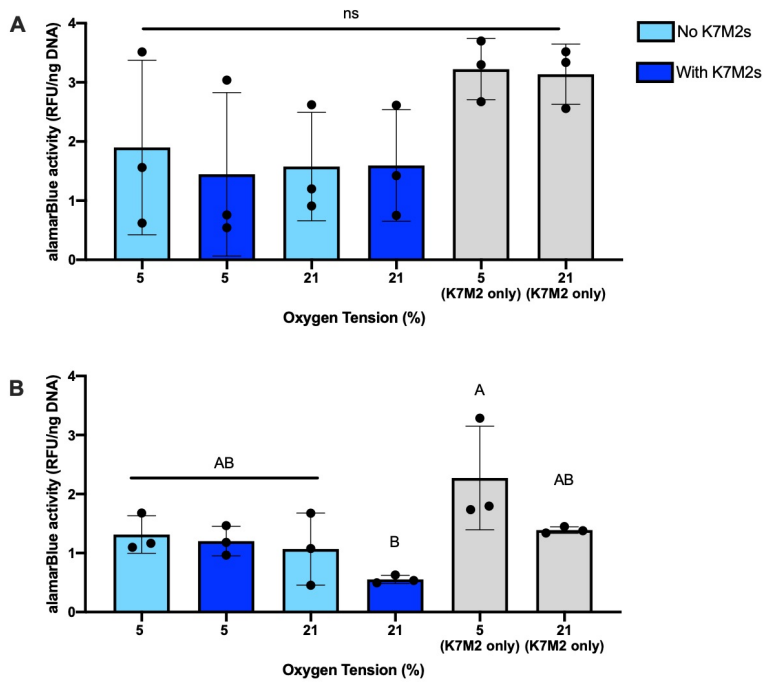


Figure 3. alamarBlue activity normalized to DNA content of eBM loaded with K7M2 cells cultured under ambient air (21% O₂) and normoxic (5% O₂) conditions at (A) Day 1 and (B) Day 8 timepoints. K7M2s in monolayer were used as a control. Data presented as mean ± SD. Letters denote statistical significance between groups.

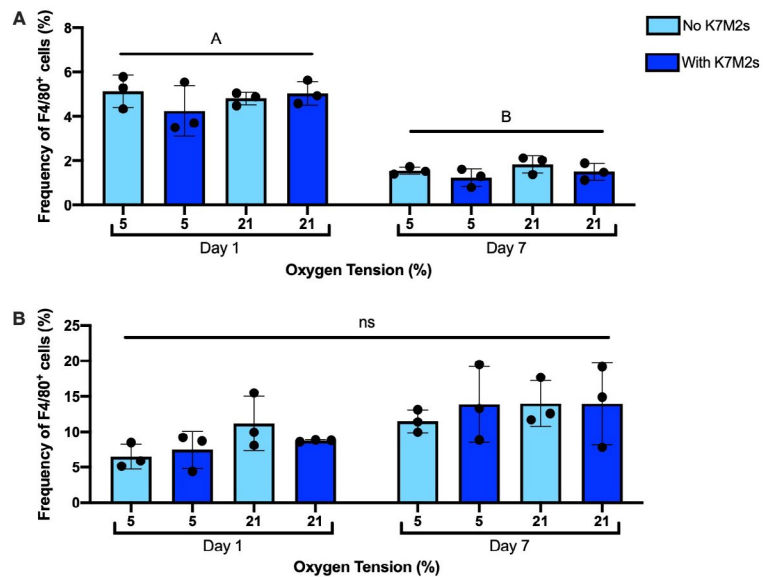


Figure 4. Flow cytometric analysis of macrophage polarization within eBM loaded with K7M2 cells cultured under ambient air with K7M2 cells cultured within ambient air with K7M2 cells cultured under ambient air (21% O₂) and normoxic (5% O₂) conditions. (A) M1 populations, CD86⁺ and (B) M2 populations, CD206⁺ cells were evaluated Day 1 and Day 7 timepoints. Data presented as mean ± SD. Letters denote statistical significance between groups.



Poster #070 #1819018

LONG-TERM INHIBITION OF PARP SENSITIZES A THREE-DIMENSIONAL CHONDROSARCOMA MODEL TO CHEMO- AND RADIOTHERAPY

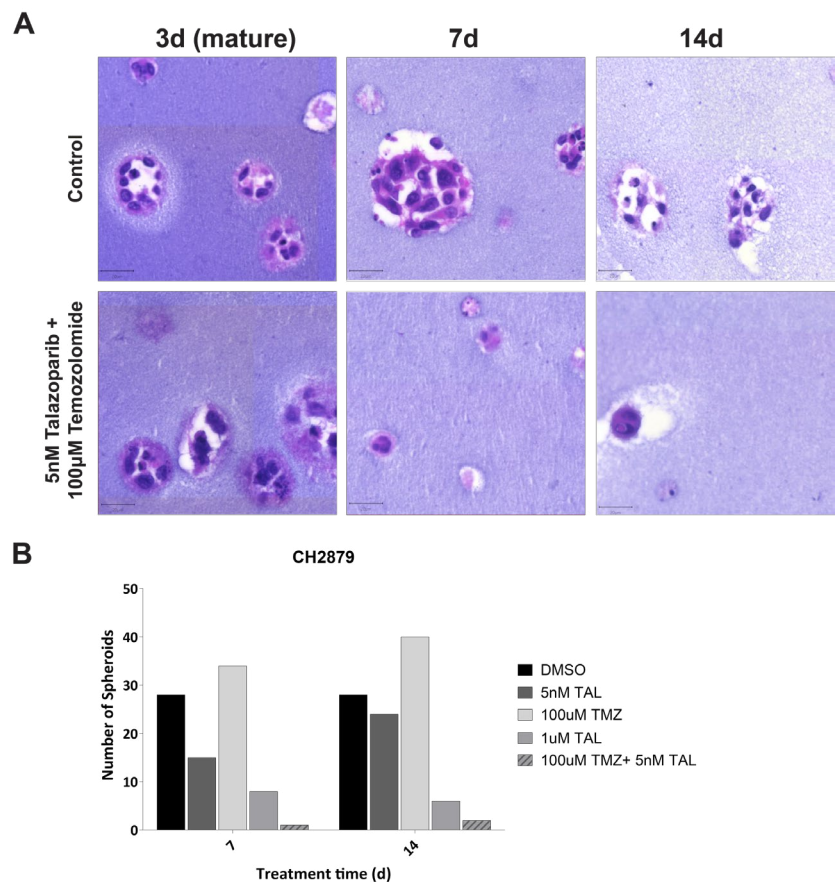
Ieva Palubeckaite, PhD; Sanne Venneker, MSc; Brendy E. van den Akker; Inge H. Briare - de Bruijn; Judith V.M.G. Bovée, MD PhD
 Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS

Objective: Chondrosarcoma tumors display a variable clinical behavior leading to an approximate 5-year survival rate of 74–99% for grade II and 31–77% for grade III chondrosarcoma patients. Low survival rates for high grade chondrosarcoma patients are a result of their low response rate to conventional therapy and their high metastatic potential. Currently, the only curative treatment for chondrosarcoma is surgical removal. Around 50% of conventional central chondrosarcomas, harbor an NADP+-dependent isocitrate dehydrogenase 1/2 (IDH1/2) enzyme mutation, making it the most common genetic abnormality within this neoplasm. These mutations are associated with various human malignancies, including gliomas, cholangiocarcinoma and acute myeloid leukemia (AML), where they appear to occur in early oncogenesis. DNA repair defects and synthetic lethality with poly(ADP-ribose) polymerase (PARP) inhibition occur in IDH mutant glioma and leukemia models. Therefore, sensitization to chemo- and radiotherapy using PARP inhibition was previously applied to conventionally cultured chondrosarcoma cell lines. The study indicated that talazoparib treatment (PARP inhibitor) combined with temozolomide or radiation were promising therapeutic strategies for chondrosarcoma, irrespective of IDH mutation status. We assessed the effect of the combination therapies further using our more representative alginate spheroid model.

Methods: Three chondrosarcoma cell lines, CH2879, JJ012 and SW1353, were cultured in alginate beads as clonal spheroids. The spheroids were either treated throughout growth for 7/14 days or cultured for 14 days to maturity then treated for 3 days. Treatment was performed with talazoparib or temozolomide alone as well as combination of the two. Cell viability was assessed using a Presto blue assay and 3D colony counting. Immunohistochemical stains (Ki67 and cleaved caspase-3) were performed to assess changes in spheroid proliferation and apoptotic levels. Combination of radiotherapy and talazoparib combination treatment was additionally assessed by 3D colony formation assay following one dose of radiation (0-6 Gy) at day 1 and treatment with talazoparib on day 1 and 8. The samples were harvested and assessed after 14 days.

Results: Effectiveness of spheroid treatment with talazoparib alone was greatly increased at longer treatment times (7 and 14 days) in all three cell lines, allowing for a reduction in treatment concentration. Treatment time dependent synergy was observed when combining talazoparib and temozolomide and was also increased with longer treatment times (Fig 1A). In all three cell lines, 14 day chemotherapy combination treatment was most effective at reducing cell viability and spheroid number (Fig 1B). Radiotherapy in combination with talazoparib was synergistic in only the JJ012 cell line and produced variable results in the other cell lines.

Conclusion: Assessment of combination therapies identified long-term talazoparib therapy



or talazoparib and temozolomide combination therapy as effective at reducing spheroid viability and number in all three chondrosarcoma cell lines. Further testing would be required to confirm whether to pursue radiotherapy combination treatment in a chondrosarcoma subset. The effect of the talazoparib and temozolomide combination on spheroids is promising, providing a rationale and information for further in vivo testing.



Poster #071 #1818979

PROGNOSTIC AND THERAPEUTIC VALUE OF T-LYMPHOKINE-ACTIVATED KILLER CELL-ORIGINATED PROTEIN KINASE (TOPK) IN OSTEOSARCOMA

Pichaya Thanindratarn, MD¹; Zhenfeng Duan, MD, PhD²; Francis J. Hornicek, MD, PhD²; Scott D. Nelson, MD³; Arun Singh, MD⁴; Noah C. Federman, MD⁵; Dylan Dean, MD²

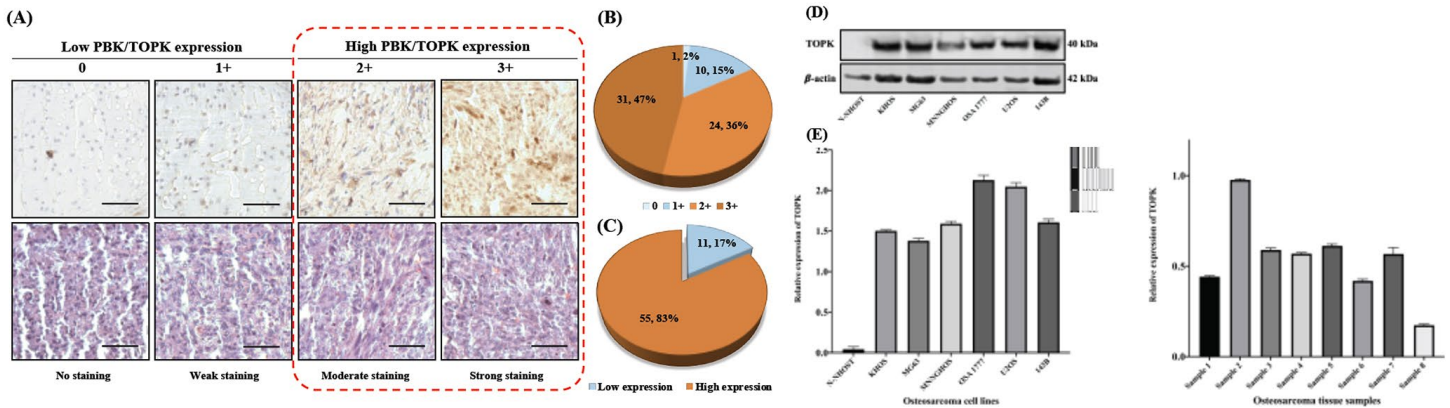
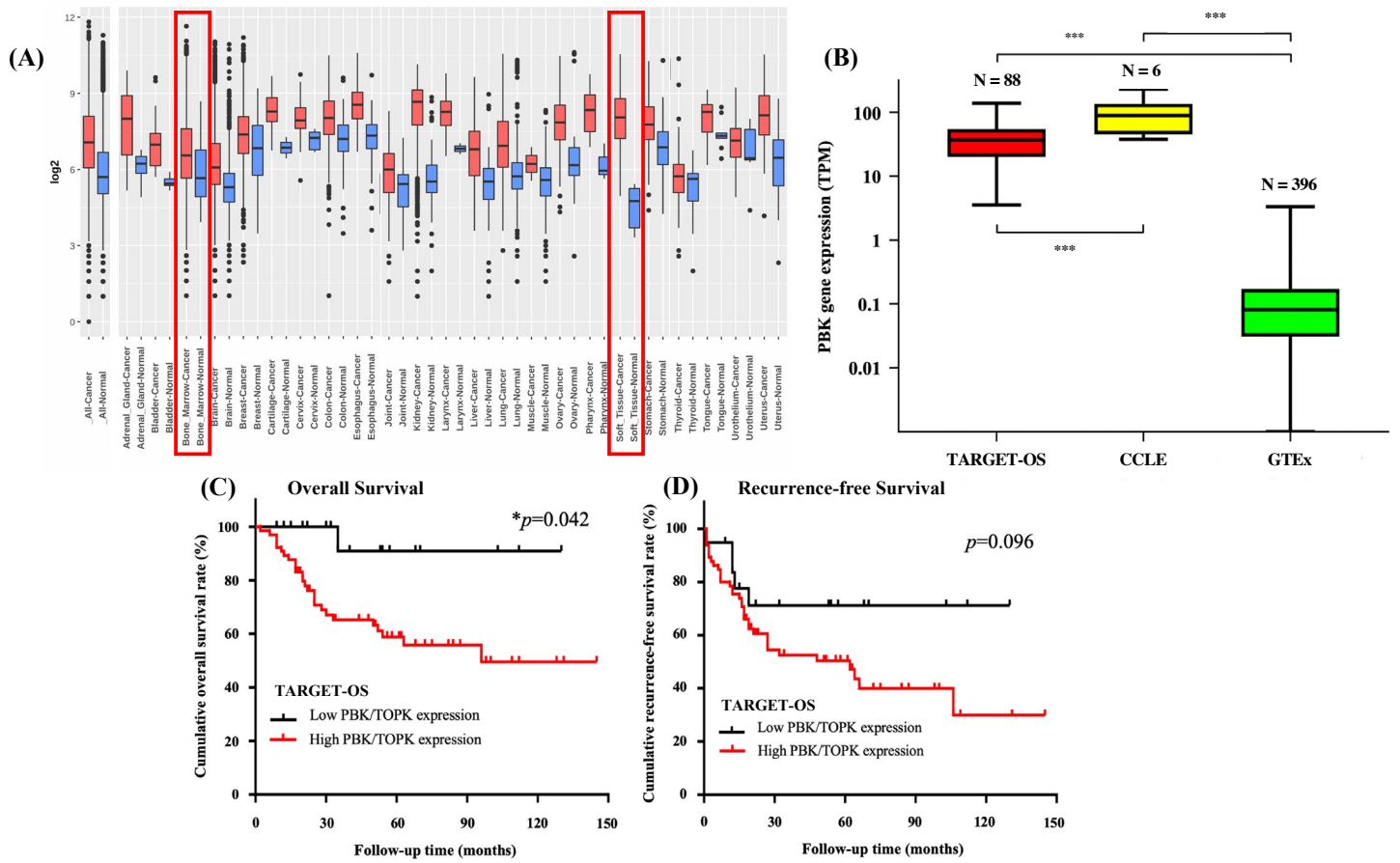
¹Department of Orthopedic Surgery, Chulabhorn Hospital, HRH Princess Chulabhorn College of Medical Science, Chulabhorn Royal Academy, Bangkok, Krung Thep, THAILAND, ²Department of Orthopaedic Surgery, David Geffen School of Medicine at UCLA, Los Angeles, California, UNITED STATES, ³UCLA Medical Center, Santa Monica, California, UNITED STATES, ⁴University of California, Los Angeles, Santa Monica, California, UNITED STATES, ⁵UCLA Medical Center, Los Angeles, California, UNITED STATES

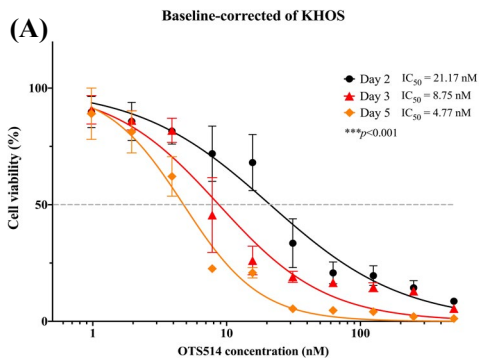
Objective: T-lymphokine-activated killer (T-LAK) cell-originated protein kinase (TOPK) is an emerging target with critical roles in various cancers; however, its expression and function in osteosarcoma remain unexplored. Therefore, we assessed its expression, clinical prognostic value, and functional role in osteosarcoma.

Methods: Expression of TOPK was evaluated using RNA sequencing and gene expression data from public databases (TARGET-OS, CCLE, GTEX, and GENT2). We subsequently confirmed this bioinformatic data with immunohistochemistry in an osteosarcoma tissue microarray (TMA), and explored possible correlations between TOPK expression and patient clinical characteristics. After finding TOPK overexpression in osteosarcoma cell lines and patient tissues via western blot, we reduced TOPK expression in the cell lines with small interfering RNA (siRNA) and the selective inhibitor OTS514 and analyzed markers of pathogenesis. The effects of TOPK expression on osteosarcoma cell clonogenicity and migration were also investigated using clonogenic and wound healing assays, respectively. We used a 3D cell culture to model in vivo osteosarcoma growth and validate the effects of TOPK inhibition in a more predictive environment.

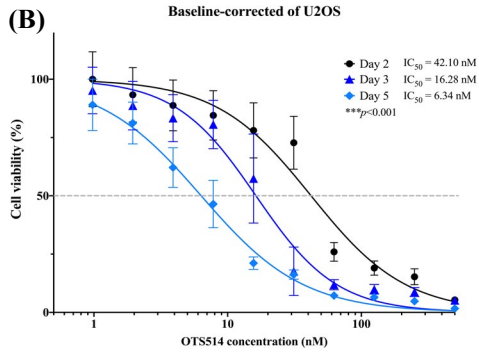
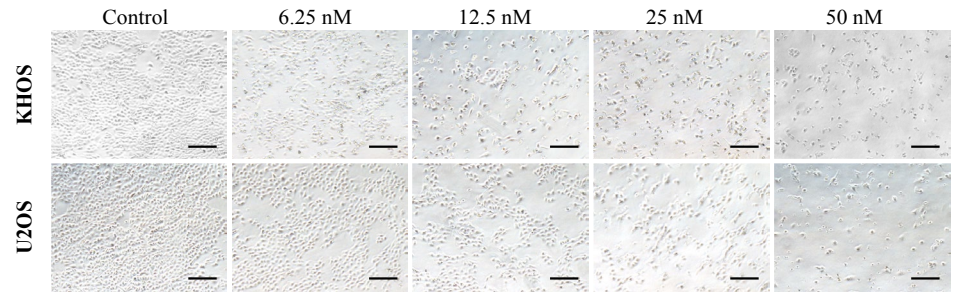
Results: TOPK gene expression was significantly higher in osteosarcoma than normal tissues and directly correlated with shorter overall survival. TOPK was overexpressed and validated in 83.3% of the osteosarcoma specimens within our TMA and all osteosarcoma cell lines, while normal osteoblast cells had no aberrant expression. High TOPK expression correlated with metastasis, disease status, and shorter overall survival. Silencing of TOPK with siRNA decreased cell viability, and inhibition with OTS514 suppressed osteosarcoma cell growth, proliferation, migration, colony-forming ability, and spheroid growth. Enhancing of chemotherapeutic sensitivity and a synergistic effect was also observed in the combination of OTS514 and either doxorubicin or cisplatin treating osteosarcoma cells.

Conclusion: High expression of TOPK is an independent predictor of poor prognosis in osteosarcoma patients. Our findings strongly support the biological and clinical importance of TOPK in osteosarcoma as a novel prognostic biomarker and target for personalized therapy.

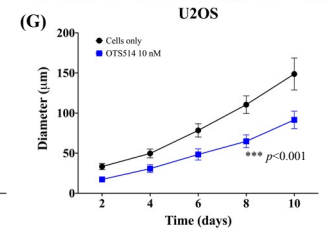
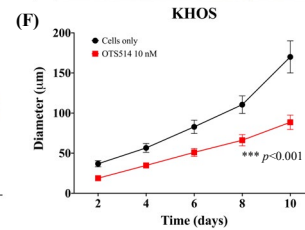
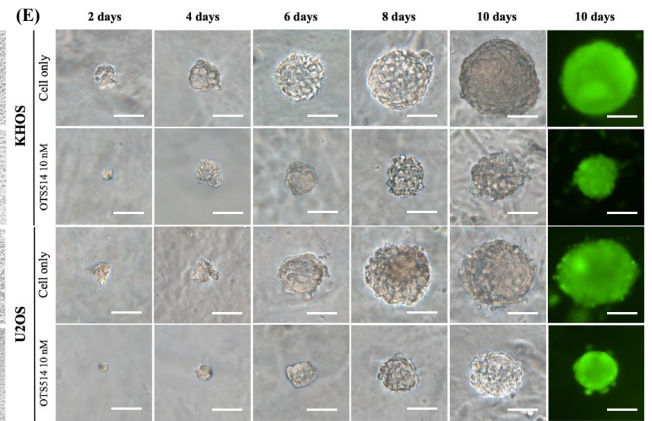
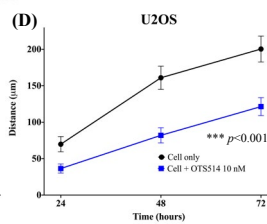
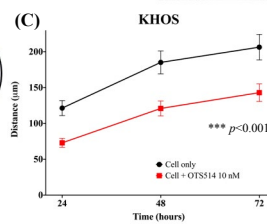
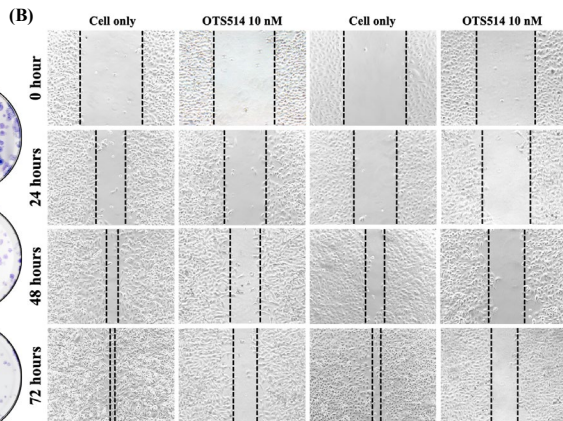
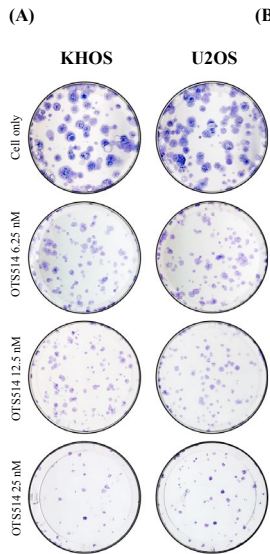
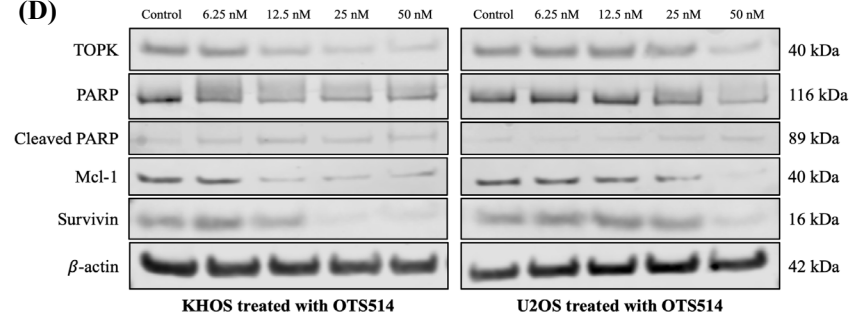




(C)



(D)





Poster #072 #1818997

UPDATED OUTCOMES FOR PATIENTS WITH COMPLETELY RESECTED PULMONARY RECURRENT OSTEOSARCOMA: A REPORT FROM THE CHILDREN'S ONCOLOGY GROUP

Alexander J. Chou, MD¹; Mark D. Krailo, PhD²; Ruxu Han, MS³; Allen Buxton, MS³; Damon R. Reed, MD⁴; Richard Gorlick, MD⁵; Steven G. DuBois, MD⁶; Michael Isakoff, MD⁷; Katherine A. Janeway, MD⁶; Pooja Hingorani, MD⁵, ¹Weill Cornell Medicine, NY, New York, UNITED STATES, ²Department of Preventive Medicine, Keck School of Medicine of the University of Southern California, Los Angeles, California, UNITED STATES, ³Children's Oncology Group, Monrovia, California, UNITED STATES, ⁴Moffitt Cancer Center, Tampa, Florida, UNITED STATES, ⁵MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁶Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, Massachusetts, UNITED STATES, ⁷Connecticut Children's Medical Center, Hartford, Connecticut, UNITED STATES

Objective: Amongst patients with recurrent osteosarcoma (OS), those with resectable pulmonary-only relapse appear to have the best outcomes. Prior analysis of patients with completely resected recurrent OS enrolled on a Children's Oncology Group (COG) Phase 2 trial AOST0221, which studied the efficacy of inhaled GMCSF, showed a 12-month disease control rate (DCR12) of only 20% (95% CI, 10 – 34%). DCR12 based on this analysis was used as the historical benchmark for efficacy analysis in two recently completed trials, AOST1321 (completely resected cohort only) and AOST1421. We analyzed the stability of the DCR12 benchmark using data from these contemporary studies.

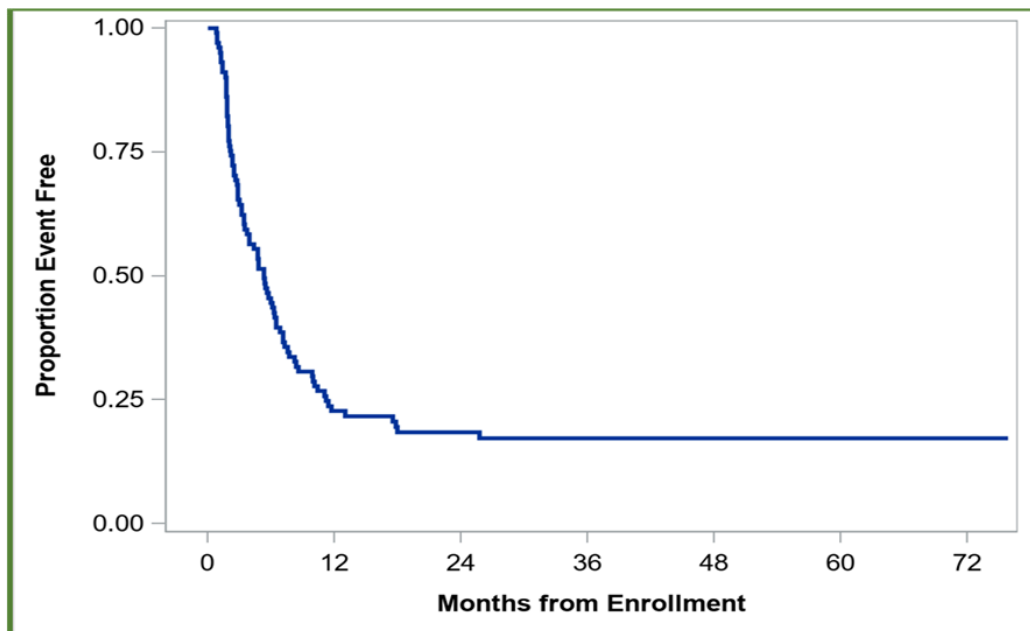
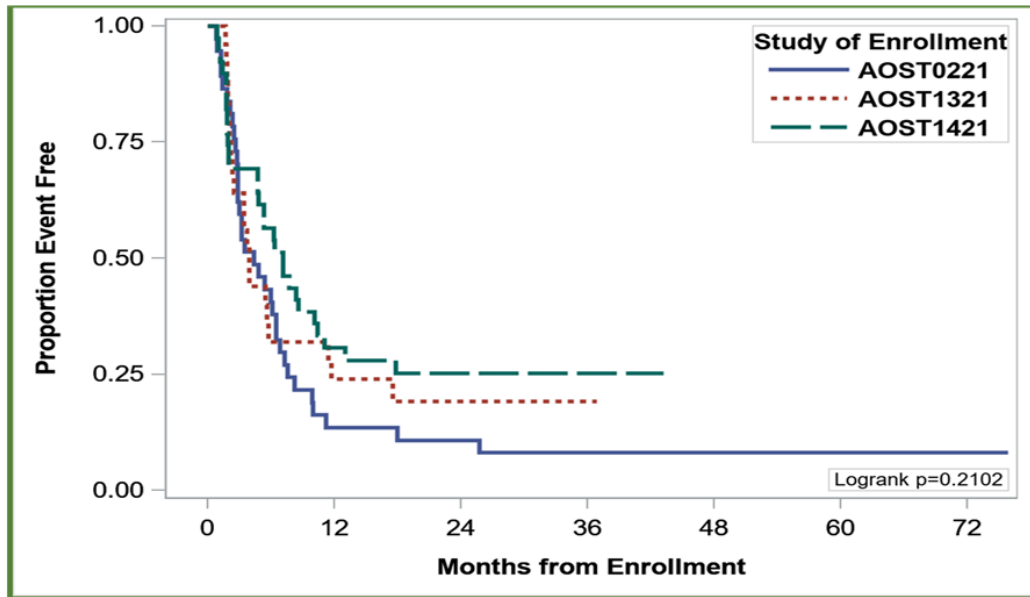
Methods: Patients were eligible for AOST1321 if they had undergone resection of all sites of recurrent or refractory OS within 30 days of enrollment and for AOST1421 if they had lung only recurrent OS completely resected within 4 weeks of enrollment. AOST1321 evaluated denosumab while AOST1421 evaluated dinutuximab. Patients with refractory disease, extrapulmonary recurrence or without histological confirmation of relapse were excluded from this analysis. DCR12 was defined as having at least stable disease 12 months after the start of protocol therapy. We report the DCR12 observed on AOST1321, AOST1421 and AOST0221.

Results: One hundred and twenty-eight evaluable patients with completely resected recurrent OS were enrolled on AOST0221 (N=49), AOST1321 (N=38) and AOST1421 (N=41). One hundred and one patients were included in this analysis (AOST0221: 37, AOST 1321: 25, AOST1421:39). DCR12 was 14 % (95% CI, 5% – 26%) for AOST0221, 24% (95%CI 10-42%) for AOST1321, and 31% (95% CI, 17% - 45%) for AOST1421. Risk for disease progression did not differ across the 3 included studies. DCR12 for all three studies combined was 23% (95% CI, 15% – 31%).

Conclusion: Prognosis for recurrent OS remains dismal, even for those with resectable pulmonary-only disease. The previously described benchmark of disease control at 12 months remained relatively consistent in recent studies for those patients who have resectable pulmonary-only relapse. Therefore, DCR12 remains a useful outcome measure in fully resected OS with lung only metastases. Analyses are ongoing to better define the appropriate threshold to define investigational agent activity in this specific patient population.

Trials Included	Agent Studied	Eligibility for original study	Total # eligible patient on original study	Number of patients included in this analysis
AOST0221	inhaled GmCSF	FIRST relapse of lung only disease; surgery allowed	43	37
AOST1321 (cohort 2)	Denosumab	s/p resection of all sites of recurrent or refractory OS within 30 days of enrollment	38	25
AOST1421	Dinutuximab	lung only recurrent OS completely resected within 4 weeks of enrollment	39	39

Patient Characteristic		AOST0221	AOST1321 (cohort 2)	AOST1421	Total
Number of Prior Regimens	1	37	14	28	79
	2+	0	11	11	22
Age in Years at Enrollment	≤9	2	0	4	6
	10 - 17	23	14	22	59
	18+	12	11	13	36
Patient Sex	Male	25	14	22	61
	Female	12	11	17	40
Patient Race	White	28	19	27	74
	Black	6	1	4	11
	Other	3	5	8	16





Poster #073 #1819050

WEEKLY CISPLATIN +/- IMATINIB IN ADVANCED CHORDOMA: A RETROSPECTIVE CASE-SERIES ANALYSIS FROM THE ITALIAN RARE CANCERS NETWORK (RTR)

Giacomo Giulio Baldi, MD¹; Salvatore Lo Vullo²; Giovanni Grignani, MD³; Bruno Vincenzi, MD, PhD⁴; Giuseppe Badalamenti, MD, PhD⁵; Marinella Mastore, MD⁶; Ciriaco Buonomenna, MD⁷; Carlo Morosi, MD⁸; Alessandro Gronchi, MD⁹; Anna Maria Frezza, MD¹⁰; Salvatore Provenzano, MD¹⁰; Noemi Simeone, MD¹⁰; Luigi Mariani²; Paolo G. Casali, MD¹⁰; Silvia Stacchiotti, MD¹⁰

¹Department of Medical Oncology, Hospital of Prato, Prato, Italy, Prato, Toscana, ITALY, ²Unit of Clinical Epidemiology and Trial Organization, IRCCS Fondazione Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY, ³Department of Medical Oncology-Sarcoma Unit, Candiolo Cancer Institute FPO-IRCCS, Candiolo (TO), Italy, Candiolo, Piemonte, ITALY, ⁴Department of Medical Oncology, Università Campus Bio-Medico di Roma, Rome, Italy, Roma, Lazio, ITALY, ⁵Department of Medical Oncology, Policlinico "Paolo Giaccone", University of Palermo, Palermo, Italy, Palermo, Sicilia, ITALY, ⁶Department of Medical Oncology, San Gerardo Hospital, Monza, Italy, Monza, Lombardia, ITALY, ⁷Department of Radiology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, Milan, Lombardia, ITALY, ⁸Department of Radiology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, Milan, Lombardia, ITALY, ⁹Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, Milan, Lombardia, ITALY, ¹⁰Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY

Objective: Chordoma is an ultra-rare bone sarcoma refractory to anthracycline-based regimens usually administered in sarcoma. We report on a retrospective study of the efficacy of weekly cisplatin (wCDDP) +/- imatinib in patients with advanced chordoma treated within the Italian Rare Cancer Network (RTR).

Methods: Adult patients with a confirmed pathological diagnosis of locally advanced/metastatic and brachyury-positive chordoma treated with wCDDP (ranging from 20 to 30 mg/sqm once a week) +/- imatinib (ranging from 400 to 800 mg/day, continuously) within the RTR starting from 2007 were retrospectively identified. Response by Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 was retrospectively recorded. Overall survival (OS) and progression free survival (PFS) were estimated using the Kaplan-Meier method.

Results: From April 2007 to October 2020, 33 consecutive patients were retrospectively identified (conventional chordoma = 25 [75.8%], dedifferentiated chordoma = 3 [9.1%]; wCDDP as front-line treatment = 8 [24.2%]; further-line = 25 [75.8%]; prior line with imatinib = 25 [75.8%]). All patients had progressive disease before starting wCDDP. Thirty-two (97.0%) patients were evaluable for response (22 [68.8%] wCDDP alone; 10 [31.3%] wCDDP plus imatinib). Nine of 10 patients treated with wCDDP plus imatinib were pretreated with imatinib monotherapy with progression. All patients have completed their treatment. In all patients treated with wCDDP plus imatinib, imatinib was stopped at the time of CDDP interruption. In the evaluable population best response was: 27 (84.3%) stable disease (SD), 5 (15.6%) progressive disease (PD) and a clinical benefit rate (CBR) of 40.6%. At a 54-months median follow-up, median OS was 30.3 months (IQR: 18.1-56.6), median PFS was 8.0 months (IQR: 5.1-17.0) with a 6-month PFS of 66.7% (95% CI, 52.4%-84.9%) and with 10 (30.3%) patients free from progression at 12 months. In 22 (evaluable) patients treated with wCDDP monotherapy best response was: 18 SD (81.8%), 4 PD (18.2%) and a CBR of 40.9%. mPFS was 8.0 months (IQR: 5.1-17.0) with a 6-month PFS of 65.2% (95% CI, 48.4%-87.9%); median OS was 30.3 months (IQR: 18.1-56.7). In 10 (evaluable) patients treated with wCDDP plus imatinib best response was: 9 SD (90.0%) and 1 PD (10.0%), and a CBR of 40.0%. Median PFS was 9.3 months (IQR: 4.9-26.5) with a 6-month PFS of 70.0% (95% CI, 46.7%-100%); median OS was 35.3 months (IQR: 17.3-49.7). Definitive treatment discontinuation for grade 3-4 toxicity (NCI-CTCAE v4.03) was required for 6/33 patients (18,1%) (5/22 [22.7%] of pts treated with wCDDP alone; 1/10 [10%] treated with wCDDP plus imatinib).

Conclusion: This retrospective series suggests that wCDDP, both as a single agent and in combination with imatinib, can be an option for systemic treatment of advanced chordoma. Although no dimensional responses were seen, >65% of patients with evidence of disease progression before starting CDDP were progression-free at 6 months and 30% at 12 months. Those data support a prospective study to confirm wCDDP antitumor effect in the disease and to better understand if the combo of wCDDP and imatinib may be superior to wCDDP as a single-agent.



Poster #074 #1818999

EPIGENETIC MODULATION OF NK CELLS TO IMPROVE TUMOR TRAFFICKING AND ENHANCE THERAPEUTIC EFFICACY AGAINST OSTEOSARCOMA

Ariana R. Anjier, MS; Shinji Maegawa, PhD; Vidya Gopalakrishnan, PhD; Juan Bournat, PhD; Donghang Cheng, PhD; Yanwen Yang, PhD; Charles V. Kingsley; Adam Kulp; Eugenie Kleinerman, MD; Nancy Gordon, MD
UT MD Anderson Cancer Center, Houston, Texas, UNITED STATES

Objective: To determine whether epigenetic modulation of allogeneic NK cells with the HDAC inhibitor Entinostat (MS-275) will improve tumor trafficking and enhance therapeutic efficacy against osteosarcoma (OS) lung metastases.

Methods: Human NK cells were purified and expanded from healthy donor buffy coats using recombinant human IL-2 and genetically engineered K562 feeder cells (Somanchi et al. 2011). Cytotoxicity against the human OS17 OS cells was confirmed using the calcein release assay. NK cells were kept in culture for at least 48 hours with IL-2 prior to use and pre-treated for 24 hours with 0.5uM Entinostat (MS-275) prior to injection into mice.

RNA was extracted from untreated and MS-275 pre-treated NK cells and submitted for RNA seq to determine differentially expressed genes. ChiPseq was also performed to determine the histone post-translational modifications. Fifteen female NSG mice were injected IV with 3×10^6 luciferase labeled OS17 cells. Three weeks after injection, when lung tumors were confirmed by bioluminescence imaging, mice were divided into three groups (5 mice/group): ¹untreated, ²NK cells, and ³MS-275 pre-treated NK cells. NK cells (50×10^6) were administered via tail vein twice/week (five total treatments). For two of the five treatments, NK cells were stained with near-infrared DiR dye prior to injection (Somanchi et al 2016). Distribution of NK cells was determined at 2, 24, 48 and 72 hours after injection by imaging using the IVIS lumina system. All groups were euthanized 24 hours after the final NK cell treatment and lungs were harvested and processed for histologic analysis.

A pilot study was done using two additional female NSG mice: one treated with DiR-NK cells and one with MS-275 pre-treated DiR-NK cells for 3D imaging in the Xerra imaging system as an additional way to determine distribution of NK cells. 24 hours after treatment, animals were sacrificed, and carcasses frozen for processing and visualization.

Results: MS275 upregulates expression of immunomodulatory genes on NK cells and promotes histone H3 and H4 acetylation. 547 differentially expressed genes were identified between the untreated and MS-275 treated NK cells. In addition, four immune related genes (L1CAM, IFNG, C3 and CD28) were found to be upregulated in the MS-275 treated NK cells and histone H3 and H4 acetylation was found at the identified immunomodulatory genes. Pre-treatment of NK cells with MS-275 enhances adoptive transfer of NK cells therapeutic efficacy against OS. There was a significant decrease in the number of micro-metastasis in the MS-275 pre-treated NK cell group as compared to the untreated control group (199 vs 97 $p=0.05$). There was greater DiR signal detected in the mice and the lungs from mice that received pure NK cells as compared to those who received MS-275 pre-treated NK cells and, in these mice, greater signal was detected in the liver at the 24 hours post-injection time point. Lastly, Xerra imaging demonstrated DiR fluorescence in the lungs of the NK cell treatment mouse and in the liver of the MS-275 pre-treated NK cell treatment mouse, suggesting that tumor burden might have an impact on NK cell migration and persistence. Low to no tumor leads to NK cells arriving to the lung and leaving to reach the liver whereas high tumor burden allows NK cells to arrive and remain longer within the lungs.

Conclusion: We conclude that MS-275 has an immunomodulatory effect on NK cells (increases L1CAM, IFNG, C3 and CD28). It also increases H3 and H4 acetylation suggesting transcriptional activation of the immune-related genes that contribute to NK cell increased cytolytic function. Pre-treatment of NK cells with MS-275 enhances NK cell therapeutic efficacy. Localization and persistence of NK cells in the lungs potentially correlates with tumor burden. The Xerra imaging system is an effective tool to visualize DiR-stained NK cells as detection was consistent with data obtained from the IVIS lumina imaging system.

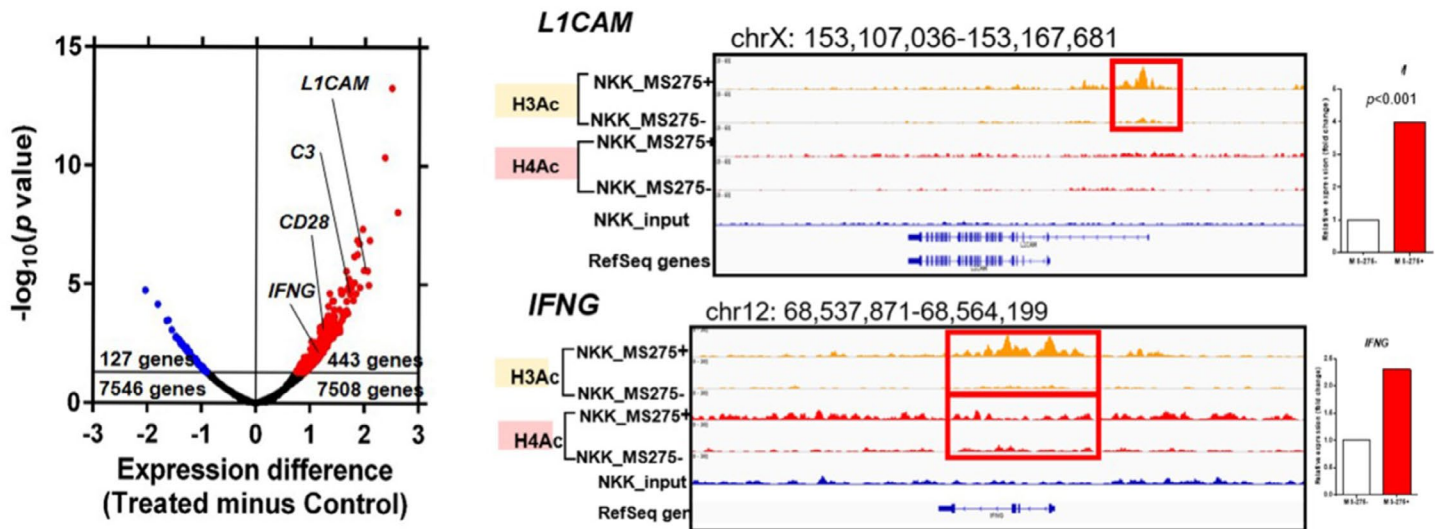


Fig. 1 MS-275 upregulates expression of immunomodulatory genes in human NK cells and promotes histone H3 and H4 acetylation at immunomodulatory genes in NK cells.

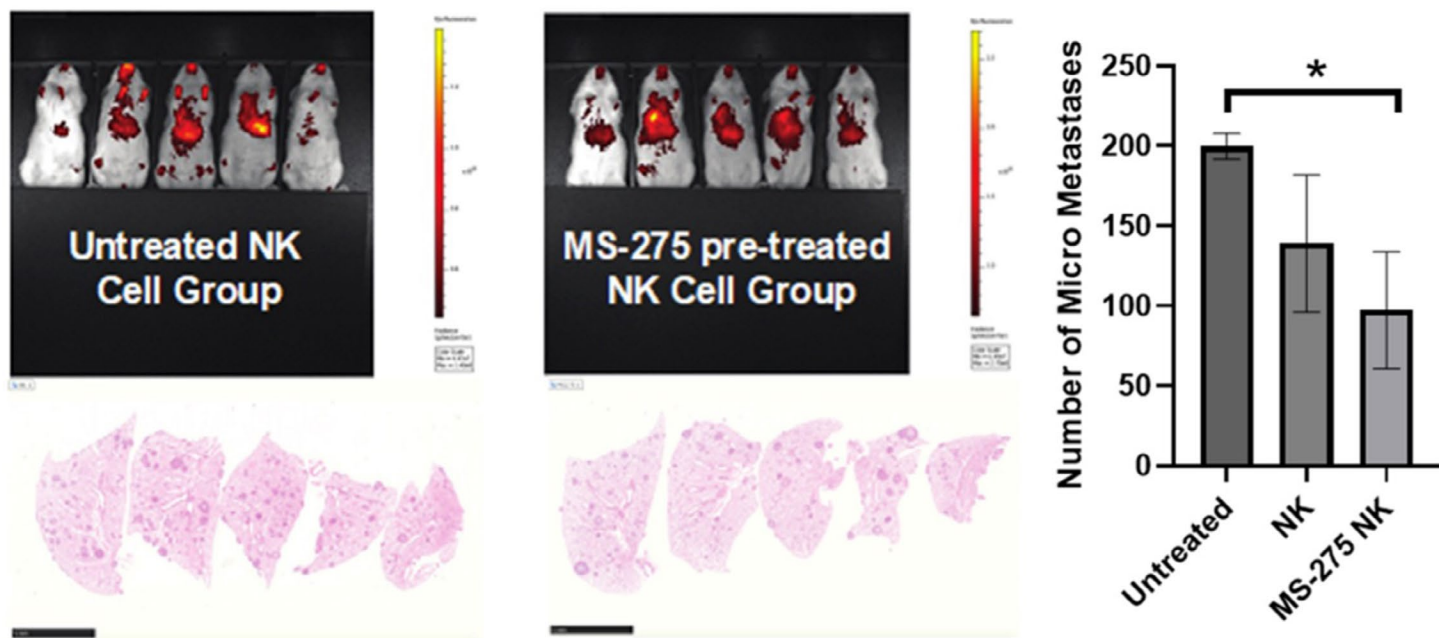


Fig. 2 DiR fluorescence of NK cells *in vivo* and H&E sections of OS17 osteosarcoma tumor burden in the lungs of NSG mice treated with human NK cells (left) and MS-275 pre-treated human NK cells (right). Number of micro-metastases in NSG mice with human OS17 osteosarcoma lung metastases are significantly reduced when treated with MS-275 pre-treated NK cells.



Poster #075 #1818980

FIRST-IN-CLASS CDC45-MCM-GINS HELICASE INHIBITORS OFFER THERAPEUTIC POTENTIAL FOR OSTEOSARCOMA TREATMENT

Darcy L. Welch, MS¹; Shengyan Xiang, PhD¹; Xingju Luo, PhD¹; Damon R. Reed, MD²; Mark Alexandrow, PhD¹,
¹H Lee Moffitt Cancer Center and Research Institute, Tampa, Florida, UNITED STATES, ²Moffitt Cancer Center, Tampa, Florida, UNITED STATES

Objective: Osteosarcoma (OS) is the most common bone cancer affecting children and young adults with suboptimal outcomes. The Cdc45-MCM-GINS (hCMG) replicative helicase is required for tumor cell growth and may be a novel therapeutic target in OS. Mammalian cells assemble more CMG precursor complexes (MCM hexamers) than needed for DNA replication in order to recover from replicative stresses, with the excess being referred to as reserve MCMs. Oncogene-driven mismanagement of MCM/CMG activation depletes these reserve complexes, creating a potential weakness in CMG function that can increase sensitivity to fork-stalling chemotherapy drugs.

Methods: hCMG enzyme was produced via Sf9 or High-5 insect cells that were co-infected with 11 baculoviruses that each expressed one subunit of the hCMG. The Sld5 protein was tagged with GST and included a PreScission site behind the tag, while Cdc45 was tagged with His6-Flag epitopes. Several purification steps were performed, which resulted in the isolation of the hCMG complex enriched in fractions 6-9 after glycerol gradient centrifugation. An ADP-sensing fluorescent-polarization based primary assay was optimized for CMG measurements, followed by a classical fork-unwinding helicase assay as a secondary verification step. Two OS cell lines (143B and OS252) were treated with potential CMG inhibitors (CMGi) and then assessed for viability. For comparison, non-tumor HaCaT keratinocytes were treated similarly.

Results: The aminocoumarins clorobiocin and coumermycin-A1 (C-A1) inhibit ATP hydrolysis and fork-unwinding activity of the hCMG at low micromolar concentrations. A closely related compound, novobiocin, has no inhibitory effect on the hCMG. C-A1 targets the hCMG in OS cells, suppressing MCM hexamer loading and DNA unwinding, both dependent on ATP binding and/or hydrolysis. C-A1 reduces viability at concentrations similar to other chemotherapy drugs in OS cells, but less capably in non-tumor HaCaT cells indicating a therapeutic window.

Conclusion: The discovery of these aminocoumarins as first-in-class, effective CMGi provides an architecture for the development of targeted therapeutics against the hCMG that can be used clinically as innovative interventions in OS management.



Poster #076 #1818865

IDH1 MUTATION INDUCES HIF-1 α AND CONFERS ANGIOGENIC PROPERTY IN CHONDROSARCOMA JJ012 CELLS

Luyuan Li, PhD; Xiaoyu Hu, MD; Josiane E. Eid, MD; Jonathan C. Trent, MD, PhD

Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES

Objective: Chondrosarcomas constitute a heterogeneous group of primary bone cancers and are the second most common primary malignancy of bone. Conventional chondrosarcoma is resistant to standard chemotherapy and radiotherapy, thus there is no effective treatment for patients with inoperable or metastatic chondrosarcoma. IDH1/2 mutations were recently discovered in gliomas, leukemia, cholangiocarcinoma, as well as dedifferentiated and conventional chondrosarcoma. Importantly, IDH mutation represents a targetable and common genetic abnormality in 50-70% of chondrosarcomas. However, their role in the pathogenesis of chondrosarcoma remains largely unknown. In this study, we sought to determine the potential association of IDH1 mutation and HIF-1 α in chondrosarcoma.

Methods: We employed the IDH1-mutant chondrosarcoma JJ012 cell line, CRISPR/Cas9 mutant IDH1 knockout (KO) JJ012 clones, and their derived xenografts. Expression of HIF-1 α target genes were evaluated by qRT-PCR. Protein levels in cells and tissues were assessed by Western Blotting and Immunohistochemistry, respectively. Cell angiogenic and tumorigenic potential were determined by in vitro vascular-endothelial tube formation assay and soft-agar colony formation assay, respectively.

Results: We found that CRISPR/Cas9 knockout of mutant IDH1 reduced HIF-1 α levels in vitro and in vivo. Loss of mutant IDH1 decreased the expression of angiogenic markers including the HIF-1 α target gene VEGF in tumors, and attenuated the angiogenic capacity of JJ012 cells. Moreover, we observed that restoring HIF-1 α levels with exogenous expression significantly enhanced the anchorage-independent growth of mutant IDH1 KO cells.

Conclusion: Our study suggest IDH1 mutation confers angiogenic and tumorigenic properties of JJ012 cells by inducing HIF-1 α . Thus, the HIF pathway represents a promising candidate for combinatorial regimens to target IDH1 mutated chondrosarcomas.



Poster #077 #1819025

ADVERSE PROGNOSTIC IMPACT OF LOSS OF STAG2 PROTEIN EXPRESSION IN PATIENTS WITH NEWLY DIAGNOSED LOCALIZED EWING SARCOMA: A REPORT FROM THE CHILDREN'S ONCOLOGY GROUP (COG)

 David S. Shulman, MD¹; Kelly Klega, BS¹; Alanna J. Church, MD²; Sonja Chen, MD³; Aaron R. Thorner, PhD⁴; Anwasha Nag, PhD⁴; David Hall, MS⁵; Donald A. Barkauskas, PhD⁶; Mark D. Krailo, PhD⁶; Katherine A. Janeway, MD¹; Steven G. DuBois, MD¹; Brian D. Crompton, MD¹
¹Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, MA, ²Department of Pathology, Boston Children's Hospital and Harvard Medical School, Boston, Massachusetts, UNITED STATES, ³Department of Pathology and Laboratory Medicine, Rhode Island Hospital, Providence RI, Providence, Rhode Island, UNITED STATES, ⁴Center for Cancer Genomics, Dana-Farber Cancer Institute, Boston, Massachusetts, UNITED STATES, ⁵Children's Oncology Group, Monrovia, California, UNITED STATES, ⁶Department of Preventive Medicine, Keck School of Medicine of the University of Southern California, Los Angeles, California, UNITED STATES

Objective: Ewing sarcoma (EWS) is an aggressive sarcoma of the bone and soft tissues. At present, there are no available molecular biomarkers to inform risk-stratified therapeutic approaches. STAG2 mutations leading to loss of protein expression are found in 10-15% of patients with EWS. These mutations have been associated with poor outcomes in a small series. We studied a large cohort of patients with localized and metastatic EWS with tissue available for immunohistochemistry (IHC) to determine: ¹frequency of STAG2 protein loss detected by IHC; ²whether protein expression is associated with pathogenic gene alterations; and ³whether loss of expression is associated with inferior outcomes.

Methods: We performed a retrospective cohort study of patients with localized and metastatic EWS and available diagnostic tissue for STAG2 IHC. All patients had previously enrolled to one of three COG biology or therapeutic studies (AEWS0031, AEWS02B1, AEWS07B1). We obtained two unstained slides from 239 patients, as well as isolated tumor DNA for sequencing, if available. Tissue was stained for STAG2 and scored according to the combinative semiquantitative H-score method. Tumors with >50% 2+ or 3+ were considered as "expressed", those with >50% 0 were considered "loss of expression" and those with >50% 1+ were "intermediate." 155 cases passed initial quality control. 27 patients had available whole genome amplified material and amplicon sequencing was performed to identify STAG2 mutations. STAG2 expression was tested for association with clinical features (age, sex, race, ethnicity, stage, primary site) and survival was estimated using Kaplan-Meier methods with log-rank tests of significance.

Results: Of the 155 patients with evaluable slides for IHC analysis, 20 (13%) had staining that was intermediate. Of the remaining 135 patients, 35 (26%) had STAG2 loss of protein expression 29/108 (27%) in the localized cohort and 6/27 (22%) patients in the metastatic cohort. Among the patients with material for sequencing, no patients with STAG2 expression had mutations and two of the 7 patients with STAG2 protein loss had pathogenic STAG2 mutations. STAG2 loss of expression was not associated with clinical or demographic features including stage. Among patients with localized disease (n=108), 5-year event-free survival was 52% (95% CI 33-68%) and 75% (95% CI 63-84%) for patients with STAG2 loss vs. STAG2 expression (Figure 1; p=0.0018). Among the same group, 5-year overall survival was 61% (95% CI 40-76%) and 90% (95% CI 79-96%), for patients with STAG2 loss and STAG2 expression, respectively (p=0.0002).

Conclusion: This is the first report of STAG2 protein expression in a large homogeneous cohort of patients with newly diagnosed EWS. STAG2 loss of protein expression is readily evaluable from minimal amounts of FFPE and occurs at a higher rate than STAG2 mutations. STAG2 expression represents a key prognostic biomarker for stratification of patients with localized EWS and warrants validation in a large cohort of patients with localized tumors.

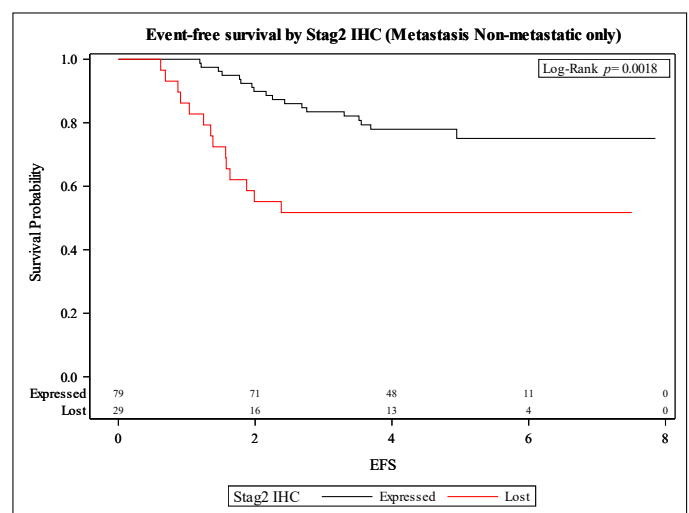


Figure 1: Study schema (A) and STAG2 IHC loss of expression (B) and STAG2 retained expression (C).



Poster #078 #1819068

METASTATIC LUNG COLONIZATION BY OSTEOSARCOMA CELLS IS A MULTI-STEP PROCESS REQUIRING COOPERATION BETWEEN TUMOR SUBPOPULATIONS WITH DISTINCT PHENOTYPES

 Ryan D. Roberts, MD, PhD¹; James B. Reinecke, MD, PhD¹; John M. Hinckley¹; Sanjana Rajan¹; Amy Gross²; Maren Cam, PhD¹,

¹Nationwide Children's Hospital, Columbus, Ohio, UNITED STATES, ²Center for Childhood Cancer, Nationwide Children's Hospital, The Ohio State University James Comprehensive Cancer Center, Columbus, Ohio, UNITED STATES

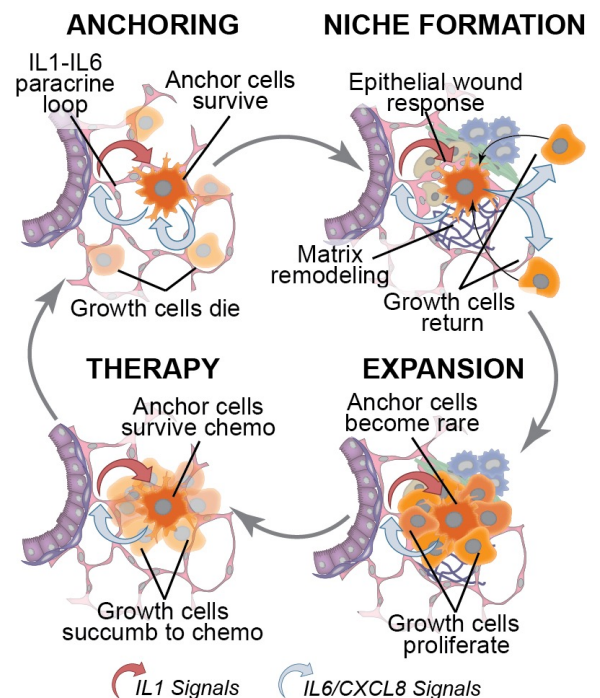
Objective: Four decades of intense multinational efforts have not improved outcomes for children and teenagers with osteosarcoma. Our standard of care remains unchanged since 1982, even though 35-40% of young people so treated still die from the disease—usually from complications related to lung metastasis. While effective metastasis-targeting interventions could transform clinical care, our unsophisticated understanding of the mechanisms that drive lung-specific metastasis handicaps efforts to develop rational, targeted therapeutic interventions. Focused on this problem, our laboratory had previously shown that concurrent inhibition of IL6 and CXCL8 could prevent metastases in up to 85% of osteosarcoma-bearing mice, though the mechanisms behind this disease prevention remained unclear.

Methods: Seeking to understand how IL6 and CXCL8 inhibition prevent metastasis, we generated single-cell RNA-seq datasets from the lungs from osteosarcoma-bearing mice collected at multiple time points during lung colonization. We employed niche-labeling technology to isolate tumor and tumor-associated cells from microscopic to fully established lesions. We used this data to perform inter-cellular signaling analyses and to characterize changes occurring in the cellular content and in the phenotypes of cells occupying the metastatic niche over developmental time. Immunofluorescent staining of both murine and human metastatic lesions confirmed these findings, which we also validated in tumor-on-lung organoid systems. We used several mouse models to evaluate the *in vivo* significance of our results.

Results: We found that a small subpopulation of osteosarcoma cells triggers an IL1-IL6 paracrine loop upon interaction with epithelial cells in the lung, driving IL6/CXCL8 production within the early metastatic niche. This subset of osteosarcoma cells has distinct characteristics: it is hypo-proliferative, hyper-secretory, p21+, and survives the stresses of dissemination to the lung. We have come to call these metastasis-initiating cells "anchor" cells and to call their rapidly proliferative counterparts "growth cells." Very early metastases show near-complete enrichment for anchor-phenotype osteosarcoma cells, while growth cells become dominant as lesions expand.

Our preliminary data suggest that cytokines made by anchor cells block the resolution of a wound-healing response that occurs in response to tumor cells, creating a "wound that never heals." These wound-like changes alter the cellular, cytokine, and matrix composition to promote colonization by growth cells. Anchor-derived signals can recruit circulating growth cells into a developing niche, although it remains unclear whether this or state changes in anchor cell progeny are the primary mechanism for the appearance of growth cells within a lesion. Intriguingly, anchor cells appear resistant to chemotherapy, providing a potential mechanism for relapse after treatment.

Conclusion: These data suggest that the establishment of lung metastases arises through cooperation among osteosarcoma cells with distinct phenotypes. Anchor cells survive the initial stresses of the pulmonary environment, then modify that environment by invoking and manipulating the wound-healing programs of the lung. Proliferating growth cells are subsequently recruited to anchored niches to produce clinically relevant metastatic lesions. Effective treatment of metastatic disease will likely require combinations of agents that target both of these osteosarcoma subtypes, which exhibit highly divergent sensitivity to conventional therapies.





Poster #079 #1818849

FACTORS ASSOCIATED WITH ONCOLOGIC OUTCOME IN PATIENTS WITH SCAPULAR CHONDROSARCOMA

Matthew T. Houdek, MD; Elizabeth P. Wellings, MD; Chad W. Parkes, MD; Adam J. Tagliero, MD; Peter S. Rose, MD, Mayo Clinic, Rochester, Minnesota, UNITED STATES

Objective: Chondrosarcomas are common primary bone tumor in adults, often affecting the flat bones. Since these tumor are historically resistant to chemotherapy and radiotherapy, surgical resection with negative margins remains the mainstay of treatment. The scapula is a common location for these tumors, however there is a relative lack of outcome studies, with previous series having conflicting results. Previous series examining patients with chondrosarcomas of the scapula have reported rates of local recurrence ranging from 0-40% and metastatic disease occurring in 10-20% of patients. The goal of the study was to examine the oncologic and functional outcome of a modern series of patients with scapular chondrosarcoma.

Methods: We retrospectively reviewed 39 patients (26 males:13 females) with a mean age of 46 ± 17 undergoing surgical resection of a scapular chondrosarcomas. Most patients had Grade I ($n=24$) tumors, with 26 (67%) having an associated soft-tissue mass. Chondrosarcomas were grouped based on if they were a primary tumor ($n=31$, 79%) or a secondary tumor (arising from an osteochondroma or enchondroma, $n=8$, 21%). Grade I and II tumors were considered to be "low grade" and Grade III and dedifferentiated were considered "high grade". The mean follow-up was 8 years. In patients with a limb salvage procedure ($n=36$), reconstructions included soft tissue alone ($n=16$) where the remnants of the rotator cuff and scapular stabilizers were sutured to the surrounding soft tissue and scapula. Bony reconstruction (Table 2) included suspension an endoprosthesis proximal humerus or the residual proximal humerus to the remaining clavicle ($n=11$), scapulothoracic fusion ($n=2$), osteoarticular allograft of the glenoid ($n=2$), scapular allograft ($n=2$), cementation of the defect ($n=3$), and reverse total shoulder arthroplasty with autologous bone grafting ($n=1$).

Results: The 10-year disease specific survival was 77%. High grade tumors (HR 18.15, $p < 0.01$) were associated with death due to disease. The 10-year local recurrence- and metastatic free survival were 77% and 74%. Positive surgical margins (HR 8.85, $p < 0.01$) was associated with local recurrence and local recurrence was associated with metastatic disease (HR 3.37, $p = 0.04$). All disease recurrences and death due to disease occurred in patients with a soft-tissue mass ($p < 0.05$). Following surgery the mean MSTS93 rating was $77 \pm 19\%$ and the mean shoulder elevation was $81 \pm 66^\circ$. When examining the patient function based on the type of resection patients who underwent had a partial scapulectomy which preserved the glenoid had improved outcome in terms of mean MSTS93 ($p < 0.01$) and mean forward elevation of the shoulder ($p < 0.01$).

Conclusion: Overall surgical resection of a scapular chondrosarcoma was associated with a relatively high rate of local tumor recurrence, which imparts a worse oncologic outcome. The presence of a soft-tissue mass was associated with a worse oncologic outcome, even in the setting of a low-histological grade, highlighting the potentially aggressive nature of these tumors. As such we recommend an en-bloc resection for all patients, regardless of histological grade.

Table 1: Comparison of Patients with Primary and Secondary Chondrosarcoma of the Scapula

Demographic	All Patients (n=39)	Primary Chondrosarcoma (n=31)	Secondary Chondrosarcoma (n=8)	P Value
Males	26 (67%)	20 (65%)	6 (75%)	0.69
Females	13 (33%)	11 (35%)	2 (25%)	0.69
Mean Age (Years)	46 ± 17	50 ± 16	31 ± 14	< 0.01
Tumor Size (cm)	8 ± 6	7 ± 5	12 ± 7	0.03
Tumor Volume (cm ³)	$714 \pm 1,733$	402 ± 636	$1,792 \pm 3,527$	0.04
High Grade Tumor	7 (18%)	6 (19%)	1 (12%)	0.65

Table 2: Limb Salvage Reconstruction following Resection of a Scapular Chondrosarcoma

Type of Resection	Type of Reconstruction
Extraarticular Partial Scapulectomy	Soft Tissue Alone (n=14) Scapulothoracic Fusion (n=2) Scapular Allograft (n=1)
Partial Scapulectomy Including Glenoid	Cement and Pin (n=3) Osteoarticular Allograft (n=2) Soft Tissue Alone (n=2) Staged Bony Autograft with Reverse Total Shoulder (n=1)
Total Scapulectomy	Soft Tissue with Suspension of Humerus to Clavicle (n=5) Total Scapular Allograft (n=1)
Scapulectomy and Proximal Humerus	Endoprosthesis Proximal Humerus Suspended to Clavicle (n=6)

Table 3: Factors Associated with Oncologic Outcome Following Scapular Resection for Chondrosarcoma

Demographic	Disease Specific Survival (HR 95% CI)	P Value	Local Recurrence (HR 95% CI)	P Value	Metastatic Disease (HR 95% CI)	P value
High Grade Tumor	18.15 (3.53-93.35)	<0.01	10.60 (2.23-50.23)	<0.01	13.30 (3.38-52.37)	<0.01
Primary Tumor	0.79 (0.15-3.97)	0.78	0.69 (0.13-3.62)	0.66	0.51 (0.13-1.99)	0.33
Male Gender	0.84 (0.20-3.56)	0.82	3.16 (0.37-26.41)	0.28	1.12 (0.29-4.37)	0.85
Age \geq 55 years	1.55 (0.36-6.62)	0.54	4.66 (0.96-22.60)	0.055	1.53 (0.43-5.42)	0.50
Soft Tissue Mass	∞	<0.01	1.72 (0.33-9.01)	0.51	∞	<0.01
Tumor Size \geq 8 cm	4.97 (0.99-24.93)	0.051	4.65 (0.89-24.60)	0.06	3.55 (0.91-13.78)	0.06
Local Recurrence	3.30 (0.78-13.87)	0.10	N/A		3.73 (1.05-13.26)	0.04
Positive Margins	0.85 (0.10-6.99)	0.88	8.85 (1.97-39.69)	<0.01	0.65 (0.08-5.14)	0.68

Table 4: Functional Outcome Following Resection of a Scapular Chondrosarcoma

Surgical Procedure	Partial Scapulectomy	Total Scapulectomy	Resection Involving Humerus	Glenoid Resection	P Value
Mean MSTS93	90 \pm 9%	70 \pm 9%	67 \pm 9%	80 \pm 12%	<0.01
Mean Forward Shoulder Elevation	140 \pm 38 $^\circ$	17 \pm 22 $^\circ$	28 \pm 19 $^\circ$	63 \pm 57 $^\circ$	<0.01



Poster #080 #1818868

SAFETY AND EFFICACY OF MULTIPLE TYROSINE KINASE INHIBITOR THERAPY FOR PEDIATRIC/ADOLESCENT AND YOUNG ADULT PATIENTS WITH RELAPSED OR REFRACTORY OSTEOSARCOMAS: SINGLE-INSTITUTION RETROSPECTIVE STUDY

Masanaka Sugiyama, MD; Ayumu Arakawa, MD; Nami Shirakawa, MD; Kayoko Tao, MD; Kazuki Tanimura, MD; Miho Nakajima, MD; Yuko Watanabe, MD; Tadashi Kumamoto, MD; Junnosuke Maniwa, MD; Akihiro Yoneda, MD; Shintaro Iwata, MD; Eisuke Kobayashi, MD; Akira Kawai, MD; Chitose Ogawa, MD
National Cancer Center Hospital, Chuo-ku, Tokyo, JAPAN

Objective: Relapsed or refractory osteosarcomas still have poor prognosis because of a small repertoire of effective chemotherapy regimens, which consequently indicates the need for a new treatment strategy. Some recent reports have described that molecular targeting agents, including the multiple tyrosine kinase inhibitors (MTKIs), are effective against relapsed or refractory adult osteosarcomas. However, there are only a few reports describing the administration of these agents for pediatric osteosarcomas. Therefore, to clarify the safety and efficacy of MTKI-including therapy for children and adolescent and young adults (AYAs), we conducted a retrospective examination of the adverse events and treatment outcomes.

Methods: We retrospectively reviewed the electronic medical records of pediatric and AYA patients with relapsed or refractory osteosarcomas who received MTKI-including therapies at the Department of Pediatric Oncology, National Cancer Center Hospital, from December 2013 to May 2021. The adverse events due to these therapies, the clinical courses, and the treatment outcomes were analyzed retrospectively. The Kaplan–Meier method was used to estimate the progression-free survival at 95% confidence interval (CI).

Results: We included 31 patients consisting of 15 male and 16 female subjects who received MTKIs, including sorafenib monotherapy (7 patients), sorafenib and everolimus (14 patients), and regorafenib monotherapy (10 patients). Their median age was 17 years (range: 11–22 years). Additional radiotherapy was administered to 11 patients. The incidence rates of treatment-related grade 3 nonhematological adverse events were 14.3% in the sorafenib monotherapy group (palmar-plantar erythrodysesthesia syndrome (1 patient)), 21.4% in the sorafenib and everolimus group (pneumothorax, rash, bronchial fistula, skin ulceration, and palmar-plantar erythrodysesthesia syndrome (each 1 patient: rash, skin ulceration, and palmar-plantar erythrodysesthesia syndrome occurred in a same patient)), and 20.0% in the regorafenib monotherapy group (palmar-plantar erythrodysesthesia syndrome (2 patients)). There were no grade 4 nonhematological adverse events. One patient discontinued sorafenib and everolimus because of grade 3 skin ulceration, and one patient discontinued regorafenib because of grade 3 pericardial effusion due to an uncertain cause. The 4-month median progression-free survival rate was 36.7% (95% CI: 22.9%–58.7%) in the entire study population, whereas it was 14.3% (95% CI: 2.33%–87.7%) in the sorafenib monotherapy group, 30.8% (95% CI: 13.6%–69.5%) in the sorafenib and everolimus group, and 60% (95% CI: 36.2%–99.5%) in the regorafenib monotherapy group. The median progression-free survival was 94 days (95% CI: 56–160 days) in the entire study population, whereas it was 51 days (95% CI: 38–not available (NA) days) in the sorafenib monotherapy group, 101 days (95% CI: 64–NA days) in the sorafenib and everolimus group, and 167 days (95% CI: 43–NA days) in the regorafenib monotherapy group. None of the patients died from treatment-related toxicity.

Conclusion: The safety profile of MTKI-including therapy for pediatric and AYA patients with osteosarcomas was similar to that of adult patients, and these agents were tolerable even in heavily treated pediatric patients. Especially, regorafenib appeared to be more effective than sorafenib-based therapy. Patients could achieve a certain period of survival time and maintain a favorable performance status during and after the treatment. MTKI-including therapy is useful against relapsed or refractory pediatric and AYA osteosarcomas.



Poster #081 #1818925

TYROSINE KINASE INHIBITORS IN RECURRENT BONE TUMOURS. A REAL WORLD EXPERIENCE

Tushar Vora, MD¹; Sarah Cohen-Gogo, MD, PhD²; David Malkin, MD, FRCP(C)²; Daniel A. Morgenstern, MB BChir, PhD³; Paul Nathan, MD, M.Sc., FRCPC²; Avram Denburg, MD, M.Sc., PhD, FRCPC²; Furqan Shaikh, MD, M.Sc., PhD, FRCPC²; Jack Brzezinski, MD²; Anita Villani, MD²; Sevan Hopyan, MD, PhD, FRCSC²; Jay S. Wunder, MSc., MD⁴; Peter C. Ferguson, MD, PhD, FRCSC⁵; Kim M. Tsoi, MD, PhD⁶; Albiruni Ryan Abdul Abdul Razak, MD, MB, MRCPI⁷; Abha A. Gupta, MD, M.Sc., FRCPC⁸; Hagit Peretz Soroka, PhD⁹

¹Hospital for Sick Children, Princess Margaret Cancer Center, University of Toronto, Toronto, Ontario, CANADA,

²Hospital for Sick Children and University of Toronto, Toronto, Ontario, CANADA, ³Hospital for Sick Children,

Toronto, Ontario, CANADA, ⁴The Lunenfeld-Tanenbaum Research Institute, Toronto, Ontario, CANADA, ⁵Division of

Orthopaedic Surgery, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, CANADA, ⁶University of Toronto,

Mount Sinai Hospital, Toronto, Ontario, CANADA, ⁷Division of Medical Oncology, Princess Margaret Cancer Centre,

University Health Network, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, CANADA, ⁸Hospital for Sick

Children and Princess Margaret Cancer Center and University of Toronto, Toronto, Ontario, CANADA, ⁹Princess Margaret

Cancer Center, Canadian Sarcoma Research and Clinical Collaboration (CanSarCC), Toronto, Ontario, CANADA

Objective: Median survival for patients with relapsed or metastatic Osteosarcoma (OS) and Ewing sarcoma (ES) are dismal and have not improved in the last few decades despite varied multi-agent chemotherapeutic approaches. Recent reports suggest promising role for tyrosine kinase inhibitors (TKIs) such as regorafenib (R) and cabozantinib (C) in this setting. We have analyzed the toxicities and outcomes of using these agents, obtained through compassionate access, in paediatric and adult patients with bone sarcoma after relapse, outside of a clinical trial setting.

Methods: After Research Ethics Board approvals, pediatric and adult bone sarcoma patients in relapse, from Hospital for Sick Children and Princess Margaret Cancer Center, who had received either R or C, from January 01, 2018 to May 01, 2021 (for minimum one month duration) were retrospectively analyzed. Data collected included patient characteristics, disease parameters, treatment details, toxicity and outcomes. Response was defined as per RECIST v.1.1. Progression-free and overall survival were estimated using Kaplan-Meier survival analysis. SPSS version 27 was used for data analysis.

Results: Twenty-two patients received R or C for relapsed bone sarcoma. Patient demographics, TKIs, line of therapy and toxicities are listed in Table 1. The median starting dose of R was 80 mg (range 40 – 160 mg) and C was 60 mg (range 40 – 60 mg). Four (18.2%) required dose reductions; most common toxicities were hypertension and hand-foot-syndrome. (Table 1) Response evaluation was available in 20 patients. Waterfall plot (Figure 1) shows best response of a single target lesion. Best overall response was partial response, 2 (10%); stable disease, 13 (65%); and progressive disease, 5 (25%). Median time to best response was 2.0 months (range 1 – 17 months). At a median follow up of 9 months (range 1 – 27), 7 (31.8%) had died of progressive disease and the rest (n=15, 68.2%) were alive with disease. Swimmer's plot (Figure 2) shows time to progression or censor. Median time to progression on TKI was 5.8 months (± 1.5 , 95% CI 2.9 – 8.73, Figure 3) and median OS was 10 months (± 2.7 , 95% CI 4.7 – 15.3).

Conclusion: Comparable to the originally published trials, our analysis shows that TKIs have meaningful activity in patients with recurrent bone tumours with acceptable toxicities, in real-world settings. Lower doses may be sufficient at maintaining meaningful responses and requires further study. REGOSTA like trials, looking at role of TKIs in earlier lines of therapies or maintenance settings, will be pivotal.

Table 1. Demographics, Diagnosis, Disease sites, Line of Treatment and Toxicities

		Total (n=22, %)	R (n=6, 27.3%)	C (n=16, 72.7%)
Age years at start of TKI	Median (Range)	19.46 (12-54)	16.66 (14-46)	22.04 (12- 54)
	≤18 years	10 (45.5)	5	5
	>18 years	12 (54.5)	1	11
Male		13 (59.1)	3	10
Diagnosis	OS	15 (68.1)	5	10
	ES	3 (13.6)	0	3
	Chondrosarcoma	4 (18.2)	1	3
Disease at start of TKI	Lung	18 (81.8)	5	13
	bone	7 (31.8)	2	5
	local	4 (18.2)	1	3
Line of therapy of TKI	1 st	1 (4.5)	0	1
	2 nd	10 (45.5)	3	7
	3 rd	8 (36.4)	3	5
	≥4	3 (13.6)	0	3
Toxicities (Grade ≥ 2)	Dose Reduction	4 (18.2)	2	2
	Hypertension	4 (18.2)	3	1
	Bleeding	2 (9.1)	0	2
	Mucositis	1 (4.5)	1	0
	HFS	3 (13.6)	2	1
	Elevated LFTs	1 (4.5)	0	1

HFS – Hand Foot Syndrome, LFTs- Liver Function Tests

Figure 1 – Waterfall chart for a targeted lesion in each evaluable patient

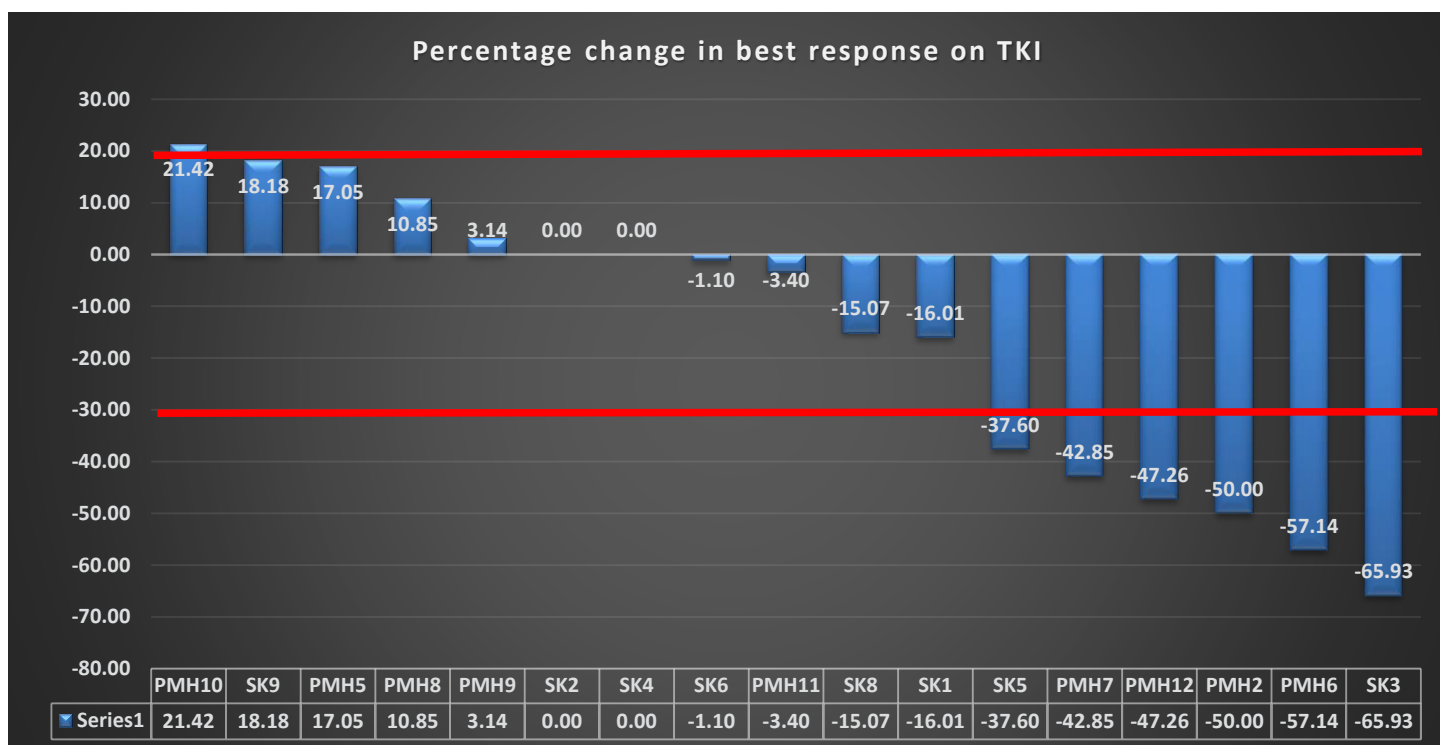


Figure 2 – Swimmers Plot for Time to Progression or Censor

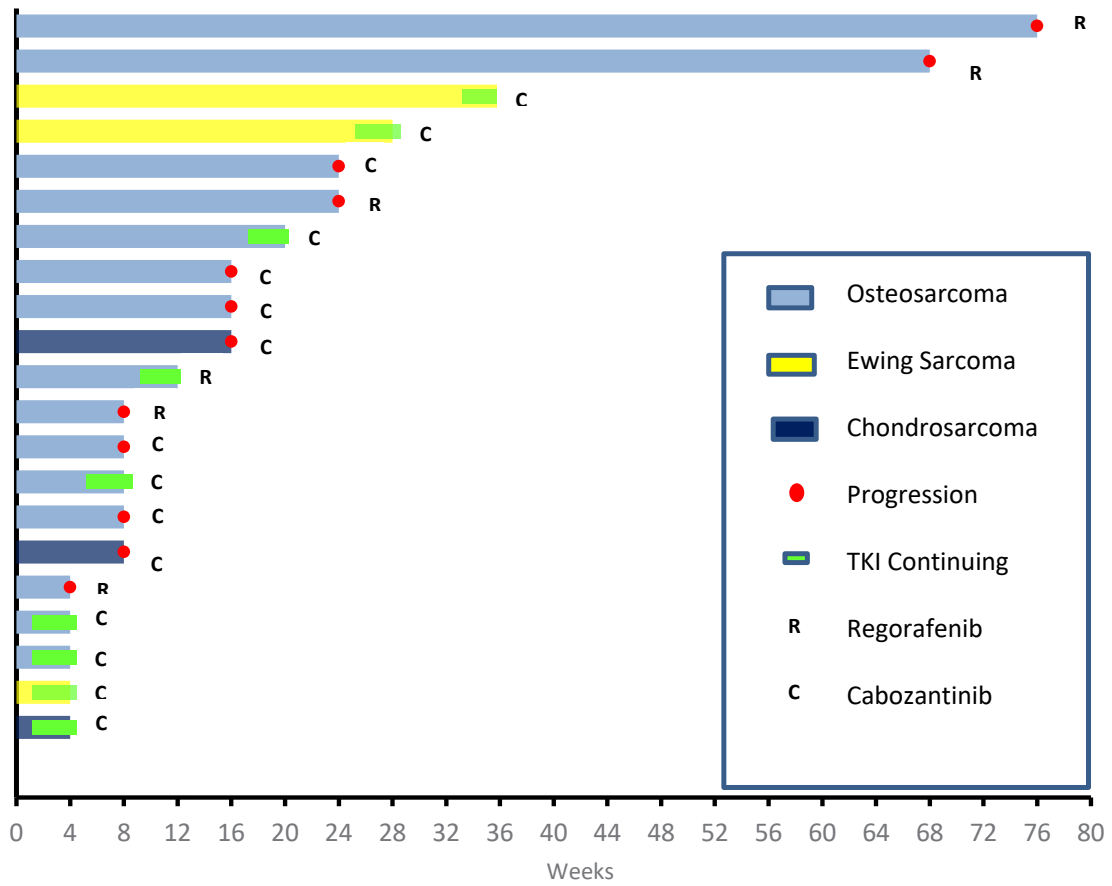
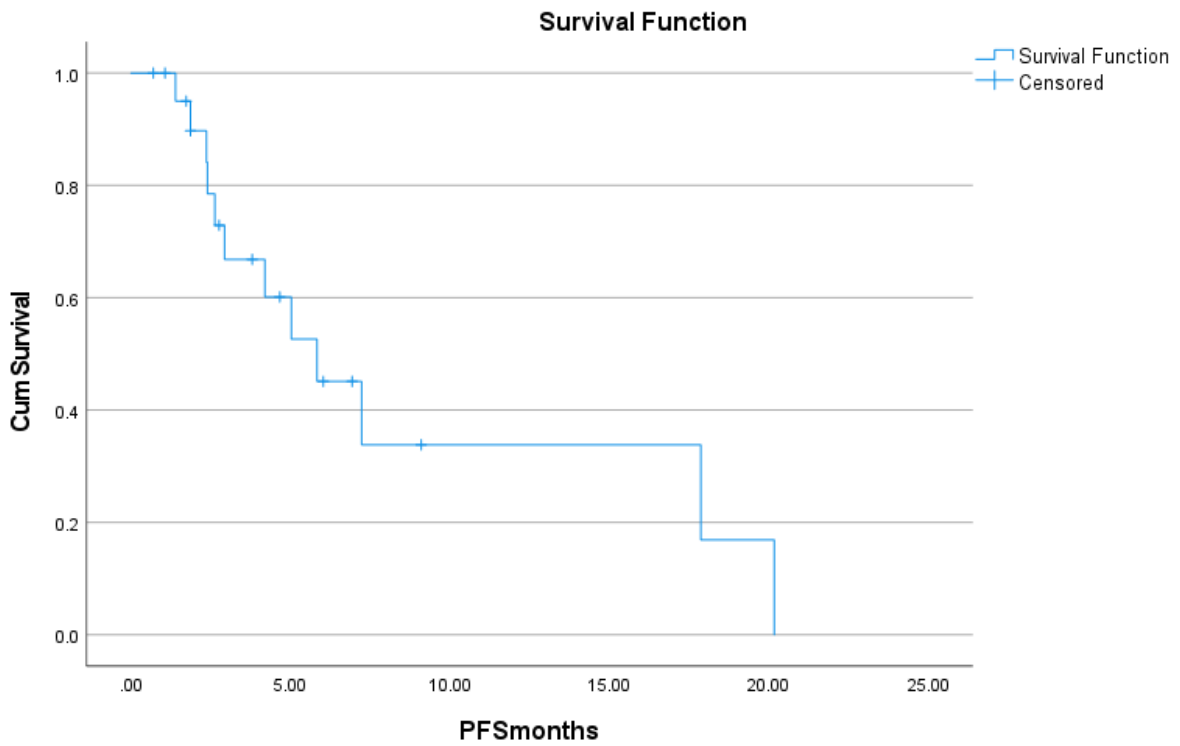


Figure 3. Progression-free Survival of entire cohort





Poster #082 #1818989

PRESENTING CHARACTERISTICS AND SURVIVAL OF EWING SARCOMA OF THE PELVIS

Jeffrey Brown, BS¹; Kyla Rakoczy, BS¹; John Groundland, MD²

¹University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES,

²Huntsman Cancer Institute, Salt Lake City, Utah, UNITED STATES

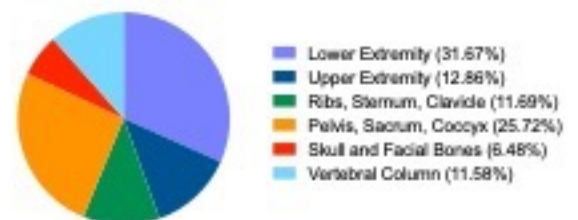
Objective: Ewing tumors are an aggressive malignancy representing the second most common sarcoma of bone in children and adolescents. While survival rates have improved with combined surgery, radiation, and systemic chemotherapy, the disease still carries significant morbidity and mortality. Additionally, the clinical course of Ewing sarcoma is impacted by the anatomic site of the primary tumor. Ewing sarcoma of the pelvic bones broadly represents the second most frequent primary tumor location but carries a poorer prognosis in comparison to tumors originating at other anatomic sites. This study aims to further describe the clinical presentation and survival of Ewing sarcoma of the bony pelvis.

Methods: The National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) program was reviewed for Ewing sarcoma of the bony pelvis diagnosed between 2004-2013. Tumors were broadly categorized into one of six categories: lower extremity, upper extremity, skull and facial bones, vertebral column, pelvic bones including the sacrum, and thoracic bones including ribs, sternum, and clavicle. Cases were analyzed by age at diagnosis, sex, tumor size, tumor extension, surgical intervention, use of radiotherapy, and presence of metastases. Overall survival was assessed with Kaplan-Meier log rank tests and compared to primary tumors at other anatomic locations.

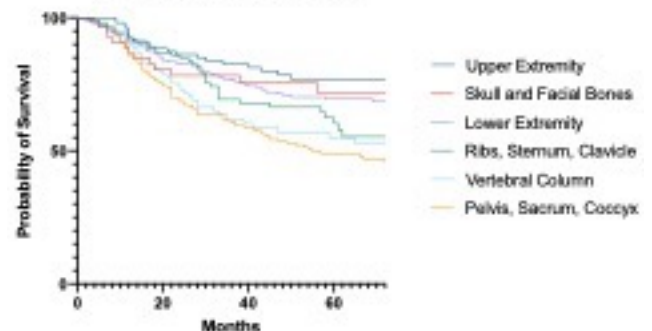
Results: In total 941 cases of Ewing sarcoma were identified across all anatomic sites, 242 of which were tumors of the pelvis. The most frequent location was lower extremity tumors (31.67%, n=298), followed by pelvic tumors (25.72%, n=242), upper extremity (12.86%, n=121), thoracic cage (11.69%, n=110), vertebrae (11.58%, n=109), and facial bones (6.48%, n=61). The 5-year survival rates were 48.7% for tumors of the pelvis, compared to 68.5% for lower extremity tumors, 76.3% at upper extremities, 62.7% at thoracic bones, 74.5% at skull and facial bones, and 54.9% at the vertebral column. At the time of diagnosis 48.28% of pelvic tumors were >10 cm, 82.81% extended beyond the periosteum, and 48.05% had clinically apparent metastatic disease. While 67.77% of pelvic tumors received radiotherapy, only 30.42% underwent any form of surgical intervention.

Conclusion: This review of the SEER database contextualizes presenting characteristics of pelvic Ewing sarcoma relative to tumors at other anatomic sites. This study indicates poor survival of pelvic Ewing sarcoma when presenting with tumor size >10 cm, tumor extension beyond periosteum, presence of metastases at diagnosis, external hemipelvectomy or lack of surgical resection, and isolated radiotherapy. These findings provide additional guidance for therapeutic decisions and clarify conditions affecting the prognosis of pelvic Ewing sarcoma.

Anatomic Distribution of Primary Tumor



Survival All Anatomic Sites





Poster #083 #1818967

ESTABLISHMENT OF SIMPLE SCREENING SYSTEM FOR MOLECULAR TARGET THERAPY IN OSTEOSARCOMA

Keita Sasa, MD¹; Tsuyoshi Saito, MD, PhD²; Taisei Kurihara, M.D, PhD²; Nobuhiko Hasegawa, MD, PhD²; Kei Sano, MD, PhD²; Daisuke Kubota, MD, PhD²; Keisuke Akaike, MD, PhD²; Taketo Okubo, MD, PhD²; Takuo Hayashi, MD, PhD²; Tatsuya Takagi, MD, PhD²; Muneaki Ishijima, MD, PhD²; Yoshiyuki Suehara, MD, PhD²
¹Juntendo University, Bunkyo-ku, Tokyo, JAPAN, ²Juntendo University, Bunkyo-ku, Tokyo, JAPAN

Objective: Osteosarcoma is the most common primary malignant bone tumor. Although the treatment protocol was established 30 years ago (perioperative chemotherapy, resection), the treatment results of the advanced cases at the first visit are still extremely poor. This would be in part due to the fact that new anti-cancer drugs were not emerged. Recently, next-generation sequencing (NGS)-based research open a possibility for new molecular target therapy on osteosarcoma. Our group and others conducted a comprehensive analysis using clinical sequence such as MSK-IMPACT and identified mutually exclusive co-occurrence of gene amplification for molecular target therapy in approximately 40% of osteosarcoma (Suehara Y. Clin Cancer Res, 2019, Sayles LC. Cancer Discov. 2019, Zhao J. Cancer Lett. 2020). However, the cost of NGS is expensive, and the formalin-fixed paraffin embedded (FFPE) sample is generally not suitable for NGS analysis due to nucleic acid degradation due to the decalcification process in addition to the sample age, hampering this kind of analysis. We aimed to establish a simple method to examine gene amplification status in osteosarcoma using NanoString.

Methods: To elucidate co-amplification status of genes previously reported to occur mutually exclusive manner (PDGFRA/KIT/KDR, VEGFA/CCND3, MDM2/CDK4, MYC et al.: 24 genes) in osteosarcoma, we created a custom probe set in NanoString assay. As samples, 9 cell lines (prepared as frozen and FFPE samples, respectively), 13 clinical frozen samples of osteosarcoma, and 3 corresponding decalcified FFPE samples were used. Genomic DNA was extracted using the Qiagen kit (QIAamp DNA Mini Kit, QIAamp DNA FFPE Tissue Kit).

Results: The same pattern of gene amplification was obtained between the frozen and the corresponding FFPE samples in all 9 cell lines and the obtained gene amplification status was concordant with those described in the cell line database in Cancer Cell Line Encyclopedia (CCLE). These findings confirmed the quality of this custom probe set. Then, we analyzed 13 clinical samples of osteosarcoma and confirmed mutual exclusive co-occurrence pattern of gene amplification (PDGFRA/KIT/KDR, VEGFA/CCND3 and MDM2/CDK4) in 4 cases (30.8%). Analysis using FFPE samples after decalcification was also available for 10 cases and the obtained findings were concordant with those from frozen samples in 6 cases (60%).

Conclusion: For NGS analysis of bone tumors, degradation of nucleic acids due to decalcification and sample aging are main problems hampered for this analysis. In addition, the NGS analysis is very expensive (about \$5,000 in Japan). Therefore, the establishment of simple method is desired. The results were highly reproducible across many cancer cell lines, suggesting the reliability of our custom probe set. Furthermore, this NanoString-based CNV assay using frozen samples revealed mutual exclusive co-occurrence pattern of gene amplification in 4 of 13 cases (approximately 30%), being consistent with the previously reported frequency (Suehara Y. Clin Cancer Res, 2019). In addition, almost the same findings were obtained in FFPE samples after decalcification. This analysis is relatively cheap (\$300 per sample: tumor-derived and the corresponding normal tissue-derived DNA is required). This analysis will contribute to design the therapeutic strategy based on genome profiling in osteosarcoma.



Poster #084 #1819038

AN EXPLORATORY PILOT TRIAL EVALUATING TUMOR INFILTRATING LYMPHOCYTES THERAPY ON RELAPSED OSTEOSARCOMA

Yingqi Hua, MD, PhD¹; Chongren Wang, MD²; Hongliang Fang, PhD³; Yafei Jiang, MD²; Mengxiong Sun, MD²; Dongqing Zuo, MD²; Xiaojun Ma, MD²; Suxia Xue, MD³; Wei Sun, MD²; Yu Lv, MD²; Jing Xu, PhD²; Zhengdong Cai, MD²; Xiaowen He, PhD, MD³

¹Shanghai General Hospital, Shanghai Jiao Tong University, Shanghai, Shanghai, CHINA (PEOPLE'S REPUBLIC),

²Shanghai General Hospital, School of Medicine Shanghai Jiao Tong University, Shanghai, Shanghai, CHINA (PEOPLE'S REPUBLIC), ³Origincell Technology Group Co., Ltd, Shanghai, Shanghai, CHINA (PEOPLE'S REPUBLIC)

Objective: Osteosarcoma is the most common primary malignancy of bone, and typically affects adolescents and young adults. Once spreading to the lung, there has been few advances in survival and treatment for metastatic disease. Only two-thirds of patients with initially localized disease are expected to be cured, with long-term survival occurring in <20% of patients with metastatic or recurrent tumors. Given that outcomes of metastatic or unresectable osteosarcomas are still unsatisfactory, novel treatment approaches are needed.

Based on recent studies about the role of the immune system in malignancies, immunotherapies including immune modulators such as interleukin-2, immune checkpoint inhibitors, and engineered T cells have been utilized in patients with malignancies. Osteosarcoma have a higher percentage of CD8+ infiltrating lymphocytes than other sarcoma subtypes, and the degree of infiltration correlates positively with survival. In addition, there are multiple cell surface proteins that are potentially targetable with antibodies. Although there are limited reports of immunotherapies for osteosarcoma, immunotherapy is thought to be a promising treatment option for osteosarcomas.

Adoptive Cell Therapy (ACT) with tumor-infiltrating lymphocytes (TILs) capitalize on the underlying genomic instability of cancer cells, which causes the accumulation of genetic mutations that give rise to antigens for which expression is limited to tumors (neoantigens), upon recognition of these neoantigens, cytotoxic T lymphocytes (CTLs) become activated, provoking an antitumor immune response. TILs therapy is a one-time treatment that involves the adoptive transfer of autologous T cells isolated from the tumor tissue and expanded ex vivo to a patient after lymphodepletion. Therefore, we initiated an exploratory clinical study to establish the safety and feasibility of TILs in adolescent and young adults with osteosarcoma pulmonary metastases (ChiCTR1900026789).

Methods: This is an exploratory pilot single-arm trial in adolescent and young patients with relapsed and refractory advanced osteosarcoma pulmonary metastases (PMs). Fresh tumor tissues from relapse sites were obtained from each patient by thoracoscopic or local surgery and sent to Origincell Therapeutics for the cGMP production of therapeutic TIL cells. The total culture and expansion process required approximately 21-28 days. In preparation for the therapeutic TILs infusion, all subjects underwent lymphodepletion with Flu (30~40 mg/m²) and Cy (300~700 mg/m²) daily for 3 days to eliminate potentially suppressive immune cells. The patients were then infused with their autologous expanded TIL cells (Ori-TILs) with total dose of 6~13.6x10⁹ cells. Immediately after autologous TIL infusion, all subjects received up to 6~16 times of IL-2 (100,000~200,000 IU/kg) to promote activation, proliferation, and anti-tumor cytolytic activity of TILs. Adverse Event (AE) grade categorization is according to CTCAE 5.0, and tumor response was assessed per RECIST 1.1. As the trial progressed, the subjects' PK/PD data were also measured.

Results: As of June 20, 2021, 12 subjects with Enneking IIIB pathological diagnosed osteosarcoma with PMs were enrolled (Table.1). All subjects had progressed after standard treatment with chemotherapy. Some of them were treated with second-line off-label targeted therapy such as anlotinib or apatinib, or anti-PD-1 antibody. 11 subjects received autologous TIL cells via single infusion, of which 6 patients received the higher dose level of 1.0x10⁹. 11 patients reached at least 1 month of follow-up and tolerated the treatment well. One subject did not receive treatment due to unsuccessful preparation of the TIL manufacture. The most common adverse events reported were fever (80%), constipation (40%) and increased GGT (40%). High incidence of fever was due to IL2 infusion. All patients experienced transient decrease in lymphocyte count and leukopenia resulting from the lymphodepletion regimen. Grade 4 hematologic toxicities include lymphocytosis (8/11), neutropenia (2/11) and thrombocytopenia (1/11). No neurotoxicity was observed. Among the 11 evaluable subjects, the best responses achieved are 9 SD, 2 PD. The disease control rate (DCR) was observed in 9 patients (82%) and the median duration of SD is more than 4 months. The duration of remission of one patient with SD is more than 6 months and the

maximal % reduction in tumor size is more than 20 %. Subjects 1, 5, 8 and 9 had pulmonary metastases and the tumor samples for TIL expansion were obtained from these PMs. Notably subject 9 has sustained SD for over 6 months as of May 2021. Follow up is ongoing.

Conclusion: Current immune oncology approaches are not yet effective in osteosarcoma, and pulmonary metastases in osteosarcoma remain the major cause of cancer related mortality. Ligon et al presented data which supported that osteosarcoma PMs are more highly infiltrated by immune cells compared with primary tumors. Notably, tumors that demonstrate increased CD8 T cell infiltration and decreased PD-L1 expression were associated with improved PFS, suggesting that even in these relatively cold tumors the degree of immune response may influence the patient's outcome.

Our study results provide evidence that autologous TILs infusion therapy, combined with non-myeloablative lymphodepletion with cyclophosphamide and fludarabine, and accompanied by high dose IL-2 infusion, is safe and holds promising antitumor potential. This study supports continuing development of TIL in the treatment of r/r osteosarcoma with pulmonary metastases. Follow up research can explore optimization of the lymphodepletion and IL regimens, and finding ways to strengthen the cytotoxicity of TILs and their ability to overcome the mechanism of immune evasion.

Table 1: Comparison of Patients with Primary and Secondary Chondrosarcoma of the Scapula

Demographic	All Patients (n=39)	Primary Chondrosarcoma (n=31)	Secondary Chondrosarcoma (n=8)	P Value
Males	26 (67%)	20 (65%)	6 (75%)	0.69
Females	13 (33%)	11 (35%)	2 (25%)	0.69
Mean Age (Years)	46±17	50±16	31±14	<0.01
Tumor Size (cm)	8±6	7±5	12±7	0.03
Tumor Volume (cm ³)	714±1,733	402±636	1,792±3,527	0.04
High Grade Tumor	7 (18%)	6 (19%)	1 (12%)	0.65

Table 2: Limb Salvage Reconstruction following Resection of a Scapular Chondrosarcoma

Type of Resection	Type of Reconstruction
Extraarticular Partial Scapulectomy	Soft Tissue Alone (n=14) Scapulothoracic Fusion (n=2) Scapular Allograft (n=1)
Partial Scapulectomy Including Glenoid	Cement and Pin (n=3) Osteoarticular Allograft (n=2) Soft Tissue Alone (n=2) Staged Bony Autograft with Reverse Total Shoulder (n=1)
Total Scapulectomy	Soft Tissue with Suspension of Humerus to Clavicle (n=5) Total Scapular Allograft (n=1)
Scapulectomy and Proximal Humerus	Endoprosthetic Proximal Humerus Suspended to Clavicle (n=6)

Table 3: Factors Associated with Oncologic Outcome Following Scapular Resection for Chondrosarcoma

Demographic	Disease Specific Survival (HR 95% CI)	P Value	Local Recurrence (HR 95% CI)	P Value	Metastatic Disease (HR 95% CI)	P value
High Grade Tumor	18.15 (3.53-93.35)	<0.01	10.60 (2.23-50.23)	<0.01	13.30 (3.38-52.37)	<0.01
Primary Tumor	0.79 (0.15-3.97)	0.78	0.69 (0.13-3.62)	0.66	0.51 (0.13-1.99)	0.33
Male Gender	0.84 (0.20-3.56)	0.82	3.16 (0.37-26.41)	0.28	1.12 (0.29-4.37)	0.85
Age ≥55 years	1.55 (0.36-6.62)	0.54	4.66 (0.96-22.60)	0.055	1.53 (0.43-5.42)	0.50
Soft Tissue Mass	∞	<0.01	1.72 (0.33-9.01)	0.51	∞	<0.01
Tumor Size ≥8 cm	4.97 (0.99-24.93)	0.051	4.65 (0.89-24.60)	0.06	3.55 (0.91-13.78)	0.06
Local Recurrence	3.30 (0.78-13.87)	0.10	N/A		3.73 (1.05-13.26)	0.04
Positive Margins	0.85 (0.10-6.99)	0.88	8.85 (1.97-39.69)	<0.01	0.65 (0.08-5.14)	0.68

Table 4: Functional Outcome Following Resection of a Scapular Chondrosarcoma

Surgical Procedure	Partial Scapulectomy	Total Scapulectomy	Resection Involving Humerus	Glenoid Resection	P Value
Mean MSTS93	90±9%	70±9%	67±9%	80±12%	<0.01
Mean Forward Shoulder Elevation	140±38°	17±22°	28±19°	63±57°	<0.01



Poster #085 #1818959

CLINICAL OUTCOME OF EXTRA-AXIAL CHORDOMA: AN INTEGRATIVE DATA ANALYSIS

Toshihiko Nishisho, MD, PhD¹; Toki Shunichi, MD²; Ryo Miyagi, MD³; Koichi Sairyo, MD, PhD²

¹Tokushima Pref. Miyoshi Hospital, Tokushima, Tokushima, JAPAN, ²Tokushima University, Tokushima, Tokushima, JAPAN,

³Tokushima Prefectural Central Hospital, Tokushima, Tokushima, JAPAN

Objective: Chordomas are commonly located in axial bone, such as the skull base, vertebral bodies, and the sacrococcygeal bone. A quite small number of cases of chordoma can initially develop in extra-axial bone, which are referred to as extra axial chordoma (EAC). Brachyury, a highly specific marker of chordoma, are useful to diagnose of EAC and reports of EAC increased in these days. However, the definition, clinical future and the outcome remain unclear. In this study, we tried and integrative data analysis of EAC including our case.

Methods: A electronic search in PubMed until May 31, 2020, was performed using the keyword of “extra axial chordoma”. We extracted chordoma cases which show positive brachyury immunostaining and arise from bone and soft tissue of extremities, pelvis, thoracic wall. We excluded studies as follows: clinical information was insufficient, visceral cases, and cases which are difficult to distinguish from axial chordoma. All statistical analyses were performed using R version 3.6.3.

Results: This study included 32 EAC cases including one case from our institute, 20 men and 12 women, whose age was 13-87 years (mean 41 years, SD 19). The median follow-up period was 38.2 months (range 2–167 months). Seventeen tumors occurred in the upper extremities, 17 cases in the lower extremities, 2 cases in the pelvis, 2 cases in the thoracic wall. Twenty three patients were continuous disease free (CDF), 4 cases had no evidence of disease (NED), 4 patients were alive with disease (AWD), no patients died of disease (DOD), and one patient died of other diseases (DOOD). Two cases had lung metastases and one case had lymph node metastases. The 5-year local recurrence-free survival was 75.2% and the 5-year overall survival was 93.8%. Wide resection was significant favorable prognostic factor for local control in univariate analyses although multivariate analyses showed no prognostic factor.

Conclusion: EAC occurred in relatively younger age and had better prognosis compared to conventional axial chordoma. Wide local resection could control local recurrence of EAC. Therefore, initial image diagnosis is especially important for this quite rare disease.



Poster #086 #1819023

PATHOGENIC GERMLINE VARIANT OF PALB2 IN A PATIENT WITH EWING SARCOMA: IMPACT OF PALB2 LOSS ON RESPONSE TO DNA DAMAGE

Jessica D. Daley, MD¹; Sreya Dey²; Noah Brown, MD³; Elena Kessler, MS, CGC⁴; Julia Meade, MD⁵; Elena Mukherjee, MS⁶; Alexandra Superdock, MD⁷; James Cooper, MD⁵; Kelly M. Bailey, MD, PhD⁵

¹UPMC Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES, ²University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES, ³University of Michigan, Ann Arbor, Michigan, UNITED STATES, ⁴UPMC, Pittsburgh, Pennsylvania, UNITED STATES, ⁵University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES, ⁶University of Pittsburgh Dept of Pediatrics, Pittsburgh, Pennsylvania, UNITED STATES, ⁷UPMC Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES

Objective: Pathogenic germline variants in genes involved in DNA damage repair have been increasingly identified in patients with Ewing sarcoma. We have previously reported a patient with a germline variant in BARD1 (a binding partner of BRCA1), and demonstrated that loss of BARD1 enhances sensitivity to PARP inhibition and radiation. We now describe an adolescent diagnosed with two occurrences of distinct site, localized Ewing sarcoma greater than five years apart. This patient was found to have a germline variant in PALB2 (partner and localizer of BRCA2). PALB2 is a part of the BRCA pathway and is involved in homologous recombination in DNA damage repair. Heterozygous mutations in this gene have been associated with increased risk of breast and pancreatic cancer in adults. Here, we investigate the role of PALB2 in the DNA damage response in Ewing sarcoma.

Methods: This patient enrolled in the IRB-approved UPMC Musculoskeletal Oncology Registry and Tissue Bank. PCR analysis was performed to determine EWS-FLI1 fusion status. A Blueprints Genetics Comprehensive Hereditary Cancer Panel Plus was performed. An extensive family history of cancer was obtained. To investigate effect of PALB2 loss on Ewing cell sensitivity to DNA damage, control or PALB2 siRNA was transfected into A673, TC32, and CHLA-10 Ewing sarcoma cell lines, followed by exposure to DNA damage (PARP inhibition, radiation, or a combination). Cells were monitored for confluence and apoptosis using a live-cell IncuCyte 3/7 caspase assay. BARD1, BRCA1, and RAD51 siRNA were also utilized for comparison.

Results: RNA isolated from FFPE slides was subjected to PCR analysis and revealed that this tumor harbors a type 1 EWS-FLI1 fusion. Blueprints Genetics Comprehensive Hereditary Cancer Panel Plus revealed a likely pathogenic variant in PALB2: c.3469_3482del, p.(Gln1157Cysfs*28). PALB2 expression was successfully knocked down in Ewing sarcoma cell lines via PALB2 siRNA. Ongoing studies reveal the ability of PALB2 loss to impact Ewing cell response to DNA damage as compared to control siRNA. Additionally, the effect of PALB2 knockdown on response to DNA damage is compared to knock down of other DNA damage pathway genes described in patients with Ewing sarcoma. The culmination of these data suggest that Ewing tumors occurring in the setting of germline DNA damage repair gene defects may be more responsive to combinatorial therapy targeting the DNA damage response pathway.

Conclusion: We have identified a novel PALB2 germline variant in patient with a unique history of two distinct, localized Ewing tumors that developed >5 years apart. This variant has implications for future cancer screenings for this patient. Loss of PALB2 was studied in additional Ewing sarcoma cell lines in order to determine the impact on DNA damage response following exposure to radiation or PARP inhibitors. This work adds to the growing body of literature pertaining to the role of germline DNA damage repair gene variants in the response of Ewing tumors to DNA damage. Future prospective analysis of outcomes for this unique subset of patients with Ewing sarcoma is warranted.



Poster #087 #1818933

CAN LOW-GRADE CHONDROSARCOMA IN FLAT BONES BE TREATED WITH INTRALESIONAL CURETTAGE AND CRYOTHERAPY?

Kwangwon Park, MD, PhD¹; John Krumme, MD²; Moses Adebayo, MD³; Brock Adams, MD⁴; Robert Henshaw, MD⁴
¹Arnold Palmer Children's Hospital, Oviedo, Florida, UNITED STATES, ²University of Missouri, Leawood, Kansas, UNITED STATES, ³Howard University Hospital, Washington, District of Columbia, UNITED STATES, ⁴Washington Hospital Center, Washington, District of Columbia, UNITED STATES

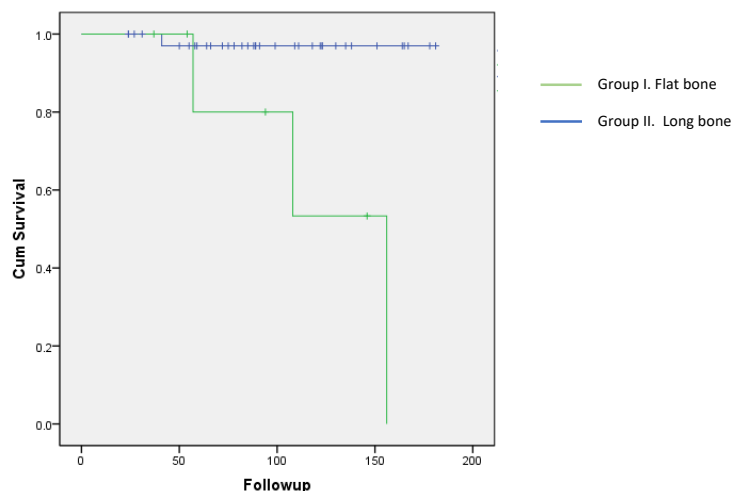
Objective: Various surgical options are available for chondrosarcomas including wide or radical resection or intralesional curettage with adjuvants such as cryotherapy. Chondrosarcoma in flat bones such as pelvis or scapula are thought to be more aggressive in behavior, and little is known about treatment outcome of low-grade chondrosarcoma in flat bones utilizing intralesional curettage and adjuvant cryotherapy. We tried to determine whether there are any differences between patients who had low-grade chondrosarcoma in their flat bones and long bones with regards to ¹disease outcome, ²functional outcome, and ³treatment complications.

Methods: We retrospectively reviewed 45 patients with primary low-grade chondrosarcoma who were treated with intralesional curettage and cryotherapy between 1993 to 2016. The minimum follow-up period was 2 years (average: 7.8 years). The patients were divided by location of tumor, group I (flat bones, 7 patients) and group II (long bones, 37 patients). Clinical data including gender, age, grade and size of the tumor, and disease outcome including local recurrence-free survival and disease-free survival were evaluated. Functional outcome was assessed using Musculoskeletal Tumor Society (MSTS) functional score. Complications related with the procedure were also analyzed.

Results: There were 4 local recurrences, 1 in proximal femur, 1 in sacrum, and 2 in periacetabular area. The local recurrence rate was higher in group I with 5 years disease-free survival of 80.0% in group I and 97.0% in group II (Log-rank test, p = 0.001). All recurrent cases were noted to have initially presented with soft tissue extension (grade IB); recurrences were treated with secondary wide resection. One recurrent case in periacetabular area showed change to high grade IIB chondrosarcoma and treated with salvage hemipelvectomy, however there was no disease related mortality noted in either cohort. There were no statistically significant relationships between age, grade or size of the tumor and local recurrence. The mean MSTS score at the last follow up was 21.7 in group I and 27.9 in group II (Mann-Whitney test, p = 0.045). 5 complications were reported in group II, 1 stress fracture of femur treated conservatively, and 4 implant related complications (extravasation of the cement, interlocking screw irritation) which resolved after revision surgery.

Conclusion: Intralesional curettage and cryotherapy for low-grade chondrosarcoma may be appropriate for patients with lesions confined to bone. Patient with stage IB lesions should be treated with alternative surgical options such as wide excision to ensure optimal local control. Locally recurrent tumors are at risk of transformation into higher grade lesions but may still be treatable with salvage wide resection.

1 Figure 1. Survival estimates of study population by tumor location.



2

3 Figure 1 shows the time to recurrence of chondrosarcoma by tumor location. A higher proportion of tumors
4 located in flat bones undergoes recurrence per unit time compared to those located in long bones (p = 0.001).



Poster #088 #1818848

PREOPERATIVE SARCOPENIA IS ASSOCIATED WITH LOCAL TUMOR RECURRENCE BUT NOT WOUND COMPLICATIONS FOLLOWING SACRAL TUMOR RESECTION

Matthew T. Houdek, MD; Elyse Brinkmann, MD; Doris E. Wenger, MD; Joshua D. Johnson, MD; Syed M. Karim, MD; Daniel Blezek, PhD; Peter S. Rose, MD
Mayo Clinic, Rochester, Minnesota, UNITED STATES

Objective: Sacral tumor resection is known for a historically high rate of complications, namely wound complications. Various risk factors for wound complications exist, including high sacral resections, tumor size and use of radiotherapy. Recent series have shown the association of sarcopenia on the incidence of wound complications following sarcoma surgery, however there is a paucity of data examining the impact of sarcopenia on the outcome of sacral tumor resection. The purpose of this study is to investigate the impact of preoperative sarcopenia on ¹complications and reoperation and ²patient outcome.

Methods: A group of 103 patients undergoing a sacrectomy (Mayo Type 1) for a malignant tumor from 2005-2017 were reviewed. Of this, 50 (49%) of patients had a preoperative CT scan which included the L4 vertebral level within 90-days of surgery. Two patients with perioperative deaths were removed, for a remaining group of 48 (47%) patients. The group included 25 males and 23 females with a mean age and body mass index (BMI) of 54±13 years and 28.6±6.8 kg/m². 31 (65%) cases were performed for a primary sarcoma, and 17 (45%) were performed for locally recurrent colorectal carcinoma. The mean tumor size and volume were 9±5 cm and 594±932 cm³. 27 (56%) were considered high sacrectomies (S2 or higher), and included 7 (15%) total sacrectomies requiring reconstruction (Mayo 1A), 2 (4%) subtotal sacrectomies requiring reconstruction (Mayo 1B) and 39 (77%) subtotal sacrectomies not requiring reconstruction (Mayo Type 1C). Radiotherapy was given to 25 (52%) of the patients, with a mean total dose of 47±13 Gy. Central sarcopenia was measured by measuring the psoas:lumbar vertebra index (PLVI), with the 50th percentile (0.97) used to determine which patients were high (>0.97) versus low (<0.97). Of which 24 (50%) patients were considered to have a high PLVI and 24 (50%) were considered to have a low PLVI (sarcopenic).

Results: There was no difference (p>0.05) in comparing the base demographic of patients without sarcopenia compared to those with sarcopenia in terms of age, BMI, gender, tumor size or volume, high sacral resections or history of radiotherapy (Table 1).

There was no difference (p>0.05) in the total operative time or units of red blood cells transfused during the sacrectomy between patients with sarcopenia and those without (Table 2). When comparing patients with sarcopenia and those without, there was no difference in the incidence of postoperative wound complications (n=13, 54% vs. n=13, 54%, OR 1.0 (95% CI 0.32-3.11), p=1.0), deep infection (n=8, 33% vs. n=9, 38%), OR 0.83 (95% CI 0.25-2.72), p=1.0) or reoperation (n=13, 54% vs. n=10, 42%, OR 1.65 (95% CI 0.52-5.18), p=0.56). Patients with sarcopenia were noted to have a lower mean MST593 rating compared to those without (56±27% vs. 69±24%, p=0.10), however this failed to reach statistical significance.

Conclusion: Contrary to previous studies which highlighted an association between sarcopenia and postoperative wound complications, in the current study sarcopenia was not predictive of wound complications, infection or reoperation following sacral tumor resection. Sarcopenia was however an independent risk factor for local tumor recurrence following sacrectomy, and as such should be considered when counseling patients on the outcome of sacral tumor resection.

Table 1: Comparison and Surgical Outcomes of Patients With and Without Sarcopenia Undergoing Sacral Tumor Resection

Patient Demographic	Sarcopenia (PLVI<0.97)	No Sarcopenia (PLVI >0.97)	P Value
Mean Patient Age	57±13 Years	51±12 Years	0.08
Mean BMI	27.9±6.9 kg/m ²	29.3±6.9 kg/m ²	0.49
Male Gender	10 (42%)	15 (62%)	0.24
Female Gender	14 (48%)	9 (38%)	0.24
Mean Tumor Size	8±3 cm	10±6 cm	0.30
Mean Tumor Volume	384±384 cm ³	813±1,251 cm ³	0.11
Primary Sarcoma	13 (54%)	18 (75%)	0.22
High Sacrectomy	13 (54%)	14 (58%)	1.0
Radiotherapy	11 (46%)	12 (50%)	1.0
Diabetes Mellitus	3 (13%)	3 (13%)	1.0
Tobacco Use	7 (29%)	6 (25%)	1.0
Outcome	Sarcopenia (PLVI<0.97)	No Sarcopenia (PLVI >0.97)	P Value
Mean Total Operative Time	1,093±502 minutes	1,048±623 minutes	0.77
Red Blood Cells Units Transfused	12±15 Unites	10±18 Units	0.75
Wound Complications	13 (54%)	13 (54%)	1.0
Deep Infection	8 (33%)	9 (38%)	1.0
Sacral Stress Fracture	3 (13%)	1 (4%)	0.60
Mean MSTs93 Score	56±27%	69±24%	0.10
Ambulatory	19 (79%)	21 (88%)	0.41
Reoperation	13 (54%)	10 (42%)	0.56

Table 2: Cox Hazard Regression on the Impact of Sarcopenia on Oncologic Outcome

Oncologic Outcome	Sarcopenia Cox Hazard Ratio (95% CI)	P Value
Disease Free Survival	2.04 (0.68-6.12)	0.20
Overall Survival	1.57 (0.60-4.06)	0.34
Metastatic Disease	2.47 (0.66-9.22)	0.17
Local Recurrence	6.60 (1.47-29.56)	0.01



Poster #089 #1819084

PRELIMINARY SAFETY RESULTS OF A PILOT STUDY OF HIGH DOSE PEMETREXED FOR CHORDOMA

Kamlesh K. Sankhala, MD¹; Tiffany Juarez, MD²; Jose Carrillo, MD³; Naveed Wagle, MD³; Akanksha Sharma, MD⁴; Judy Truong, PAC³; Minhdan Nguyen, PAC³; Annie Heng, RN³; Jaya Gill, RN³; Raffi Nersesian, Clinical Research³; Santosh Kesari, MD, PhD³

¹NextGen Oncology, Cedars Sinai Medical Center, Beverly Hills, California, UNITED STATES, ²Saint John's Cancer Institute and Pacific Neuroscience Institute at Providence Saint John's Health Center, Santa Monica, CA, Santa Monica, California, UNITED STATES, ³Saint John's Cancer Institute and Pacific Neuroscience Institute at Providence Saint John's Health Center, Santa Monica, CA, Santa Monica, California, UNITED STATES, ⁴Saint John's Cancer Institute and Pacific Neuroscience Institute at Providence Saint John's Health Center, Santa Monica, CA, Santa Monica, California, UNITED STATES

Objective: Chordomas are ultra-rare tumors that arise along the axial spine and no standard of care exists for refractory disease. Pemetrexed is a multitargeted antifolate that inhibits thymidylate synthase (TS) and other enzymes involved in nucleotide biosynthesis. Considering the majority of chordomas do not express TS, we sought to obtain preliminary data on the therapeutic activity and safety of high-dose pemetrexed.

Methods: Adults with chordoma were treated on an open-label, single-arm, uncontrolled trial. Pemetrexed 900 mg/m² is administered by intravenous infusion every 3 weeks, along with supportive medications of folic acid, vitamin B12, and dexamethasone. The primary endpoint is the objective response rate according to RECIST v1.1. Secondary and exploratory endpoints include adverse events, progression-free survival (PFS), tumor molecular profiles, and alterations in potential tissue and blood-based biomarkers before and after treatment.

Results: Fifteen patients with chordoma were enrolled between February 2020 and June 2021. Adverse events have been similar to those expected for pemetrexed, with the most common being rash, creatinine increased, diarrhea, fatigue, mucositis, and pruritus. Adverse events have been relatively mild, with one Grade 3 creatinine increase and 1 Grade 4 lymphopenia. No Grade 5 adverse events, unexpected toxicities, or dose-limiting toxicities have been observed to date. One patient discontinued study treatment after four cycles due to psychosocial issues during the Covid-19 pandemic, one patient switched to receiving treatment in her home state after 13 cycles, and three patients discontinued due to disease progression; the other 10 patients continue on study.

Conclusion: High-dose pemetrexed is safe and well-tolerated in the 15 patients treated on the ongoing pilot study. Enrollment is closed and assessment of efficacy is ongoing. (Funded by Chordoma Foundation and Lilly; ClinicalTrials.gov number, NCT03955042).



Poster #090 #1818985

TETRAVALENT DEATH RECEPTOR 5 AGONIST INBRX-109 IN EWING SARCOMA: PLANNED PHASE 1 COHORT EXPANSION GUIDED BY PRECLINICAL DATA

Emily Rowell, PhD¹; Vasily Andrianov, MD²; Analeah Heidt, PhD³; Klaus Wagner, MD, PhD³; Chase Deveraux³; Will Crago³; Brendan Eckelman, PhD³; Quinn Deveraux, PhD³; Victoria T. Chua-Alcala, MD⁴; Joseph Chao, MD⁵; Warren Chow, MD⁵; Rashmi Chugh, MD⁶; Anthony P. Conley, MD⁷; Vivek Subbiah, MD⁸

¹Inhibrx, inc., La Jolla, California, UNITED STATES, ²Inhibrx Inc., La Jolla, California, UNITED STATES, ³Inhibrx, Inc., La Jolla, California, UNITED STATES, ⁴Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES, ⁵City of Hope Comprehensive Cancer Center, Duarte, California, UNITED STATES, ⁶University of Michigan, Ann Arbor, Michigan, UNITED STATES, ⁷MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁸The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES

Objective: INBRX-109 is a single domain-based agonist antibody targeting death receptor 5 (DR5). Activation of DR5 can induce programmed cell death through the extrinsic apoptosis pathway in a cancer-biased manner. Precisely engineered, the valency of INBRX-109 was empirically selected to include four DR5 binding domains to overcome the limitations of earlier generation agonists that lacked efficacy or ceased development due to hepatotoxicity. INBRX-109 shows robust anti-tumor activity in patient derived models of numerous tumor types, including Ewing sarcoma. Based on this encouraging pre-clinical data, we are planning to initiate an Ewing sarcoma expansion cohort to explore the combination of INBRX-109 with irinotecan and temozolomide (IT).

Methods: A three-part, Phase 1 clinical trial (NCT03715933) evaluating the safety and efficacy of INBRX-109 in a variety of tumor types was initiated in November 2018. Part 1, dose escalation, was completed in August 2019 with enrollment of 20 patients. INBRX-109 was well-tolerated, with no significant toxicities observed at doses up to and including the maximum administered dose of 30 mg/kg; a maximum tolerated dose was not reached and a dose level of 3 mg/kg was chosen for further investigation. Single agent and chemotherapy combination expansion cohorts are currently enrolling in Part 2 and Part 3 of the study, respectively. In these expansion cohorts, safety, PK, immunogenicity, efficacy and potential predictive diagnostic biomarkers of INBRX-109 are being evaluated. An additional chemotherapy combination cohort in Ewing sarcoma is planned to start in 2H 2021.

Results: In in vitro preclinical studies, DR5 receptor clustering by INBRX-109 potently induced cancer cell death across a variety of tumor cell lines, with minimal observed cytotoxicity on the human hepatic cell line, HepaRG. This activity translated to potent in vivo anti-tumor activity in patient derived xenograft models derived from numerous cancers, including Ewing sarcoma (Figure 1). Based on the observed single-agent activity in Ewing sarcoma, in vitro studies were initiated to investigate the combinatorial activity of INBRX-109 with SN-38, the active metabolite of the chemotherapeutic irinotecan. As shown in Figure 2, INBRX-109 demonstrates single agent activity, as well as combination activity with SN-38 across multiple Ewing sarcoma model cell lines. Our pre-clinical data suggest added benefit of the combination of DR5 agonism and SN-38, with INBRX-109 mediated DR5 crosslinking providing a key pro-apoptotic signal in Ewing sarcoma cell lines and patient derived xenografts.

The Phase 1 trial Ewing sarcoma expansion cohort will investigate safety and efficacy of INBRX-109 (1 or 3 mg/kg IV Day 1 Q21D) in combination with irinotecan (50 mg/m²/day IV Days 1-5 Q21D) and temozolomide (100 mg/m²/day PO Days 1-5 Q21D). This cohort will enroll 20 patients with locally advanced or metastatic, non-resectable, Ewing sarcoma, who have received at least one prior line of systemic treatment with a preferred first line chemotherapy regimen (e.g., VDC/IE, VAI, VIDE, VDC), and who are candidates for irinotecan and temozolomide given as second, third or fourth line therapy.

Conclusion: Encouraging pre-clinical anti-cancer activity warrants further investigation of INBRX-109 in unresectable or metastatic Ewing sarcoma in combination with irinotecan based chemotherapy. The Ewing sarcoma cohort is planned to start in 2H 2021 and any clinical updates if available will be shared at the CTOS meeting in November 2021.

Figure 1. *In vivo* activity of INBRX-109 in an Ewing sarcoma patient-derived xenograft model

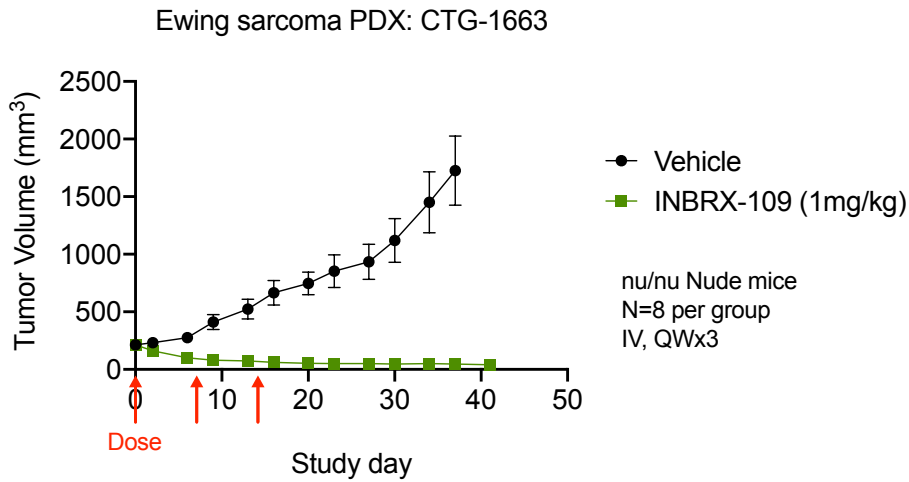
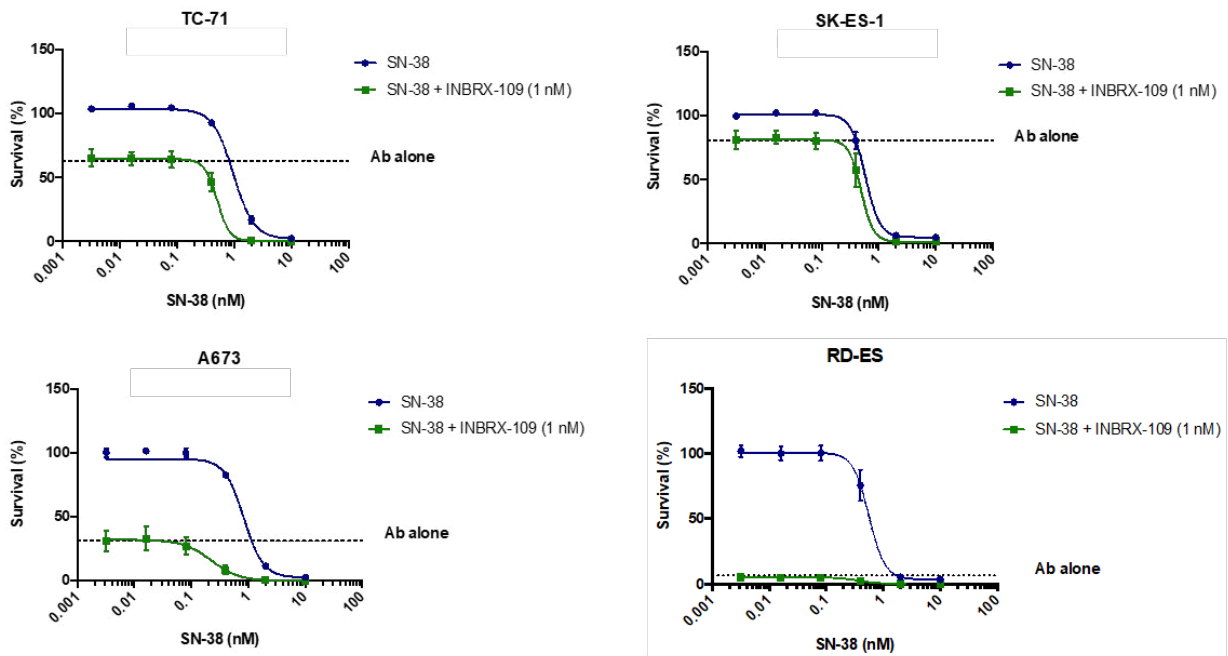


Figure 2. Example of combinatorial INBRX-109 and SN-38 activity in Ewing sarcoma cell line





Poster #091 #1819036

MORE TO CONSIDER: THE MISDIAGNOSIS OF ACUTE LYMPHOBLASTIC LEUKEMIA AS EWING'S SARCOMA

Lauren Riggs¹; Madeline Link¹; Paul M. Kent, MD²

¹Rush University Medical Center, Chicago, Illinois, UNITED STATES, ²Rush University Medical Center, River Forest, Illinois, UNITED STATES

Objective: Acute lymphoblastic leukemia/lymphoma (ALL/NHL) is the most common childhood cancer, with 3000 cases/yr. Ewing's sarcoma (EWS) is 10X less common. EWS and pediatric pre-B cell ALL can share similarities clinically, radiographically, and immunohistochemically (IHC). For example, both: are small round blue cell tumors with abundant glycogen, can have bone marrow replacement, can have lytic bone lesions and bone pain, and can stain for FLI1 and CD99. Because of age, EWS is often seen by adult oncologists and may have a workup looking for the more mature adult B-cell ALL/NHL, which does not include IMC markers for immature pre-B cell lymphoblasts (CD10/CD22) (table 1). These malignancies are differentiated by FISH for the FLI1-EWS fusion (in 95% of EWS), but this takes time. Our objective is to inform clinicians about the potential to misdiagnosis ALL for EWS. We report 4 cases of ALL mimicking EWS.

CASE 1: A 7 year old male presented with a painful destructive iliac mass (Figure 2-left side) and CBC with mild thrombocytopenia. Biopsy of the mass showed small round blue cells which were FLI-1/CD99(+) and CD20/CD45(-), both characteristic of EWS and thought to rule out B cell-NHL. However, the mass was negative by FISH for the EWSR1 rearrangement, which prompted further workup, revealing: CD10/CD22/TdT(+), which changed the diagnosis to pre-B cell lymphoblastic lymphoma of bone.

CASE 2: A 14 year old male presented with a painful destructive distal femur mass (Figure 2-right) with normal CBC and LDH. Biopsy of mass again showed small round blue cells FLI-1/CD99 (+) and CD20/CD45(-), and as before, negative for EWSR1 rearrangement. Because of the experience of the previous case, IHC studies were expanded, showing PAX5/CD22/TdT(+), confirming diagnosis of pre-B cell lymphoma of bone.

Methods: A literature review on PubMed and Google Scholar with search terms: "childhood acute lymphoblastic leukemia," "Ewing's sarcoma," and "misdiagnosis of childhood acute lymphoblastic leukemia" in conjunction with a review of patient records.

Results: In addition to our patients, in our literature review we found 2 cases of misdiagnoses between EWS and ALL. One misdiagnosis of ALL arose 5-year-old boy after receiving treatment for EWS. The ALL was misdiagnosed as bone marrow metastasis of the EWS. Another of a two-year-old girl originally diagnosed with extraosseous EWS, which was later found to be an extramedullary disease as a part of ALL.

Conclusion: The misdiagnosis of ALL as EWS has been reported in at least two patients in literature in the past. We found 2 additional cases of ALL misdiagnosed as EWS at our institution. As EWS is typically found in young adults, the IMC markers specific to pediatric pre-B cell ALL are often overlooked. CD99 and FLI1 can both be positive in pediatric ALL/NHL and therefore cannot completely confirm the presence of EWS. We recommend testing for CD10, CD22, and TdT as these are specific to pediatric ALL.

Table 1

Marker	EWS	Adult B-cell ALL / Lymphoma	Pediatric Pre-B cell ALL /Lymphoma
FLI1	positive	negative	positive (Rarely)
CD99	positive	negative	positive (Occasionally)
CD45	negative	positive	negative
CD20	negative	positive	negative
CD10	negative	negative	positive
CD22	negative	negative	positive
TdT	negative	positive	positive

Table 2

Patient	Our Patient/ From Literature	Original Diagnosis	Positive IMC Markers Found	Revised Diagnosis
1	Patient 1	EWS	CD99, FLI-1, CD22, CD19, TdT	ALL
2	Patient 2	EWS	CD99, PAX5, CD22, TdT	ALL / NHL
3	From Literature (Li et al, Medicine, 97(3))	EWS	FLI-1, CD10, CD34, CD99	ALL
4	From Literature (Jakovljević et al, Pediatr. Blood Cancer, 54: 606-609)	EWS	CD10, CD19, CD34, CD99, TdT, FLI-1, cCD79a	ALL

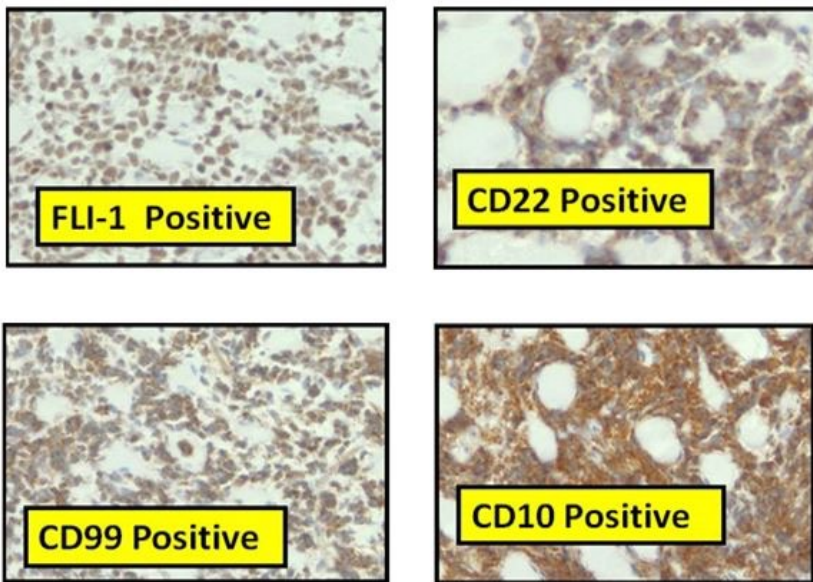


Figure 1: IMC Markers for classic EWS: CD99/FLI-1(+) (left side images), CD20/CD45(-) – thought to rule out B cell leukemia/lymphoma (not shown). On re-study patient was found to be CD10/CD22(+) (right side images) and TdT(+) (not shown) thus changing the diagnosis to pre-B ALL.

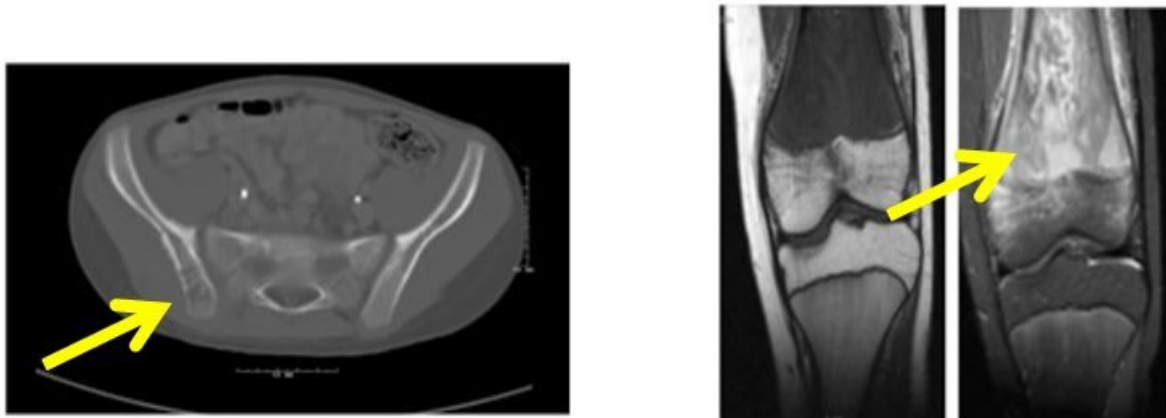


Figure 2: CT scans of patients 1 and 2.



Poster #092 #1819010

PRESENCE OF TUMORAL STEM CELLS AS A PROGNOSTIC FACTOR IN OSTEOSARCOMA OSTEOLASTIC IN ADULTS

Miguel Angel Clara-Altamirano, MD, MSc¹; Claudia HS Caro-Sanchez, MD, MSc¹; Alethia Alvarez-Cano, MD, MSc²; Carlo C Cortés-González, PHD¹; Silvio A Namendys-Silva, MD, MSc¹; Dorian Y. Garcia-Ortega, MD, MSc, FACS³
¹Instituto Nacional de Cancerología, Tlalpan, Distrito Federal, MEXICO, ²Christus Muguerza, Monterrey, Nuevo Leon, MEXICO, ³Instituto Nacional de Cancerología, Mexico, Distrito Federal, MEXICO

Objective: Osteosarcoma (OS) is the most common sarcoma of the bone. Currently, the most important factor in predicting survival of patients with osteosarcoma is the degree of response to neoadjuvant chemotherapy. The existence of osteosarcoma stem cells has been proposed as a mechanism of chemotherapy resistance, recurrence, and perhaps distant metastasis. These theories remain unconfirmed.

The aim of this work is to demonstrate the presence of tumor stem cells in osteosarcoma biopsies through the detection of CD117, ALDH1, CD133, and CD44, and to analyze their relationship with prognosis of this group of patients.

Methods: A descriptive, retrospective, and analytical study was carried out. We included samples from patients with a diagnosis of high-grade osteosarcoma, treated in a sarcoma referral center from March 1, 2013 to February 28, 2018. Paraffin-embedded blocks with >60% cellularity was selected. Histological sections were obtained from each block in electro-charged slides, with which immunofluorescence studies were carried out for the identification of CD117, ALDH1, CD133, and CD44 using the Axio Scan Z1 microscope.

Results: Samples from 14 patients were analyzed, the median age was 24.1 years, and male:female ratio was 2:1, the most frequent location was the distal femur (35.7%). The presence of ALDH 1 was demonstrated in 71.4%, CD44, and ALDH1 in 28.6%, CD133 and ALDH1 in 64.3% and tumor stem cells in 35.7%. No association was found between the expression of these markers and worse overall survival or response to chemotherapy.

Conclusion: We found no difference between the presence of CD117, ALDH1, CD133 and CD44 with the response to neoadjuvant chemotherapy, however, the high prevalence of stem cells in the analyzed tumor tissue is striking, which opens the possibility of future studies, since our sample is small.

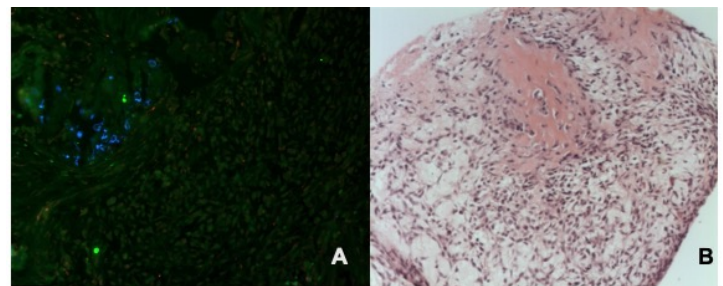
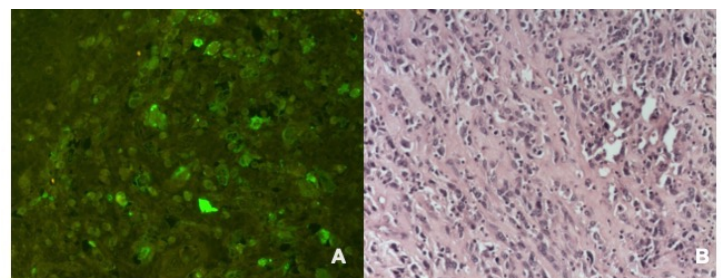
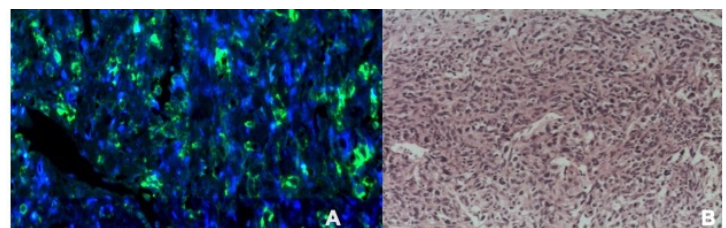


Figure 1 A. Multiplex 20X. with the presence of ALDH1 (green) and CD44 (Blue). B. Hematoxylin and Eosin section of the case (20X).



A. Multiplex 40X. presence of ALDH1 (green). B. Cut in Hematoxylin and Eosin of the case (20X)



A. Multiplex 20X. presence of CD133 (red), ALDH1 (green) and CD44 (Blue). B. Hematoxylin and Eosin section of the case (20X).



Poster #093 #1819062

SUCCESSFUL TREATMENT OF A CHILD WITH SYMPTOMATIC BRACHIAL PLEXUS OSTEOSARCOMA METASTASIS WITH MICROSPHERE EMBOLIZATION

Rhea M. Nambiar¹; Madeline Link²; Paul M. Kent, MD³

¹Rush University Medical Center, Boston, Massachusetts, UNITED STATES, ²Rush University Medical Center, Chicago, Illinois, UNITED STATES, ³Rush University Medical Center, River Forest, Illinois, UNITED STATES

Objective: Osteosarcoma (OST) is a highly prevalent malignant bone tumor for pediatric patients (Chu et al., 2007). The only proven therapy for gross disease, whether primary, metastatic or relapsed, is surgical excision. However, many patients are not surgical candidates, their disease is too extensive or too inaccessible for resection. Arterial embolization is used in practice to reduce a tumor's blood supply and thereby reduce or stagnate growth (Chu et al., 2007), and as an adjunct to definitive limb salvage surgery. We report a case of a successful arterial microsphere embolization of multiply relapsed OST for a large lung mass compressing on a patient's brachial plexus.

Methods: The patient is a female, now 15, with multiply (five) relapsed disseminated osteosarcoma (Fig 1). The patient experienced tightness and numbness in the right upper extremity, right axillary, right midclavicular, and right lateral neck. She had mild relief at first with gabapentin, but despite systemic chemotherapy, Samarium and stereotactic radiotherapy, the mass grew, became more PET avid and led to diminished sensation and motor impairment of her dominant hand. This mass was entrapped between the pleural space and chest wall cavity at the site of a previous pleurodesis for refractory pneumothorax, which rendered the tumor as inaccessible and inoperable. The patient was planning for a very important event (Quinceañera), so every effort was made for her to feel as good as possible. Therefore, microsphere embolization therapy was offered after being discussed at our Tumor board, and with an understanding that this was not standard therapy in the hopes of palliating the pain.

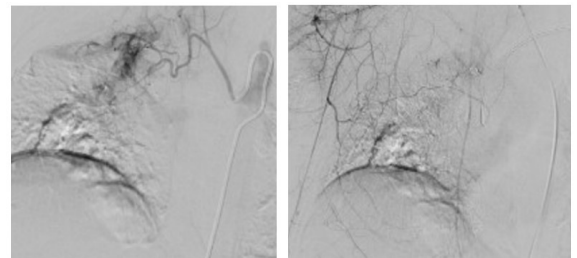
The microsphere embolization successfully hindered blood flow to the mass, which is shown in the pre- and post-embolization angiograms (Fig 1).

Within 5 days post-op the patient had better hand movement and motor control, less numbness and a marked reduction in pain. Her serum alkaline phosphatase, which had previously served as a reliable marker of response to treatment, had decreased (Fig 2 and 3). She was able to enjoy her Quinceañera.

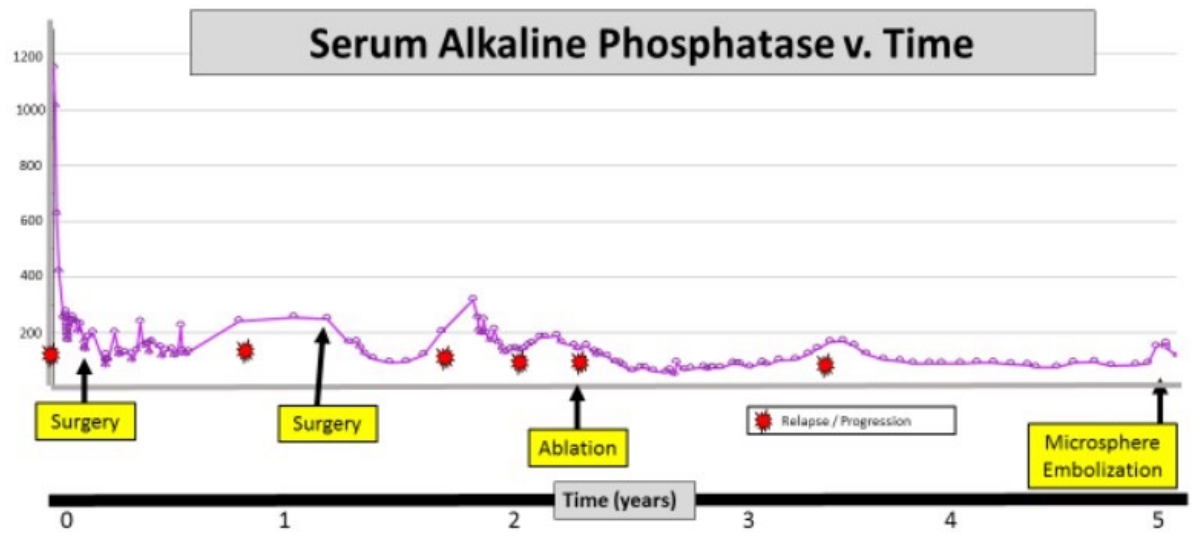
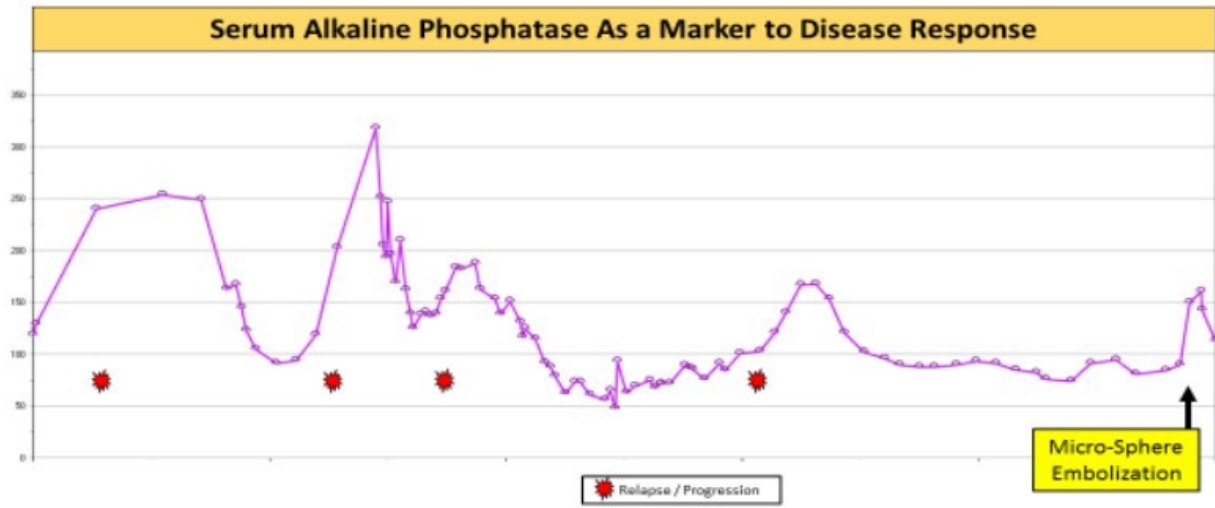
A literature review limited to the last 15 years was conducted on PubMed and Google Scholar using the keywords: "brachial plexus", "osteosarcoma", "arterial embolization", and "children".

Results: Out of the 20 results listed using arterial embolization, this appears to be the first pediatric case where arterial microsphere embolization was used for pain palliation and as a primary treatment for an inaccessible OST mass that compressed the patient's brachial plexus.

Conclusion: Using an arterial microsphere embolization procedure can be beneficial for pain relief in pediatric patients with multiply relapsed sarcoma (Mavrogenis et al., 2014). This minimally invasive procedure to effectively and safely block blood supply to a symptomatic metastatic site may be considered as an option for rapid palliation of pain and improvement of quality of life. Our hope is that further experience and research into arterial microsphere embolization can be informed by our report.



Pre-embolization angiogram Post-embolization angiogram





Poster #094 #1818838

APATINIB PLUS IFOSFAMIDE AND ETOPOSIDE (IE) FOR RELAPSED OR REFRACTORY OSTEOSARCOMA: A RETROSPECTIVE STUDY IN TWO CENTERS IN CHINA

 Lu Xie, MD¹; Jie Xu, MD¹; Xin Sun, MD¹; Xiaowei Li, MD¹; Kuisheng Liu, MD¹; Xin Liang, PhD¹; Zuli Zhou, MD¹; Hongqing Zhuang, MD²; Kunkun Sun, MD¹; Jin Gu, MD³; Wei Guo, MD and PhD¹
¹Peking University People's Hospital, Beijing, Beijing, CHINA (PEOPLE'S REPUBLIC), ²Peking University Third Hospital, Beijing, Beijing, CHINA (PEOPLE'S REPUBLIC), ³Peking University Shougang Hospital, Beijing, Beijing, CHINA (PEOPLE'S REPUBLIC)

Objective: Apatinib has led to positive responses in the treatment of osteosarcoma refractory to first-line chemotherapy. However, apatinib demonstrates only short-lived activity, and the disease control rate of musculoskeletal lesions is worse than that of pulmonary lesions. This treatment failure has been partly overcome by the addition of ifosfamide and etoposide (IE). Here, we retrospectively compared the activity of apatinib + IE in relapsed or refractory osteosarcoma in two sarcoma centres in China.

Methods: We retrospectively analyzed medical files and radiographic materials of patients with osteosarcoma relapsed or refractory to first-line chemotherapy, who had received combination of apatinib and IE regimen between June 3rd, 2017 and July 17th, 2020. Thirty-three patients were included.

Results: The included patients had received a combination of apatinib 500 mg (orally) daily and the IE regimen (n = 33) between June 3, 2017, and July 17, 2020. The tumour burden was considerable in these patients: 16/33 (48.5%) patients had lung and musculoskeletal lesions, and 31/33 (93.9%) patients had progressed to two lines of therapies at baseline. With a median follow-up duration of 28.4 (interquartile range [IQR], 16.1–38.3) months, 21/33 (63.6%) patients had objective responses, and the median event-free survival was 11.4 (IQR, 6.7–18.4) months. The median overall survival was 19.8 (IQR, 13.1–30.6) months. At the last follow-up, 16/33 patients had tumour downstaging, and all lesions had been completely resected.

Conclusion: For osteosarcoma with multiple sites of metastasis, apatinib + IE demonstrated clinically meaningful anti-tumour activity and delayed disease progression in patients with recurrent or refractory osteosarcoma after failure of chemotherapy. This combination with manageable toxicity deserves further investigation in prospective trials.

Calculation method for progression-free survival (PFS) and event-free survival(EFS) in this study

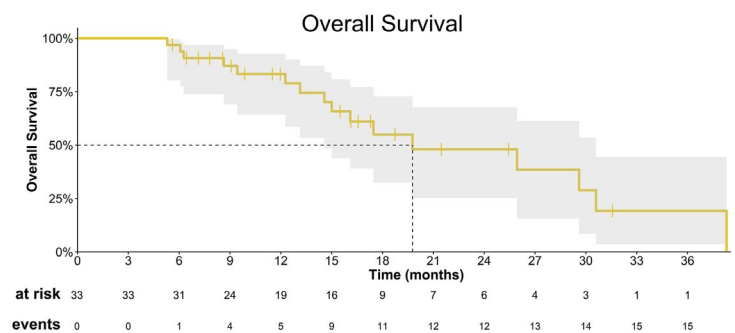
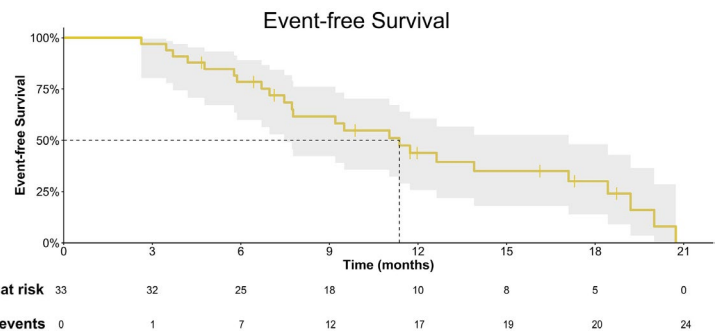
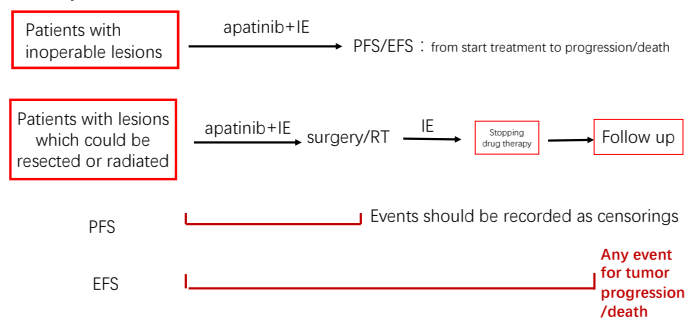


Table IV. Comparison of the patients' demographics and efficacy of different apatinib-based therapeutic strategies for advanced osteosarcoma.

Items	Apatinib+IE (N=33)	Apatinib (N=37)	Apatinib+Camrelizumab (N=41)	IE (N=46)
Study types	Retrospective study	Prospective trial	Prospective trial	Retrospective study
Trial registration number	NCT04690231	NCT02711007	NCT03359018	NCT04690231
Age (year; average±standard deviation) (95% CI)	19.1±8.5 (16.0, 22.2)	21.7±11.5 (17.9, 25.6)	19.7±9.0 (17.1, 22.4)	17.7±9.3 (14.9, 20.5)
Target lesions before treatment, N (%)				
Pulmonary lesions	13 (39.39)	27 (72.97)	18 (41.86)	39 (84.78)
Musculoskeletal lesions	3 (9.09)	4 (10.81)	3 (6.98)	1 (2.17)
Lung+ Musculoskeletal lesions	16 (48.48)	6 (16.22)	22 (51.16)	6 (13.04)
Lung+bone+other lesions ^a	1 (3.03)	0 (0.00)		0 (0.00)
Lines of systemic therapy				
1 st line (MAPI ^b)	15 (45.45)	31 (83.78)	37 (86.05)	40 (86.96)
2 nd line (IE/GT)	16 (48.48)	5 (13.52)	6 (13.95)	5 (10.87)
3 rd line	2 (6.06)	1 (2.70)		1 (2.17)
ECOG status before treatment, N (%)				
0	20 (60.60)	27 (72.97)	34 (79.07)	44 (95.65)
1	11 (33.33)	10 (27.03)	9 (20.93)	2 (4.35)
2	2 (6.06)	0 (0.00)	0 (0.00)	0 (0.00)
Osteosarcoma subtypes, canonical types, N (%)	32 (96.97)	35 (94.59)	42 (97.67)	46 (100.00)
Complete response, N (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Partial response, N (%)	21 (63.6)	16 (43.2)	9 (20.9)	13 (26.1)
Stable disease, N (%)	12 (36.4)	8 (21.6)	26 (60.5)	28 (60.9)
Progressive disease, N (%)	0 (0.0)	13 (35.1)	8 (18.6)	5 (10.9)
ITT Event-free survival				
Delete loss rate, N (%)	9 (27.3)	11 (29.7)	7 (16.3)	12 (42.9)
KM median (Q1, Q3) months	11.4 (7.5, 17.1)	4.5 (3.5, 6.3)	6.2 (3.6, 8.9)	11.7 (7.6, 15.7)
6 months	78.5%	36.8%	50.9%	71.7%
12 months	39.5%	<10%	<10%	56.8%
ITT Overall survival				
KM median (Q1, Q3) months	19.8 (9.4, 51.8)	9.9 (8.0, 19.0)	11.3 (8.1, 14.8)	30.4 (26.9, NR)
Complete Surgical Remission, N (%)	16 (48.5)	0.0 (0.0)	0.0 (0.0)	23 (50.0)

^aOther sites including lymph nodes, visceral metastasis and/or brain metastasis; ^bMAP/I, including high-dose methotrexate (12 g/m²), doxorubicin (75 mg/m²), cisplatin (100–120 mg/m²) with or without ifosfamide (12 g/m²). We defined these four agents as first-line chemotherapy; we usually choose IE as the second-line chemotherapy, which included ifosfamide 1.8 g/m²/d d₁₋₅ and etoposide 100 mg/m²/d d₁₋₅ Q3W (IE). AWD, alive with disease; CBR, clinical benefit rate (6 months); CI, confidence interval; DCR, disease control rate; DOD, died of disease; IE, ifosfamide and etoposide; IQR, interquartile range; ITT, intention-to-treat population; KM, Kaplan Meier; MAP/I, high-dose methotrexate, doxorubicin, cisplatin with or without ifosfamide; NED, no evidence of disease; NR, not reached; ORR, overall response rate.



Poster #095 #1819072

THE THERAPEUTIC REGIMEN INCLUDING BEVACIZUMAB, SORAFENIB AND CYCLOPHOSPHAMIDE PROVIDES CLINICAL BENEFIT FOR THE TREATMENT OF CHILDREN AND YOUNG ADULTS WITH RECURRENT OR REFRACTORY OSSEOUS SARCOMAS

Jessica L. Bodea, MD; Sara M. Federico, MD

St. Jude Children's Research Hospital, Memphis, Tennessee, UNITED STATES

Objective: In spite of therapeutic advances and improved survival rates for pediatric patients with cancer, there is a lag in survival rates of children and adolescents with recurrent and/or metastatic solid tumors. New therapies targeting alternative mechanisms of action are needed. Angiogenesis is critical for tumor growth and metastatic spread. Inhibition of vascular endothelial growth factors and platelet-derived growth factor receptors impacts angiogenesis and can lead to tumor response. A previous phase 1 dose-escalation study with an expansion cohort evaluated the combination of an anti-angiogenic regimen including: bevacizumab, sorafenib, and oral cyclophosphamide. These agents demonstrated a signal of activity in patients with sarcomas (F. Navid, *Clinical Cancer Research*, 2013; S.M. Federico, *European Journal of Cancer*, 2020). Here we report a cohort of 39 pediatric patients treated at the recommended phase 2 doses of this treatment regimen.

Methods: Charts of patients with refractory or recurrent solid tumors were reviewed. The treatment regimen lasted 21 days and included: bevacizumab (15 mg/kg, IV, day 1), sorafenib (90 mg/m² PO twice daily, days 1-21), and low-dose oral cyclophosphamide (50mg/m² PO daily, days 1-21). Toxicities were assessed using Common Terminology Criteria for Adverse Events, v5.0. Responses were independently evaluated by 2 reviewers using the Response Evaluation Criteria in Solid Tumors (RECIST1.1) criteria. Outcome data are reported.

Results: Thirty-nine patients (22 male, 17 female; median age 15 years; range 1-22 years) received the treatment regimen and had previously received a median of 3 prior systemic therapies (range 1-6). The most common diagnoses included bone sarcomas (n=21; 14 Ewing sarcoma, 7 osteosarcoma) and soft tissue sarcomas (n=9; 2 rhabdomyosarcoma, 3 synovial sarcoma, 2 desmoplastic small round cell tumors, 2 high-grade sarcoma). The most common grade III non-hematologic toxicities included hypertension (2, 5.4%), hematuria (2, 5.4%). Grade III nausea/vomiting, elevated lipase, weight loss, transaminitis, and hyperbilirubinemia occurred in 1 patient (2.7%) each, respectively. Five patients (13.5%) had pneumothorax, 4 were grade I and asymptomatic, with 1 grade II. Pneumothorax occurred at the time of progressive disease (n=3), following cycle 3 (n=1, after a lung biopsy) and spontaneously (n=1, patient with stable disease following 9 cycles.) The most common grade III/IV hematologic toxicities were lymphopenia (19, 51%) and leukopenia (13, 35%). Sixteen patients (43.2%) developed hand/foot exanthem grade II or less. A total of 297 courses of therapy were administered to the cohort with a total of 8 hospitalizations and 33 unplanned clinic visits due to treatment related toxicities. Twenty-three patients required a dose reduction of either cyclophosphamide, sorafenib or bevacizumab during therapy. The most common reasons included: hand/foot exanthem (n=13), suppression of counts (n=8) and poor wound healing (n=7). Patients who required a dose modification continued to respond to therapy following the modification. One patient (Ewing sarcoma) achieved a complete response after 11 cycles. Two patients (Ewing sarcoma, high grade sarcoma) achieved a partial response following cycles 2 and 4 respectively, and 20 patients had stable disease. The median duration of therapy for all patients was 4 cycles (range 1-46). The median duration of therapy for patients with bone tumors was 7 cycles (range 1-46). For patients with bone tumors, the median time to progression was 6 cycles (range 2-46).

Conclusion: Intravenous bevacizumab combined with oral sorafenib and low-dose cyclophosphamide was well tolerated with minimal need for supportive care, additional clinic visits, or hospital admissions. Numerous patients experienced disease stabilization for prolonged time periods. This regimen may be beneficial as a palliative therapy to prolong life, maintain stable disease and limit major treatment-related toxicities in this heavily pretreated patient population. For bone tumors, this regimen demonstrated a signal of activity and may be beneficial as a treatment incorporated into upfront therapy or as a maintenance therapy.



Poster #096 #1818929

SUCCESSFUL COMBINATION OF DENOSUMAB AND SCLEROTHERAPY FOR SYMPTOMATIC LARGE RECURRENT SPINAL ANEURYSMAL BONE CYST IN A CHILD

Paul M. Kent, MD¹; Sreekumar Madassery, MD²

¹Rush University Medical Center, River Forest, Illinois, UNITED STATES, ²Rush University Medical Center, Chicago, Illinois, UNITED STATES

Objective: Aneurysmal bone cyst (ABC) is a rare (0.15 cases/million), clonal, non-cancerous bone tumor, of unknown cause, composed of multiple variable sized blood filled cysts. It presents with pain and swelling in the affected bone and mass effect on adjacent tissues. After treatment, up to 1/3 can recur, especially in children. Spinal ABCs, found in 16% of patients, if not successfully treated, can cause permanent neurologic deficits, even quadriplegia (J Bone Joint Surg Am. 2011;93(16):1534).

There are no agreed upon standard treatment. Options include: en bloc excision, high speed burr, phenol or doxycycline infusion, argon beam coagulation, cryosurgery, curettage, bone cement, radiation, bone grafting, surgically removing the affected bone or selective arterial embolization [Curr Rev Must Med 2016, 9:435]. Present and emerging therapies include sclerotherapy, bisphosphonate and RANKL-inhibitor therapy.

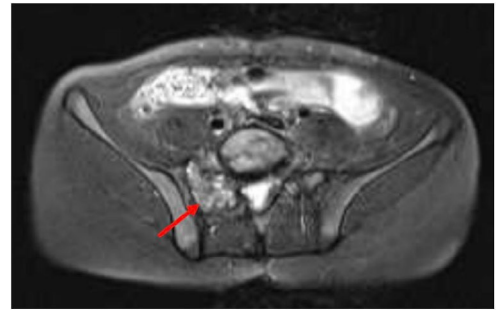
We describe successful treatment of child with recurrent symptomatic massive sacral ABC with a novel combination therapy of sclerotherapy (albumin, doxycycline, and air), followed by a year of intensive denosumab.

Methods: Case Report: A 7 year old girl with gluten sensitive enteropathy, controlled by diet, presented with a recurrence of symptomatic ABC of the entire right hemi-sacrum with impingement of the S1 nerve and canal. The patient recurred after pre-op IR embolization followed by immediate surgical excision of the tumor with bone grafting. Although she initially had significant relief of symptoms after the interventions, her recurrence showed a new onset of progressive RLE pain, weakness, footdrop, and progressive refusal to bear weight.

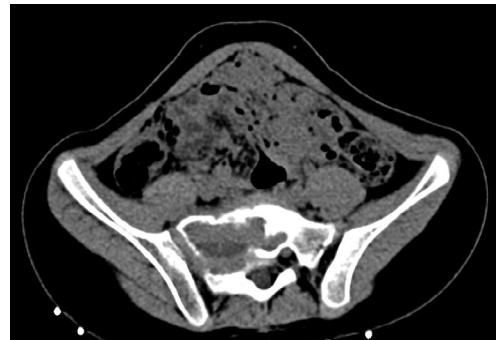
Repeat MRI showed the ABC had completely re-developed with numerous mixed hemorrhage cysts and again causing nerve impingement (figure 1 and 2). Therefore, after multi-disciplinary and multi-institutional discussion, decision was made to attempt sclerotherapy with bone grafting and biological therapy in the form of the RANKL – inhibitor monoclonal antibody denosumab.

Results: Procedure: Under anesthesia, while prone, multiple coaxial needles were advanced into the multi-cystic areas of the ABC (figure 3), and aspiration of approximately 400cc of blood under high pressure was obtained. Dilute contrast was injected to see if there was communication with the cysts and additional needles were placed in areas not communicating. Following this, the sclerosant cocktail (albumin, doxycycline, and air) was injected through several of the access needles in order to coat the entirety of the cysts. Finally, through two of the needles, biologic bone graft material was instilled.

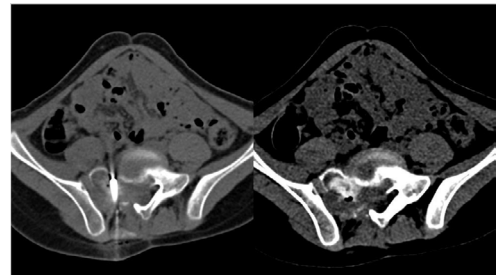
Post Procedure the patient had significant immediate pain relief. She was immediately started on intensive denosumab therapy (65mg SQ weekly x 4, then every 28 days x 12. Patient has maintained the symptomatic relief for approximately 12 months now and has returned to full activity and strength. Follow-up MRI showed interval bone formation and minimal residual cysts (figure 4).



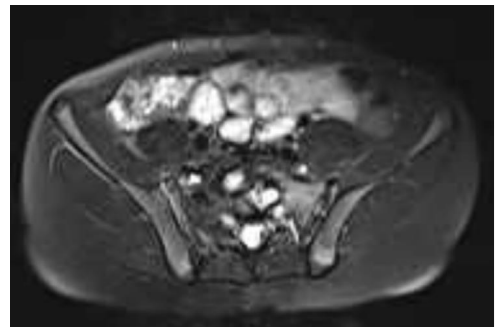
Initial MRI showing Right Sacral ABC (arrow) with numerous cyst



Procedural CT shows Right sacral ABC, with devoid osseous area and cystic components



Left image with one of several access needles into the ABC. Right image showing areas of contrast communication after aspiration of blood products.



Follow up MRI after sclerotherapy and with ongoing Denosumab therapy showing interval bone growth with marked reduction of cystic areas.

Conclusion: Effective treatment of recurrent massive, symptomatic ABC requires a multidisciplinary team approach. Percutaneous minimally invasive sclerotherapy with a sclerosant cocktail and adjuvant denosumab is an option to consider in such cases, especially when surgery is impossible or morbid. We believe this is a first report of this combination therapy and may provide an alternative to morbid surgery for some patients. We hope to inform the discussion of treatment options for recurrent massive ABCs by providing an example of a successful, safe and minimally invasive therapy. More research is required to establish best practices for difficult to treat ABCs.



Poster #097 #1818847

ACTIVATION OF EFFICIENT DNA REPAIR MECHANISMS AFTER PHOTON AND PROTON IRRADIATION OF HUMAN CHONDROSARCOMA CELLS

Birgit Lohberger, PhD MSc¹; Sylvia Kerschbaum-Gruber, PhD MSc²; Tobias Madl, Prof. Dr.³; Karl Kashofer, PhD MSc⁴; Andreas Leithner, Prof. Dr.⁵; Dietmar Georg, Prof. Dr.²

¹Medical University Graz, Department of Orthopedics and Trauma, Graz, Steiermark, AUSTRIA, ²Department of Radiation Oncology, Medical University of Vienna; MedAustron Ion Therapy Center, Wiener Neustadt, Vienna, Wien, AUSTRIA, ³Gottfried Schatz Research Center for Cell Signaling, Metabolism and Aging Molecular Biology and Biochemistry, Medical University of Graz, Graz, Steiermark, AUSTRIA, ⁴Institute of Pathology, Medical University of Graz, Graz, Steiermark, AUSTRIA, ⁵Department of Orthopedics and Trauma, Medical University of Graz, Graz, Steiermark, AUSTRIA

Objective: Although particle therapy with protons has proven to be beneficial in the treatment of chondrosarcoma compared to photon-based radiation therapy, the cellular and molecular mechanisms have not yet been sufficiently investigated.

Methods: Cell viability, proliferation behavior, and colony forming ability were analyzed after photon and proton irradiation (IR). Cell cycle were analyzed using flow cytometry and corresponding regulator genes and key players of the DNA repair mechanisms were measured using next generation sequencing, protein expression, immunohistochemistry and immunofluorescence staining. Changes in metabolic phenotypes were determined with nuclear magnetic resonance spectroscopy.

Results: Radiation with both, photons as well as protons, resulted in reduced cell survival and a G2/M phase arrest of the cell cycle. Especially 1 h after IR, a significantly higher level of phosphorylated γ H2AX foci was observed. This was accompanied with a reprogramming in cellular metabolism. Interestingly, within 24 h the majority of clearly visible DNA damages were repaired and the metabolic phenotype restored. Involved DNA repair mechanisms are, besides the homology directed repair (HDR) and the non-homologous end-joining (NHEJ), especially the mismatch mediated repair (MMR) pathway with the key players EXO1, MSH3, and PCNA. Protons, as compared to 160 kV x-rays, resulted in more pronounced effects.

Conclusion: Chondrosarcoma cells have a highly efficient DNA repair program which regenerates the majority of DNA damages within 24 h. These molecular mechanisms represent an important basis for an improved therapy.



Poster #098 #1818839

COMPLETE REMISSION OF METASTATIC OSTEOSARCOMA USING COMBINED MODALITY THERAPY: A RETROSEPTIVE ANALYSIS OF UNSELECTED PATIENTS IN CHINA

Lu Xie, MD¹; Jie Xu, MD¹; Xiaowei Li, MD¹; Zuli Zhou, MD¹; Hongqing Zhuang, MD²; Xin Sun, MD¹; Kuisheng Liu, MD¹; Xingyu Liu, MD¹; Kunkun Sun, MD¹; Jin Gu, MD³; Wei Guo, MD and PhD¹

¹Peking University People's Hospital, Beijing, Beijing, CHINA (PEOPLE'S REPUBLIC), ²Peking University Third Hospital, Beijing, Beijing, CHINA (PEOPLE'S REPUBLIC), ³Peking University Shougang Hospital, Beijing, Beijing, CHINA (PEOPLE'S REPUBLIC)

Objective: Complete surgical remission (CSR) is the best predictor of overall survival (OS) for patients with metastatic osteosarcoma. However, metastasectomy has not been widely implemented in China in the last decade due to various factors, and instead, most physicians choose hypofractionated radiotherapy to treat pulmonary lesions. This study aimed to retrospectively evaluate the outcomes of different local treatments for pulmonary lesions and identify the best local therapy strategies for these patients.

Methods: We reviewed the clinical courses of osteosarcoma patients with pulmonary metastases who were initially treated in two sarcoma centres in Beijing, China, from June 1st, 2009, to March 26th, 2020. With a median follow-up of 32.4 (95% confidence interval (CI): 30.8, 36.1) months, a total of 127 patients with 605 pulmonary nodules, all of whom had received local therapy and firstly achieved CSR or complete radiated/metabolic remission (CRR), were included in the analysis. A total of 102 patients with 525 nodules were initially diagnosed with resectable lung metastases, while 25 patients had 80 indeterminate nodules at presentation and relapsed with pulmonary metastases within 6 months after the completion of adjuvant chemotherapy.

Results: Eighty-eight of 127 (69.3%) patients had fewer than 5 nodules at the time of local therapy, with 48 of 127 (37.8%) located in the unilateral pleura. No patient underwent thoracotomy, and 42 of 127 patients (85 nodules) received video-assisted thoracoscopic surgery (VATS). In addition, 79 of 127 patients (520 nodules) received hypofractionated stereotactic body radiotherapy (RT), such as Gamma Knife radiosurgery or CyberKnife radiosurgery. The twelve-month event-free survival (EFS) (from local therapy to progression) rate of this entire study cohort was 35.6% (95% CI: 26.8%, 44.4%), without a significant difference between the two groups (44.7% for VATS vs. 28.4% for RT, P = 0.755). Radiation-induced pneumonitis was observed in 62 of 86 (72.1%) patients, with one patient (1/86, 1.2%) in grade 4.

Conclusion: Our past data showed a similar prognosis with the use of hypofractionated radiotherapy and VATS for the treatment of pulmonary metastasis and no inferiority to thoracotomy regarding historical outcomes. Currently, high-resolution chest computed tomography (CT) provides sufficient information on nodules, and less invasive modalities can thus be considered for treatment.

Table 1. Patient characteristics (N = 127)

Items	Number of patients	Percentage (%)	p for 2-y EFS ^a
Sex			0.759
Male	83	65.4	
Female	44	34.7	
Age (median: 15.0 years)	Range: 5–56 (Q1, Q3, 15.1, 18.0) years		0.025
<40 years	124	97.6	
≥40 years	3	2.4	
Pathological Subtypes			0.526
Conventional:chondroblastic	12	9.4	
Conventional: osteoblastic	78	61.4	
Conventional: not defined	24	18.9	
Telangiectatic	5	3.9	
Small cell	3	2.4	
High-grade surface	1	0.8	
Missing	4	3.1	
Primary site			0.328
Distal femur	62	48.8	
Proximal tibia and/or fibula	38	29.9	
Proximal femur	4	3.2	
Proximal humerus	9	7.1	
Axial skeleton	7	5.5	
Maxillofacial site	1	0.8	
Others	6	4.7	
Total number of pulmonary nodules for observation	605	100	0.963
Lung metastasis			0.464
≤5 nodules	88	69.3	
>5 nodules	39	30.7	
Lung metastasis			0.063
Monolateral	48	37.8	
Bilateral	79	62.2	
Local therapy for pulmonary nodules			0.476
Resection ^b	42 (85 nodules)	33.1	
Radiotherapy ^c	79 (520 nodules)	62.2	
Combined with resection and radiotherapy	6	4.7	
Missing nodules during follow-up ^d	52	7.9 (52/657)	N/A ⁱ
For resection	15	15.0 (15/100)	
For radiotherapy	37	6.6 (37/557)	
Failed local resection ^e	8	9.4 (8/85)	
Failed local radiotherapy ^f	14	2.7 (14/520)	
D _{max} ^g for pulmonary nodule/nodules			0.286
3–5 mm	18	14.1	
5–10 mm	29	22.8	
10–20 mm	50	39.4	
>20 mm	30	23.6	

Systematic treatment during local therapy of pulmonary nodules ^h			0.426
MAPI first-line chemotherapy	56	44.1	
IE second-line chemotherapy	53	41.7	
Targeted therapy	13	10.2	
Combination of TKIs and IE chemo	4	3.2	
None	1	0.8	
Median time for follow-up (months)	32.4	(95% CI: 30.8, 36.1)	(Range: 10.4, 106.5)

^a2-y EFS: 2-year event-free survival, which was calculated from start of the local therapy (resection or radiotherapy) to any kind of progression as defined by RECIST 1.1.

^bPulmonary metastasectomies were video-assisted thoracoscopic Surgery (VATS).

^cRadiotherapy usually involves GammaKnife or Cyber Knife with radio-dose >60 Gy.

^dBy comparing initial chest thin-layer computed tomography (CT) before local therapy and during follow-up, we observed that nodules had resolved or were undetectable with local treatment, most of which were observed as tiny or blurry nodules or even hardly been detected between infection and malignancy and would relapse after stopping systemic treatment.

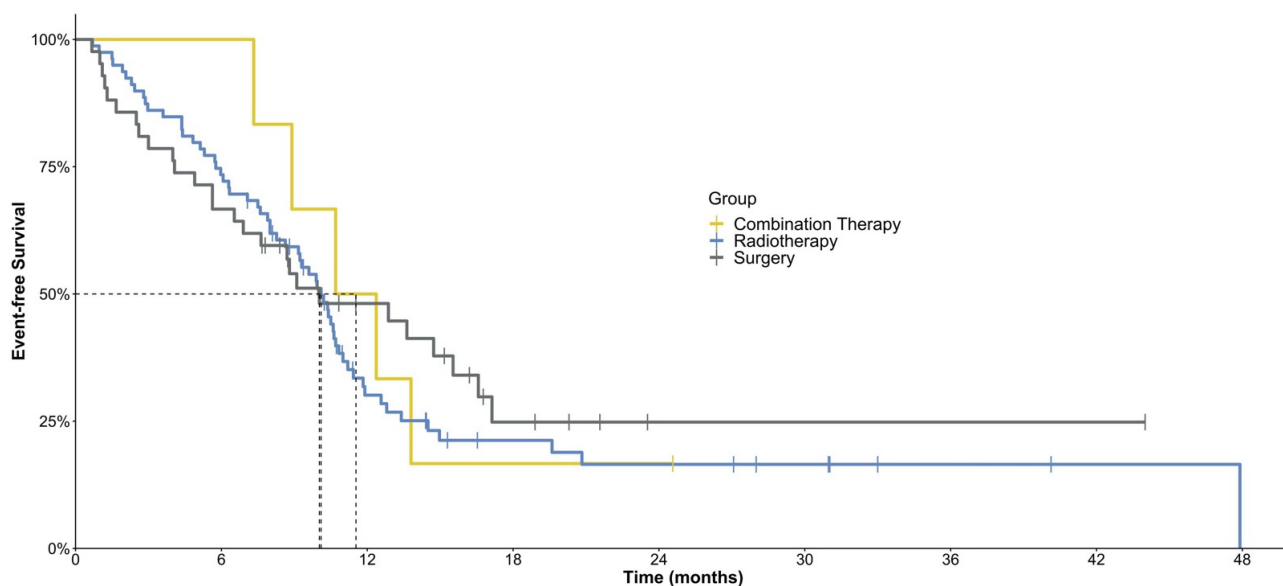
^eFailed local resection: local tumor relapse where previous tumor resection had been done.

^fFailed local radiotherapy: local tumor relapse where previous radiation had been performed for curative tumor eradication.

^gPatients were classified into four groups based on maximal nodule diameter: 1) 3 mm–5 mm; 2) 5 mm–10 mm; 3) 10 mm–20 mm; 4) >20 mm.

^hAt the Musculoskeletal Tumor Center of Peking University People's Hospital and Peking University Shougang Hospital, a chemo-protocol that includes high-dose methotrexate, cisplatin, doxorubicin, and ifosfamide (MAPI) is used as first-line chemotherapy (seen in appendix fig. 1); ifosfamide and etoposide (IE) as second-line systematic therapy; anti-angiogenesis tyrosine kinase inhibitors (TKIs) such as apatinib, anlotinib, cabozantinib, and regorafenib as third-line therapy; the combination of TKIs and IE chemotherapy as fourth-line therapy.

ⁱData not available.



	0	6	12	18	24	30	36	42	48
Combination Therapy	6	6	3	1	1	0	0	0	0
Radiotherapy	79	58	18	9	7	5	2	1	0
Surgery	42	28	14	5	1	1	1	1	0

Table 2. Comparison of clinical manifestations of patients who underwent VATS^a or radiation

Items	VATS (N = 42)	Radiotherapy (N = 79)	Combination (N = 6)
Number of pulmonary nodules /person			
≤5 nodules	41 (97.6%)	55 (69.6%)	4 (66.7%)
>5 nodules	1 (2.4%)	24 (30.4%)	2 (33.3%)
Lung metastasis			
Monolateral	33 (78.6%)	11 (13.9%)	4 (66.7%)
Bilateral	9 (21.4%)	68 (86.1%)	2 (33.3%)
D _{max} ^b for pulmonary nodule/nodules			
3–5 mm	3 (7.1%)	15 (19.0%)	0 (0.0%)
5–10 mm	6 (14.3%)	22 (27.8%)	1 (16.7%)
10–20 mm	24 (57.1%)	25 (31.6%)	1 (16.7%)
>20 mm	9 (21.4%)	17 (21.5%)	4 (66.7%)
Systematic treatment during local therapy of pulmonary nodules ^c			
MAPI first-line chemotherapy	14 (33.3%)	40 (50.6%)	2 (33.3%)
IE second-line chemotherapy	24 (57.1%)	25 (31.6%)	4 (66.7%)
Targeted therapy	2 (4.8%)	11 (13.9%)	0 (0.0%)
Combination of TKIS and IE chemo	2 (4.8%)	4 (5.1%)	0 (0.0%)
None	0 (0.0%)	1 (1.3%)	0 (0.0%)

^aVATS: Video-assisted thoracoscopic surgery.

^bPatients were classified into four groups based on nodule maximal diameter: 1) 3 mm–5 mm; 2) 5 mm–10 mm; 3) 10 mm–20 mm; 4) >20 mm.

^cAt the Musculoskeletal Tumor Center of Peking University People's Hospital and Peking University Shougang Hospital, a chemo-protocol that includes high-dose methotrexate, cisplatin, doxorubicin, and ifosfamide (MAPI) is used as first-line chemotherapy (seen in appendix fig. 1); ifosfamide and etoposide (IE) as second-line systematic therapy; anti-angiogenesis tyrosine kinase inhibitors (TKIs) such as apatinib, anlotinib, cabozantinib, and regorafenib as third-line therapy; and the combination of TKIs and IE chemotherapy as fourth-line therapy.

Table 3. Comparison of survival in different groups of patients

Items	Patients with Resections (N = 42)	Patients with Radiotherapy (N = 79)	Patients with combination of resections and radiotherapy (N = 6)	p for survival
2-year no local recurrence survival rate [\pm SD]	81.0% [\pm 7.1%]	92.8% [\pm 3.1%]	66.7% [\pm 36.7%]	0.652
Local relapse of nodules without new lesions	2/42 (4.8%)	1/79 (1.3%)	1/6 (16.7%)	N/A ^a
Local relapse of nodules with new lesions	6/42 (14.3%)	10/79 (12.7%)	1/6 (16.7%)	N/A ^a
Progression without local relapse	19/42 (45.2%)	49/79 (62.0%)	3/6 (50.0%)	
Events for progression in total	27/42 (64.3%)	60/79 (75.9%)	5/6 (83.3%)	
From resections/radiotherapy to any event (median, Q1, Q3) months	10.0 (4.1, 17.1)	10.1 (5.8, 14.5)	N/A	0.755
From resections/radiotherapy to death (mean, 95%CI) ^b months	37.6 (32.5, 42.7)	67.0 (58.7, 75.3)	21.5 (17.3, 25.7)	0.712

^aN/A data not available;

^bmedian overall survival has not reached yet, thus we use mean overall survival to replace the data.



Poster #099 #1818859

FACTORS INFLUENCING RISK FOR DEEP SURGICAL WOUND COMPLICATIONS IN PEDIATRIC PATIENTS AFTER LIMB SALVAGE SURGERY FOR OSTEOSARCOMA

Lindsay J. Talbot, MD¹; Aaron Ross, MS²; Andrew Miller, BS²; Xiaoqing Wang, PhD¹; Zhaohua Lu, PhD¹; Carla Cartwright, RDN, LDN, CNSC¹; Karen Ringwald-Smith, RDN, CSP, LDN¹; Madison Tyler, RDN, CSP, LDN¹; Najat C. Daw³; Fariba Navid, MD⁴; Hafeez Abdelhafeez, MD⁵; Michael Neel, MD¹; Michael Bishop, MD¹

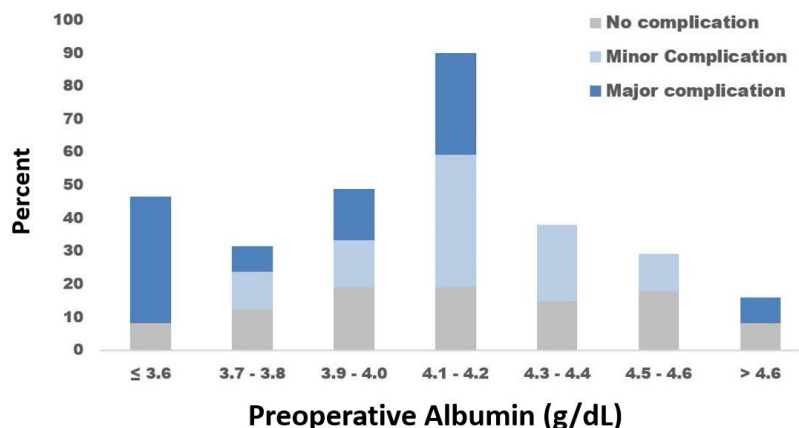
¹St. Jude Children's Research Hospital, Memphis, Tennessee, UNITED STATES, ²University of Tennessee School of Medicine, Memphis, Tennessee, UNITED STATES, ³Pediatrics, MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁴Keck School of Medicine, Los Angeles, California, UNITED STATES, ⁵St. Jude Children's Research Hospital, Memphis, Tennessee, UNITED STATES

Objective: Limb salvage surgery is the preferred method for complete resection of extremity osteosarcoma because of the potential to maintain function while achieving complete surgical resection, a critical factor in achieving long-term survival. Postoperative wound complications represent a challenge in these patients due to morbidity, need for further surgical procedures, and potential to delay postoperative chemotherapy, elevating risk of reduced overall survival and ultimate limb loss. We sought to identify modifiable factors associated with superficial and deep surgical wound complications after limb salvage procedures in a pediatric cohort of osteosarcoma patients.

Methods: We conducted a retrospective review of patients who underwent primary limb salvage surgery for osteosarcoma from 2010 to 2020 at a tertiary pediatric oncology hospital. Inclusion criteria included age <21 years and limb salvage procedure performed with a curative intent. Patients undergoing limb salvage surgery for recurrent tumors or for hardware revision/failure were excluded. Data collected included demographic, clinical, nutrition and treatment-based variables, operative data, and wound complications. A subset of patients (n=22) received bevacizumab as part of a clinical trial (NCT00667342). Wound complications were defined as minor if superficial to muscular fascia and as major if deep to fascia and further categorized based on required intervention (routine wound care, advanced wound care, antibiotics, surgical debridement, hardware removal, amputation). Primary outcome was presence of wound complication at 3 months post-resection. Univariate analysis was performed for all variables, followed by iterative forward-backwards multivariable evaluation for variables achieving a p-value < 0.2 on univariate analysis. P value of < 0.05 after multivariable analysis was considered significant.

Results: Among 123 patients who met inclusion criteria, 36 (29.3%) had a minor wound complication and 13 (10.6%) a major complication at 3 months post resection, for an overall complication rate of 39.8%. No significant difference was noted in demographic and diagnostic characteristics or operative data between the two complication groups. Treatment with bevacizumab was statistically significant between complication groups (p = 0.006), whereas other chemotherapy-specific data showed no statistically significant differences. Within nutrition-specific parameters, preoperative serum albumin and postoperative serum albumin were both statistically significant between complication groups (p = 0.043 and 0.035, respectively). On multivariable analysis, only treatment with bevacizumab and preoperative serum albumin maintained independent predictive value (Table 1). Bevacizumab treatment contributed to both minor and major wound complications (p = 0.015 and p = 0.005, respectively), but after adjustment for bevacizumab treatment, only preoperative albumin level predicted major wound complications (p = 0.007). Categorical evaluation of preoperative serum albumin demonstrated that 12/13 major complications (92.4%) occurred in patients with preoperative serum albumin < 4.3 g/dL (normal range 3.6 – 4.9 g/dL), while minor complications and no complications were evenly distributed across serum

Figure 1. Postoperative Complications Stratified by Preoperative Albumin Subgroup



albumin levels (Figure 1). Nearly all major wound complications occurred in patients with a preoperative serum albumin < 4.3 g/dL, a level higher than the typical preoperative target level (3.0 – 3.4 g/dL).

Conclusion: Pediatric patients with osteosarcoma are at high risk for wound complications after limb salvage procedures for primary tumor local control. Treatment with bevacizumab and preoperative serum albumin were both predictors of major wound complications within 3 months of limb salvage surgery. Preoperative optimization of serum albumin may reduce the risk of major postoperative wound complications in these patients. Prospective studies, potentially under the auspices of enhanced recovery after surgery (ERAS) protocols in limb salvage surgery, are warranted to confirm these findings.

Table 1. Final multivariate model after iterative regression. All variables achieving a significance of $p > 0.20$ were included in iterative regression and are shown. Those achieving statistical significance on multivariable analysis have relevant statistical data displayed.

Variable	Odds Ratio (95% CI)		P-value	
	Minor* (n = 36)	Major* (n = 13)	Minor*	Major*
Complication type				
Bevacizumab treatment (Y/N)	3.803 (1.302 – 11.11)	8.436 (1.911 – 37.24)	0.015	0.005
Anatomic site	ns			
Total lymphocyte count (count x 10³/mL)	ns			
Preoperative BMI Z score	ns			
Preoperative albumin (g/dL)	0.934 ** (0.600 – 1.453)	2.837 ** (1.314 – 5.348)	0.762	0.007
Postoperative albumin (g/dL)	ns			
Estimated blood loss (mL/kg)	ns			
Postoperative hemoglobin (g/dL)	ns			
Postoperative platelet count (count x 10³/mL)	ns			

* Reference group: no complication

** Odds increase in wound complication per g/dL decrease in preoperative albumin



Poster #100 #1818944

CLINICAL OUTCOMES OF PATIENTS TREATED WITH CARBON FIBER NAILS: AN INTERNATIONAL STUDY

Santiago A. Lozano-Calderon, MD, PhD¹; Zeger Rijs, MD²; Nelson Merchan, MD¹; Caleb Yeung, MD¹; Emily Berner, BS¹; Vania Oliveira, MD, PhD³; Giuseppe Bianchi, MD⁴; Eric Staals, MD⁴; Debora Lana, MD⁵; Davide Donati, MD⁴; Ortal Segal, MD⁶; Stefano Marone, MD⁷; Raimondo Piana, MD⁷; Simone De Meo, PhD⁷; Pietro Pellegrino, MD⁷; Nicola Ratto, MD⁷; Carmine Zoccali, MD, PhD⁸; Maurizio Scorianz, MD⁹; Guido Scocciati, MD⁹; Domenico A. Campanacci, MD⁹; Lorenzo Andreani, MD¹⁰; Silvia de Franco, MD¹⁰; Michele Boffano, Dr/ MD-MSc¹¹; Thomas Cosker, FRCS¹²; Varunprasanth Sethurajah¹²; Manuel Peleteiro Pensado, MD, PhD¹³; Irene Barrientos Ruiz, MD¹³; Esperanza Holgado Moreno, MD¹³; Eduardo J. Ortiz-Cruz, MD, PhD¹³; Michiel van de sande, MD, PhD²

¹Massachusetts General Hospital, Boston, Massachusetts, UNITED STATES, ²Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ³Centro Hospitalar Universitário do Porto, Portugal / Oporto University Hospital Center, Portugal, Porto, Porto, PORTUGAL, ⁴IRCCS Istituto Ortopedico Rizzoli, Bologna, Emilia-Romagna, ITALY, ⁵Ospedale Maggiore Trauma Center, Bologna, Emilia-Romagna, ITALY, ⁶Tel Aviv Sourasky Medical Center, Tel Aviv, Tel Aviv, ISRAEL, ⁷Centro Traumatologico Ortopedico, Turin, Piemonte, ITALY, ⁸IRCCS Regina Elena National Cancer Institute, Rome, Lazio, ITALY, ⁹Careggi University Hospital, Florence, Toscana, ITALY, ¹⁰University Hospital of Pisa, Pisa, Toscana, ITALY, ¹¹Regina Margherita Children's Hospital, Turin, Piemonte, ITALY, ¹²Nuffield Orthopaedic Centre, Oxford, England, UNITED KINGDOM, ¹³Hospital Universitario La Paz, Madrid, Madrid, SPAIN

Objective: Hardware in orthopaedics typically consists of the successful use of nails, plates, and screws made from titanium or cobalt-chromium alloys. However, these implants create artifacts on imaging studies. These artifacts have an impact on oncologic follow up and in radiation planning in patients with metastatic bone disease. Carbon fiber implants have become an attractive option for the oncologic patient given their radiolucency. Additionally, their modulus of elasticity is closer to the one from bone when compared to titanium implants. The aim of this study was to evaluate the imaging, indications, and complications from carbon fiber implants, specifically looking at carbon fiber nails.

Methods: We performed a review of 274 patients involving 11 institutions from around the world who have used carbon fiber nails. Data was collected internationally through Castor EDC.

Results: 141 patients (51%) were females, 132 (48%) were males, and 1 (0.4%) was unknown. The average patient age was 60 years. Of the 283 patients, 133 (47%) had a pathological fracture. 30 (11%) of these patients had a primary musculo-skeletal tumor, 181 (66%) had metastatic disease, 14 (5%) had a benign musculoskeletal tumor, 46 (17%) had multiple myeloma, 2 (0.7%) resulted from trauma, and 1 (0.4%) was unknown. Regarding location, 154 patients (56%) received femoral intramedullary nailing, 97 (35%) received humeral intramedullary nailing, and 23 (8%) received tibial intramedullary nailing. 7 (0.3%) implants failed due to structural failure, 1 (0.4%) failed due to infection, and 1 (0.4%) failed due to non-infected wound adhesion.

Conclusion: Carbon fiber implants are a safe alternative for the treatment of pathologic fractures. Their radiolucency facilitates the use of X-ray, MRI, and CT for surveillance purposes. There is also potential benefit for radiation planning. Implant failure rate and infection rates are low with the use of this technology.

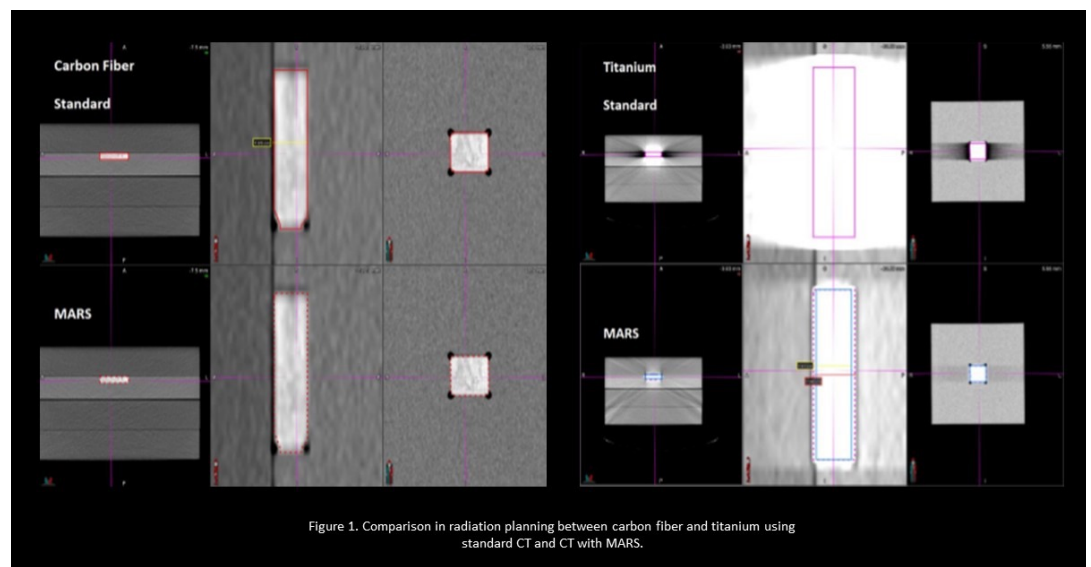
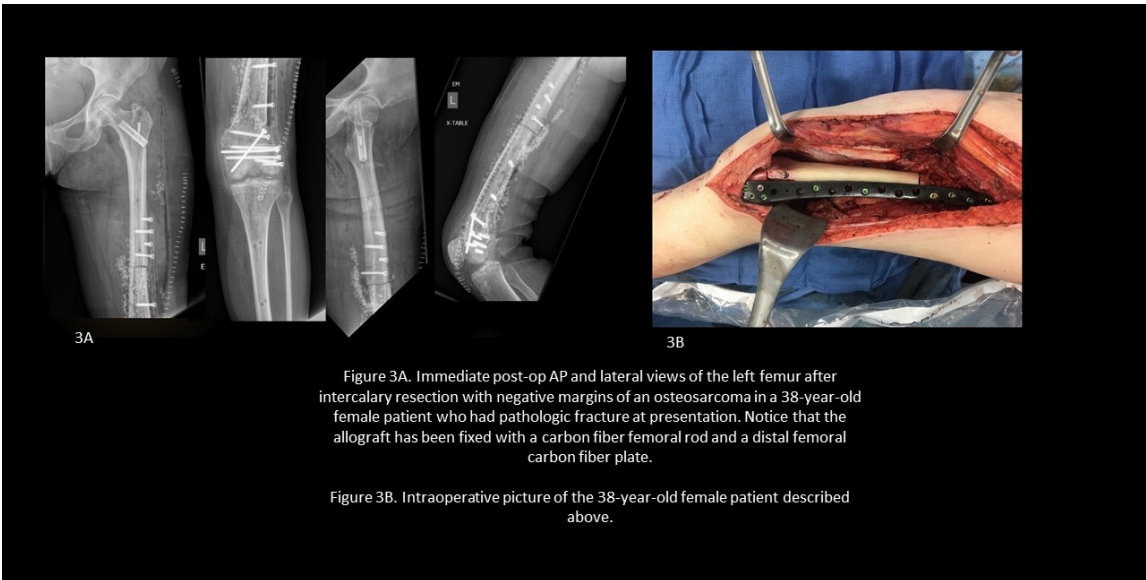
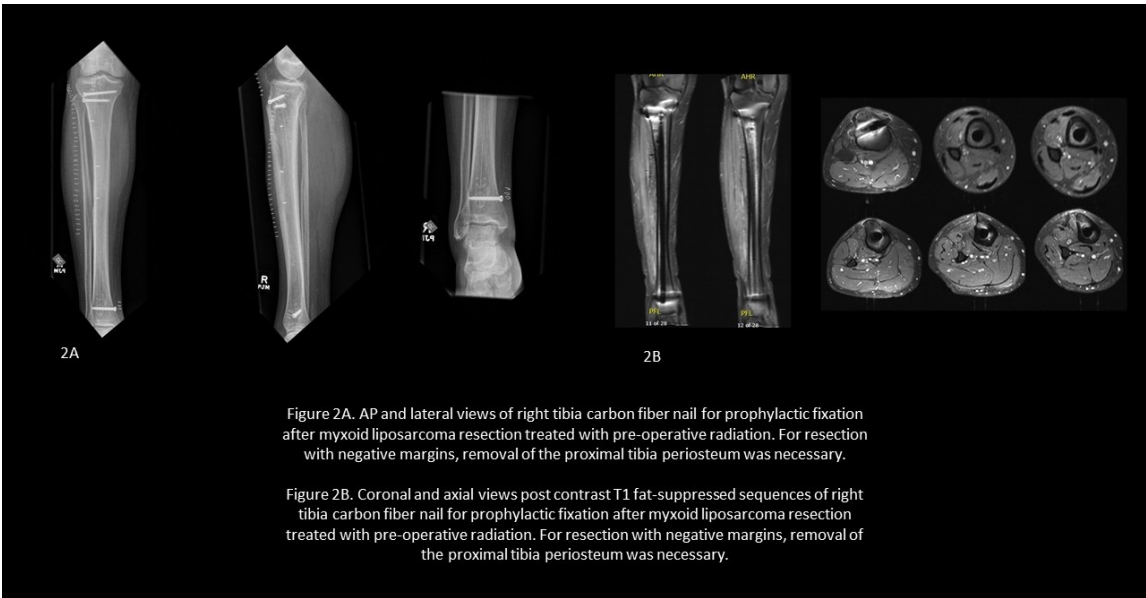


Figure 1. Comparison in radiation planning between carbon fiber and titanium using standard CT and CT with MARS.





Poster #101 #1818995

CLINICAL OUTCOMES OF PATIENTS TREATED WITH CARBON FIBER PLATES: AN INTERNATIONAL STUDY

Zeger Rijs, MD¹; Santiago A. Lozano-Calderon, MD, PhD²; Emily Berner, BS²; Nelson Merchan, MD²; Caleb Yeung, MD²; Vania Oliveira, MD, PhD³; Giuseppe Bianchi, MD⁴; Eric Staals, MD⁴; Debora Lana, MD⁵; Davide Donati, MD⁴; Ortal Segal, MD⁶; Stefano Marone, MD⁷; Raimondo Piana, MD⁷; Simone De Meo, PhD⁷; Pietro Pellegrino, MD⁷; Nicola Ratto, MD⁷; Maurizio Scorianz, MD⁸; Guido Scoccianti, MD⁸; Amber Weekhout, BSc¹; Domenico A. Campanacci, MD⁸; Lorenzo Andreani, MD⁹; Silvia de Franco, MD⁹; Michele Boffano, Dr/ MD-MSc¹⁰; Thomas Cosker, FRCS¹¹; Varunprasanth Sethurajah¹¹; Manuel Peleteiro Pensado, MD, PhD¹²; Irene Barrientos Ruiz, MD¹²; Esperanza Holgado Moreno, MD¹²; Eduardo J. Ortiz-Cruz, MD, PhD¹²; Michiel van de sande, MD, PhD¹

¹Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ²Massachusetts General Hospital, Boston, Massachusetts, UNITED STATES, ³Centro Hospitalar Universitário do Porto, Portugal / Oporto University Hospital Center, Portugal, Porto, Porto, PORTUGAL, ⁴IRCCS Istituto Ortopedico Rizzoli, Bologna, Emilia-Romagna, ITALY, ⁵Ospedale Maggiore Trauma Center, Bologna, Emilia-Romagna, ITALY, ⁶Tel Aviv Sourasky Medical Center, Tel Aviv, Tel Aviv, ISRAEL, ⁷Centro Traumatologico Ortopedico, Turin, Piemonte, ITALY, ⁸Careggi University Hospital, Florence, Toscana, ITALY, ⁹University Hospital of Pisa, Pisa, Toscana, ITALY, ¹⁰Regina Margherita Children's Hospital, Turin, Piemonte, ITALY, ¹¹Nuffield Orthopaedic Centre, Oxford, England, UNITED KINGDOM, ¹²Hospital Universitario La Paz, Madrid, Madrid, SPAIN

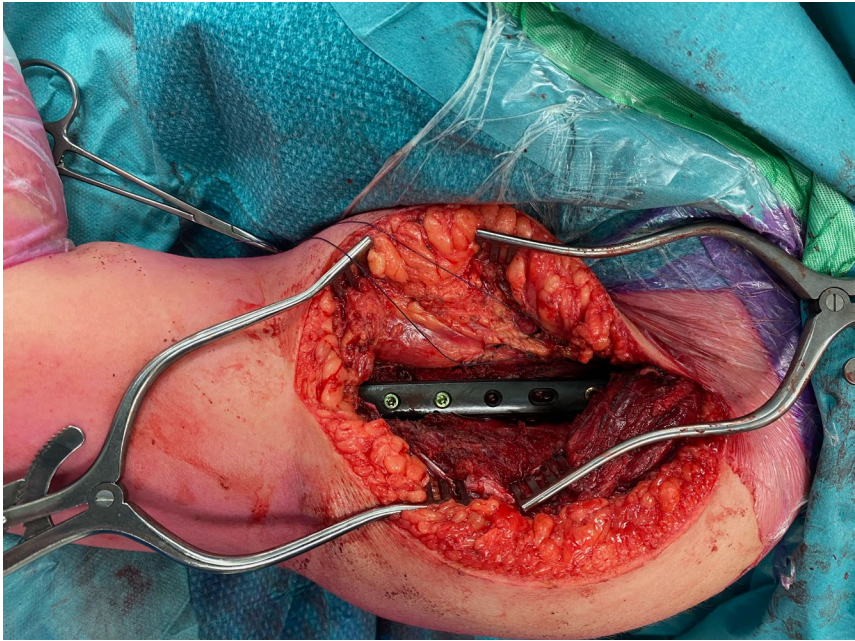
Objective: Carbon fiber implants are a promising alternative to current implants due to their radiolucency which allows for precise radiation planning and facilitates visualization of local recurrences. Additionally, their biomechanical properties should theoretically enhance bone healing and reduce complication risks. Our aim was to investigate the imaging, indications, and complications of carbon fiber plates.

Methods: This international multicenter retrospective registry involved 105 patients who have received a carbon fiber plate for different oncologic indications. Plates were used as a mean for fixation after excision and curettage of bone tumors packed with allograft or cement, intralesional resection and curettage with cement packing of metastatic bone lesions and lastly as a mean of fixation of osteoarticular, hemicondylar, intercalary, or hemi-intercalary structural allografts used for reconstruction after wide resection of malignant neoplasms.

Results: 66 (63%) females and 39 (37%) males with an average age of 40 years were included. The diagnoses were 34 (32%) chondrosarcomas or atypical cartilaginous tumors, 24 (23%) benign primary bone lesions, 12 (11%) osteosarcomas, 11 (10%) adamantinomas, 8 (8%) metastasis, 4 (4%) multiple myelomas, 4 (4%) soft tissue sarcomas, 2 (2%) ewing sarcomas, and for 6 (6%) patients the diagnosis was not reported. Regarding location, 41 (39%) received a femoral condyl plate, 25 (24%) received a proximal humerus plate, 25 (24%) received diaphyseal plate and for 14 patients (13%) this was not reported. 9 patients (9%) with benign bone tumors received an autograft, 39 (37%) received an allograft and 39 (37%) received cement. Eight (8%) plates failed due to structural bone or construct failure, 8 (8%) due to infection and 4 (4%) due to soft tissue failure.

Conclusion: Carbon fiber plates provide a safe and viable alternative for the treatment of bone tumors. Their radiolucency facilitates a better oncological follow up and there is a potential benefit for radiation planning. The implant failure rate which can be attributed to the use of the carbon fiber plates were low.







Poster #102 #1818907

ROLE OF 3D PRINTED IMPLANTS IN THE DEFECT RECONSTRUCTION IN PATIENTS WITH CHEST WALL TUMORS

Aslan Valiev, PhD; Pavel Kononets, PhD; Timur Charatishvili, Prof; Nikolay Petrochenko, PhD; Alexander Salkov, Fellow, Federal State Budgetary Institution

N.N. Blokhin National Medical Research Center of Oncology of the Ministry of Health of the Russian Federation (N.N. Blokhin NMRCO), Moscow, Moskva, RUSSIA

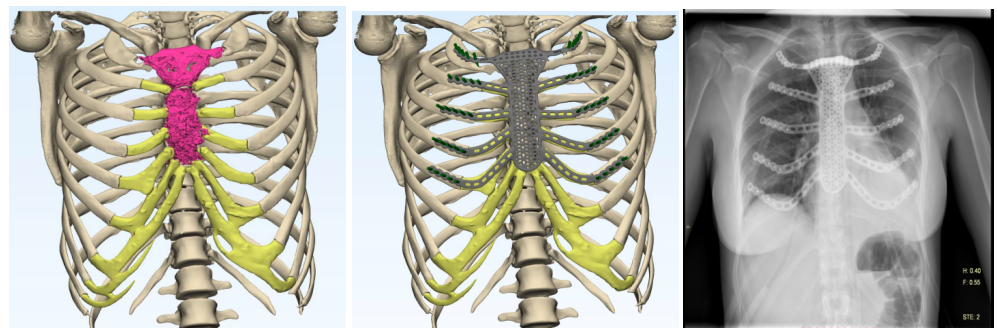
Objective: The primary malignant tumors of the chest wall are very rare. It constitutes 3,1% localizing in sternum and 10,1% localizing in ribs and clavicle of all the primary bone tumors. Metastatic tumors occur 2–4 times more often than primary lesions of the chest wall. 9% of all metastatic bone tumors are locating in the sternum. From all the tumors of the sternum 30% are metastatic, and mostly the primary tumors are: breast, prostatic gland, lungs, renal and thyroid, ovaries. Rarity of these tumors, technical difficulties in reconstruction of the chest wall (traditional and 3D custom made implants) and small amount of publications still make this problem very controversial.

Methods: From 2019 to 2021 21 patient with chest wall tumors were treated in the Soft Tissue and Bone Tumors Department of N.N. Blokhin National Medical Research Center of Oncology, Moscow (Russia). The 3D custom made implant was used in 5 patients (table 1): 2 chondrosarcoma cases, lung cancer, osteosarcoma and undifferentiated pleomorphic soft tissue sarcoma. The custom prostheses of the chest wall were made by 3D printing using individual anatomical features of each patient, made by 1,0 mm CT scanned virtual model.

Results: The follow up after the patients was 3-12 months. There were 4 R0 margins and 1 R1 margin resection. Local recurrences were found in 2 patients (1 patient: chondrosarcoma of the sternum, 9 months after surgery, 2 patient osteosarcoma of the rib – 2 months after surgery). Three patients alive without evidence of recurrence. Four patients had a good respiratory function after surgery, 1 was needed respiratory support until death. No one of the patients had signs of paradoxical breathing. The mean hospital stay time after surgery was 28 days. The most often complications were: seroma, hydro-pneumothorax, pneumonia.

Conclusion: 3D custom made implants can moderately increase the results of surgical treatment of patients with chest wall tumors, but the results gotten after surgery says, that there is a big need in very thorough indications use to this category of the patients.

Fig 1.



1a

1b

1c

Chondrosarcoma of the sternum (1a), virtual template (1b), chest radiograph (1c)

Tumor type	Age	Distant metastases	Method of reconstruction	Recurrence
Chondrosarcoma sternum	47	no	3D-implant, thoracic major flaps both sides	+ (9 mths)
Lung cancer	62	no	3D-implant, left thoracic major flap	no
Chondrosarcoma 5th rib	65	no	3D-implant, left thoracic major flap	no
Osteosarcoma sternum	63	yes	3D-implant, thoracodorsal flap	+ (2mths)
Undifferentiated pleomorphic soft tissue sarcoma	29	no	3D-implant, thoracic major flaps both sides	no



Poster #103 #1818971

RESTORATION OF PELVIC RING CONTINUITY IN INTERNAL HEMIPELVECTOMY DEFECTS WITH THE VASCULARIZED FIBULA OSSEOUS FREE FLAP

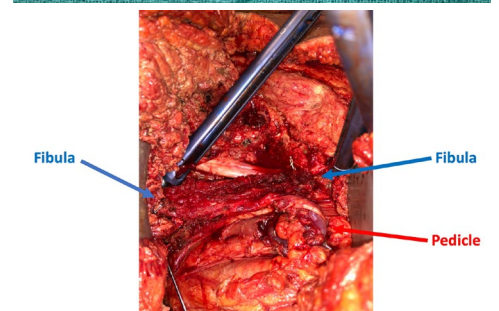
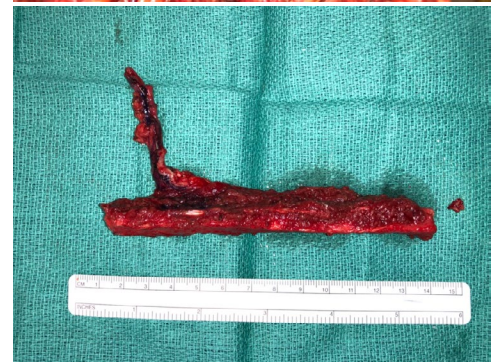
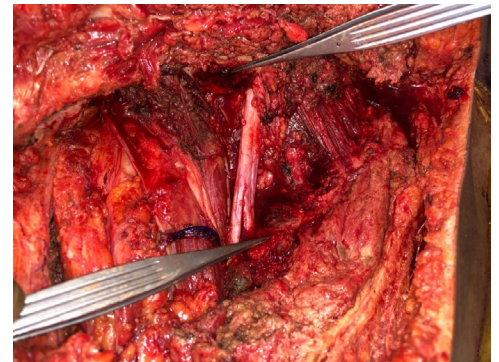
 Max Vaynrub, MD; Leslie N. Kim, MD; Farooq Shahzad, MBBS, MS
 Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES

Objective: Internal hemipelvectomy defects are classified into types I to IV depending on the part of the pelvis resected (I: ilium; II: acetabulum; III: ischiopubic rami; IV: sacrum). Complete type I resections result in unilateral loss of spinopelvic continuity. Bony reconstruction with the fibula free flap uses a reliable source of vascularized bone graft to restore the pelvic ring, which preserves limb length equality and permits direct transmission of forces from the lower extremity to the trunk. This study presents our 30-year experience with internal hemipelvectomy reconstruction with the fibula free flap.

Methods: This is a retrospective review of all patients who underwent internal hemipelvectomy reconstruction with fibula free flap at our institution from 1991-2021. Data were collected for patient demographics, tumor pathology, neoadjuvant and adjuvant therapy, type of resection and details of reconstruction. Outcomes of interest were post-operative complications, weight bearing status, and Musculoskeletal Tumor Society (MSTS) functional outcome score.

Results: 14 patients met inclusion criteria. There were 10 females. Mean age was 24 years (range 9.2 to 52.5 years). Ewing's sarcoma was the most common diagnosis (n=9), followed by osteosarcoma (n=2), immature teratoma (n=1), chondrosarcoma (n=1), and giant cell tumor of bone (n=1). Patient received neoadjuvant chemotherapy (n=12), neoadjuvant radiation (n=7), and adjuvant chemotherapy (n=11). Type I/IV defects were the most common (n=12) followed by type I only (n=1) and type I-II (n=1). Reconstruction was performed with 2 fibula struts in 9 patients, 1 strut in 3 patients and 3 struts in 1 patient. The struts were docked on the sacrum or L5 transverse process proximally and at the supraacetabular iliac bone distally (figure 1: defect; figure 2: fibula flap; figure 3: flap inset; figure 4: post-operative X ray). The fibula was fixated with wires and/or plates and screws in 10 patients, while 4 patients underwent spinopelvic pedicle screw instrumentation. Microvascular arterial anastomoses were performed to the superior gluteal, inferior gluteal, internal iliac, external iliac, deep inferior epigastric, deep circumflex iliac and hypogastric arteries. Venous anastomoses were performed to the external iliac, common iliac, superior gluteal, inferior gluteal, deep inferior epigastric and deep circumflex iliac veins. Follow up duration was a mean of 40.3 months (range 2.7 to 230 months). Mean MSTS score was 19.87 (range 7-30). Mean time to full weight bearing was 6.8 months (range 2 weeks-13 months). Of the nine patients who had at least 3-month postoperative imaging available, 6 had union at both junction sites, and 1 had union at the proximal site only. There were no intraoperative flap complications. Reoperations were performed in 6 patients, for wound revision (n=5) and hematoma evacuation (n=1). Another patient with seroma had a drain placed by interventional radiology. Two patients experienced foot drop, 1 patient had chronic pain, and 2 had scoliosis.

Conclusion: The fibula free bone flap reliably restores spinopelvic continuity in complete iliac or ilio-sacral resections. Although technically challenging, the procedure is safe and effective for restoring skeletal stability, even in the face of chemotherapy and radiotherapy.





Poster #104 #1818887

INTRAMEDULLARY NAIL VERSUS PLATE FIXATION OF METASTATIC LESIONS OF THE HUMERUS

Danielle Greig, MD¹; Rishi Trikha, MD¹; Erik J. Geiger, MD²; Nicholas M. Bernthal, MD²; Brooke Crawford, MD³

¹University of California, Los Angeles, Santa Monica, California, UNITED STATES, ²David Geffen School of Medicine at UCLA, Santa Monica, California, UNITED STATES, ³University of California, Los Angeles, Los Angeles, California, UNITED STATES

Objective: Up to 20% of all bony metastases are located in the upper extremities, and more than half of these are found in the humerus. These lesions are associated with substantial pain, functional impairment, and a high rate of pathologic fracture. Goals of surgical management include pain relief and functional restoration through prophylactic fixation. There is, however, no consensus on the optimal implant, and the decision to utilize intramedullary nail (IMN) or plate fixation is currently based on surgeon preference. The aim of this study was to compare outcomes of IMN and plate fixation of pathologic or impending pathologic humerus fractures. Specifically, we analyzed differences in surgical time, complications, postoperative pain and range of motion between the two groups.

Methods: A retrospective review was performed of all metastatic lesions to the humerus with pathologic or impending pathologic fractures that were treated surgically at a single institution over an 8-year period. Patients with at least 6 weeks of follow-up were included for analysis. 51 patients underwent either IMN (n=22) or curettage, cementation and lateral locked plating (n=29) based on clinical presentation and surgeon preference. Patient demographic, oncologic, procedural, and outcome data were analyzed.

Results: Average follow-up of surviving patients was 9.5 months (range: 1.5 mos – 3.8 yrs). The mean age at the time of surgery was 67.5 years (range: 35.5 – 91.4 yrs), which was not significantly different between IMN and plate groups (71.4 yrs vs 64.3 yrs, p=0.071) (Table 1). The most common diagnosis was multiple myeloma (11/51, 23.6%), followed by metastatic breast cancer (7/51, 13.7%) and metastatic renal cell carcinoma (5/51, 9.8%). Fracture location was classified as either proximal third (28/51, 54.9%), middle third (17/51, 33.3%), or distal third (11.8%). While a trend toward plating of proximal third fractures was observed, there was no significant difference in fracture location between the IMN and plate groups (40.9%/50.0%/9.1% vs 65.5%/20.7%/13.8% proximal/middle/distal, p=0.089).

IMN fixation was associated with a significant reduction in surgical time over plating (189.2 vs 252.6 mins, p=0.003). There was no significant difference between IMN and locked plate fixation with regard to estimated blood loss (177.3mL vs 245.7mL, p=0.149), blood transfusion (9.1% vs 3.4%, p=0.571), or postoperative length of stay (4.8 vs 3.0 days, p=0.219). At final follow-up, 27.3% (6/22) of patients in the IMN group had died of disease, compared with 10.3% (3/29) in the plate group (p=0.267). Overall, 42.1% of patients were pain free, and there was no significant difference in the proportion of pain free patients between IMN and plate groups (53.8% vs 36.0%, p=0.323). Postoperative range of motion was not significantly different between IMN and plate groups with regard to forward flexion (111.4° vs 110.8°, p=0.966), abduction (91.9° vs 105.3°, p=0.377), or external rotation (41.7° vs 39.2°, p=0.595). There were 8 complications overall (17.6%), 5 in the IMN group and 3 in the plate group (22.7% vs 10.3%, p=0.268) (Table 2). Two nails required revision to plating for nonunion with persistent pain, while one plate was revised to an IMN for nonunion with associated hardware cutout.

Conclusion: IM nailing of pathologic humerus fractures was associated with shorter surgical time than plating, with no difference in postoperative outcomes including complication rates, postoperative pain, and range of motion. Both IM nailing and plating were associated with pain relief and adequate postoperative function. Given the low overall complication and revision surgery rates, both present reasonable surgical options for patients with metastatic lesions of the humerus.

Table 2: Postoperative Complications Following Fixation

	Complication	Treatment
Intramedullary Nail (n=22)	Nonunion with persistent pain	Revision to plate
	Nonunion with persistent pain	Revision to plate
	Acromion fracture	Activity limitation
	Wound dehiscence	Packing, local wound care
	Wound infection	Operative I&D
Plate (n=29)	Nonunion and hardware failure	Revision to IMN
	Radial nerve palsy	Observation, bracing, therapy
	Radial nerve palsy	Observation, bracing, therapy



Poster #105 #1819066

LONG-TERM OUTCOMES AND DIFFERENCES IN THERAPY FOR PEDIATRIC AND ADULT EWING SARCOMA PATIENTS IN BRITISH COLUMBIA, CANADA

Christine Simmons, FRCPC, MD, MSc¹; Omar Hajjaj, BSc²; Lauren Corke, BSc²; Caron Strahlendorf, FRCPC, FCP, MB³; Sarah Hamilton, MD, FRCPC⁴

¹BC Cancer - Vancouver, Vancouver, British Columbia, CANADA, ²BCCA Vancouver, Vancouver, British Columbia, CANADA, ³BC Children's Hospital, Vancouver, British Columbia, CANADA, ⁴BC Cancer Agency, Vancouver, British Columbia, CANADA

Objective: Ewing Sarcoma (EWS) is an exceptionally clinically challenging disease for sarcoma specialists. Although it is known to be responsive to chemotherapy and radiation, the number of lines of therapy available is limited. EWS affects both pediatric patients (PP) and adult patients (AP), however, the literature states that reported outcomes are worse for AP compared to PP. There is no known explanation for the difference in outcomes. It is undetermined if this is a result of a biological difference in AP compared to PP, or if this is due to differences in the number of lines of therapy and/or types of treatment. The goal of this study is to identify the types of treatment, number of lines, and outcomes of both PP and AP in a multi-institutional real-world setting.

Methods: Five cancer centers across British Columbia contribute data to the Sarcoma Outcomes Database at BC Cancer. This cohort study identifies and analyzes patients diagnosed with EWS in British Columbia, from January 1, 2000, to December 31, 2018, from this database. Data on the frequency, amount, and regimen of chemotherapy were collected. As well as baseline Charlson Comorbidity Index, age at diagnosis, presence of surgical intervention, use of radiation, progression-free survival, and overall survival.

Results: 108 patients with EWS were identified from the database. This included 66 AP and 42 PP. AP had a median age of 37 (19-86) and the median age for pediatric patients was 14 (1-18). Overall, the mean lines of treatment for both groups were 1.6. The mean number of lines was 1.76 for PP, and 1.52 for AP. There was no significant difference in the number of lines of therapy received between PP and AP (p=0.21). There was, however, a difference in the type of therapy received by these two cohorts. PP were provided with more dose-dense therapy than AP (85% vs 28% for dose-dense chemo). See table 1 for overall survival (OS) outcomes and progression-free survival (PFS) data. PP who received dose-dense regimens were found to have a longer five-year overall survival compared to PP with non-dose-dense regimens (HR 0.87). There was no difference in five-year overall survival for dose-dense and non-dose-dense regimens in AP (HR 0.95), even when controlling for co-morbidities. Vincristine, Adriamycin, Cyclophosphamide alternating with Ifosfamide and Etoposide q3weeks was the most prevalent chemotherapy regimen for AP. The most common regimen in PP was the same, however, alternation occurred q2weeks. Overall, 22.2% of patients did not get radiation and 40.7% did not get surgery. All PP received chemotherapy whereas 5% of AP did not get chemotherapy.

Conclusion: PP with EWS received dose-dense chemotherapy regimens more often than AP. Despite the similarities between the number of lines of therapy and type of chemotherapy regimen PP were found to have better survival outcomes than AP. Extrapolating pediatric protocols to the adult setting may not be appropriate given the differences in outcomes. It remains unclear whether it is biological differences in EWS between PP and AP that affect survival outcomes. Further work to identify effective therapies and predictive biomarkers in the disease is necessary as there is potential that this could further distinguish reasons for discrepant outcomes in PP and AP.

Table 1: Survival outcomes in PP and AP

	Median overall survival (OS)	Median progression-free survival (PFS)
Adult patients (AP)	79 mos.	23 mos.
Pediatric patients (PP)	NE	32 mos.



Poster #106 #1818843

DEDIFFERENTIATED CHONDROSARCOMA: A REVIEW OF THE CLINICOPATHOLOGICAL FEATURES AND OUTCOMES OF 16 CASES TREATED AT A SINGLE INSTITUTION

 Charles A. Gusho, BS¹; Athan Zavras, BS²; Ira Miller, MD, PhD²; Matthew W. Colman, MD²; Linus Lee, BE²; Steven Gitelis, MD²; Alan T. Blank, MD, MS²
¹Rush University Medical Center, Milwaukee, Wisconsin, UNITED STATES, ²Rush University Medical Center, Chicago, Illinois, UNITED STATES

Objective: Dedifferentiated chondrosarcoma (DCS) is a rare and aggressive malignancy with a poor prognosis. The purpose of this investigation was to assess the clinicopathological features and outcomes of DCS patients treated at a single institution.

Methods: This study was a retrospective review over a consecutive twenty-year period. Data including treatment details and outcomes were recorded.

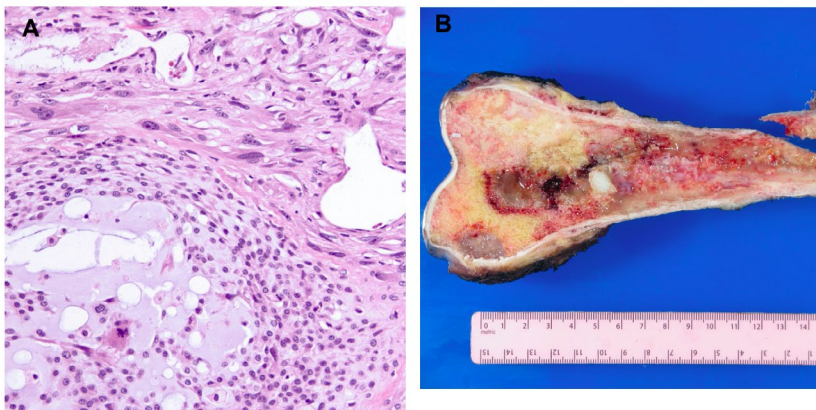
Results: A total of 16 cases from 2000 to 2018 were reviewed. The median age was 62 years (IQR, 52-69 years) and the majority of DCS arose in the femur (50%, n = 8) and pelvis (25%, n = 4). Fourteen (88%) cases received limb salvage/wide margin resection (n = 13) or intralesional surgery (n = 1). For all DCS, the median estimated overall survival (OS) was 46 months (95% CI, 1-90 months) with both a five and ten-year survival probability of 32%. On Kaplan-Meier analysis there was no difference between operative versus nonoperative management (p = 0.747), surgery alone versus surgery/chemotherapy (p = 0.265), nor surgery alone versus surgery/chemotherapy/radiation (p = 0.698).

Conclusion: Our findings confirm the poor prognosis of DCS patients, with a five-year estimate of 32%. Together with existing literature, our data may enable future strategic recommendation of DCS patients.

Table I. Characteristics of included cases.

Dedifferentiated chondrosarcoma (n = 16)	Frequency (%)
Age (years) †	62.5 (39-83)
Race	
White	13 (81.3)
Other/Unknown	3 (18.8)
Sex	
Male	7 (43.8)
Female	9 (56.3)
Location	
Femur	8 (50)
Pelvis	4 (25)
Ribs	1 (6.3)
Periscapula	1 (6.3)
Tibia	1 (6.3)
Initial metastasis	3 (18.8)
Initial biopsy	14 (87.5)
NLR ‡	3.83 (2.54)
Neoadjuvant chemotherapy	2 (12.5)
Neoadjuvant radiation	2 (12.5)
Surgery	14 (87.6)
Limb salvage/wide resection	13 (81.3)
Intralesional	1 (6.3)
Size (cm) ‡	9.77 (5.02)
Negative margins	
Yes	12 (75)
No	2 (12.5)
Missing	2 (12.5)
Dedifferentiated component	
Osteosarcoma	5 (31.3)
UPS	6 (37.5)
Rhabdomyosarcoma	1 (6.3)
Low-grade dedifferentiation	1 (6.3)
Mixed	1 (6.3)
Reoperation	6 (37.5)
Adjuvant chemotherapy	5 (31.3)
Adjuvant radiation	7 (43.8)
Follow-up (months) †	18.5 (1-140)
Disease relapse	15 (93.8)
Mortality	13 (81.3)

† median, range. ‡ mean, standard deviation. NLR, preoperative neutrophil-lymphocyte-ratio. UPS, undifferentiated pleomorphic sarcoma.





Poster #108 #1819061

DETECTION OF DNA COPY-NUMBER CHANGES IN CIRCULATING TUMOUR DNA IN PATIENTS WITH UPS AND LPS BY ULTRA LOW-PASS WHOLE GENOME SEQUENCING AND DIGITAL DROPLET PCR

Heidi M. Namløs, PhD¹; Marie K. Gillstrøm, MSc¹; Justine Abdelli, MSc¹; Nitin Sharma, PhD¹; Ksenia Khelik, PhD¹; Ola Myklebost, PhD²; Kjetil Boye, MD, PhD¹; Leonardo A. Meza-Zepeda, MSc, PhD¹

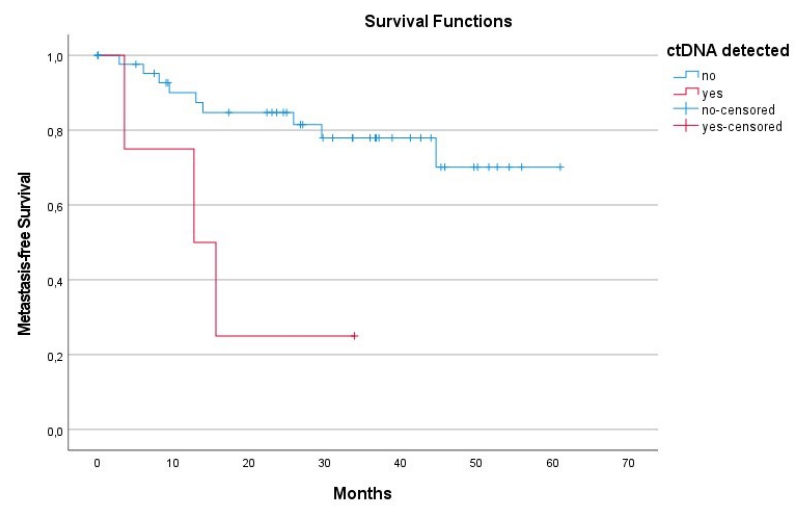
¹Oslo University Hospital, Oslo, Oslo, NORWAY, ²University of Bergen, Bergen, Hordaland, NORWAY

Objective: The molecular landscape of soft-tissue sarcoma (STS) can range from simple karyotypes to complex karyotypes. The latter group being characterized by multiple chromosomal aberrations and amplifications, as frequently observed in undifferentiated pleomorphic sarcoma (UPS) and liposarcoma (LPS). Therapeutic decisions increasingly rely on the molecular characteristics of the individual tumour. The discovery of circulating cell-free tumour DNA (ctDNA) in plasma facilitates the use of liquid biopsy as a minimally invasive method to obtain information about the genomic landscape of a tumour. However, ctDNA constitutes only a fraction of the total circulating DNA and high sensitivity methods are required to detect it. Considering the broad range of somatic changes observed in sarcomas, different approaches must be considered for the detection of genomic changes in ctDNA. Still ctDNA provides a promising new field for the diagnosis and prognosis of cancer patients. The aim of this project is to investigate if detection of ctDNA is associated with clinicopathological parameters like tumor size, mitotic count, or development of metastases in UPS or LPS.

Methods: We have profiled tumour and plasma for 72 sarcoma patients from Oslo University Hospital. The patient cohort consisted of 41 UPSs, 17 dedifferentiated liposarcomas (DDLPSs), and 14 well-differentiated liposarcomas (WDLPSs). Sixty patients had a primary disease and 12 patients were metastatic at the time of diagnosis and blood sampling. Thirteen patients developed metastasis at a later time point. Ultra-low pass whole genome sequencing (ULP-WGS) was performed to detect large DNA copy number aberrations in tumour and plasma for all 72 patients. Droplet digital PCR (ddPCR) with copy number variation (CNV) was done to detect increased MDM2 copy number in the plasma of 30 of the LPS patients as well as 15 healthy controls. Statistical analysis was performed to investigate the association between the detection of ctDNA and clinicopathological parameters. The project will be extended with plasma samples from a cohort of 50 UPS and LPS patients from KU Leuven Cancer Institute.

Results: We identified 12 patients out of 72 with detectable ctDNA in plasma. Six patients had detectable ctDNA by ULP-WGS and eight patients had increased MDM2 copy number by ddPCR. For two patients, ctDNA was detected by both methods. Overall, this gives a positive detection of 10% for ULP-WGS and 25% for ddPCR. Of the patients with detectable ctDNA, four patients had a diagnosis of UPS, six were DDLPS and two were WDLPS. A prognostic analysis was done for the ULP-WGS patient cohort, and a significant statistical difference ($p = 0.01$) for metastasis-free survival was found between patients with detectable ctDNA and patients without detectable ctDNA (Figure). No association was found between detectable ctDNA and tumour size or mitotic count.

Conclusion: Our results show that ULP-WGS and ddPCR can be used to detect copy number changes in plasma of LPS and UPS patients. However, although many of the patients included in the study had large tumours, the shedding capacity of these sarcoma subtypes seems to be relatively low. Detection of ctDNA may depend on disease aggressiveness as patients with detectable ctDNA by ULP-WGS had a higher chance of developing metastases than patients without detectable ctDNA. However, the analysis is based on only four patients with detectable ctDNA. These results substantiate prior studies to address if the presence of ctDNA reflects disease aggressiveness, and international collaboration has been set up to profile an extended sample cohort.





Poster #109 #1818892

TOWARDS ELIMINATING LOCAL TUMOUR RECURRENCE: DETECTION OF SATELLITE TUMOUR CELLS IN PERI-TUMOURAL EDEMA IN MYXOFIBROSARCOMA AND UNDIFFERENTIATED PLEOMORPHIC SARCOMA USING TARGETED GENE SEQUENCING

Miguel Alfonso V. Principe¹; Nalan Gokgoz, Ph.D²; Patrick Prochazka³; Peter C. Ferguson, MD, PhD, FRCSC⁴; Simin Dewji, MD⁵; Jay S. Wunder, MSc., MD²; Irene L. Andrulis, Ph.D²; Brendan C. Dickson, MD MSc⁶; Kim M. Tsoi, MD, PhD⁷

¹Lunenfeld-Tanenbaum Research Institute, Toronto, Ontario, CANADA, ²The Lunenfeld-Tanenbaum Research Institute, Toronto, Ontario, CANADA, ³The Lunenfeld-Tanenbaum Research Institute, Toronto, Ontario, CANADA, ⁴Division of Orthopaedic Surgery, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, CANADA, ⁵Department of Laboratory Medicine and Pathobiology, Toronto, Ontario, CANADA, ⁶Mount Sinai Hospital, Toronto, Ontario, CANADA, ⁷University of Toronto, Mount Sinai Hospital, Toronto, Ontario, CANADA

Objective: Myxofibrosarcoma (MFS) and undifferentiated pleomorphic sarcoma (UPS) are soft tissue sarcomas associated with high local recurrence rates following resection. Our group previously showed these tumours frequently present with peri-tumoural edema (so-called 'tumour tails') possibly containing neoplastic satellite cells. Our current practice is to include the areas of peri-tumoural edema on resection of the tumour mass, however, this is presumed to result in over-treatment of a subset of patients.

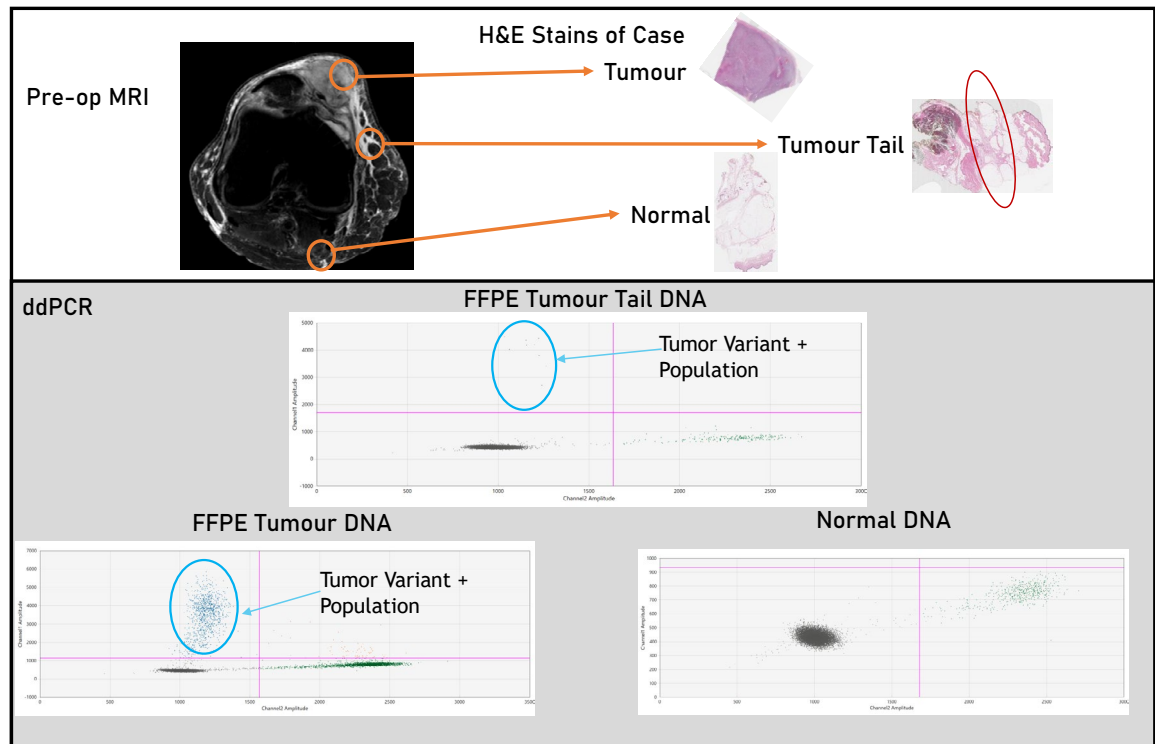
A sensitive and accurate method for detecting neoplastic satellite cells in tails is required. Advances in targeted next generation (t-NGS) sequencing and digital droplet PCR (ddPCR) allow for identification of small amounts of tumour DNA. We recently characterized the mutational profile of a cohort of patients with MFS and UPS, and have developed protocols to detect these mutant alleles. The objective of this study is to determine whether targeted gene sequencing reveals the presence of neoplastic satellite cells in peri-tumoural edema associated with MFS and UPS.

Methods: This was a retrospective, proof-of-principle, study using archival formalin-fixed paraffin-embedded (FFPE) tissue for patients diagnosed with UPS or MFS at Mount Sinai Hospital (Toronto, Canada) and whose tumours had previously undergone whole genome or exome sequencing (WGS or WXS; n=45). Staging MRI scans were re-reviewed for the presence of tumour tails, defined as increased T2 signal change extending peripherally along juxta-tumoural soft tissue fascial planes, with corresponding homogeneous low T1 signal replacement. Surgically resected cases with radiologic evidence of tumour tails (n=20) underwent histologic re-review and those with atypical spindle cells in the regions surrounding the tumour were selected for targeted gene sequencing (n=8). DNA was extracted from areas of FFPE tissue corresponding to 'tumour', 'tumour tails' and 'normal' and quality analysis performed. Tumour-specific single-nucleotide variants (TSVs) were selected from the WGS/WXS data and primers/probes for ddPCR were designed (n=3-5 per case) for t-NGS. The reactions were performed using the QX200 ddPCR System and analysis of resulting droplet populations was undertaken using Quantasoft Analysis Pro. Tumour and normal tissue served as positive and negative controls, respectively. A droplet population positive with the variant probe within the tails indicated the presence of satellite tumour cells.

Results: DNA was successfully extracted from tumour tails tissue in 6 of 8 cases (range 400-2,000 ng DNA/case), including two cases in which the patients received neoadjuvant radiation. In two cases, quality analysis showed the amount of DNA suitable for ddPCR was below its threshold of detection. Using ddPCR, TSVs were detected in the tails tissue of five cases (range 1 to 4 positive probes/case; Figure 1), while one case presented with no TSVs within their tumour tails. Investigation into the minimum input required through dilutional assays demonstrated that TSVs could be detected within the tail tissue using as little as 10ng of DNA.

Conclusion: This proof-of-principle study demonstrates t-NGS can identify tumour-specific variants in the peri-tumoural edema of MFS and UPS, confirming our previous work regarding the presence of neoplastic cells within this area. Current work is now comparing t-NGS and standard histology in a blinded, prospective study using fresh frozen tissue in a larger patient cohort. Future studies will investigate the impact of neoadjuvant radiotherapy on satellite tumour cells. Together, this work will form the foundation for development of a pre-operative diagnostic assay for differentiating malignant from reactive peritumoral edema in MFS and UPS. Ultimately, this work is expected to enable patient-specific surgical precision that will result in lower rates of both local recurrence as well as excessive resection.

Figure 1. Detection of tumour-specific variant, C778T-BCAR3 in a 81 year-old patient presenting with a tumour in the quadriceps histologically defined as Grade 3 undifferentiated pleomorphic sarcoma. Pre-operation T₂-staging MRI is shown with corresponding hematoxylin and eosin (H&E) staining for three areas of interest: the primary tumour, tumour tail, and normal. Below is the ddPCR results, using DNA extracted from patient's FFPE tissue within the same areas of interest. Highlighted are tumour variant positive populations found within both tumour and tumour tail DNA.



Case	Histology	Tumour Location	Pre-op Radiation	Sufficient DNA for ddPCR	TSV Probes used	TSV+ Tumor Tails
IHRT2929	MFS	Inguinal Canal	N	Y	5	4
IHRT4357	MFS	Adductor	N	Y	3	2
IHRT4141	MFS	Upper Arm	Y	Y*	3	2
IHRT3270	UPS	Quads	Y	Y	4	0
IHRT6941	MFS	Hamstrings	N	Y	4	1
IHRT6766	UPS	Quads	N	Y	3	3
IHRT3223	MFS	Forearm	Y	N	N/A	N/A
IHRT3177	MFS	Shoulder	Y	N	N/A	N/A

Table 1. Summary of all cases which fit our selection criteria; Mount Sinai Hospital patients histologically diagnosed and re-reviewed with MFS or UPS, with available T₂ MRI with present tumour tails, WGS/WXS data, as well as FFPE archival tissue of tumour, tumour tail, and normal tissue. Of 8 cases, only 5 had sufficient DNA for ddPCR in all three conditions, while 1 was only sufficient for its tumour and tumour tails condition. Of the 6 cases with available Tumour Tails DNA, 4 had at least one probe with a TSV+ signal.

*IHRT4141 only had sufficient amplifiable DNA for Tumour and Tails conditions.



Poster #110 #1818871

CIRCULATING TUMOUR DNA DETECTION: A POTENTIAL TOOL FOR SARCOMA MANAGEMENT

Paige E. Darville-O'Quinn¹; Nalan Gokgoz, PhD²; Kim M. Tsoi, MD, PhD³; Jay S. Wunder, MSc., MD²; Irene L. Andrulis, PhD²

¹Lunenfeld Tanenbaum Research Institute, Aurora, Ontario, CANADA, ²The Lunenfeld-Tanenbaum Research Institute, Toronto, Ontario, CANADA, ³University of Toronto, Mount Sinai Hospital, Toronto, Ontario, CANADA

Objective: Within two years of an initial surgical resection, 40-50% of sarcoma patients develop either local recurrence or distant metastases – at which point the survival rate drops significantly. As there are currently no biomarkers for the early detection of recurrent disease, we instead rely on clinical examination and radiographic imaging (such as CT and PET scans). However, by the time recurrent disease can be clinically detected it is often extensive and difficult to treat. Circulating tumour DNA (ctDNA) is able to capture the complete genetic landscape of a tumour, making it a promising potential biomarker to monitor disease progression and response to treatment. It is possible to detect ctDNA in the blood of adult sarcoma patients, however since it is present in extremely low quantities and recurrent driver mutations are infrequent, there is a need for highly sensitive methodologies. Droplet digital PCR (ddPCR) has been shown to be capable of detecting and quantifying ctDNA as shown in Figure 1, however it is limited in that it can only be used to target one tumour variant sequence at a time. The purpose of the present study is to investigate methods of targeting multiple tumour variants simultaneously to increase the chances of detecting ctDNA in patient blood, and assess the viability as a way to monitor disease.

Methods: Plasma was isolated from 20mL peripheral blood samples collected from 300 pre-operative sarcoma patients, and matched tumour samples from surgical resection were frozen and stored. Cell-free DNA (cfDNA) extracted from plasma was quantified using qPCR, and the quality was assessed using capillary electrophoresis. 12 cases were selected to undergo whole exome sequencing (WES) of bulk tumour and whole blood to identify tumour specific mutations. These cases were chosen based on the corresponding cfDNA having a relatively high concentration and being free of contamination with genomic DNA. Five of the 12 cases had an additional blood draw at a later time point from which cfDNA was also extracted. For four cases (Table 1), 6 to 8 of the tumour variants identified by WES were selected as targets to be used as a marker of ctDNA within cfDNA samples. Primers were designed to amplify these sequences simultaneously using multiplex PCR (mPCR). These mPCR products will then undergo targeted amplicon sequencing to determine whether the tumour mutations can be found in patient plasma. Additionally, sensitivity assays will be conducted to assess the accuracy of this system.

Results: To date, cfDNA has been extracted from 90 cases and quantified by qPCR. Capillary electrophoresis found peaks at approximately 170bp in size, confirming the presence of cfDNA. For each of the 12 cases sequenced, a variety of tumour-specific variations were identified. The variants chosen as targets were selected based on having the highest variant allele frequency (VAF), with priority being given to mutations that alter the protein coding sequence (non-synonymous SNVs, stopgain mutations, indels). Thus far, primers have been designed and an mPCR protocol has been optimized for 4 separate cases – each case requiring different primer ratios and PCR conditions. Before proceeding to sequencing, it is important that each target sequence be amplified with similar efficiency in the same reaction as shown in Figure 2.

Conclusion: The ability to detect a tumour-specific mutation in the plasma of sarcoma patients using ddPCR was an important first step in developing a ctDNA testing protocol for clinical use. However, it is important to explore other methodologies that will allow for the targeting of multiple mutations simultaneously, as this will increase the chances of detecting ctDNA. Blood samples from these patients will continue to be collected at follow-up visits, so that plasma may be analyzed for the presence of ctDNA, thus identifying risk of disease recurrence. Additionally, the association between presence of ctDNA and clinical outcome is currently being investigated.

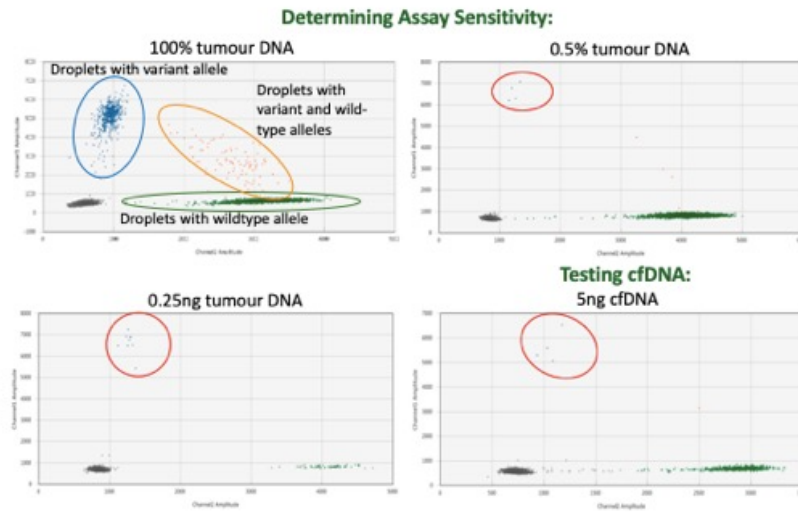


Figure 1: ddPCR is highly sensitive and was able to detect ctDNA in the plasma of pre-operative sarcoma patients.

Study ID	Primary CT#	Diagnosis	Secondary CT#
RT-7417	CT110	MFS	N/A
RT-7418	CT87	Well differentiated liposarcoma	CT115 (resection after biopsy)
RT-7421	CT114	UPS	N/A
RT-7860	CT247	Pleomorphic liposarcoma	CT281 (resection after radiation)

Table 1: Four cases for which an mPCR protocol has been optimized and will analyzed for ctDNA through targeted amplicon sequencing.

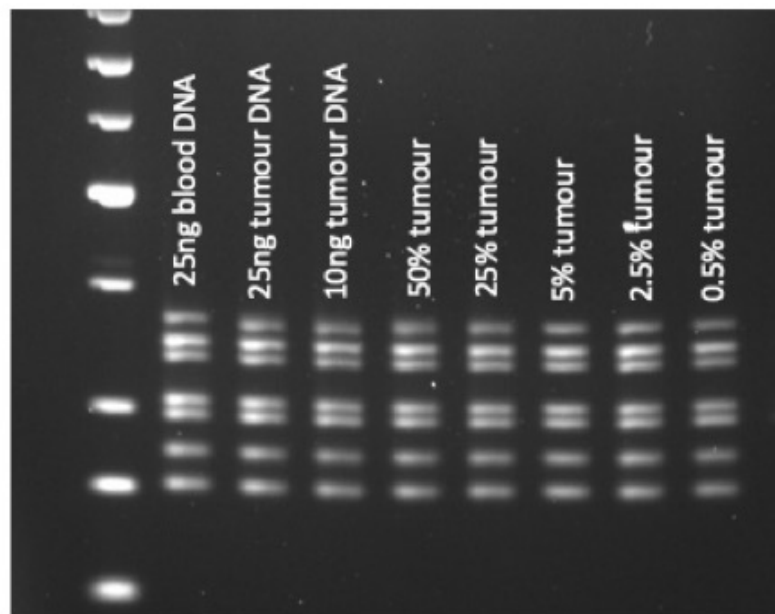


Figure 2: Agarose gel depicting the mPCR products for case RT-7421.



Poster #111 #1819051

CIRCULATING TUMOR DNA (CTDNA) LANDSCAPE IN BONE AND SOFT TISSUE SARCOMAS

Gabriel Tinoco, MD, FACP¹; David Liebner, MD¹; Lesli Kiedrowski, MS, MPH, CGC²; Leslie Bucheit, MS, CGC²

¹The Ohio State University, Columbus, Ohio, UNITED STATES, ²Guardant Health, Redwood City, California, UNITED STATES

Objective: ctDNA is a proven tool to accelerate comprehensive biomarker identification for clinical practice and clinical trial enrollment in various cancer types. However, there is a dearth of genomic biomarker analyses for prognostication, therapeutic matching, and longitudinal monitoring for patients with bone and soft tissue sarcomas; exploration is warranted to determine if the benefits of ctDNA can extend to this population as well. Here, we characterize the ctDNA genomic alteration (GA) landscape across a large bone and soft tissue sarcoma dataset and assess trends in two subtypes.

Methods: Analysis of genomic results from ctDNA samples prospectively collected between 2014 and 2021 for clinical Guardant360 testing and a diagnosis of sarcoma, with subtype documented by ordering providers on the test requisition form (TRF) was performed. GIST is designated elsewhere on the TRF and was excluded.

Results: 970 patients were tested with Guardant360 of which 516(53%) were male; the median age was 59 years (range: 4-93). Of reported diagnoses, 427(44%) patients had sarcoma NOS, 207(21%) leiomyosarcoma, and 335 (34%) had various other subtypes reported including soft tissue sarcoma (81, 8%), osteosarcoma (68, 7%), liposarcoma (65, 7%), chondrosarcoma (48, 5%). All other reported subtypes were observed in <5% of patients. 79 patients had more than one test for a total of 1,096 tests; most analyzed >70 genes (1034/1096, 94%). MSI could be assessed in 644 (59%) tests; 2 (<1%) had MSI-H detected. ctDNA GA were identified in 828/1096 (76%) tests of which 309/1026 (28%) had non-synonymous characterized GAs. The most commonly altered genes were TP53 (30%), BRAF (10%), ATM (8%); 5% of patients had GAs in CCNE1, CDK4 and/or EGFR while ARID1A, IDH1, GNAS, KIT, KRAS, FGFR1, PIK3CA GAs were each identified in 4% of patients. Of patients with Osteosarcoma, 45(66%) were male and the median age was 40 years (range: 8-85). Eighty-six tests were submitted of which 63(73%) had GAs identified; 52 (60%) had non-synonymous characterized GAs. GAs were observed most frequently in TP53 (43%) with all other GAs identified at <5% frequency. Notably, 9 patients were tested more than once representing 27 tests; 66% of patients had new GAs identified on subsequent tests. Of patients with chondrosarcoma, 15 (31%) were male and the median age was 57 years (range: 20-89). Fifty-one tests were submitted of which 34 (67%) had GAs identified; 28 (56%) had non-synonymous characterized GAs. One patient had multiple tests, of which one was included for further analysis. Of the remaining 26 patients/tests, GAs were identified in IDH1 most frequently (42%); 82% had co-occurring GAs, most commonly in TP53 (44%), TERT promoter (22%) or both (11%). All IDH1 GAs were identified at the R132 hotspot. Amplifications in CCNE1, CDK6, FGFR1, and PIK3CA and mutations in PTEN, ARID1A, STK11 were also identified.

Conclusion: ctDNA can be assessed in sarcoma patients seeking liquid biopsy and can identify a wide arrange of GAs that may identify opportunities for expanded biomarker research. Longitudinal testing may highlight cancer evolution and should be further interrogated in other subtypes. Frequencies of GAs of interest for therapy and/or prognostication – such as MSI-H or IDH1 – are similar to published tumor-derived rates. Future research using paired ctDNA and clinical outcomes will help elucidate the impact of genomic biomarkers in this population.



Poster #112 #1818978

UPREGULATION OF LCP1 IN CHONDROSARCOMA CORRELATES WITH AGGRESSIVE BEHAVIOR AND POOR PROGNOSIS

Caleb A. Watson¹; Emily Peairs, MS²¹; John Martin, PhD¹; Trudy Zou, MS¹²; Jianhong Ou, PhD¹; Julia D. Visgauss, MD³,
¹Duke University School of Medicine, Durham, North Carolina, UNITED STATES, ²University of Pittsburgh School of Medicine, Durham, North Carolina, UNITED STATES, ³Duke University Hospital, Department of Orthopaedic Surgery, Durham, North Carolina, UNITED STATES

Objective: Chondrosarcoma (CHS) is a primary malignancy of the bone, whose chemoresistent nature and metastatic potential have driven the focus of our research into the specific drivers of metastatic progression. No treatment currently exists for the management of distant metastatic disease. Thus, it is crucial that research focuses on understanding the molecular mechanisms associated with metastatic progression in chondrosarcomas in order to identify and develop targeted systematic therapies. Through a combination of gene expression and validation studies, we aim to identify dysregulated genes in chondrosarcomas with known metastatic potential.

Methods: Cell lines

We used primary cell cultures from the primary tumors of deidentified patients from our institution's biobank. Clinical information including metastatic status at final follow up (at least 2 years) was known for all tumors.

RNA-seq

To ensure quality control, RNA-seq reads were trimmed by Trim Galore, then mapped using the TopHat algorithm to the human genome (GRCh38). The mapped reads were filtered by a MAPQ no smaller than 30 which were then counted using featureCounts. The Bioconductor package DESeq2 was employed to analyze differential expressions in the mapped reads. Coverage depth were normalized by deeptools using the Reads Per Kilobase per Million mapped reads (RPKM) for RNA-seq. Transcripts Per Million (TPM) values were quantified from Salmon and summarized through tximport.

qPCR

RNA concentration and quality were quantified using the NanoDrop 2000/2000c program. Primers for the genes of interest were custom designed using the IDT PrimerQuest Tool, with optimum amplicon size of 100 bp and optimum melting temperature of 60°C. Fold change was calculated by normalization to GAPDH internal control, and significance of expression was assessed using one-way ANOVA and post-hoc student's t-test.

Survival Analysis

To further validate the generalizability of our results, we generated survival curves using the Kaplan-Meier technique from the R survival package, using microarray mRNA expression data from the dataset published in Nicolle et al. of 102 chondrosarcomas. The Cox proportional hazard regression, performed using the coxph R function, was used to measure statistical significance of the Kaplan-Meier hazard ratios.

Results: We performed RNA sequencing on primary cell cultures from 4 chondrosarcomas: two with known development of metastasis and two without, then compared the differently expressed genes (DEGs) across the metastasizing and non-metastasizing tumors. These DEGs, including CNTN1, CXADR, EGLN3, GABRA3, LCP1, and TSPAN15, revealed statistically significant upregulation in our metastatic chondrosarcoma cell lines ($\log_2\text{FoldChange} > 5$). Individual replicate counts were analyzed for these genes through a heat map, along with other significantly dysregulated genes highlighted in our preliminary volcano plots (Figure 1a). qPCR validation was then performed to validate these results, showing significant difference in the log 2-fold change expression values for LCP1 (lymphocyte cytosolic protein 1) comparing the nonmetastatic and metastatic cell lines (Figure 1b). Statistical significance was quantified using one-way ANOVA followed by post-hoc student's t-test ($p\text{-adj} < 0.001$).

Kaplan Meyer survival analysis of LCP1 expression in chondrosarcoma revealed significantly decreased survival of patients with high expression of LCP1. Examination of expression by quartiles reveals significant dose dependent inverse relationship of LCP1 expression and survival (Figure 2a), with statistically significant differences in the Hazard Ratio (HR) between quartiles with $p\text{-value} = 0.002$ (Figure 2b).

Conclusion: Increased expression of LCP1 in chondrosarcoma correlates with metastatic phenotype and worse survival. Further work is needed to identify if LCP1 is a biologic marker of aggressivity, or may itself contribute to metastatic progression in chondrosarcoma, and can be therapeutically targeted.

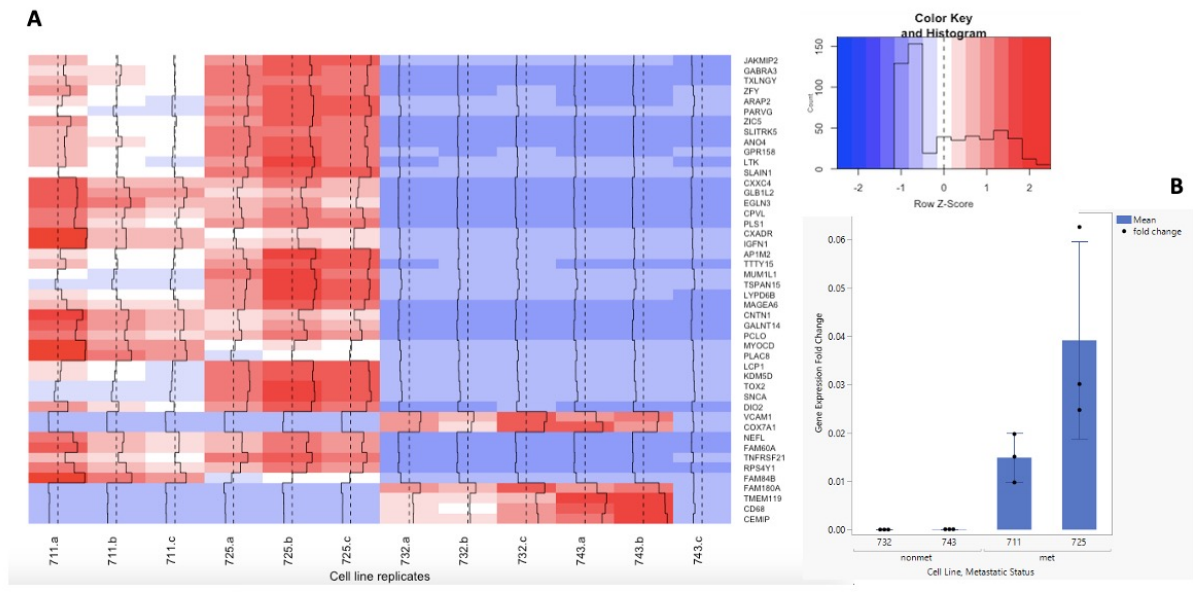


Figure 1. Gene expression data of from primary chondrosarcoma tumor cells. A) Heatmap comparing normalized counts from 2 metastatic (711, 725) and 2 nonmetastatic cell lines (735, 743) in triplicate (Z-scores processed and clustered by row). Genes listed constitute the most highly dysregulated genes with statistical significance. Density lines correspond to deviations from the mean of individual gene counts within each replicate. B) qPCR validation of LCP1 expression, showing individual data points for all 3 replicates for each metastatic (711, 725) and nonmetastatic (732, 743) cell line.

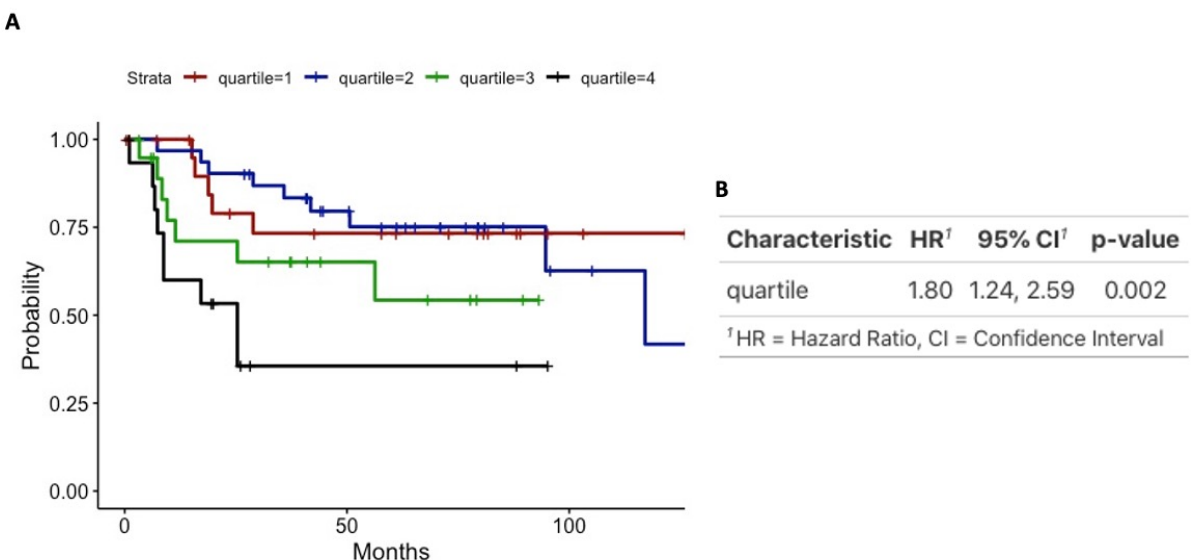


Figure 2. Kaplan-Meier survival curve depicting 10-year overall survival (OS) for patients with chondrosarcoma based on LCP1 expression. LCP1 expression was stratified by quartiles with 1 being lowest expression and 4 being highest, with statistically significant differences in the Hazard Ratio (HR) between quartiles (p-value = 0.002).



Poster #113 #1818840

THE PROGNOSTIC SIGNIFICANCE OF LYMPHOVASCULAR TUMOR INVASION IN LOCALIZED HIGH-GRADE OSTEOSARCOMA: OUTCOMES OF A SINGLE INSTITUTION OVER TEN YEARS

Charles A. Gusho, BS¹; Ira Miller, MD, PhD²; Bishir Clayton, MD²; Linus Lee, BE²; Matthew W. Colman, MD²; Steven Gitelis, MD²; Alan T. Blank, MD, MS²

¹Rush University Medical Center, Milwaukee, Wisconsin, UNITED STATES, ²Rush University Medical Center, Chicago, Illinois, UNITED STATES

Objective: Lymphovascular invasion (LVI) has shown evidence of an association with worse survival in high-grade osteosarcoma patients. The purpose of this investigation was to prognosticate LVI as a predictor of survival.

Methods: This was a retrospective review of high-grade, localized osteosarcoma patients over a consecutive ten-year period. Proportional hazards regression was used to identify prognostic factors. Cumulative mortality incidence was estimated with recurrence as a competing risk.

Results: Forty-two cases with a median follow-up of 64 months (range, 6-158 months) were reviewed. LVI was present in 21.4% (n = 9). The five- and ten-year survivals in LVI (+) were 40% and 20%, compared to 93% and 81% in LVI (-), respectively ($p < 0.001$). After controlling for confounders, advanced age (HR, 1.134; 95% CI, 1-1.2; $p = 0.01$) and LVI (HR, 21.768; 95% CI, 3-135; $p = 0.001$) were negative prognosticators. The cumulative incidence of recurrence was no different between LVI (+) and LVI (-) ($p = 0.811$), though the incidence of mortality was significantly higher in LVI (+) ($p = 0.003$).

Conclusion: The presence of LVI in the setting of high-grade, localized osteosarcoma is associated with greater rates of mortality and appears to portend a dismal prognosis.

Table 1. Characteristics of included cases.

High-grade, localized osteosarcoma	LVI + (n = 9) Frequency (%)	LVI - (n = 33) Frequency (%)	p-value‡
Age (years) at diagnosis †	16 (6 - 49)	17 (8 - 49)	0.909
BMI (kg/m ²)	21.9 (2.9)	21.1 (5.3)	0.470
Sex			0.523
Male	7 (77.8)	22 (66.7)	
Female	2 (22.2)	11 (33.3)	
Race			0.259
White	4 (44.4)	21 (63.6)	
Black	4 (44.4)	6 (18.2)	
Other/Unknown	1 (11.1)	6 (18.2)	
Location			0.114
Distal femur	4 (44.4)	10 (30.3)	
Proximal femur	1 (11.1)	1 (3.0)	
Proximal tibia	-	10 (30.3)	
Distal tibia	-	3 (9.1)	
Humerus	-	4 (12.1)	
Pelvis	2 (22.2)	2 (6.1)	
Head & neck	1 (11.1)	2 (6.1)	
Foot	-	1 (3.0)	
Proximal fibula	1 (11.1)	-	
Co-morbidities			0.934
Hypertension	1 (11.1)	2 (6.1)	
Diabetes	1 (11.1)	-	
Prior cardiac event	-	1 (3.0)	
Congestive heart failure	-	1 (3.0)	
Smoking history	1 (11.1)	3 (9.1)	
Pre-treatment labs			
Platelets (x1000/mL)	410 (141)	282 (129)	0.015**
White blood cell count (10 ⁹ /L)	8 (1.8)	9 (4.5)	0.534
NLR	2.5 (0.6)	3.9 (4.5)	0.390
Albumin (g/dL)	3.8 (0.6)	3.6 (0.6)	0.348
Creatinine (mg/dL)	0.77 (0.1)	0.76 (0.2)	0.812
Procedure			
Limb-salvage	7 (77.8)	25 (75.8)	
Amputation	2 (22.2)	8 (24.2)	
Operative time (minutes)	260 (227)	212 (123)	0.437
EBL (mL)	1650 (2448)	483 (627)	0.035**
Total hospitalization pRBC units	2.6 (4.5)	0.9 (1.8)	0.103

Table 1. Continued.

High-grade, localized osteosarcoma	LVI + (n = 9) Frequency (%)	LVI - (n = 33) Frequency (%)	p-value‡
Largest tumor dimension (cm)	9.7 (3.9)	8.8 (3.2)	0.495
Margin distance (cm)	1.8 (2.4)	2.4 (3.6)	0.305
Margin status (mm)			0.601
0 mm	1 (11.1)	1 (3.0)	
1 mm to 1.9 mm	1 (11.1)	4 (12.1)	
2 mm or greater	7 (77.8)	28 (84.8)	
Necrosis (%) †	50 (10 - 91)	89 (5 - 100)	0.119
Pre-treatment response			0.527
Good (90% or greater)	5 (55.6)	6 (18.2)	
Poor (< 90%)	3 (33.3)	16 (48.5)	
Missing	1 (11.1)	1 (3.0)	
Post-operative complication			0.160
Yes	4 (44.4)	7 (21.2)	
No	5 (55.6)	26 (78.8)	
Reoperation			0.957
Yes	5 (55.6)	18 (54.5)	
No	4 (44.4)	15 (45.5)	
Hospital stay (days) †	5 (2 - 54)	4 (2 - 14)	0.024**
Adjuvant radiation			0.246
Yes	2 (22.2)	3 (9.1)	
No	6 (66.7%)	30 (90.9)	
Follow-up (months) †	57 (6 - 158)	65 (14 - 142)	0.330
Deceased			0.002*
Yes	6 (66.7)	5 (15.2)	
No	3 (33.3)	28 (84.8)	
Recurrence			0.005*
Yes	8 (88.9)	12 (36.4)	
No	1 (11.1)	21 (63.6)	

BMI, body mass index. NLR, neutrophil-to-lymphocyte ratio. EBL, estimated blood loss. pRBC, packed red blood cells. † mean (range). ‡ two-tailed independent sample t-test or Chi-square test. * significant a priori hypotheses. ** significant at 0.05 though not at $p < 0.002$ when corrected for multiple hypothesis testing.

Table 2. Cox regression model outcomes for overall survival.

Variable	Univariable		Multivariable	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Age (years) at diagnosis	1.083 (1.02-1.14)	0.002	1.134 (1.0-1.2)	0.010*
Hospital stay (days)	1.066 (1.01-1.1)	0.009	1.108 (0.9-1.3)	0.292
Margin status (mm)				
0 mm	12.6 (2.1-73.8)	0.019	3.976 (0.2-63)	0.329
1 mm to 1.9 mm	2.592 (0.3-23.4)	0.396	0.041 (0-573)	0.513
2 mm or greater	Ref		Ref	
Necrosis (%)	0.979 (0.9-0.99)	0.029	1.02 (0.9-1.04)	0.299
LVI				
No	Ref	Ref	Ref	
Yes	9.449 (2.6-34.7)	0.001	21.768 (3-135)	0.001*

Ref, reference variable. HR, hazard ratio. CI, confidence interval. * significant on multivariable analysis only.



Poster #114 #1818886

COMPARISON OF NEXT GENERATION SEQUENCING IN ADOLESCENT AND YOUNG ADULT VERSUS OLDER ADULT PATIENTS WITH METASTATIC OR UNRESECTABLE SARCOMA

Amanda Parkes, MD, University of Wisconsin Carbone Cancer Center, Madison, Wisconsin, UNITED STATES

Objective: Adolescent and young adult (AYA) patients aged 15 to 39 years are underrepresented in oncology clinical trials, however factors leading to this disparity are unclear. As next generation sequencing (NGS) is used to identify molecular abnormalities that may inform clinical trial opportunities, we sought to study differences in NGS testing between AYA and older adult patients with metastatic or unresectable sarcoma.

Methods: We identified all patients with metastatic or unresectable sarcoma seen at the University of Wisconsin Carbone Cancer Center (UWCCC) between 5/1/2020-4/30/2021. Sarcoma patients were selected to serve as a model to represent the care of AYA patients given the relative frequency with which sarcomas are seen in AYAs and work suggesting that sarcoma should serve as a standard AYA care model. Metastatic or unresectable sarcomas were selected given their relatively poor outcomes for which clinical trials should be considered. We conducted retrospective chart review to identify demographics, tumor characteristics, and NGS testing. As UWCCC has a Precision Medicine Molecular Tumor Board (PMMTB) during which all NGS test results are reviewed and patient specific targeted therapies including clinical trials are recommended and documented in a tumor board note, we were able to then review clinical trials or other treatments identified at the time of NGS testing.

Results: We identified 61 patients seen at UWCCC between 5/1/2020-4/30/2021 with metastatic or unresectable sarcoma, including 18 AYAs aged 15-39 years (18/61, 30%) and 43 older adults (43/61, 70%). The majority of cases were soft tissue sarcomas, seen in 61% of AYAs (11/18) and 98% of older adults (42/43). NGS was requested in only 61% of AYAs with metastatic or unresectable sarcoma (11/18) as compared with 86% of older adults (37/43, $p = 0.0425$). Notably, all 7 AYAs with bone sarcoma (7/7, 100%) had NGS requested, as compared with only 36% of AYAs with soft tissue sarcoma (4/11, $p = 0.0128$). Ten molecular abnormalities were identified by NGS in the 11 AYA patients with NGS requested (range: 0-3 molecular abnormalities/NGS), as compared with 38 molecular abnormalities identified by NGS in the 37 older adult patients with NGS requested (range: 0-4 molecular abnormalities/NGS). The PMMTB only identified patient specific targeted therapies including clinical trials based on NGS for one AYA patient, as compared with 10 older adult patients. All patients with PMMTB identified therapies had soft tissue sarcoma.

Conclusion: While AYAs with metastatic or unresectable sarcoma represent a vulnerable population at high risk for poor outcomes, we found a statistically significant lower frequency of NGS testing requests in AYAs as compared with older adults. This disparity was specific to AYAs with soft tissue sarcoma, as all AYAs with metastatic or unresectable bone sarcoma had NGS testing requested. Lower frequency of NGS testing requests in AYAs led to lower identification of targeted therapies including clinical trials by our PMMTB, suggesting inequalities in NGS testing may contribute to the underrepresentation of AYAs with sarcoma in clinical trials.



Poster #115 #1818893

PHOTOACOUSTIC MICROSCOPY OF UNDECALCIFIED BONE

 Brooke Crawford, MD, FAAOS¹; Rui Cao, PhD²; Scott D. Nelson, MD³; Yu Liang, MD⁴; Yilin Luo, PhD²; Yide Zhang, PhD²; Lihong Wang, PhD²
¹UCLA, Los Angeles, California, UNITED STATES, ²California Institute of Technology, Pasadena, California, UNITED STATES, ³UCLA Medical Center, Santa Monica, California, UNITED STATES, ⁴City of Hope Cancer Center, Duarte, California, UNITED STATES

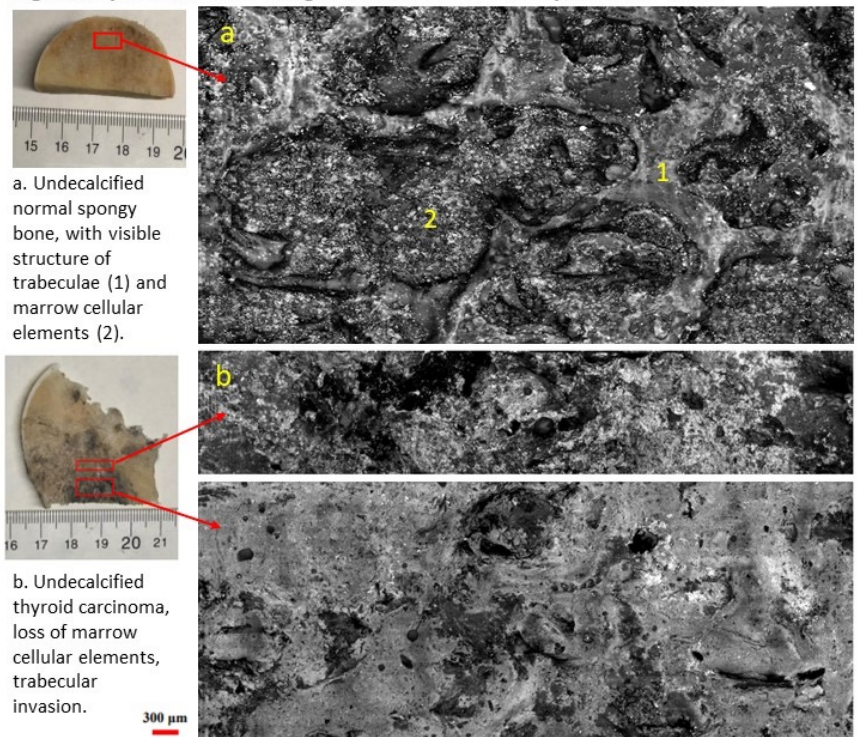
Objective: Bone tissue is especially difficult to process for pathologic analysis. The calcification of the tissue prevents smooth slicing of the specimen, and decalcification can take up to 7 days. Intra-operative margin status is therefore limited to soft tissue margins. Orthopaedic oncologists have worked around this issue by taking wider bone margins in bony sarcomas, the standard is 2cm from the tumor, to prevent a positive margin surgery. Depending on the anatomic location, 2cm in multiple directions can lead to significant functional morbidity. In soft tissue sarcoma, negative margins as close as 2mm have been shown to have similar positive outcomes to wider margins; however, this data has not been shown in bone, likely due to the inability to confirm a closer margin as negative for bone tissue. A possible solution to this problem is photoacoustic imaging. It involves a short laser pulse into tissue, with an ultrasound transducer detecting the reflective heat-induced pressure-wave that propagates in tissue as an ultrasonic wave. An image is produced from the original optical energy deposition inside the tissue. Recently, photoacoustic imaging has been applied to breast cancer tissue as an alternative to frozen and permanent section; images are nearly identical to pathology slides obtained with normal processing. This is a proof of concept project to determine whether photoacoustic imaging is a viable modality in calcified bone specimens.

Methods: Harvested bone sarcoma specimens were obtained through an institutional tissue repository IRB. The capability of this label-free contour-scan photoacoustic microscopy (PAM) system was demonstrated by imaging undecalcified thick bone (>1cm) with rough surfaces. Both undecalcified and decalcified bone were imaged by UV-PAM and compared with gold-standard hematoxylin and eosin (H&E) stained scanned images to validate the PAM results. Bone PAM images were converted into pseudo-color virtual histology images, allowing the pathologist to readily identify the cancerous features.

Results: 3D contour scanning with PAM was successfully used to image thick, undecalcified normal bone, creating recognizable spongy bone structures and elements (Fig 1). Although this capability is invaluable, historically undecalcified specimens are done for metabolic bone disease rather than bone tumors, so there is no strong comparison for the pathologic bone, although visible differences were apparent in this study (Fig 1).

For a gold standard comparison, specimens with calcification that was not so dense as to prevent sectioning were obtained and H&E slides were created and high resolution photographs were taken. Photoacoustic images were then taken as well, matching the magnification. A well-known sarcoma pathologist subsequently examined the PAM images, and was able to distinguish normal from pathologic bone (Fig 2).

Conclusion: Our results indicate that photoacoustic microscopy is a valid option for imaging undecalcified bone. The 3D

Figure 1. photoacoustic images of undecalcified, unprocessed bone


contouring allows direct imaging of thick, hard specimens with a rough surface without prior knowledge of the surface contour, and produced recognizable images of spongy bone (Fig 1). Furthermore, we were able to compare PAM images to undecalcified H&E specimens and distinguish pathologic bone (Fig 2). This study serves as proof of concept for this modality, and more refinement of the process and further studies are needed to verify these results.

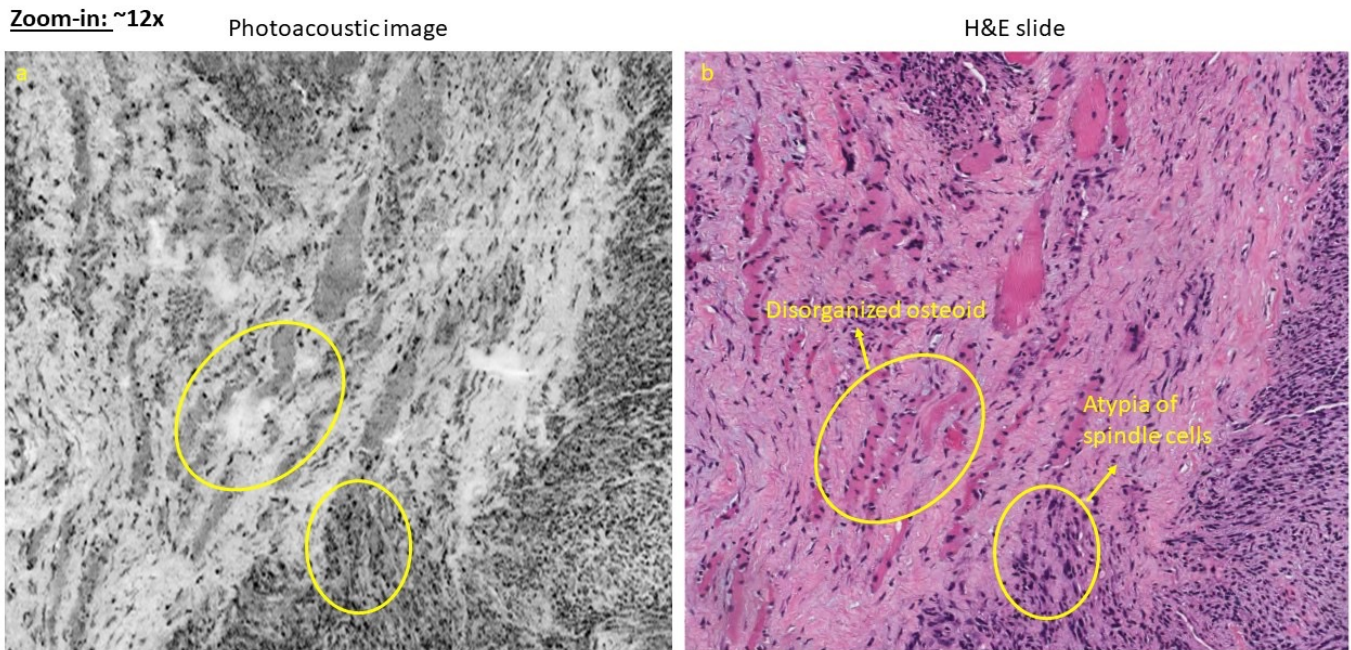


Figure 2. Osteosarcoma specimen, undecalcified, sectioned and processed for and H&E slide (b). A photoacoustic image was taken of the slide for direct comparison (a). Notice the disorganized osteoid and spindle cell atypia visible in H&E slide and PAI.

100 um



Poster #116 #1819079

THE SARCOMA MICROBIOME AS A NOVEL PROGNOSTIC TOOL

Gabriel Tinoco, MD, FACP¹; Marium Husain, MD¹; Rebecca Hoyd, Biostatistician¹; Malvenderjit Jagjit Singh, Biostatistician¹; James L. Chen, MD²; David Liebner, MD¹; Daniel Spakowicz, PhD¹

¹The Ohio State University, Columbus, Ohio, UNITED STATES, ²Ohio State University, Columbus, Ohio, UNITED STATES

Objective: Sarcomas are a heterogeneous group of malignant tumors of mesenchymal origin consisting of numerous histological and molecular subtypes, with unique biologic features and different clinical outcomes. The application of immunology and its development as a therapeutic tool in cancer care has revolutionized the field over the past decade; however, its application in sarcomas has led to underwhelming outcomes. Thus, there is an urgent need to understand the immunologic interactions in cancer patients better. Evaluating the tumor microbiome is a promising new approach that could be used as a diagnostic and therapeutic tool, leading to improved treatment options and better clinical outcomes.

Methods: We utilized sarcoma tumor biopsy RNAseq data from two independent datasets, ¹The Cancer Genome Atlas (TCGA) and ²the Oncology Research Information Exchange Network (ORIEN). Due to the large number of sarcoma subtypes, we focused on three main groups: dedifferentiated liposarcoma (DDLPS), leiomyosarcoma (LMS), and "other," representing all other sarcoma subtypes. We utilized ExoTIC, "Exogenous sequences in Tumors and Immune cells," a tool recently developed by Dr. Daniel Spakowicz and Dr. Xaiokui Mo. ExoTIC takes raw RNAseq reads and carefully aligns to both human and non-human reference genomes to identify low-abundance microbes. Models of association were analyzed based on each of the three groups as well as all the samples: "All" group. We performed Cox proportional hazards regression to identify the microbes associated with overall survival (OS).

Results: We evaluated 94 RNAseq samples from TCGA and then validated those associations on an independent dataset of 95 samples from ORIEN (Table 1). For TCGA, a total of 11 microbes were statistically associated only with DDLPS, 6 only with LMS. However, for LMS, those six microbes did not validate in the ORIEN dataset. Interestingly, for DDLPS, three microbes associated with lower survival across both datasets: Peptoniphilus hari (HR 20.49 [ORIEN]; HR 3.39 [TCGA]), Desulfosarcina alkanivorans (HR 20.49 [ORIEN]; HR 2.61 [TCGA]), and Pseudomonas parafulva (HR 4.84 [ORIEN]; HR 2.50 [TCGA]). The presence of no organisms was associated with improved survival.

Conclusion: We found a specific relationship between microbial presence and histological sarcoma subtype (DDLPS, LMS), which significantly correlated with OS and validated in an independent dataset. Assessing individual characteristics of a sarcoma histological subtype with its particular microenvironment (e.g., microbes) can lead to personalized treatment insights and improved outcomes. Our future research will validate and correlate the microbial profile of sarcoma subtypes with clinical outcomes retrospectively and prospectively.

	ORIEN	TCGA	p test
n	95	94	
Age (mean (SD))	55.93 (15.71)	63.68 (14.12)	<0.001
Sex = Male (%)	46 (48.4)	39 (41.5)	0.417
Histology (%)			0.314
Leiomyosarcoma	31 (32.6)	39 (41.5)	
Liposarcoma	23 (24.2)	24 (25.5)	
Other	41 (43.2)	31 (33.0)	



Poster #117 #1818988

VALIDATION OF MDM2 FLUORESCENCE IN SITU HYBRIDIZATION TESTING IN THE DIAGNOSIS OF WELL-DIFFERENTIATED ADIPOCYTIC NEOPLASMS: A RETROSPECTIVE REVIEWAshley N. Flaman, MD, FRCPC¹; Brendan C. Dickson, MD MSc²; Elizabeth G. Demicco, MD PhD³¹University of Toronto / Mount Sinai Hospital, Toronto, Ontario, CANADA, ²Mount Sinai Hospital, Toronto, Ontario, CANADA, ³Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, Ontario, CANADA

Objective: There is a high level of concordance between morphology and MDM2 fluorescence in situ hybridization (FISH) testing in the classification of lipoma and atypical lipomatous tumour / well-differentiated liposarcoma (ALT/WDLPS). Occasionally, however, atypia may be minimal or focal, and FISH is currently recommended for confirming the diagnosis of well-differentiated adipocytic tumours arising in the retroperitoneum, abdomen, and pelvis; recurrent 'lipomas'; those with equivocal cytologic atypia; and deep extremity tumours lacking cytologic atypia (> 10 cm, in patients > 50). Clarity remains necessary for situations in which relevant history and/or imaging are unavailable. The aim of this validation study was to assess the applicability of existing MDM2 testing criteria, including cases for which size and depth criteria are lacking, in triaging lipomatous neoplasms.

Methods: A retrospective review of the laboratory information system was conducted to retrieve 250 consecutive cases for which MDM2 FISH had been performed, including both in-house and consultation specimens. Well-differentiated adipocytic neoplasms with at least one archival slide available for review were included. Data, including patient age/sex, tumour size, anatomic site, depth, and specimen type, was obtained from the pathology reports, requisitions, consult letters, and electronic medical record where available. H&E slides were reviewed to document the presence/absence of nuclear atypia (enlarged, hyperchromatic tumour nuclei), cellular or myxocollagenous septa, fat necrosis, acellular collagen bands, myxoid change, and lipoblasts.

Results: 58 cases (23%) were diagnosed as ALT/WDLPS, 162 (65%) were benign (e.g., lipoma, hibernoma, spindle-cell/pleomorphic lipoma, etc.), and 30 (12%) were non-diagnostic (e.g., fat necrosis, scant fragments of skeletal muscle and adipose tissue, etc.). For non-diagnostic samples, 87% were core biopsies, where adequacy of sampling was often uncertain. ALT/WDLPS were significantly larger than benign tumours (14.8 cm vs 10.9 cm, p=0.01). Correlations between testing indications and final diagnosis are summarized in Table 1. With strict application of current testing recommendations, only one ALT would have been missed (a 10.6 cm superficial tumour of thigh with no atypia). The remaining 6 superficial tumours diagnosed as ALT all showed atypia. Recurrent tumours not meeting other testing criteria were uniformly benign (n=10), whereas recurrent tumours with additional testing indications were ALT/WDLPS in 5/7 cases. Three of 43 (7%) of cases with no atypia and unknown depth and size information were diagnosed as ALT on the basis of FISH results.

Conclusion: This study validates the indications for MDM2 FISH proposed by Clay et al. (2015) for lipomatous neoplasms. While our findings suggest that recurrent tumours lacking additional indications for testing may not require FISH, it is conceivable that a subset of these cases may simply represent residual gross disease rather than true local recurrence. As nearly 20% of cases were missing size/depth information, this study also reinforces the importance of providing these details to prevent over-testing.

Table 1: Indications for testing in well-differentiated lipomatous neoplasms.

Indication for testing	Total (n)	Benign (%)	Atypical/ malignant (%)	Non-diagnostic (%)
Clay (2015) criteria	146	50.0	37.0	13.0
Size/deep	18	77.8	22.2	0.0
RP/pelvic/intra-abdominal	20	55.0	0.0	45.0
Recurrent	10	100.0	0.0	0.0
Atypia	47	51.1	38.3	10.6
Meet multiple criteria	51	27.5	62.7	9.8
Missing clinical data	43	79.1	7.0	14.0
Do not meet criteria	61	90.2	1.6	8.2



Poster #118 #1819030

A REPORT ON THE REVIEW OF ARCHIVED OSTEOSARCOMA AND EWING SARCOMA SPECIMENS AT THE BIOPATHOLOGY CENTER - BONE SARCOMA COMMITTEE, CHILDREN'S ONCOLOGY GROUP

 Archana Shenoy, MD¹; Sonja Chen, MD²; Jonathan Bush, MD³; Alyaa Al-Ibraheemi, MD⁴; Jessica L. Davis, MD⁵; Mark D. Krailo, PhD⁶; Damon R. Reed, MD⁷; Katherine A. Janeway, MD⁸
¹Nationwide Childrens Hospital, Columbus, Ohio, UNITED STATES, ²Brown University, Providence, Rhode Island, UNITED STATES, ³British Columbia Children's Hospital, Vancouver, British Columbia, CANADA, ⁴Boston Children's Hospital, Boston, Massachusetts, UNITED STATES, ⁵Oregon Health & Science University, Portland, Oregon, UNITED STATES, ⁶Department of Preventive Medicine, Keck School of Medicine of the University of Southern California, Los Angeles, California, UNITED STATES, ⁷Moffitt Cancer Center, Tampa, Florida, UNITED STATES, ⁸Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, Massachusetts, UNITED STATES

Objective: The Children's Oncology Group (COG) Biorepository at the Biopathology Center (BPC), Nationwide Children's Hospital, Columbus, OH contains archived tumor specimens submitted for various COG study protocols. The BPC repository is utilized for numerous biology study aims, with the goal of helping to better understand the pathophysiology of tumors. This in turn may influence design of future clinical trials and patient care. BPC pathologists perform quality assurance (QA) reviews of archival material before biospecimens are released for study. Since QA reviews are not routinely included in the submission process into the BPC, the quality and utility of tissue is often unclear. Therefore, a pathology quality assurance review was conducted to explore the utility of future testing on banked formalin fixed paraffin embedded (FFPE) Ewing Sarcoma and Osteosarcoma specimens

Methods: The BPC staff retrieved archival tumor cases for review between 06/2020 and 08/2020. One hematoxylin and eosin-stained slide per FFPE block of tissue was digital scanned for whole slide image (WSI) analysis and uploaded with a copy of the de-identified pathology report on a virtual slide-viewing platform. Four board certified pediatric pathologists with expertise in sarcomas (AA, JB, SC, AS) designed a digital QA review form and performed reviews. The QA review data collection form included diagnosis, volume of viable tumor, decalcification techniques, ancillary molecular/cytogenetic studies and a comment box to include miscellaneous noteworthy information.

Results: During the study period, 530 cases (of 1257 cases requested) were digitally prepared for review and 462 reviews were completed. Of the reviewed cases, 414 (90%) were concordant with the diagnosis and had variable volumes of viable tumor (scant to adequate), while 34 (7%) of cases had no viable tumor (extensive tissue necrosis or no tumor on the slide) and 14 (3%) had an alternative diagnosis (e.g. tumor submitted as osteosarcoma, re-classified as a chondromyxoid fibroma on review). Of the reviewed concordant cases, 324 (78%) were consistent with OS, 90 (21.7%) were consistent with ES and 3 (<1%) were consistent non-ES round cell sarcomas (e.g. BCOR or CIC- rearranged sarcomas).

Conclusion: Ninety percent of reviewed specimens passed QA review, whereas the remaining failed due to diagnostic discordance or lack of viable tumor. Among specimens with diagnostic concordance, variable volumes of tumor were present, including specimens with scant viable tumors. Although QA reviews are time consuming, these results suggest QA reviews at tissue submission could potentially improve tissue quality available for research and timeliness of sample delivery for research. In addition, it would provide an opportunity for follow-up with sites to request submission of higher quality specimens and mitigate storage of tissue without potential for future use.



Poster #119 #1818948

CELL-CYCLE PHASE PROGRESSION ANALYSIS IDENTIFIES DISTINCT PHENOTYPES OF PROGNOSTIC SIGNIFICANCE IN SARCOMA

Mark M. Cullen, MD¹; Alexander L. Lazarides, MD²; Etienne M. Flamant, BA³; Patricia D. Pittman, MD⁴; Harrison R. Ferlauto, MD⁵; David L. Kerr, IV, MD¹; Daniel Evans, BS, MSc³; Zuwei Su, PhD⁴; Kai Stoebber, PhD⁶; David G. Kirsch, MD, PhD⁷; Nicole A. Larrier, MD, MS⁷; Lars M. Wagner, MD⁸; Julia D. Visgauss, MD¹; Brian E. Brigman, MD, PhD¹; Richard F. Riedel⁹; Jason A. Somarelli, PhD⁹; Dianna M. Cardona, MD⁴; William C. Eward, MD¹

¹Duke University Hospital, Department of Orthopaedic Surgery, Durham, North Carolina, UNITED STATES,

²Duke University Hospital, Department of Orthopedic Surgery, Durham, North Carolina, UNITED STATES

³Duke University School of Medicine, Durham, North Carolina, UNITED STATES, ⁴Duke University Hospital, Department of Pathology, Durham, North Carolina, UNITED STATES, ⁵Icahn School of Medicine at Mt. Sinai, Department of

Orthopaedic Surgery, New York, New York, UNITED STATES, ⁶University of Cambridge, London, England, UNITED

KINGDOM, ⁷Duke University Hospital, Department of Radiation Oncology, Durham, North Carolina, UNITED STATES,

⁸Duke University Hospital, Department of Pediatrics, Durham, North Carolina, UNITED STATES, ⁹Duke Cancer Institute, Duke University Medical Center, Durham, North Carolina, UNITED STATES

Objective: Cell-cycle markers, such as Mcm2, Geminin, Plk1, and H3S10ph have prognostic value and have been used to reclassify individual carcinomas by their unique cell-cycle phenotypes. It's been suggested that this method of classification allows for better alignment of adjuvant therapies with the unique biology of each tumor; however, this strategy has not been thoroughly explored for sarcomas. Our goal was to correlate the protein expression of specific markers and cell-cycle phenotypes with prognosis of patients with bone or soft tissue sarcoma.

Methods: A total of 142 sarcomas were collected from a single institution. Of these 26 were of bone, with the majority of these being osteosarcoma, and 116 were from the soft tissue, with the majority of these being undifferentiated pleomorphic sarcoma and liposarcoma (Table 1). Most of the tumors were found to be grade 3 (64.4%) and were between 6 and 10 cm (34.8%). After primary diagnosis 39.4% of these tumors had a local recurrence and 49.3% were found to have a distant metastasis (Table 1). Tumors were fixed in formalin, embedded in paraffin, and stained for Mcm2, Geminin, Plk1, and H3S10ph. Each marker and its cell-cycle phenotypes were evaluated for their prognostic significance in several outcome measures: 5-year local recurrence-free survival, metastasis-free survival, disease-free survival and overall survival. Cut-offs of "high" or "low" expression of a certain protein were determined through optimization utilizing cox-regression analysis. Three cell-cycle phenotypes were generated by a combination of the optimization cut-offs for Mcm2 and Geminin as prognostic markers of overall survival. Tumors were classified into the following three subtypes: Phenotype I included tumors with low expression of Mcm2 regardless of their Geminin levels (Table 2); Phenotype II included tumors that expressed high levels of Mcm2 and low levels of Geminin (Table 2); Phenotype III tumors included tumors that expressed high levels of both Mcm2 and Geminin (Table 2). Cox-regression analysis was utilized to evaluate each marker and phenotype with an alpha value of 0.05. Covariates were chosen based on backward likelihood ratio selection.

Results: High expression of H3S10ph was found to be associated with an increased time to local recurrence (HR: 0.39 (0.20 – 0.74), $p = 0.004$; Table 3). High expression of Mcm2 (HR: 2.79 [1.60-4.86], $p = <0.001$; Table 2) and Plk1 (HR: 1.90 [1.11-3.24], $p = 0.02$; Table 3), were all found to be associated with a decreased metastasis-free survival time. High expression of Mcm2 (HR: 1.76 [1.01-3.08], $p = 0.048$; Table 3) was found to be associated with a shorter disease-free survival time. Finally, High Geminin (HR: 2.13 [1.07-4.21], $p = 0.03$) and Plk1 (HR: 1.89 [1.08-3.33], $p = 0.03$) were shown to be associated with a decreased survival time. After placing tumors in each cell-cycle phenotype it was found that Phenotype III was found to be associated with a decreased metastasis-free survival time when compared to Phenotype I (HR: 2.30 [1.02-5.22], $p = 0.046$; Table 4). Phenotype III (HR: 3.23 [1.33 – 7.83], $p = 0.01$; Figure 1; Table 4) was associated with a decreased survival time when compared to Phenotype I. When the phenotype I and II tumors were combined and compared to the phenotype III tumors, significant differences in overall survival (HR: 2.13 (1.01 – 4.47), $p = 0.047$) were identified.

Conclusion: This study demonstrated that Mcm2, Geminin, Plk1, and H3S10ph may be important individual histopathologic markers that can be utilized for prognostication of sarcomas. A subset of these markers (Mcm2 and Geminin) demonstrated a means of classifying sarcomas by unique phenotypes representing abnormalities of each phase of cell cycle progression;

importantly, this appeared to provide meaningful prognostic value and may help sarcoma specialists plan adjuvant therapies. Future clinical studies are needed to validate the prognostic significance of these markers.

Table 1: Expression profile based on the Labelling Index of each Cell-cycle Phenotype

Phenotype	Mcm2 (BM28)*	Geminin*	Plk1&	H3S10ph&
Phenotype I (G0-Out of Cycle)	Low	-	-	-
Phenotype II (G1 delayed/ arrested)	High	Low	-	-
Phenotype III (Actively Cycling)	High	High	-.&	-.&

*With Mcm2 and Geminin being the most important for defining phenotype

&Utilized to better characterize phenotype 3

Table 2: Univariate and Multivariate Analysis of Tumor Markers for Local Recurrence-Free Survival, Metastasis-Free Survival, Disease-Free Survival, and Overall Survival. Multivariate analysis is controlling for age, grade, tumor size, and tumor type.

5-Year Local Recurrence-Free Survival									
<u>Univariate</u>	Labelling Index	Hazard Ratio	95% CI	p-value	<u>Multivariate</u>	Labelling Index	Hazard Ratio	95% CI	p-value
H3S10ph	≤3	1			H3S10ph	≤3	1		
	>3	0.41	0.23-0.73	0.003		>3	0.39	0.20-0.74	0.004
5-Year Metastasis-Free Survival									
<u>Univariate</u>	Labelling Index	Hazard Ratio	95% CI	p-value	<u>Multivariate</u>	Labelling Index	Hazard Ratio	95% CI	p-value
Mcm2	≤72	1			Mcm2	≤72	1		
	>72	2.15	1.28-3.63	0.004		>72	2.79	1.60-4.86	<0.001
Geminin	≤2	1			Geminin	≤2	1		
	>2	2.21	1.28-3.80	0.004		>2	1.48	0.80-2.72	0.22
Plk1	≤2	1			Plk1	≤2	1		
	>2	2.11	1.27-3.49	0.004		>2	1.90	1.11-3.24	0.02
ATRX	≤5	1			ATRX	≤5	1		
	>5	0.40	0.24-0.67	0.001		>5	0.57	0.33-1.00	0.048
5-Year Disease-Free Survival									
<u>Univariate</u>	Labelling Index	Hazard Ratio	95% CI	p-value	<u>Multivariate</u>	Labelling Index	Hazard Ratio	95% CI	p-value
Mcm2	≤32	1			Mcm2	≤32	1		
	>32	1.88	1.18-3.01	0.008		>32	1.76	1.01-3.08	0.048
ATRX	≤80	1			ATRX	≤80	1		
	>80	0.57	0.36-0.89	0.01		>80	0.68	0.42-1.10	0.12
5-Year Overall Survival									
<u>Univariate</u>	Labelling Index	Hazard Ratio	95% CI	p-value	<u>Multivariate</u>	Labelling Index	Hazard Ratio	95% CI	p-value
Mcm2	≤45	1			Mcm2	≤45	1		
	>45	2.72	1.45-5.12	0.002		>45	1.67	0.86-3.26	0.13
Geminin	≤16	1			Geminin	≤16	1		
	>16	2.52	1.34-4.73	0.004		>16	2.13	1.07-4.21	0.03
Plk1	≤2	1			Plk1	≤2	1		
	>2	2.02	1.16-3.52	0.01		>2	1.89	1.08-3.33	0.03
ATRX	≤5	1			ATRX	≤5	1		
	>5	0.38	0.21-0.66	0.001		>5	0.55	0.30-0.99	0.047

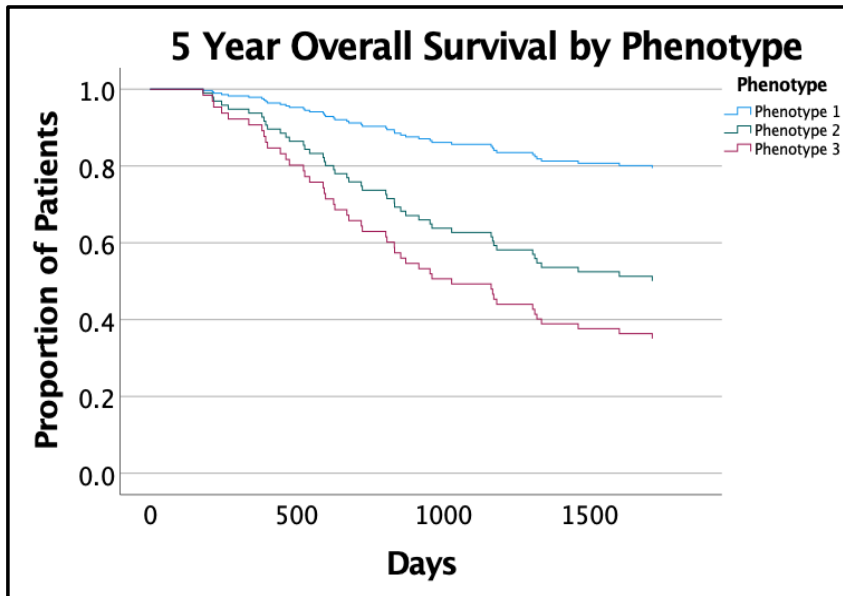


Figure 1: 5-Year Overall Survival by Phenotype. Significant differences in 5-year survival were found between phenotype I and phenotypes II (HR: 3.01 (1.42-6.36), $p = 0.004$) and III (HR: 4.56 (2.02-10.29), $p < 0.0001$) in univariate analysis. After controlling for grade, tumor size, and stratifying by tumor type only differences between phenotypes I and phenotypes III remained (HR: 3.23 (1.33-7.83), $p = 0.01$). When the phenotype I and II tumors were combined and compared to the phenotype III tumors, significant differences in overall survival (HR: 2.13 (1.01 – 4.47), $p = 0.047$) were identified.

Table 3: Univariate and Multivariate Analysis of Phenotype for Local Recurrence-Free Survival, Metastasis-Free Survival, Disease-Free Survival, and Overall Survival. Multivariate analysis is controlling for age, grade, tumor size, and tumor type.

5-Year Local Recurrence-Free Survival							
<u>Univariate</u>	Hazard Ratio	95% CI	p-value	<u>Multivariate</u>	Hazard Ratio	95% CI	p-value
Phenotype			0.72	Phenotype			0.71
I	1			I	1		
II	1.11	0.58-2.10	0.76	II	1.14	0.54-2.42	0.73
III	0.74	0.28-1.97	0.54	III	0.69	0.18-2.55	0.57
5-Year Metastasis Free Survival							
<u>Univariate</u>	Hazard Ratio	95% CI	p-value	<u>Multivariate</u>	Hazard Ratio	95% CI	p-value
Phenotype			0.01	Phenotype			0.14
I	1			I	1		
II	1.99	1.09-3.64	0.03	II	1.43	0.74-2.77	0.29
III	2.72	1.33-5.56	0.01	III	2.30	1.02 – 5.22	0.046
5-Year Disease-Free Survival							
<u>Univariate</u>	Hazard Ratio	95% CI	p-value	<u>Multivariate</u>	Hazard Ratio	95% CI	p-value
Phenotype			0.08	Phenotype			0.20
I	1			I	1		
II	1.60	0.98-2.61	0.06	II	1.44	0.82-2.54	0.21
III	1.82	0.98 – 3.39	0.06	III	1.99	0.92–4.28	0.08
5-Year Overall Survival							
<u>Univariate</u>	Hazard Ratio	95% CI	p-value	<u>Multivariate</u>	Hazard Ratio	95% CI	p-value
Phenotype			0.001	Phenotype			0.03
I	1			I	1		
II	3.01	1.42-6.36	0.004	II	1.80	0.82-3.95	0.14
III	4.56	2.02-10.29	<0.001	III	3.23	1.33–7.83	0.01



Poster #120 #1818981

THE EFFICACY OF MOLECULAR ANALYSIS IN THE DIAGNOSIS OF BONE AND SOFT TISSUE TUMORS: A 15 YEARS MONO-INSTITUTIONAL EXPERIENCE

Marco Gambarotti, MD¹; Stefania Benini, Bsci¹; Gabriella Gamberi, Bsci¹; Stefania Cocchi, Bsci¹; Giovanna Magagnoli, Bsci¹; Marta Sbaraglia, MD²; Alberto Righi, MD¹; Angelo Paolo Dei Tos, MD³
¹Rizzoli Orthopaedic Institute, Bologna, Emilia-Romagna, ITALY, ²Azienda Ospedaliera Università di Padova (UniPD), Padova, Veneto, ITALY, ³Università di Padova (UniPD), Padova, Veneto, ITALY

Objective: Histological diagnosis of bone and soft tissue tumors can be challenging, sometimes requiring a combination of morphology, immunophenotype and ancillary molecular tests. Many tumors are associated with characteristic genetic aberrations that can be assessed using fluorescence in situ hybridization (FISH), reverse-transcription-PCR (RT-PCR), anchored multiplex PCR (AMP) for next-generation sequencing (NGS) or other mutational analysis. Since this last years, routine molecular testing has been implemented and a novel technique termed anchored multiplex PCR (AMP) for next-generation sequencing (NGS) has recently been introduced, using the Archer FusionPlex Sarcoma Panel. The experience has also increased within our Department as more molecular tests are routinely performed. We now reassess 15 years, comparing the use of formalin-fixed, paraffin-embedded (FFPE) tissue vs frozen tissue, to see whether there were discernible improvements in test efficacy.

Methods: 2638 consecutive cases from January 2006 until December 2020 that had undergone FISH, RT-PCR/quantitative RT-PCR (qRT-PCR), NGS or mutational analysis were assessed to evaluate the diagnostic utility of these molecular techniques in order to confirm the histopathological assessment.

Results: In total, 3242 analyzes were carried out; 1720 of which were RT-PCR/qPCR investigations (1622 fusion gene research and 98 gene variation analysis) and 1495 were FISH analysis (1099 gene rearrangement status and 396 MDM2 status). The 68% of samples analyzed were from undecalcified FFPE tissue, the 32% from frozen tissue. A total of 3307 analyzes were performed. The most frequent requests were for Ewing sarcoma (761 cases), well dedifferentiated/dedifferentiated liposarcoma (451 cases), synovial sarcoma (393 cases), myxoid liposarcoma (383 cases), and extraskelatal myxoid chondrosarcoma (121 cases). RT-PCR analyzes showed a 5% failure rate on frozen tissue vs 17% on undecalcified FFPE tissue, while FISH total surveys showed a 15% failure rate on undecalcified FFPE tissue. In sixteen (5%) of these cases, it was furtherly necessary to apply NGS analysis on undecalcified FFPE tissue samples; only one case (6%) failed the result, while 6 cases (37%) showed strong fusions.

Conclusion: We demonstrated the continuing utility of RT-PCR/qRT-PCR, FISH and NGS for tumor diagnosis, and that each has advantages in specific contexts. These ancillary molecular tests are important tools in both defining and excluding diagnoses of tumors. Despite the fact that false-negative results due to poor quality samples can be encountered, these methods demonstrated excellent diagnostic utility for translocation detection in bone and soft tissue tumors.



Poster #121 #1818938

FIBROBLAST ACTIVATION PROTEIN EXPRESSION IN SARCOMAS

Jacquelyn Crane, MD¹; Danielle S. Graham, MD²; Christine Mona, PhD²; Scott D. Nelson, MD³; Alireza Samiei, MD²; David Dawson, MD²; Sarah Dry, MD²; Joseph Crompton, MD PhD⁴; Matthias Benz, MD²; Johannes Czernin, MD²; Fritz C. Eilber, MD²; Thomas Graeber, PhD⁵; Jeremie Calais, MD²; Noah C. Federman, MD²

¹Stanford University, Cupertino, California, UNITED STATES, ²UCLA Medical Center, Los Angeles, California, UNITED STATES, ³UCLA Medical Center, Santa Monica, California, UNITED STATES, ⁴UCLA Health, Los Angeles, California, UNITED STATES, ⁵UCLA, Los Angeles, California, UNITED STATES

Objective: Cancer-associated fibroblasts (CAFs) are a key component of tumor stroma. CAFs have been shown to promote cancer cell survival, growth, metastasis, and chemoresistance. Fibroblast activation protein (FAP) alpha is a type II membrane bound glycoprotein enzyme with protease activity. FAP has been shown to be highly expressed by CAFs in multiple epithelial cancers with limited to absent expression in normal adult tissues. This differential expression coupled with the cancer supportive role of CAFs makes FAP a promising theranostic target. The literature on FAP expression in sarcomas is limited. Thus, we analyze the expression of FAP in several sarcoma subtypes via immunohistochemistry (IHC) and RNA sequencing in order to better understand the potential diagnostic and therapeutic role of radiolabeled FAP inhibitors (FAPI) in sarcomas.

Methods: Sample Selection:

We conducted an institutional review board approved retrospective chart review of patients with a diagnosis of sarcoma. We identified 34 tumor samples with pathology confirmed sarcoma with available tissue samples from biopsy or resection and 8 available adjacent normal tissue samples.

Immunohistochemistry (IHC)

Archival formalin-fixed paraffin-embedded tissue specimens were obtained. Staining for hematoxylin and eosin (H&E) and FAP were performed on the specimens at the UCLA Tissue Pathology Core Laboratory. Polyclonal rabbit anti-FAP alpha antibody from Abcam was used. Immunostaining was performed on Leica Bond platform. A positive control was used. Slides were scanned with 20X magnification and reviewed using Orbit Image Analysis software. A semi-quantitative scoring system was used to score FAP staining intensity on a scale of 0-3 (0 = negative; 1 = weak; 2 = moderate; 3 = strong) and FAP staining density from 0-100% (none, <25%, 25-75%; >75%). Tumor stroma and tumor cells were scored separately. Additionally, a qualitative composite FAP expression score was given to each sample (not detected; low; medium; high).

RNA sequencing data acquisition, processing and analysis

Toil processed RNA sequencing data files from The Cancer Genome Atlas (TCGA) were downloaded from the Xena Browser from the UCSC Computational Genomics Lab. Raw RNA FASTQ files from the Therapeutically Applicable Research to Generate Effective Treatments (TARGET) osteosarcoma dataset and from Sayles and colleagues were downloaded from dbGAP and EGA, respectively. Data was then processed using the Toil RNA-Seq pipeline and used to generate upper quartile normalized counts. All data were log transformed ($\log_2(x+1)$). FAP expression was compared across different sarcoma subtypes.

Results: IHC

A total of 31 sarcoma samples, 8 samples from normal tissue adjacent to the sarcoma samples, and 1 positive control had adequate cellularity for review of H&E slides and quantification of FAP staining. This includes 3 cases of alveolar soft part sarcoma (ASPS), 8 cases of Ewing's sarcoma (ES), 4 cases of leiomyosarcoma, 4 cases of well-differentiated liposarcoma (WDLPS), 3 cases of de-differentiated liposarcoma, 5 cases of osteosarcoma and 5 cases of undifferentiated pleomorphic sarcoma (UPS). The details of each case including FAP scoring of tumor and stromal cells are listed in Table 1. This shows the variable FAP staining across samples. Representative images are shown in Figure 1.

RNA sequencing

Review of RNA sequencing data from cancer genomics databases shows high FAP expression in sarcoma tumor samples as shown in Figure 2.

Conclusion: In the current study, the expression of FAP was found to be variable across different sarcoma subtypes with the highest expression via IHC occurring in UPS samples. Compared to the majority of epithelial cancers, where the FAP expression is limited to stromal cells, FAP was found to be expressed in both stromal cells and the tumor cells. FAP expression was also present in the majority of normal tumor-adjacent samples examined, although the expression was generally lower

than that in the tumor sample. It is possible that the normal tumor-adjacent tissue is influenced by the nearby tumor and tumor stroma and may not be reflective of normal healthy tissue. The limitations of the current study include low number of sarcoma subtypes and samples included. However, the current results are promising that FAP may serve as a marker of sarcoma subtypes such as UPS. Further work is needed including investigation of FAP expression in other sarcoma subtypes and correlation of FAPI PET imaging results with FAP IHC results in order to better understand the utility of FAP in the diagnostic/staging/response evaluation and treatment of sarcomas.

Figure 1. Representative H&E and FAP IHC images. In panels A-D and F: top left = low power view of H&E slide; top right = high power view of H&E slide; bottom left = low power view of FAP stained slide; bottom right = high power view of FAP stained slide. In panel E: top right = low power view of FAP stained slide; bottom = high power view of FAP stained slide. A) Case 1 (ASPS) with tumor and stroma FAP scores of 2 and 2; B) Case 11 (Leiomyosarcoma) with tumor and stroma FAP scores of 2 and 3, respectively; C) Case 27 (UPS) with tumor and stroma FAP scores of 2 and 3, respectively; D) Case 29 (UPS) with tumor and stroma FAP scores of 3 and 3; E) Positive control (colon cancer) with tumor and stroma FAP scores of 0 and 3, respectively E. Normal A (normal tissue adjacent to Case 1) with other cells and stroma FAP scores of 0 and 1, respectively.

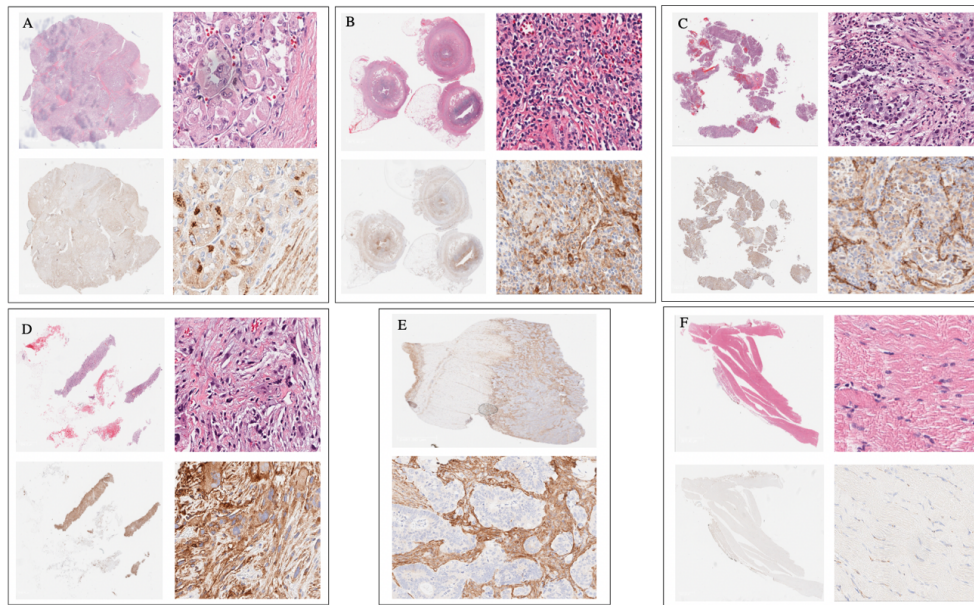


Figure 2. FAP gene expression by RNA sequencing. A) FAP gene expression across multiple cancer types from TCGA, TARGET, and Sayles et al. B) FAP gene expression by RNA sequencing across sarcoma subtypes profiled in TCGA, TARGET and Sayles et al datasets. UPS = Undifferentiated Pleomorphic Sarcoma; MPNST = Malignant Peripheral Nerve Sheath Tumor.

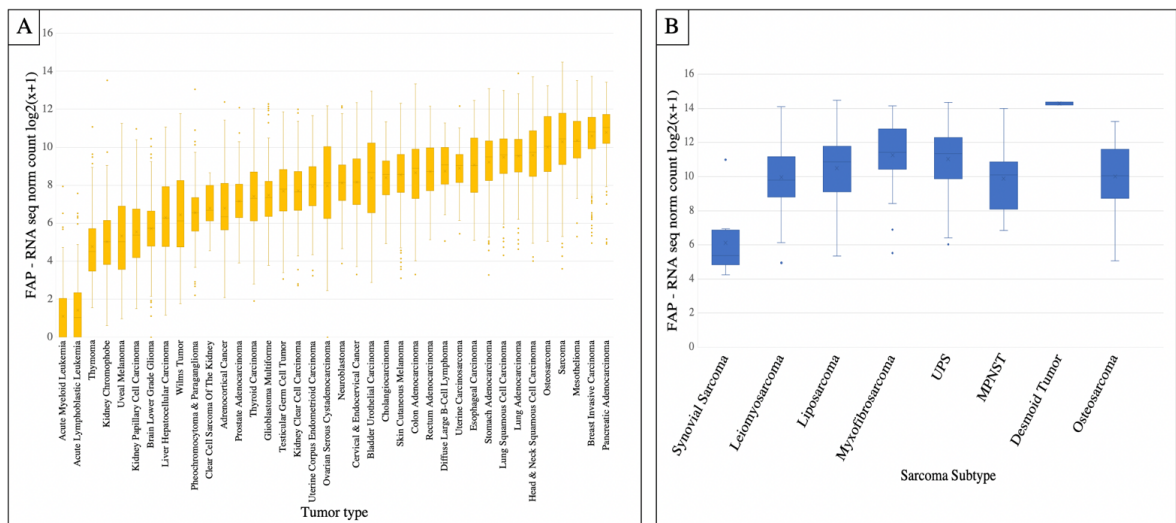


Table 1. Case information and IHC results

Case #	Diagnosis	FAP intensity score of tumor cells	FAP density score of tumor cells	FAP intensity score of stromal cells	FAP density score of stromal cells	Composite FAP score	Source	Sample treatment status
1	ASPS	2	>75%	2	>75%	Medium	Primary	Treatment naïve
1- Normal adjacent tissue	Normal tissue adjacent to ASPS	0	None	1	25-75%	Low	N/A	N/A
2	ASPS	1	<25%	3	>75%	Medium	Primary	Treatment naïve
3	ASPS	2	>75%	2	>75%	Medium	Metastasis	Treatment naïve
3- Normal adjacent tissue	Normal tissue adjacent to ASPS	1	25-75%	2	25-75%	Low	N/A	N/A
4	ES	0	None	2	>75%	Low	Metastasis	Post-chemotherapy
5	ES	0	None	3	25-75%	Low	Primary	Treatment naïve
6	ES	0	None	2	25-75%	Low	Primary	Post-neoadjuvant chemotherapy
7	ES	0	None	2	>75%	Medium	Primary	Treatment naïve
8	ES	1	<25%	1	>75%	Low	Primary	Post-neoadjuvant chemotherapy
9	ES	1	<25%	2	>75%	Low	Metastasis	Post-chemotherapy, recurrence
10	ES	0	None	1	25-75%	Low	Primary	Post-chemotherapy, recurrence
11	Leiomyosarcoma	2	>75%	3	>75%	Medium	Metastasis	Post-chemotherapy, recurrence
12	Leiomyosarcoma	1	25-75%	2	>75%	Medium	Primary	Treatment naïve
12-Normal adjacent tissue	Normal tissue adjacent to Leiomyosarcoma	0	None	2	25-75%	Low	N/A	N/A
13	Leiomyosarcoma	2	>75%	2	>75%	Medium	Primary	Post-neoadjuvant chemotherapy
13 -Normal adjacent tissue	Normal tissue adjacent to Leiomyosarcoma	2	>75%	2	>75%	Medium	N/A	N/A
14	Leiomyosarcoma	2	>75%	2	>75%	Medium	Primary	Treatment naïve
15	WDLPS	1	<25%	1	25-75%	Low	Primary	Treatment naïve, recurrence
16	WDLPS	1	<25%	2	>75%	Low	Primary	Treatment naïve, recurrence
17	WDLPS	1	25-75%	2	25-75%	Low	Primary	Treatment naïve, recurrence
18	WDLPS	1	25-75%	2	25-75%	Low	Primary	Post-chemotherapy, recurrence
19	Dedifferentiated liposarcoma	2	25-75%	2	25-75%	Medium	Primary	Post-neoadjuvant XRT
20	Dedifferentiated liposarcoma	0	None	1	<25%	Low	Primary	Treatment naïve, recurrence
21	Dedifferentiated liposarcoma	1	25-75%	2	25-75%	Low	Primary	Post-chemotherapy and XRT in distant past, recurrence
22	OS	2	>75%	2	>75%	Medium	Metastasis	Treatment naïve
23	OS	0	None	1	<25%	Low	Primary	Post-chemotherapy
24	OS	1	<25%	2	25-75%	Low	Primary	Post-neoadjuvant chemotherapy
25	OS	2	>75%	2	>75%	Medium	Metastasis	Post-chemotherapy, recurrence

26	OS	2	25-75%	3	>75%	Medium	Metastasis	Post-chemotherapy, recurrence
27	UPS	2	>75%	3	>75%	High	Primary	Treatment naïve
28	UPS	3	>75%	3	>75%	High	Primary	Treatment naïve
28- Normal adjacent tissue	Normal tissue adjacent to UPS	0	None	1	25-75%	Low	N/A	N/A
29	UPS	3	>75%	3	>75%	High	Primary	Treatment naïve
30	UPS	3	>75%	3	>75%	High	Primary	Post-chemotherapy in distant past, recurrence
30- Normal adjacent tissue	Normal tissue adjacent to UPS	0	None	2	25-75%	Low	N/A	N/A
31	UPS	2	>75%	2	>75%	Medium	Primary	Treatment naïve
31- Normal adjacent tissue	Normal tissue adjacent to UPS	0	None	2	25-75%	Low	N/A	N/A
Positive Control	Colon Cancer	0	None	3	>75%	Medium	Unknown	Unknown



Poster #122 #1818998

MAGNETIC RESONANCE IMAGING EVIDENCE OF JOINT EFFUSION IS ASSOCIATED WITH INTRA-ARTICULAR TUMOR EXTENSION

Max Vaynrub, MD; John Nolan, MD; Mohammad El Amine, MD; Anton Becker, MD PhD; Sinchun Hwang, MD
Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES

Objective: In the setting of intra-articular sarcoma extension, extra-articular excision is necessary to achieve wide margins. While limb salvage is often possible with extra-articular excision, there is greater morbidity as compared with intra-articular excision due to sacrifice of the joint capsule and surrounding soft tissue. However, failure to perform extra-articular excision in the appropriate scenario may lead to tumor recurrence, limb loss, and compromised survival. The decision to pursue extra-articular excision is a consequential one, highlighting the importance of appropriate patient selection.

The preoperative identification of intra-articular tumor extension is challenging. Physical examination is of limited utility, as the source of joint pain is often poorly localized. This leads clinicians to rely on magnetic resonance imaging (MRI). However, there are limitations to accurate MRI interpretation, such as image resolution, availability of imaging planes, distinction of tumor from edema, and varying definitions of intra-articular involvement.

In patients with sarcoma with uncertain joint invasion, the presence of effusion on preoperative MRI may suggest intra-articular pathology. However, scant literature exists to support this. Our study aims to define anatomical MRI signs of tumoral joint invasion and to determine if an association exists between pathologically confirmed intra-articular tumor extension and joint effusion on preoperative MRI.

Methods: A single-institution, retrospective cohort study was performed. The electronic medical record was searched from 2000-2020 for patients that underwent an extra-articular excision for sarcoma at the hip, knee, or shoulder. They were excluded if they lacked a diagnostic preoperative MRI, had a previous intra-articular surgery or an intra-articular fracture.

Three fellowship-trained musculoskeletal radiologists blinded to clinical and pathologic results reviewed the preoperative imaging. MRIs were evaluated on axial T1 weighted post-contrast and fluid sensitive sequences for three signs of joint invasion (capsular disruption, cortical breach and cartilage invasion) and for joint effusion/synovial thickening. Joint effusion at various anatomical recesses was measured and graded on a 4-point ordinal scale. Post hoc grouping was based on intra-articular tumor extension identified by pathologic examination. The discriminatory ability of MRI to detect intra-articular extension was determined with a receiver operating characteristic (ROC) analysis.

Results: 48 patients were included, with 10 shoulder, 9 hip and 29 knee excisions. The median age was 23.8 years (interquartile range [IQR] 14.9-46.9 years) and the median time between MRI and surgery was 2.1 weeks (IQR: 1.1-3.8 weeks).

ROC curves were constructed for all signs of joint invasion. Individually, the area under the curve (AUC) ranged between 0.65-0.76. When combined, the AUC was 0.83 (95% CI: 0.73-0.94). In 25/48 patients, only 1-2 signs of joint invasion were present, representing an uncertain radiographic determination of joint invasion. Joint effusion/synovial thickening was used to further stratify intra-articular extension. When analyzed on an ordinal scale, joint effusion had an AUC of 0.86 (95% CI: 0.71-1) (Figure 1).

When signs of invasion and effusion/ thickening were combined, the AUC was 0.89 (95% CI: 0.80-0.91, p=0.01) (Figure 2). An

Figure 1: Joint Effusion ROC Curve

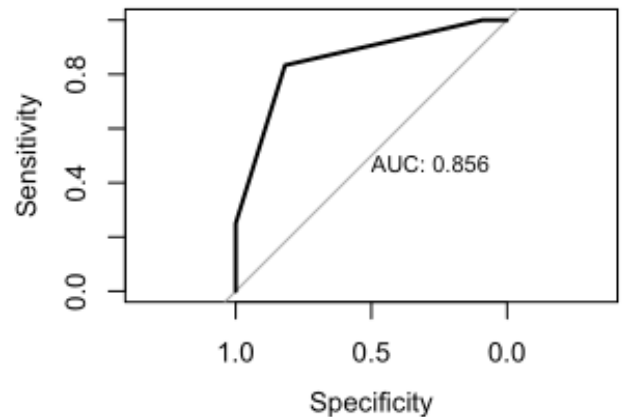
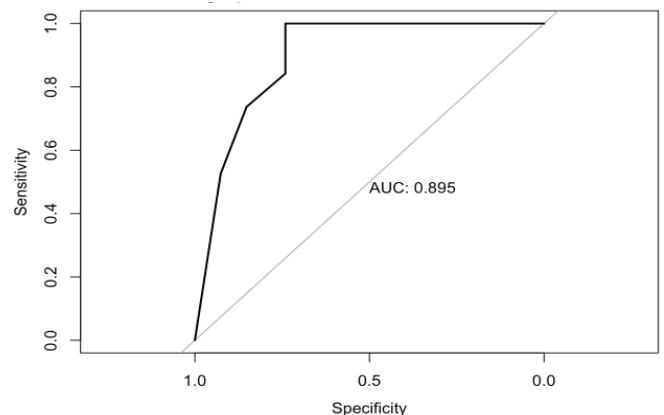


Figure 2: Combined Joint Invasion/ Effusion ROC Curve



optimal cut-off value with 100% sensitivity and 74% specificity was set at 1 sign of joint invasion and a moderate/grade 2 effusion or synovial thickening.

Conclusion: This study demonstrates excellent discrimination for MRI in determining intra-articular tumor extension when multiple signs of tumor invasion are present. In equivocal cases, joint effusion on MRI can further stratify patients and help decide whether to pursue extra-articular excision.



Poster #123 #1819060

OPTICAL COHERENCE TOMOGRAPHY FOR SURGICAL MARGIN ASSESSMENT IN SOFT TISSUE SARCOMA

Laura E. Selmic, BVetMed (Hons), MPH¹; John Alexander, MD²; Joel Mayerson, MD²; Thomas Scharschmidt, MD²; Valerie Grignol, MD²; Joal Beane, MD²; Raphael Pollock, MD²; David Konieczkowski, MD, PhD²; O. Hans Iwenofu, MD², ¹The Ohio State University College of Veterinary Medicine, Columbus, Ohio, UNITED STATES, ²James Cancer Hospital, The Ohio State University, Columbus, Ohio, UNITED STATES

Objective: Negative surgical margins are critical for optimal local control in soft tissue sarcomas (STS). The gold standard for assessment of surgical margins is histopathology, but this approach assesses only limited areas of large and complex specimens and does not provide real-time results to guide intra-operative decision-making. Optical coherence tomography (OCT) is a near-infrared imaging technology that uses light-waves to generate real-time high-resolution microscopic images of tissue microstructure. This approach has previously been shown to have high sensitivity (92-100%) for intra-operative detection of histopathologically positive margins in human breast cancer. Recently, our group has demonstrated good sensitivity (83-88%) and specificity (92-93%) of OCT for detection of microscopically positive margins in canine STS. Here, we report a pilot study evaluation of OCT in human extremity and superficial trunk STS.

Methods: OCT imaging was performed immediately after resection of 5 extremity and superficial trunk STS following informed patient consent as part of an IRB approved study. In each case, a single 1cm² area was identified intra-operatively by the surgeon as the closest surgical margin. This area was imaged with a spectral domain OCT system (Telesto, Thorlabs Inc.) and subsequently inked and processed for standard histopathological assessment. The pathologist was blinded to the OCT imaging results. A single experienced investigator evaluated the OCT images and compared them to the histopathology results.

Results: The five patients had diverse histologic subtypes of STS based on pre-treatment biopsy (Table 1). One patient received preoperative radiation therapy, one received neoadjuvant chemotherapy, and one patient received both preoperative radiation therapy and neoadjuvant chemotherapy. Of the areas selected for assessment, on histopathology two contained normal fascia, two contained skeletal muscle and one had a thin layer of fat and fascia overlying the sarcoma. All margins were classed as R0 by a distance of 0.3-2mm. On OCT imaging, differences in optical scattering intensity and tissue organization were readily detectable by tissue type (table 1). Differences in tissue microstructure between adipose and fascial tissue are shown in figure 1 (cases/panes 1,3 and 4). In case/pane 3, the sarcoma tissue could be visualized on OCT images (indicated by *) underlying a thin fascia layer, which represented a close but negative surgical margin. In contrast to normal tissues, sarcoma demonstrated high scattering, no microstructural organization, and rapid light attenuation limiting imaging depth.

Conclusion: OCT has the potential to differentiate between tumor and normal tissues in STS resection margins. Ongoing work will assess the formal diagnostic performance of OCT for detection of microscopically positive surgical margins in STS patients.

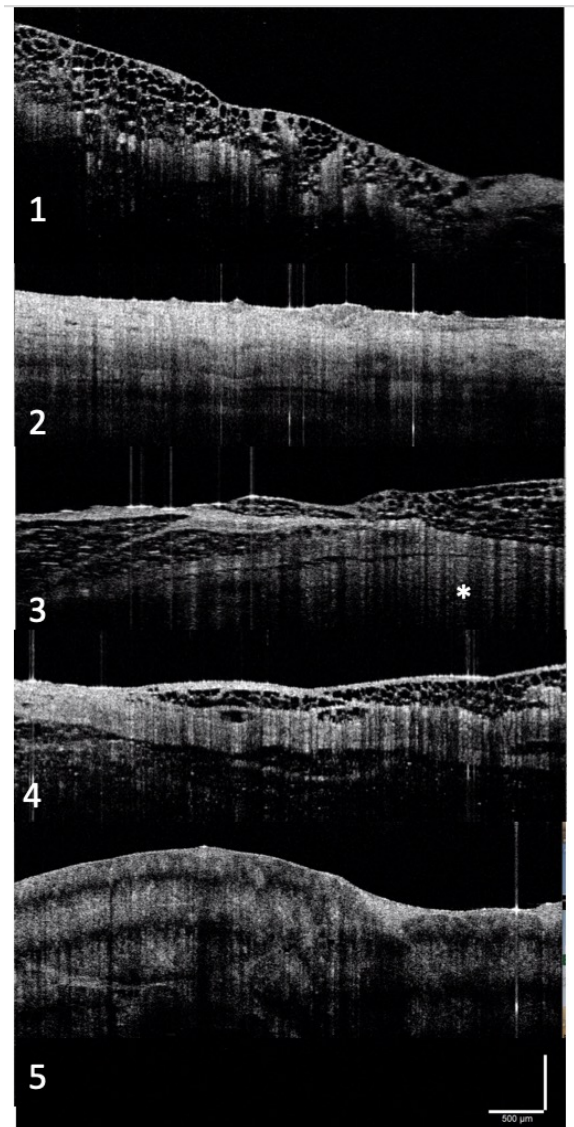


Table 1: Histopathologic and optical coherence tomography assessment for 5 soft tissue sarcoma cases

Case	Histopathology						OCT	
	Biopsy diagnosis	Neoadjuvant therapy	Diagnosis at resection	Tissue constituents of imaged area	Margin status	Margin distance	Tissue characteristics	Margin status
1.	Extraskeletal myxoid chondrosarcoma	Pazopanib x 14 months	Extraskeletal myxoid chondrosarcoma	Fascia	R0	2mm	Fat appears as low scattering honeycomb structure and fascia as white high scattering tissue deep to fat	R0
2	High grade sarcoma with myxoid features, favoring myxofibrosarcoma	Neoadjuvant ifosfamide followed by preoperative radiation therapy (50.4 Gy/28 fractions)	Necrotic soft tissue mass	Fascia	R0	2mm	Fascia appears as dense high scattering tissue.	R0
3	Dermatofibrosarcoma Protuberans and fusion analysis confirmed with COL1A1-PDGFB gene fusion	None	Dermatofibrosarcoma Protuberans	Fat and thin layer of fascia with tumor underlying	R0	0.3mm	Fat appears as low scattering honeycomb structure with thin layer of fascia appearing as dense high scattering tissue. Tumor is high scattering tissue underlying fascia	R0
4	Myxofibrosarcoma	Preoperative radiotherapy (50Gy/25 fractions)	Hematoma	Fat and skeletal muscle	n/a	n/a	Fat appears as low scattering honeycomb structure with denser organized tissue and thin layer of skeletal muscle then fat underneath.	n/a
5	Low grade myxoid fibrosarcoma	None	Myxofibrosarcoma	Skeletal muscle	R0	2mm	Skeletal muscle appears as organized alternating bands of higher and lower scattering representing organization of muscle bundles.	R0



Poster #124 #1818896

ANTIBIOTIC PROPHYLAXIS IN MEGAPROSTHETIC RECONSTRUCTIONS: IS CEFAZOLIN THE CERTAIN CHOICE?

 Isabelle S. Byers, BA¹; Daniel Evans, BS, MSc¹; Nicole Levine, MD²; Alexander L. Lazarides, MD²; Julia D. Visgauss, MD³; Brian E. Brigman, MD, PhD³; Nicholas Turner, MD, MHSc⁴; William C. Eward, MD³
¹Duke University School of Medicine, Durham, North Carolina, UNITED STATES, ²Duke University Hospital, Department of Orthopedic Surgery, Durham, North Carolina, UNITED STATES, ³Duke University Hospital, Department of Orthopaedic Surgery, Durham, North Carolina, UNITED STATES, ⁴Duke University Hospital, Department of Infectious Disease, Durham, North Carolina, UNITED STATES

Objective: For patients with malignant bone tumors, limb salvage surgery is standard of care and often involves reconstruction with a modular oncological endoprosthesis (megaprosthesis). However, these large segmental implants are at high risk for post-operative infection, with a reported range between 3-31%. Infection remains the leading cause of implant failure, often leading to amputation and major morbidity. In comparison, infection rate after a routine total joint replacement is reported to be 1-2%. Despite major differences in these patient populations, guidelines for antibiotic prophylaxis in megaprosthesis reconstructions are based on those for standard arthroplasty. Our primary objective is to assess what components of current perioperative antibiotic prophylaxis regimens are associated with risk of post-operative megaprosthesis infection. In this study, we evaluated the following: 1) Do extended post-operative antibiotics reduce the risk of infection when compared to 24-hour post-operative prophylaxis alone? 2) Is antibiotic concentration in cortical bone or adjacent soft tissue predictive of infection? 3) Do pre- and intra-operative antibiotic practices influence antibiotic penetration into cortical bone and soft tissue?

Methods: We conducted a retrospective review of all patients undergoing megaprosthesis reconstruction at Duke University from 2001-2021. This included primary and revision proximal femur replacements, distal femur replacements, total femur replacements, and proximal tibia replacements. Simple arthroplasties, cases with a wound class of "dirty" (e.g. suspected infection at the time of surgery), individuals on chronic suppressive antibiotics, and individuals who received antibiotics post-operatively for reasons other than prophylaxis were excluded. Patient, disease, procedure, and antibiotic-related risk factors were assessed for each encounter (Table 1). Infection was defined using 2018 Musculoskeletal Infection Society (MSIS) Criteria for prosthetic joint infection. For aim 1, we constructed a multivariate logistic regression model to assess whether extended post-operative antibiotics were associated with infection risk while adjusting for potential confounders. For aims 2 and 3, we conducted a pharmacokinetic subgroup analysis using tissue samples obtained from the Duke BioRepository and Precision Pathology Center (BRPC). Punch biopsies of cortical bone and adjacent muscle were collected for ten patients. Tissue samples were analyzed with liquid chromatography/mass spectrometry to quantify antibiotic concentration. Wilcoxon rank-sum tests were used to compare differences in tissue concentrations for individuals with and without post-operative infection.

Results: 185 patients (101 male, 84 female) undergoing megaprosthesis reconstruction between 2001-2021 at Duke University were included. 147 patients (79%) received recommended pre-operative antibiotics. 46 patients (25%) received vancomycin powder intra-operatively. 83 patients (82%) were appropriately re-dosed intra-operatively if procedure time exceeded four hours. 80 patients (45%) received extended post-operative antibiotics, with a mean duration of 4 days (Table 1). A total of 26 patients (14.05%) contracted megaprosthesis infection following reconstruction. On logistic regression, receipt of extended antibiotics had no significant effect on risk of post-operative infection (odds ratio [OR]: 1.61; 95% CI: 0.66 to 3.89; $p = 0.30$) after adjustment for potential confounders. Within the pharmacokinetic subgroup analysis, median cefazolin concentration in cortical bone was 0.19 ng/mL (range = 0.003 - 0.625 ng/mL) while median cefazolin concentration in adjacent muscle was 0.78 ng/mL (range = 0.108 - 15.843 ng/mL). Median bone concentration of cefazolin was significantly lower in patients with post-operative infection (0.065 ng/mL) compared to those without infection (0.42 ng/mL, $p < 0.01$). Median muscle concentration of cefazolin was also significantly lower in patients with post-operative infection (0.2 ng/mL) compared to those without infection (1.95 ng/mL, $p = 0.03$) (Table 2).

Conclusion: This study is the first to assess aspects of perioperative prophylaxis for megaprosthesis reconstructions in detail, including a pharmacokinetic analysis of antibiotic penetration into bone and adjacent soft tissue. Extended post-operative antibiotics did not reduce the risk of post-operative infection. Within the pharmacokinetic subgroup, bone concentrations of cefazolin were lower than that in muscle, while both bone and muscle concentrations were predictive of later infection. Our

results suggest that traditional or even extended antibiotics may not be effective for preventing infection in megaprosthesis reconstructions. Instead, given the strong association between antibiotic tissue concentration and infection risk, optimizing cortical bone and adjacent soft tissue concentrations at the time of surgery may be a key consideration in designing improved perioperative prophylaxis regimens.

Table 1 Characteristics of Patient Encounters (N = 185)

Patient	Median age	49.5	Procedure	Mean ASA	2.59
	Male gender (%)	101 (54%)		Procedure category (%)	
	Race (%)			PFR	50 (27%)
	White	130 (70%)		DFR	91 (49%)
	Black	38 (20.5%)		TF	9 (5%)
	Other	12 (6.5%)		PTR	25 (13.5%)
	Median BMI	26		Revision (%)	45 (24%)
	Median Charlson Comorbidity Score	2		Mean procedure duration (mins)	264
Disease	Tumor Diagnosis (%)		Mean estimated blood loss (mL)	499	
	Osteosarcoma	68 (37%)	Mean surface area of prosthesis (cm ²)	3924	
	Chondrosarcoma	27 (15%)	Mean length of stay (days)	6	
	Ewing Sarcoma	8 (4%)	Mean POD drain removal	4.9	
	Non-primary	46 (25%)	Mean POD suture removal	16.5	
	Other	35 (19%)	Antibiotic	Pre-operative antibiotics (%)	
	Metastatic (%)	68 (37%)		Ancef 1g	47 (25%)
	Pre-op chemotherapy (%)	64 (35%)		Ancef 2g	120 (65%)
	Pre-op radiation therapy (%)	34 (18%)		Ancef 3g	6 (3%)
	Post-op chemotherapy (%)	74 (40%)		Other	11 (7%)
	Post-op radiation therapy (%)	15 (8%)		Re-dosed if proc. > 4h (%)	83 (82%)
	Mean pre-op WBC	5.9		Vancomycin powder (%)	46 (25%)
Mean pre-op Hemoglobin	10.4	Extended post-op antibiotics (%)		79 (43%)	
		Ancef		46 (58%)	
		Keflex		30 (38%)	

Table 2 Pharmacokinetic Sub-Group Results: Antibiotic Tissue Penetration

	Procedure	Pre-operative antibiotics	Intra-operative antibiotic re-dose	Sample weight (mg) <i>BONE</i>	Cefazolin conc. (ng/mL) <i>BONE</i>	Sample weight (mg) <i>MUSCLE</i>	Cefazolin conc. (ng/mL) <i>MUSCLE</i>
Patient 1	DFR primary	Cefazolin 2g	Cefazolin 2g	22	0.036	23.4	0.108
Patient 2	DFR primary	Cefazolin 2g	Cefazolin 2g	30	0.097	27	0.464
Patient 3	PFR primary	Cefazolin 2g	Cefazolin 2g	29.3	0.083	12.2	0.195
Patient 4	TF revision	Cefazolin 2g	Cefazolin 3g	21	0.003	24	0.244
Patient 5	PFR primary	Cefazolin 2g	Cefazolin 2g	38	0.065	15	1.463
Patient 6	DFR primary	Cefazolin 2g	Cefazolin 2g	20.6	0.422	44.5	15.843
Patient 7	DFR primary	Cefazolin 2g	Cefazolin 2g	30.8	0.286	29	1.948
Patient 8	PFR primary	Cefazolin 2g	N/A	40	0.448	36.5	0.507
Patient 9	TF revision	Cefazolin 2g	Cefazolin 2g	40	0.536	45.5	11.429
Patient 10	PFR primary	Cefazolin 2g	N/A	35.1	0.625	44.2	1.043

Patients 1-5: development of post-operative infection

Patients 6-10: no development of post-operative infection



Poster #125 #1818915

MULTI-OMIC PREDICTORS OF CLINICAL OUTCOMES FOLLOWING CURATIVE INTENT SURGICAL RESECTION IN SOFT-TISSUE SARCOMAS

Nathan D. Seligson, PharmD¹; Yan W. Asmann, PhD²; Tariq Almerey, MD²; Steven Attia, DO²; Sanjay Bagaria, MD²

¹University of Florida, Jacksonville, Florida, UNITED STATES, ²The Mayo Clinic, Jacksonville, Florida, UNITED STATES

Objective: Surgical resection of early stage soft-tissue sarcomas (STS) provides the potential of curative treatment to patients with these rare malignancies. Even with significant improvements in surgical care, a large proportion of STS tumors resected will recur. Clinical studies have identified phenotypic markers of recurrence risk including tumor size, grade, and vascularity. Despite these findings, predicting recurrence and survival outcomes for patients with early stage STS remains a challenge. In this study, we retrospectively analyze clinical and multi-omic data for a large set of STS to identify novel prognostic biomarkers.

Methods: Primary tumor samples from 100 subjects with soft-tissue sarcomas were collected from the Mayo Clinic Sarcoma Biobank. Samples were sequenced using the Tempus xT targeted DNA and whole transcriptome next-generation sequencing platform. After quality control, 93 and 69 samples with DNA and RNA level data respectively were returned. Clinical data was collected by retrospective chart review. Overall survival (OS) was defined as time from first resection to death or last follow-up. Descriptive statistics, principle component analysis (PCA), differential expression, and pathway analysis were used as appropriate.

Results: Of the 93 samples included in this study, the most common histologies represented included liposarcomas (n=27, LPS), gastrointestinal stromal tumors (n=21, GIST), and leiomyosarcomas (n=15, LMS). Tumor grade and histology were correlated with clinical outcomes following curative intent surgical resection. High-grade tumors were associated with a decreased OS (p=0.01) but no difference was found for local recurrence (p=0.07) risk. Angiosarcoma was associated with the worst OS (p < 0.001) and local recurrence outcomes (p=0.01) while LPS were associated with mixed response (p < 0.001). Genomic variants identified were indicative of the known genomic variants in advanced STS. In GIST, pathogenic variants in KIT (71%) and PDGFRA (19%) were most common. In LMS, pathogenic variants in TP53 (80%), ATRX (33%), and RB1 (27%) were most common. In LPS, pathogenic variants in MDM2 (81%), YEATS4 (78%), FRS2 (78%), and CDK4 (74%) were most common. RNA expression signatures were calculated for each tumor using gene set variant analysis on hallmark gene sets. PCA on these signatures were driven by inflammatory and proliferation signatures (Dimension 1: TNFA Signaling, Inflammatory Response, Interferon Gamma Response; Dimension 2: E2F Targets, Oxidative Phosphorylation, MYC Targets). In LPS, oxidative phosphorylation signaling demonstrated a bimodal distribution (p=0.03). Elevated oxidative phosphorylation signaling correlated with increased risk of recurrence following resection (HR 11.1, 95%CI 1.2-107.9, p=0.03), but was not correlated with OS (HR 2.2, 95%CI 0.4-13.4, p=0.38).

Conclusion: Prognosis for the treatment of early stage STS remains difficult. Genomic alterations in this set of tumors was similar to previous reports of the genomic landscape in advanced STS. Transcriptomic analysis suggests that expression biomarkers may be useful in predicting recurrence following surgical resection of STS. Further analysis is underway.



Poster #126 #1818931

EXTRA-PLEURAL PNEUMONECTOMY (EPP) IN CHILDREN AND ADULTS WITH ADVANCED SARCOMA

Abha A. Gupta, MD, MSc, FRCPC¹; Hagit Peretz Soroka, PhD²; Agostino Pierro, MD³; Tom Waddell, MD⁴; Reto Baertschiger, MD³; Marcelo Cypel, MD⁴; Marc de Perrot, MD⁴; Caroline Rodrigues, Undergraduate Student²
¹Division of Medical Oncology, Princess Margaret Cancer Centre, University Health Network, University of Toronto, The Hospital for Sick Children, Canadian Sarcoma Research and Clinical Collaboration (CanSaRCC), Toronto, Ontario, CANADA, ²Princess Margaret Cancer Center, Canadian Sarcoma Research and Clinical Collaboration (CanSaRCC), Toronto, Ontario, CANADA, ³The Hospital for Sick Children, Toronto, Ontario, CANADA, ⁴University Health Network, Toronto, Ontario, CANADA

Objective: Sarcoma can present as locally advanced disease involving the pleura for which extra-pulmonary pneumonectomy (EPP) is often the only surgical option to ensure adequate local control. EPP involves removal of the parietal and visceral pleura, ipsilateral lung, pericardium, and hemi-diaphragm. Given the lack of literature on the role of EPP for local control in adults and children with sarcoma, we performed a retrospective analysis of our experience in Toronto to describe the treatment and outcome of patients who underwent an EPP for locally advanced sarcoma.

Methods: Data was collected on sequential patients who underwent EPP between January 1st, 2000 and August 1st, 2020 at Princess Margaret Hospital and SickKids Hospital in Toronto. Patient demographics, treatment (including multi-modality therapy), and outcome details were extracted from the CanSaRCC Database (Canadian Sarcoma Research and Clinical Collaboration). Surgical details and complications were also reviewed.

Results: Seven sarcoma patients diagnosed with locally advanced disease involving the pleura between the ages of 4 and 59 years (median 18 years) were identified to have undergone EPP. Four patients required EPP for primary disease and three patients underwent EPP for metastatic disease (Table 1). None of the patients had evidence of disease outside the ipsilateral chest at time of EPP. There were no significant surgical complications noted for all patients. Five patients and two patients had negative (R0) and positive margins, respectively (Table 1). All patients received pre-operative chemotherapy and had partial response (Table 2). All patients received radiation therapy, four within 2 weeks of EPP (details, Table 2). The median time to last FU from EPP was 23.2 months (range 8.2 to 78 months). At last FU, two patients had local recurrence in their pleura 4.3 and 5.8 months from EPP and both died from progressive disease 13.1 and 8.2 months from EPP, respectively. Five patients did not have a local recurrence at last FU - three were alive without disease, one died from brain metastasis (17 months from EPP), and one died from radiation associated osteosarcoma (5.5 years from EPP) (Table 1).

Conclusion: EPP offers a safe and effective surgical consideration for patients with locally advanced sarcoma involving the pleura in combination with chemotherapy and radiation and can contribute to prolongation of life. Consequently, EPP should be considered during multi-disciplinary tumour board discussions at high volume centers for patients with locally advanced disease.

Table 1: Diagnosis and Status at last FU of Patients who Underwent EPP

Patient	Age at Diagnosis of Pleural Disease	Diagnosis	Type of Disease	Time from EPP to Last FU (months)	Resection Margins	Status at Last FU
1	22	RMS	Primary	17.0	Positive: Multiple + margins (diaphragm, pericardium)	Deceased from brain met
2	59	Undifferentiated Pleomorphic Sarcoma	Recurrent distant disease (DFI = 27.7 months)	13.1	Negative	Deceased from recurrent pleural disease
3	18	Adenosarcoma	Recurrent distant disease (DFI = 40.6 months)	78.0	Negative	ANED
4	19	Synovial Sarcoma	Primary	8.2	Positive: Focal + margin at pericardium	Deceased from recurrent pleural disease
5	13	Ewing Sarcoma	Primary	66.0	Negative	Deceased from radiation associated sarcoma
6	4	RMS	Recurrent distant disease (DFI = 40.3 months)	23.2	Negative	ANED
7	4	Pleuro-pulmonary Blastoma	Primary	26.7	Negative	ANED

RMS = Rhabdomyosarcoma; DFI = Disease Free Interval; ANED = Alive, no evidence of disease

Table 2: Treatment and Outcomes of Patients who Underwent EPP

Patient	Pre-Op Chemotherapy	Response to Chemotherapy	Radiation [Dose (Gy), Fraction]	Time from Diagnosis of Pleural Disease to EPP (months)	Time between RT to EPP (months)
1	VDC/IE	PR	Post Op [60, 25]	5.5	2.3
2	Dox/Ifos	PR	Pre-Op [39, 3]	8.8	0.4
3	Dox/Ifos	PR	Pre-Op [30, 5]	6.9	0.3
4	Dox/Ifos	PR	Pre-Op [30, 5]	9.7	0.3
5	VDC/IE	PR	Post Op [50.4, UN]	4.7	0.4
6	VIDE	PR	Pre Op [45, UN]	5.0	1.0
7	IVAD x4, IVA x2	PR	Post Op (x2) [19.8, 11], [25.2, 14]	7.0	1.5, 2.1

PR = Partial Response; UN = Unknown Fractions; RT = Radiation Therapy



Poster #127 #1819015

CANDIDATE BIOMARKERS FOR SPECIFIC INTRAOPERATIVE IMAGING OF SOFT TISSUE SARCOMAS

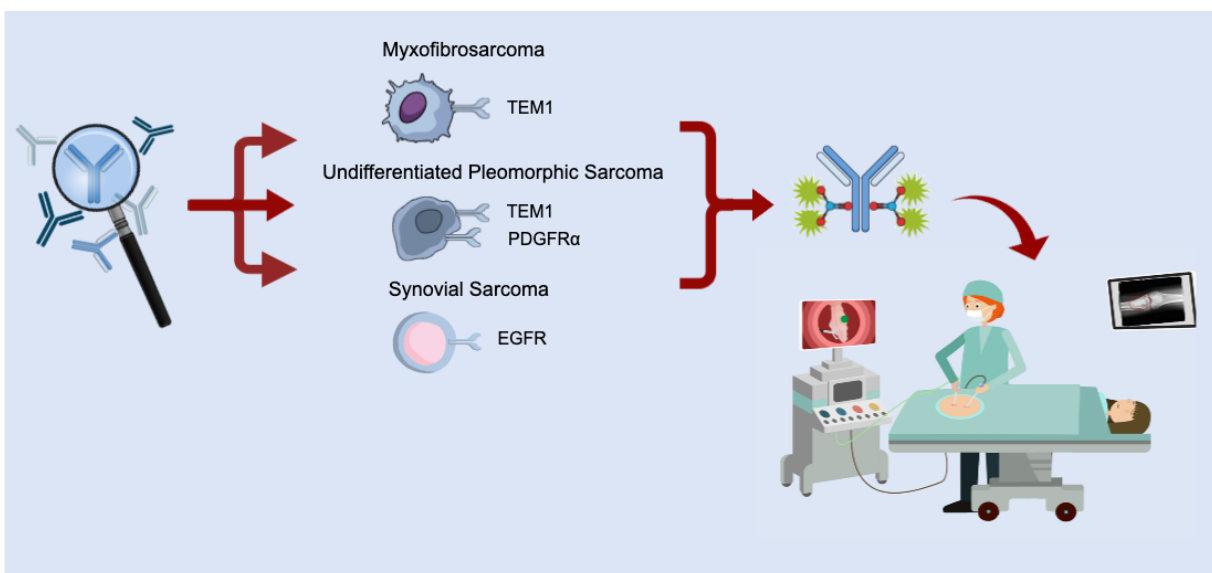
Zeger Rijs, MD¹; Naweed Shifai, BSc²; Peter Kuppen, PhD²; Alexander L. Vahrmeijer, MD PhD¹; Judith V.M.G. Bovée, MD PhD¹; Cornelis Sier, PhD²; Michiel van de Sande, MD PhD¹; Pieter van Driel, MD PhD³
¹Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ²LUMC, Leiden, Zuid-Holland, NETHERLANDS, ³Isala hospital, Zwolle, Overijssel, NETHERLANDS

Objective: Surgery is the mainstay of treatment for localized soft tissue sarcomas (STS). Curative treatment highly depends on complete tumor resection, as positive margins are associated with local recurrence and prognosis. However, determining the tumor margin during surgery is challenging. Near-infrared fluorescence (NIRF) imaging can facilitate complete resections by visualizing tumor tissue during surgery. This technique is based on fluorescent tracers binding to tumor biomarkers on malignant cells. Unfortunately, STS specific tracers are presently not clinically available. Our aim was to evaluate STS-associated cell surface-expressed biomarkers, which are currently already clinically targeted with monoclonal antibodies for therapeutic purposes, for their use in NIRF imaging of STS.

Methods: Clinically targeted biomarkers in STS were extracted from the clinical trial databases (EU Clinical Trials Register and clinicaltrials.gov) and a PubMed search was performed. Data on biomarker characteristics, sample size, percentage of biomarker-positive STS samples, pattern of biomarker expression, biomarker internalization features and previous applications of the biomarker in imaging were extracted. Biomarkers were ranked and selected utilizing a target selection scoring system. Selected targets are evaluated with immunohistochemistry in 20 myxofibrosarcomas and 20 undifferentiated soft tissue sarcomas.

Results: A total of 97 articles were included. Eleven cell surface-expressed biomarkers were identified from which 7 were selected as potential biomarkers for NIRF imaging: TEM1, VEGFR-1, EGFR, VEGFR-2, IGF-1R, PDGFR β and CD40. Promising biomarkers in common and aggressive STS subtypes are TEM1 for myxofibrosarcoma, TEM1 and PDGFR β for undifferentiated soft tissue sarcoma and EGFR for synovial sarcoma. Preliminary results from immunohistochemical evaluation identify TEM1 as the most promising biomarker for fluorescence guided imaging.

Conclusion: NIRF imaging can facilitate complete resections by visualizing tumor tissue during surgery. TEM1 is the most promising biomarker for NIRF imaging in myxofibrosarcoma and undifferentiated soft tissue sarcoma.





Poster #128 #1819011

FREE FLAP RECONSTRUCTION AFTER RADICAL RESECTION OF LIMB AND TRUNCAL SARCOMAS

Sergio Quildrian, MD¹; Gabriela vega, MD²; Walter Nardi, MD³; Jorge Chapela, MD⁴; Anabella Daffinoti, MD⁵

¹Buenos Aires British Hospital; Angel Roffo Institute of Oncology, University of Buenos Aires, Buenos Aires, Buenos Aires, ARGENTINA, ²Angel H Roffo Institute of Oncology, Tucuman, Tucuman, ARGENTINA, ³Buenos Aires British Hospital, Buenos Aires, Ciudad Autonoma de Buenos Aires, ARGENTINA, ⁴Angel H Roffo Institute of Oncology, Buenos Aires, Buenos Aires, ARGENTINA, ⁵Angel H Roffo Institute of Oncology, Buenos Aires, Ciudad Autonoma de Buenos Aires, ARGENTINA

Objective: To evaluate the surgical and oncologic results of free flap reconstruction after radical resection of truncal and limbs sarcomas.

Methods: We performed 765 sarcoma surgeries between 2008 and 2021 in two referral centers. Patients requiring free flap reconstruction after complete surgical resection were retrospectively evaluated. Demographic and tumor characteristics, primary site and type of flap used were evaluated. Tumor recurrence, morbidity and mortality of the surgical procedure were also evaluated.

Results: We used 26 free flaps in 25 patients for reconstruction after surgical resection. Eighteen (69%) patients were male; the median age was 49 years (IQR, 42-56). Eighteen (72%) patients had limb sarcomas (12 located on inferior limbs, 6 located on superior limbs) and 7 truncal sarcomas. Histology: 22(84.6%) were soft tissue sarcomas, 2 osteosarcomas and 2 chondrosarcomas. Fourteen (56%) patients had recurrent sarcomas. Median operative time was 7hs (IQR, 6-8hs). The free flaps used were anterolateral thigh flap (15), latissimus dorsi flap (4), fillet flap (3), gracilis flap (2), radial forearm flap¹ and lateral arm flap (1). With a median follow-up of 29 months, local recurrence was observed in 5(20%) patients: four patients had limb sarcomas and one patient a truncal one. Median time to disease relapse (local, regional and systemic) was 16(IQR, 4-30) months. Postoperative complication was observed in 3(11.5%) cases: 2 flap loss and 1 haematoma. The rate of free flap survival was 92.6%. There were no postoperative deaths.

Conclusion: In our series, sarcomas located on the limbs were the most common site requiring free flap reconstruction. The flap survival after sarcoma resection was >92%. Six different flaps were necessary for reconstruction and the anterolateral thigh flap was the most used (nearly 58%). The rate of local recurrence was similar to that reported for standard sarcoma surgery. Multidisciplinary management is essential in soft tissue sarcoma treatment and a multidisciplinary surgical team is also needed.



Poster #129 #1819039

PRELIMINARY RESULTS OF THE USE OF A BONE TRANSPORT NAIL AFTER TUMOR RESECTION

Lee M. Zuckerman, MD

City of Hope National Medical Center, Duarte, California, UNITED STATES

Objective: Reconstruction of large bony defects after tumor resection is challenging. The use of distraction osteogenesis and bone transport immediately after tumor resection allows for intercalary reconstruction utilizing the patient's own bone. All internal transport utilizing a bone transport nail is a newer technique for bone reconstruction. The purpose of this study was to evaluate the initial results of using a bone transport nail after tumor resection.

Methods: A retrospective review of all patients with sarcoma who had a bone transport nail placed after tumor resection was performed. Length and location of transport, complications and formation of regenerate were evaluated. Four cases of all internal distraction osteogenesis and bone transport utilizing a magnetic intramedullary bone transport nail were reviewed. Two patients were treated for conventional high-grade osteosarcoma, one for Ewing's sarcoma and one for metastatic synovial cell sarcoma. Adjuvant chemotherapy was given during transport in three cases and included cisplatin, doxorubicin, and methotrexate in two patients, and doxorubicin and cisplatin in one patient. Bone transport was started 1-2 weeks after tumor resection and chemotherapy was not delayed. The femurs started transport at 0.33 mm TID and the tibia was started at 0.25 mm TID. One case had bone grafting of the defect at the initial surgery.

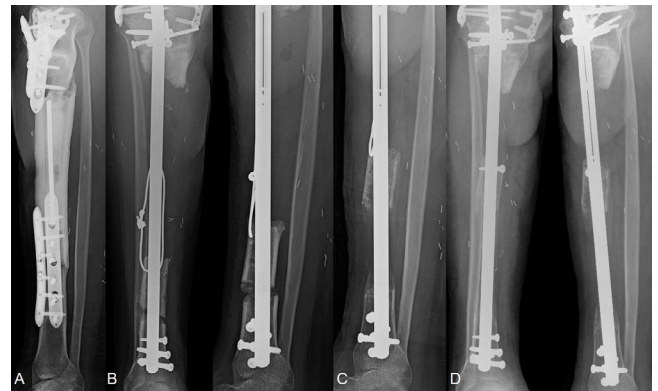


Figure 1: A) The patient sustained a fracture through his prior intercalary allograft after resection and reconstruction for Ewing's sarcoma. B) After resection of the allograft and placement of the bone transport nail, the patient underwent a cable-assisted transport. C) After completion of the initial transport of 7 cm, the cable was exchanged and continued transport was performed. D) After the second cable transport was completed, a screw was able to be placed for continued transport.

Results: A joint-preserving intercalary resection with negative margins was performed in all cases. The average age of the patient was 25 (range 13-54) and average follow-up was 14 months (range 9-25). Three femurs were treated and one tibia. The average length of transport was 11 cm (range 3.6 to 18). Three patients underwent primary tumor resection while one patient was treated for a failed intercalary allograft. No patients had radiation to the operative site. Two patients utilized all internal cable assisted transport (Figure 1). Three patients have completed transport while one patient is still completing transport. Two patients had a backing out of their distal interlocking screws and one required revision (Figure 2). Three patients required a screw exchange and/or recharge to complete transport. One patient required screw placement through the regenerate to complete transport. Regenerate was abundant in one patient who had their rate increased and was delayed in two patients, including one patient who was undergoing tibial transport and was not on chemotherapy and one patient undergoing femoral transport on cytotoxic chemotherapy (Figure 3). Otherwise, no evidence of local recurrence of tumor, infection or other complications were identified.

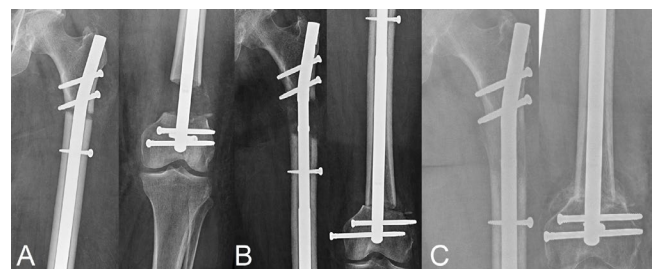


Figure 2: A) Status-post metastatic synovial cell sarcoma resection requiring vascular reconstruction after placement of a bone transport nail. B) During transport, adequate regenerate is noted in addition to backing out of the distal locking screw. C) After completion of transport and a docking procedure, the screw was advanced. Good regenerate is noted with early remodeling of the docking site.

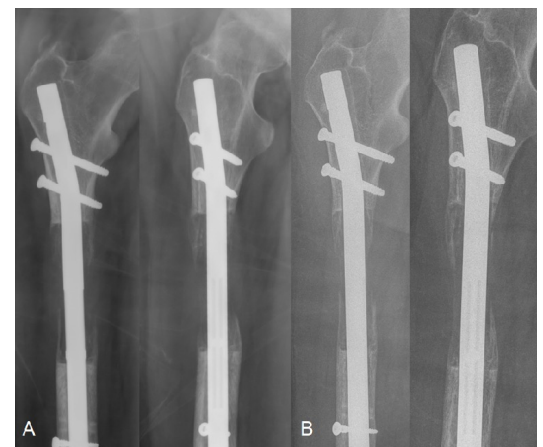


Figure 3: A) After completion of transport, the regenerate is poor while on cytotoxic chemotherapy. B) Six weeks after chemotherapy was completed, the regenerate has improved.

Conclusion: Regenerate formed in all patients, although the rate at which it formed was variable. Hardware complications were minor. There were no issues with transport, but the optimal latency and transport rate is unclear due to the variability of regenerate formation. The initial experience with this technique is promising for providing a viable method for reconstructing intercalary defects.



Poster #130 #1818846

TO WHAT EXTENT DOES PLASTIC AND RECONSTRUCTIVE SURGICAL ASSISTANCE WITH COMPLEX CLOSURE HELP AVOID AMPUTATION FOLLOWING RESECTION OF DISTAL LOWER EXTREMITY SOFT TISSUE SARCOMAS?

Charles A. Gusho, BS¹; Johnathon R. McCormick, MD²; Linus Lee, BE²; Gordan Derman, MD²; Deana Shenaq, MD²; Amir Dorafshar, MD²; Georgios Kokosis, MD²; Matthew W. Colman, MD²; Steven Gitelis, MD²; Alan T. Blank, MD, MS²
¹Rush University Medical Center, Milwaukee, Wisconsin, UNITED STATES, ²Rush University Medical Center, Chicago, Illinois, UNITED STATES

Objective: Soft tissue reconstruction following resection of distal lower extremity soft tissue sarcoma (STS) is challenging. Oftentimes, the remaining defect is a potential indication for amputation. Assistance from plastic and reconstructive surgery (PRS) may help avoid amputation and permit limb salvage with acceptable wound complication rates. However, the outcomes after PRS-assisted closure are yet to be established in this anatomical location.

Methods: This was a review of 52 patients who underwent resection of distal lower extremity STS between 2010 and 2020. PRS soft tissue management was utilized in 40.4% (n = 21) of cases, in patients who would have otherwise been considered candidates for amputation.

Results: The wound complication rate was 14.3% with PRS-assisted closure compared to 22.6% in soft tissue defects closed without PRS co-management (p = 0.46). There were zero instances of total wound or flap loss in PRS-assisted closures. When comparing patients with wound complications to those without, there was no difference in age (59.5±21 vs. 51±18 years, p = 0.42), body mass index (31.1±4.8 vs. 26.1±7.1 kg/m², p = 0.19), or tumor size (6.8±5.0 vs. 6.4±4.7 cm, p = 0.82). At final follow-up, 67% (n = 35) of patients were alive and disease-free.

Conclusion: Wound complications are not uncommon after resection of distal lower extremity STS. Without PRS-assisted soft tissue management, a large number of patients are unfortunately candidates for amputation. Involving PRS in these potential amputation cases permits successful limb salvage, while maintaining complication rates to an acceptable level.

Table 1. Cohort characteristics.

Variable	n (%)
Age (years) †	52.5 (18-88)
Body mass index (kg/m ²) ‡	29.8 (6.8)
Female	28 (53.8)
Male	24 (46.2)
Foot & ankle	19 (36.5)
Stage ^a	
I	6 (11.5)
II	16 (30.8)
III	24 (46.2)
Unknown (re-excision)	6 (11.5)
Comorbidities	
Diabetes	10 (19.2)
Smoking use at time of surgery	21 (40.4)
Histology	
Undifferentiated	16 (30.8)
Liposarcoma/leiomyosarcoma	7 (13.5)
Myxofibrosarcoma	10 (19.2)
Synovial	8 (15.4)
Other	11 (21.1)
Fungation at presentation	8 (15.4)
Greatest resected dimension (cm) ‡	6.4 (4.7)
Greatest defect dimension (cm) ‡	16.5 (10.0)
Radiation	39 (75.0)
Chemotherapy	24 (46.2)
Follow-up (months) †	36.5 (<1-127)

† median (range). ‡ mean (standard deviation).

^aAmerican Joint Committee on Cancer 7th or 8th edition.

Table 2. Wound complications.

Variable	Yes (n = 10) n (%)	No (n = 42) n (%)	P - value
Median (years) †	59.5 (18-88)	51.0 (21-83)	0.42
Body mass index (kg/m ²) ‡	32.4 (4.8)	29.2 (7.1)	0.19
Smoking	2 (20.0)	19 (45.2)	0.14
Diabetes	1 (10.0)	9 (21.4)	0.41
Tumor bed re-excision	4 (40.0)	14 (33.3)	0.69
Location (deep tumors)	7 (70.0)	29 (69.0)	0.75
Fungation	2 (20.0)	6 (14.3)	0.65
Foot and ankle soft tissue sarcoma	5 (50.0)	14 (33.3)	0.33
Tumor size (cm)	6.8 (5.0)	6.4 (4.7)	0.82
Defect size (cm)	17.9 (9.4)	16.1 (10.2)	0.63
Flap reconstruction	3 (30.0)	18 (42.9)	0.46
Vacuum assisted closure	2 (20.0)	9 (21.4)	0.96
Neoadjuvant radiation	2 (20.0)	22 (52.4)	0.065

† median (range). ‡ mean (standard deviation).



Poster #131 #1818842

A MODIFIED HARRINGTON TECHNIQUE FOR PERIACETABULAR RECONSTRUCTION IN ADVANCED METASTATIC BONE DISEASE AND A DISCUSSION OF ALTERNATIVE TREATMENT OPTIONS

Charles A. Gusho, BS¹; Linus Lee, BE²; Reagan Chapman, MS²; Alan T. Blank, MD, MS²

¹Rush University Medical Center, Milwaukee, Wisconsin, UNITED STATES, ²Rush University Medical Center, Chicago, Illinois, UNITED STATES

Objective: Management of periacetabular metastatic lesions involves complex clinical decision making. These malignancies can be extremely painful and limit function. The modified Harrington procedure with total hip arthroplasty can recreate pelvic stability with a cement rebar construct as well as a functional hip. This study analyzes a single institutional experience with the modified Harrington procedure to assess construct longevity and patient outcomes.

Methods: We queried a prospectively maintained surgical database to identify all patients at a large academic medical center from 2017 to 2019 with periacetabular metastatic disease treated with a modified Harrington. Medical records were reviewed and complications, patient outcomes, Musculoskeletal Society Tumor (MSTS) scores, and implant survival were recorded.

Results: A total of 9 consecutive patients were treated with the modified Harrington between 2017 and 2019. At maximum follow-up there were 0 revisions or long-term complications. The mean preoperative MSTS score was 2.2 (range, 0-18), compared to the mean postoperative MSTS score of 17.7 (9-25) recorded at a mean 4 (1-30) months following surgery ($p < 0.001$).

Conclusion: The modified Harrington technique total hip technique for reconstruction in periacetabular metastatic bone disease is a safe procedure with effective relief of symptoms, improvement in physical function, and excellent implant survivorship.



Poster #132 #1818908

FROZEN SECTION MARGIN ASSESSMENT IN ONCOLOGY ORTHOPEDICS

Ana C. Belzarena, MD¹; Pablo Stoppiello, MD²; Leticia Gaiero, MD²; Gottardo Bianchi, MD²; Nicolas Casales, MD²; Claudio Silveri, MD²

¹Miami Cancer Institute, Miami, Florida, UNITED STATES, ²Unidad de Patología Oncológica Musculo Esquelética, Instituto Nacional de Ortopedia y Traumatología, Montevideo, Montevideo, URUGUAY

Objective: Background The treatment cornerstone for soft tissue sarcomas is a wide margin resection. The same principle applies for some aggressive tumors as well. The surgeon performing the resection carries the burden and responsibility of surgical planning and intraoperatively decision making to achieve negative margins. Currently, resources to evaluate margins intraoperatively are limited to frozen margin section assessment. The purpose of this study is to assess the accuracy of frozen section margins in oncology orthopedic cases. Additionally, to assess if frozen result discrepancies ultimately affect patient care and final treatment.

Methods: A retrospective chart review was conducted on patients who underwent a soft tissue or bone tumor resection at our institution between July/2017 and June/2021. Demographic information along with tumor characteristics, frozen section margin result and final pathology report were recorded. Frozen sections were sent for analysis at the surgeon's discretion during the procedure. Frozen sections were then submitted for final pathology assessment. The percentage of diagnostic discrepancy was recorded and assessed for accuracy of the technique.

Results: Fifty-four patients with soft tissue or bone tumors who underwent resection at our institution were included in the study. The mean age for the sample was 44 years of age (range 28-72, SD 13). The majority of the patients had a soft tissue tumor (70.4%) localized in the lower extremity (57.4%). Most patients had a diagnosis of soft tissue sarcoma (59.3%) and the most common subtype was myxofibrosarcoma. The percentage error for the sample was of 40.7%; in all those cases there was a discrepancy in the frozen section margin result when comparing the result given intraoperatively and the final pathology report. No margin changed from benign to malignant. Twenty-six percent of margins read as malignant or suspicious for malignancy intraoperatively, were benign in the final report. Fourteen percent of margins read as inconclusive during surgery were finally read as benign. In none of the patients the difference implied a change in the patient overall treatment. No patient needed a reoperation or the addition of radiotherapy due to a modification of the frozen margin results.

Conclusion: The success of tumor resections highly depends on the status of the final margins. An extra tool surgeons can resource to, is intraoperative margin assessment by a pathologist. There is still a high rate of discrepancy in the final diagnosis and a low accuracy for this technique. However, in general pathologists seem to err towards a more malignant suspicion which is then assuaged in the final report. Surgeons should remain cognizant of this fact when making intraoperative decisions.



Poster #133 #1819070

MAJOR AMPUTATIONS FOR EXTREMITY SARCOMAS: OLD-FASHIONED SURGERY OR CHANCE OF TREATMENT? A TERTIARY REFERRAL CENTER EXPERIENCE

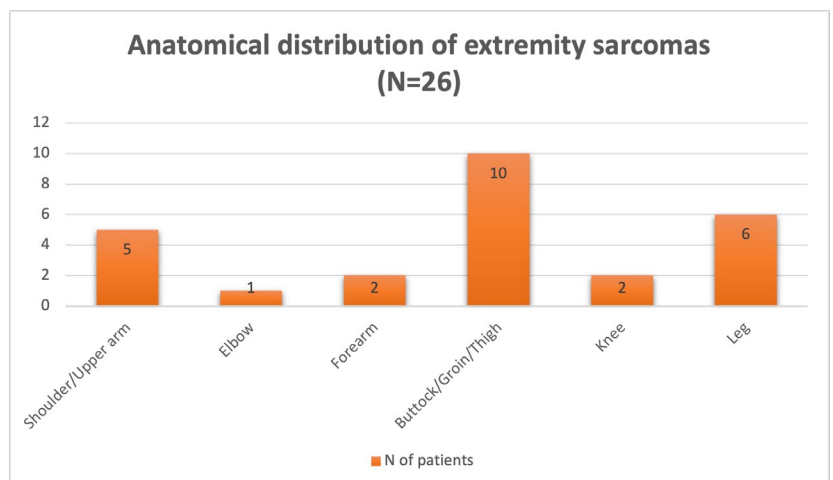
Laura Samà, MD¹; Simone Ricchitelli, MD²; Marta Tassan Mangina, Student³; Manuela Cammelli, Student³; Ilaria Santori, Student³; Laura Ruspi, MD⁴; Federico Sicoli, MD⁵; Ferdinando Cananzi, MD⁶; Vittorio Lorenzo Quagliuolo, MD⁵

¹Humanitas Clinical and Research Hospital/Humanitas University, Milan, Lombardia, ITALY, ²Humanitas Clinical and Research Center/Humanitas University, Milan, Lombardia, ITALY, ³Humanitas University, Milan, Lombardia, ITALY, ⁴Humanitas Clinical and Research Center, Rozzano (MI), Lombardia, ITALY, ⁵Humanitas Clinical and Research Hospital, Milan, Lombardia, ITALY, ⁶Humanitas Clinical and Research Center, Humanitas University, Milan, Lombardia, ITALY

Objective: Historically, amputation was the standard of care for locally advanced upper and lower extremity soft tissue or bone sarcomas. Nowadays, the treatment of choice is limb-sparing surgery combined with chemotherapy and/or radiotherapy in the preoperative or postoperative setting. Nevertheless, in some cases, major amputation is needed. The aim of this study was to recognize the cases in which major amputation remains a chance of treatment.

Methods: In this retrospective study we analyzed all patients treated with major amputation for extremity soft tissue or bone sarcoma in our institute, Humanitas Clinical and Research Center(Milan,Italy), between 2006 and 2020. We included all patients who underwent major amputation for primary or recurrence of sarcoma. We considered major amputations for upper extremities: forequarter amputations, shoulder disarticulations, and above-elbow amputations; for lower extremities: hemipelvectomy (with anterior or posterior flap), hip disarticulations, and above-knee amputations. We excluded patients who underwent minor amputations or who underwent amputations for other malignancies. We considered minor amputations: below-elbow amputations, below-knee amputations, fingers disarticulations. Patients and tumors characteristics, surgical procedures, neoadjuvant/adjuvant treatment, histology, overall survival (OS), local recurrence (LR) free survival and distant metastases (DM) free survival were considered.

Results: Out of 86 patients who underwent amputation at our center in the period of study, 26 were included. Fifteen patients(57.7%) were female. Median age was 69.0 years(IQR 51-74 years). Fifteen patients(57.7%) had a recurrence of sarcoma, of which 9(60%) presented at our center with at least a second recurrence. Only 2 patients(7.7%) had a sarcoma arising from bone. The median size was 20 cm(IQR 12-22 cm). The tumor was located in upper extremities in 8 cases(30.8%), and in lower extremities in 18 patients(69.2%) (Figure). Neoadjuvant treatment was administered in 65.4% of cases (chemotherapy N= 9,34.6%; radiotherapy N=4,15.4%; chemoradiotherapy N=4,15.4%). The type of operation performed was: above-elbow amputation in 3 patients (11.5%), shoulder disarticulation in 5 patients (19.2%), above-knee amputation in 7 patients (26.9%), hip disarticulation in 7 patients (26.9%), and hemipelvectomy in 4 patients (15.5%). Overall, postoperative morbidity rate was 30.7%. Serious postoperative complications (Clavien Dindo Classification >=3) occurred in 11.5% of cases: wound complication in 2 cases (7.7%), bleeding in 1 case (3.8%). Median length of stay was 13 days (IQR 6-30 days). The most frequent histology was undifferentiated pleomorphic sarcoma (N=10, 38.5%), followed by myxofibrosarcoma (N=6, 23.1%). All tumors were high grade sarcomas (G2-3). All patients underwent complete resection (R0). In 17 patients (65.4%), the infiltration of bone (N=13, 50%) or neurovascular bundle (N=10, 38.5%) was confirmed at histological examination. Adjuvant therapy was performed in 30.8%: chemotherapy in 4 patients (15.4%), radiotherapy in 4 patients (15.4%). Median OS was 14 months (IQR 8-8 months). Out of 19 death patients, 5 (26.3%) died of other cause than sarcoma. Median LR free survival was 11.5 months (IQR 7-27 months). Median DM free survival was 6.5 months (IQR 5-27 months). The univariate analysis didn't show



significant predicting factors for OS, LR, and DM.

Conclusion: Surgical and oncological outcomes after major amputations are considerable, but often such procedures are the only possible treatment for patients with extremity sarcomas. The most common causes of amputation were loco-regional extension and bone or neurovascular major bundle invasion. Amputation maintains an important role in extremity sarcomas and achieves durable local control in those unsuitable for limb-conserving surgery. Survival following amputation in the presence of metastatic disease is poor and should be reserved for patients with significant symptoms.



Poster #134 #1818872

CLINICAL RESULTS OF PATIENTS UNDERGOING UNPLANNED EXCISIONS OF SOFT TISSUE SARCOMAS

Sei Morinaga; Norio Yamamoto; Katsuhiko Hayashi; Akihiko Takeuchi, MD, PhD; Shinji Miwa; Kentaro Igarashi; Hirota Yonezawa; Yohei Asano; Shiro Saito; Hiroyuki Tsuchiya
Department of Orthopedic Surgery, Kanazawa University School of Medicine, Kanazawa, Ishikawa, JAPAN

Objective: Soft tissue sarcomas are rare tumors representing <1% of all malignancies. As these tumors are rare, it is not uncommon that soft tissue sarcoma excision is performed without the required preoperative imaging, staging, or wide resection margins for sarcomas. This study investigated the characteristics of unplanned excision and analyzed the recurrence, life expectancy, and proper treatment for unplanned excision. Measures to prevent unplanned excisions were also discussed.

Methods: Patients who underwent unplanned excision at another institution followed by additional wide excision at our hospital from January 2002 to December 2018 were identified. Patients with a follow-up period of less than one year or metastasis at the time of initial visit to our hospital were excluded. Forty-two patients (24 men and 18 women) met our criteria. The relationships between sex, age, tumor depth, histological grade, location, size, surgical margin at additional wide excision, residual tumor, reconstruction, kind of hospital where the primary excision was done (sarcoma or non-sarcoma center), preoperative examination, chemotherapy, radiation therapy, and The relationships between valuables and prognosis were statistically analyzed. Survival curves were generated by using the Kaplan-Meier method and compared by using the log-lank test. The Cox regression analysis was used for multivariable analysis.

Results: The mean age was 57.3 years (15–85 years) and the mean observation period was 72.5 months (14–181 months). Sixty-nine percent (29 in 42) of tumors was in the subcutaneous tissue. There were 38 high-grade tumors and four low-grade tumors. Six tumors were located in the upper extremity, 24 in the lower extremity, and 12 in the trunk. Surgical margin after additional wide excision was positive in 10 cases and negative in 32 cases. Pathological examination of specimen showed 34 of 42 cases (80.9%) had residual tumor after primary tumor excision. Fourteen patients (33.3%) required reconstructions. Of the 42 patients, 10 had undergone preoperative MRI. Among them, only one patient had enhanced MRI. Ten patients had chemotherapy while no patient had radiotherapy over the follow-up period. The mean tumor size was 5.3 cm (0.8–20 cm). The unplanned excisions were performed by orthopaedic surgeons in 18 cases, by general surgeons in eight, by plastic surgeons in seven, by dermatology surgeons in two, by a urology surgeon in one, and by a vascular surgeon in one. Four primary surgeries (9.5%) were performed in a sarcoma center. On univariate analysis, trunk tumors (p=0.02) and positive margin at additional wide excision (p < 0.01) are significantly more likely to cause recurrence. The group that needed reconstruction was significantly more likely to have distant metastasis (p=0.01). Tumor depth, histological grade, size, residual tumor, kind of hospitals where unplanned surgery was performed, preoperative examination, and chemotherapy were not significantly associated with prognosis. On multivariate analysis, positive surgical margin (HR 4.04, 95% CI 1.57-10.4, p<0.01) was significantly associated with lower 5-year recurrence-free survival (Figure 1).

Conclusion: One of the problems of unplanned excision is that there are many cases where MRI or biopsy is not performed before surgery. Hoshi et al reported that only 21% of cases of unplanned excision had MRI done before primary surgery. Our study revealed that MRI before unplanned excision was performed only in

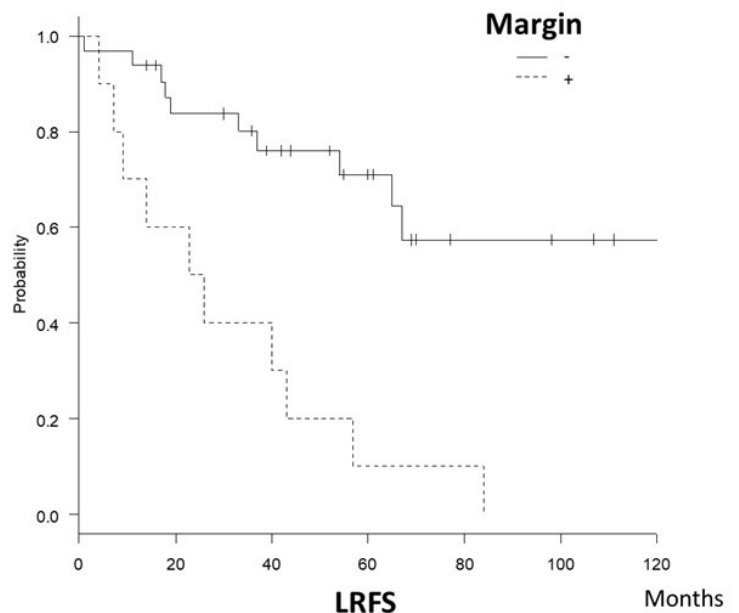


Figure 1. Locoregional recurrence-free survival (LRFS) for margin at additional wide excision

23.8% of the cases. If MRI before primary tumor excision is not done, accurate spread of the tumor cannot be confirmed and proper wide resection cannot be performed. Our data showed that positive surgical margins after additional wide excision was significantly related to high recurrence rates. It is considered that the high recurrence rate with positive margins after additional wide excision might be due to failure to recognize the nature and extent of the tumor without enhanced MRI and biopsy before primary surgery.

Surgeons should be aware that positive margin at additional wide excision is an independent risk factor for local recurrence.

Table 1. Patients characteristics

Characteristic		Number
Age (mean)		57.3
Sex	Male	24
	Female	18
Location	Upper extremity	6
	Lower extremity	24
	Trunk	12
Depth	Superficial	29
	Deep	12
	Unknown	1
Grade	Low	4
	High	38
Histology	UPS/MFH	12
	Liposarcoma	9
	Myxofibrosarcoma	7
	Leiomyosarcoma	3
	Synovial sarcoma	3
	Fibrosarcoma	2
	Others	6
Margin	-	32
	+	10
Residual tumor	-	8
	+	34
Reconstruction	Skin graft	11
	Free flap	5
	Pedicle flap	3
	Others	3
Preoperative examination	-	28
	+	32
Chemotherapy	-	10
	+	32
	-	32
	+	10

UPS; Undifferentiated pleomorphic sarcoma, MFH; Malignant fibrous histiocytoma



Poster #135 #1818984

SPECIFIC DETECTION OF THE SS18-SSX FUSION PROTEIN AND INTERACTING PARTNERS IN SYNOVIAL SARCOMA TISSUES AND MODELS

Ainiah Rushdiana Raquib, B.Sc; Torsten Nielsen, MD, PhD

University of British Columbia, Vancouver, British Columbia, CANADA

Objective: Until recently, antibodies have not existed that are specific for the SS18-SSX oncoprotein that is pathognomonic of synovial sarcoma. SS18 is ubiquitously expressed, whereas SSX (the expression of which is more specific to synovial sarcoma) is intrinsically disordered. A new rabbit monoclonal antibody directed against the SS18-SSX chimeric epitope is now commercially available that detects the protein product of the canonical fusion of SS18 exon 10 to SSX exon 6. The current study aims to validate recent reports characterising the utility of the antibody and to also test additional applications of the antibody to: 1) specifically detect SS18-SSX protein, 2) identify interactors of SS18-SSX and 3) identify regions of the chromatin associated with SS18-SSX dysregulation.

Methods: Relevant synovial sarcoma cell lines, patient tumour samples and tumour tissue from mouse models conditionally expressing human SS18-SSX2 were used to evaluate antibody applications and specificity. Assays to detect endogenous SS18-SSX included: 1) Immunoprecipitation of the bait protein visualised by western blot, 2) immunofluorescence and 3) immunohistochemistry. Interactors of SS18-SSX were detected via 1) co-IP and 2) proximity ligation assay. Identification of regions of the chromatin associated with SS18-SSX was performed using chromatin immunoprecipitation (ChIP)-qPCR.

Results: The antibody detected endogenous SS18-SSX proteins on formalin-fixed paraffin-embedded tissue from human synovial sarcoma tissue in 36 out of 37 samples. The one sample that tested negative was found to use an alternative exon splice in SSX (SSX exon 4), confirming the antibody's specificity to the canonical fusion junction found in over 90% of synovial sarcoma cases. Synovial sarcoma tumors growing in mice showed strong nuclear positivity with zero background, in the same cells that expressed green fluorescent protein (another component of the conditional transgene). By immunofluorescence on cell lines, the antibody visualised dispersed micropunctate nuclear expression of SS18-SSX. To investigate endogenous protein-protein interactions in situ, we optimised a proximity ligation assay protocol which identified distinct spots in the nucleus corresponding to positive associations between SS18-SSX and the BAF complex members BRG1 and BAF155, which are known interactors (visualised by fluorescence microscopy). These findings were validated by co-IP (visualised by western blot). The antibody was also successfully used to detect protein-chromatin interactions in cell lines by running a ChIP experiment which identified enrichment at known target gene loci (EGR1, SOX2, CDKN2a) using a qPCR read-out. Results were concordant with previously published ChIP-seq data from experiments which had to rely on SS18-SSX engineered to express immunogenic epitope tags in transfectable models.

Conclusion: The current study demonstrates the utility of an SS18-SSX specific antibody in a panel of assays used in molecular oncology applications, on a variety of sample types. The availability of a well-characterized and validated commercial antibody against SS18-SSX offers a valuable research tool for identifying relevant protein interactors and genetic targets to study the role SS18-SSX in the oncogenesis of synovial sarcoma.



Poster #138 #1819065

IMMUNE AND CANCER TESTIS ANTIGEN LANDSCAPE IN SARCOMA

Anne C. Grand'Maison, MD¹; Robert J. Seager, PhD²; Yong Hee Lee, MPH²; Mary K. Nesline, MS²; Jeffrey Conroy, PhD²; Sarabjot Pabla, PhD²

¹Roswell Park Comprehensive Cancer Center, Buffalo, New York, UNITED STATES, ²OmniSeq Inc, Buffalo, New York, UNITED STATES

Objective: Significant improvements in multiple treatments, including but not limited to surgery, targeted therapy and immunotherapy, have been made in many cancer types. However, lack of clinical benefit for sarcoma patients still remains a challenge. There remains a significant gap in our current understanding of the tumor immune microenvironment in sarcoma tissues. Additionally, the immediate need for identification of prognostic or predictive biomarkers for patient selection remains an open frontier. We aim to reveal distinct yet integrated tumor immune landscape and cancer testis antigen (CTA) landscape in sarcoma subtypes with novel clinical implications.

Methods: The cancer genome atlas (TCGA) pan-cancer normalized gene expression data was utilized for 147 sarcoma cases with transcript expression estimated immune related genes in targeted RNA-seq panel. Biomarkers of tumor inflammation gene signature (TIGS), cell proliferation (CP) signature were assessed. CTA (17 CTA genes) positivity was classified as gene expression rank ≥ 5 . Kruskal-Wallis test was used to determine the association of sarcoma subtypes with all biomarkers. Pearson's correlation was utilized to study CTA co-expression. Overall survival (OS) was studied using Kaplan Meier analysis.

Results: All five sarcoma subtypes [N=147] (leiomyosarcoma [n=104], liposarcoma [n=58], myxofibrosarcoma[n=25], pleomorphic sarcoma[n=50], and synovial sarcoma[n=10]) studied presented with significantly distinct inflammation ($p=3.5E-08$) and proliferation ($p=9.7E-07$) and PD-L1 expression ($p=0.00012$) landscapes. For instance, Leiomyosarcoma presented with significantly weakly inflamed and highly proliferative tumors and on the other hand, liposarcoma presented with more inflamed tumors and that were significantly less proliferative. To further investigate the association of tumor inflammation and survival in sarcoma, we performed Kaplan-Meier analysis. Interestingly, weakly inflamed tumors were significantly associated with worse OS ($p=0.0082$). Cell proliferation by itself was not associated with OS. Next, we looked at CTA expression landscape of 17 CTA genes. All sarcoma subtypes presented with significantly distinct NY-ESO-1 expression ($p=1.1E-10$) with all but one synovial sarcoma cases highly expressing NY-ESO-1. Interestingly, each sarcoma subtype had a distinct co-expression of multiple CTA gene groups, hinting at selection of unique pro-tumor mechanisms afforded by the CTA gene groups within sarcoma subtypes. NY-ESO-1 and LAGE-1A were associated with survival in multiple sarcoma subtypes.

Conclusion: This study investigates the wide landscape of cancer immunity, cell proliferation and cancer testis antigens in multiple sarcoma subtypes. We reveal significant association of distinct inflammation and proliferation states within these subtypes. More importantly, we describe a novel clinically relevant CTA co-expression landscape in sarcoma which can be potentially targeted with cell-based therapies or cancer vaccines.



Poster #139 #1819040

DISSECTING THE ROLE OF THE TUMOR MICROENVIRONMENT IN RESPONSE TO CHEMOTHERAPY IN LIPOSARCOMA: TRANSLATIONAL AND CLINICAL IMPLICATIONS

Alessandro De Vita, PhD, Pharm D¹; Fausti Valentina, MD²; Federica Recine, MD³; Silvia Vanni, MSc, PhD²; Giacomo Miserocchi, MSc⁴; Marcella Tazzari, PhD, Pharm D⁵; Martine Bocchini, MSc⁵; Silvia Carloni, MSc, PhD⁵; Chiara Liverani, MSc, PhD²; Chiara Spadazzi, MSc²; Claudia Cocchi, MSc¹; Roberto Casadei, MD⁶; Francesca Brandolini, MD⁶; Giorgio Ercolani, MD⁷; Davide Cavaliere, MD⁷; Alberto Bongiovanni, MD²; Federica Pieri, MD⁸; Anna Farnedi, MSc⁸; Nada Riva, MD²; Lorena Gurrieri, MD²; Toni Ibrahim, MSc, MD, PhD⁹; Laura Mercatali, MSc, PhD¹

¹IRCCS Istituto Romagnolo Per Lo Studio Dei Tumori (IRST) "Dino Amadori", Meldola, Emilia-Romagna, ITALY, ²Osteoncolgy and Rare Tumors Center, IRCCS Istituto Romagnolo Per Lo Studio Dei Tumori (IRST) "Dino Amadori", Meldola, Italy, Meldola, Emilia-Romagna, ITALY, ³Medical Oncology Unit, Azienda Ospedaliera San Giovanni Addolorata, Roma, Italy., Roma, Lazio, ITALY, ⁴Osteoncolgy and Rare Tumors Center, IRCCS Istituto Romagnolo Per Lo Studio Dei Tumori (IRST), Meldola, Emilia-Romagna, ITALY, ⁵Immunotherapy, Cell Therapy and Biobank Unit, IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) "Dino Amadori", Meldola, Italy., Meldola, Emilia-Romagna, ITALY, ⁶Orthopedic Unit, Morgagni-Pierantoni Hospital, Forlì, Italy., Forlì, Emilia-Romagna, ITALY, ⁷Unit of Surgery and Advanced Oncologic Therapies, Morgagni-Pierantoni Hospital, Forlì, Italy, Forlì, Emilia-Romagna, ITALY, ⁸Pathology Unit, Morgagni-Pierantoni Hospital, Forlì, Italy, Forlì, Emilia-Romagna, ITALY, ⁹IRCCS Istituto Ortopedico Rizzoli, Bologna, Emilia-Romagna, ITALY

Objective: Among all soft tissue sarcoma histotypes, liposarcoma (LPS) is one of the most common malignancy with an overall incidence of 15%. Morphologically LPS is divided into four different variants with distinct clinical and biological behavior: well-differentiated/atypical lipomatous tumor (ALT/WDLPS), dedifferentiated liposarcoma (DDLPS), myxoid liposarcoma (MLPS) and pleomorphic liposarcoma (PLS). A better exploration of immune infiltrates in LPS is needed and could open the door to patients stratification identifying which could benefit from chemotherapy. We aimed at picturing the LPS tumor microenvironment and its influence on chemotherapy response.

Methods: A total of 8 patients affected by LPS were enrolled in the study (6 for RNAseq and 2 for co-culture analysis). LPS cells were isolated from tumor specimens and patient-derived primary cultures were established. Pharmacological analysis was obtained exposing LPS cultures to: ifosfamide (IFO), epirubicin (EPI), IFO and EPI combination, trabectedin (TRABE) and eribulin (ERI). Cultures viability percentage was assessed through both MTT and TUNEL assays. Next, NGS analysis was performed on tumor samples combined with CIBERSORT investigation. Finally, in order to provide further evidences on the role of immune-related cells in LPS response to chemotherapy a prospective study using a co-culture model of monocytes isolated from PBMCs from healthy donors and LPS immortalized cell lines was carried out. The co-cultures were exposed to the tested drugs and cell viability was assessed through both MTT and FACS analysis.

Results: The diagnosis of the surgically-resected tumor tissues were: 1 ATL/WDLPS and DDLPS, 1 DDLPS, 3 MLPS, 1 PLS. Cytomorphologic features analysis of primary cells confirmed the establishment of a patient-derived LPS culture with a proportion of 95%, 20%, 80%, 75%, 20% and 70% cells respectively. Among all case series the most active treatment were EPI and IFO+EPI especially in 1 DDLPS, 2 MLPS. IFO did not affected cell viability excluding 1 MLPS. TRABE exhibited activity especially in 2 MLPS. ERI exhibited a slight activity excluding 1 MLPS. PLS cell survival was not affected by all the tested drugs. Next, CIBERSORT analysis showed, among all, the following absolute scores: macrophages M0 ≥ 1.3 in 1 PLS; macrophages M2 ≥ 2.1 in 1 DDLPS, 2 MLPS and 1 PLS; T cells CD4 memory resting ≥ 0.9 among all the case series excluding 1 MLPS; T cells CD4 naïve ≥ 5.7 in 1 MLPS. Next preliminary results obtained on LPS immortalized cell lines and monocytes co-culture model showed an increased in tumor cell survival of 7.9% with IFO, 5.6% with EPI, 4.1% with IFO+EPI, while a decreased cell survival of 6.1% with ERI and 7.1% with TRABE compared to mono-culture model.

Conclusion: The aim of our study was to investigate the degree of immune cell infiltration into LPS and correlate to chemotherapy response. Thus, we conceived a perspective study based on the use of LPS patient-derived primary cultures. Pharmacological profile of LPS case series showed the response to some of the main drugs used in clinical practice. In particular, the highest activity was observed with anthracycline-based regimen confirming the clinical evidence for LPS management. Moreover, the data suggested an involvement of T cells CD4 memory resting in chemotherapy responsivity

especially in MLPS while M0 macrophages were associated with chemoresistance especially in PLS. Furthermore, co-culture model analysis provide further evidences of the role of monocytes/macrophages as predictive factors of response to chemotherapy. In particular they are associated to a lower response to DNA-interfering drugs as anthracyclines and to a higher response to drugs with pleiotropic mechanism as trabectedin. Further confirmation of these results can represent a potential future direction for the management of liposarcoma.

Patient	Gender	Age at surgery (years)	Site	Size (cm)	Histological subtype	Molecular cytogenetic analysis	Grade	Tumor	Radiotherapy post surgery	Chemotherapy post/pre surgery	Follow-up (months) DFS
LPS1	Male	61	mesentery mesocolon	6 x 5.5 x 2 (primary tumor) 6.5 x 4.5 x 3 (first recurrence, 5 years later) 3.5 x 2.8 x 1.4 x 3 x 1.5 2.5 x 2 x 2 (second recurrence, 1 year later)	ATL/WDLPS and DDLPS	MDM2/CEP12>=2	low grade	Primary tumor+ local recurrence	na	Six cycles of EI (after second recurrence)	22
LPS2	Female	82	gluteus	10 x 8 x 4	DDLPS	MDM2/CEP12>=2	high grade	distant recurrence	Local adjuvant RT (50 Gy)	na	17 8 DFS
LPS3	Male	81	thigh	16 x 11 x 12	MLPS	MDM2/CEP12=1 FUS (16p11)>10%	low grade	primary tumor	Local adjuvant RT (50 Gy)	na	24
LPS4	Male	79	inguino-crural site	15 x 3 x 9	MLPS	MDM2/CEP12=1 FUS (16p11)>10%	high grade	local recurrence	Local adjuvant RT (50 Gy)	na	94
LPS5	Female	81	leg	18 x 8 x 5	RCLPS	MDM2/CEP12=1 FUS (16p11)>10%	high grade	primary tumor	Local adjuvant RT (50 Gy)	na	1
LPS6	Male	63	arm	19 x 11 x 9	PLS	MDM2/CEP12=1	high grade	primary tumor	Local adjuvant RT (50 Gy)	3 cycles of neoadjuvant EI	7 4 DFS

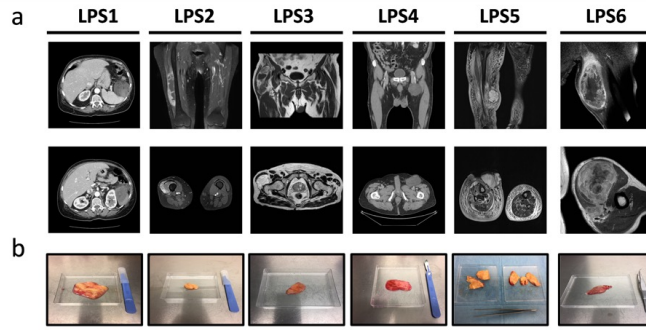


Table 1. Clinicopathological data in adipocytic sarcoma patients. a) Coronal and axial post-contrast MRI and CT images, b) Patients surgical specimens.

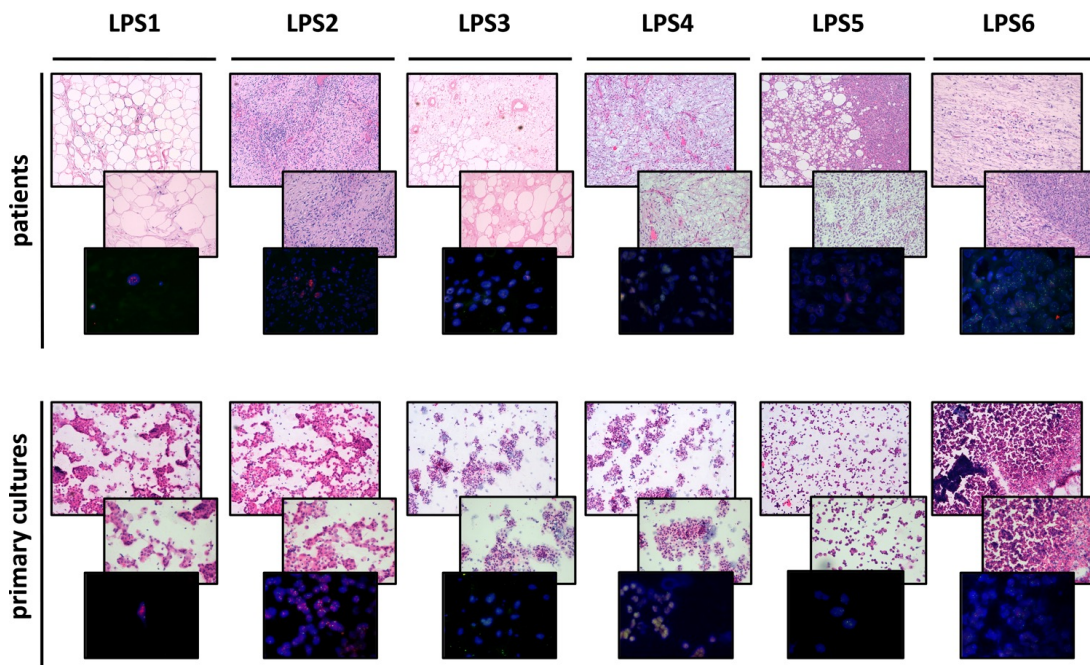


Figure 1. Hematoxylin and eosin staining of the surgical specimens and patient-derived primary cultures showing low and high grade LPS (light blue stroma) infiltrating adipose tissue, 10x and 20x magnification. FISH analysis of MDM2 amplification and FUS rearrangement 60x magnification.

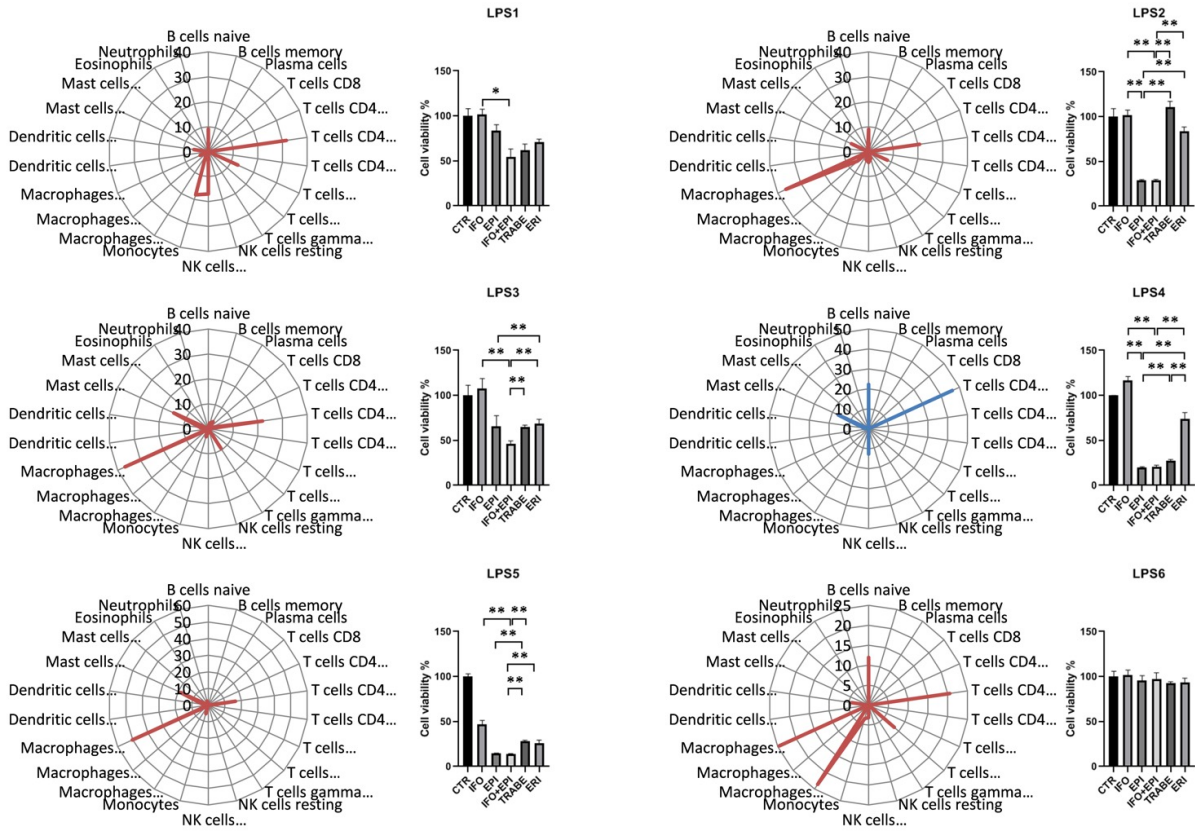


Figure 2. Chemobiogram analysis on patient-derived primary cultures and NGS analysis combined with CIBERSORT investigation on tumor samples

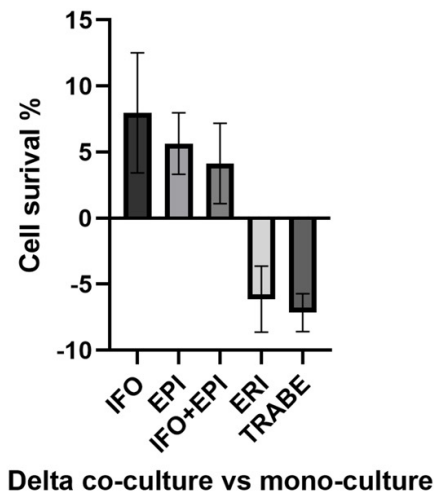


Figure 3. Preliminary results of chemobiogram analysis on monocytes isolated from PBMC healthy donors and LPS immortalized cell lines co-culture model. Cell survival percentage is represented as the delta between co-culture and mono-culture.



Poster #140 #1818909

GENOMIC AND TRANSCRIPTOMIC CORRELATES OF RESPONSE TO IMMUNE CHECKPOINT BLOCKADE-BASED THERAPY IN ANGIOSARCOMA

Evan Rosenbaum, MD¹; Cristina Antonescu, MD¹; Shaleigh Smith, MS¹; Martina Bradic, PhD¹; Allison Richards, PhD¹; Mark Donoghue, PhD¹; Daniel Kashani, MD²; Ciara Kelly, MD¹; Benjamin Nacev, MD, PhD¹; Jason Chan, MD, PhD¹; Ping Chi, MD, PhD³; Mark A. Dickson, MD¹; Mary Lou Keohan, MD⁴; Mrinal M. Gounder, MD⁴; Katherine A. Thornton, MD¹; Samuel Singer, MD, PhD¹; William D. Tap, MD¹; Sandra P. D'Angelo, MD¹

¹Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES, ²SUNY Downstate Medical College, New York, New York, UNITED STATES, ³Human Oncology and Pathogenesis Program/Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES, ⁴Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES

Objective: Angiosarcoma (AS) is a rare aggressive subtype of soft tissue sarcoma in need of novel treatment strategies. Recent reports have highlighted the efficacy of immune checkpoint blockade (ICB) in select cases, particularly in cutaneous AS. However, data describing outcome to ICB treatment in this disease remains sparse. We sought to determine outcomes to ICB in a relatively large cohort of AS patients treated at a single center.

Methods: All patients with AS treated with at least one dose of ICB at Memorial Sloan Kettering (MSK) prior to January 1, 2021 were retrospectively identified (n = 35). Available clinical features, targeted genomic sequencing (MSK-IMPACT), and whole transcriptome data were correlated with clinical benefit (defined as PFS of ≥ 16 weeks) and progression-free survival (PFS), where available. PFS was defined as time from ICB initiation until progression of disease (determined by RECIST 1.1 for those on a trial and retrospectively for those off-trial), excessive toxicity, or death from any cause.

Results: Clinical characteristics and ICB regimens utilized are presented in Table 1. Among all patients, median PFS was 11.9 weeks (95% confidence interval [CI] 7.4 – 31.9). 13 patients (37%) had PFS ≥ 16 weeks (Figure). Median tumor mutational burden (TMB) among 26 patients with IMPACT was 3.7 (interquartile range [IQR], 0.9 – 5.5); 4 patients with cutaneous AS had ≥ 10 mutations per megabase. 6 patients, all with cutaneous/head/neck (CHN) tumors, had a dominant ultraviolet (UV) mutational signature. On univariate analysis, non-Caucasian race was the only clinical factor associated with PFS (median 2.4 [CI 1.1 – not reached (NR)] vs. 14.9 [10 – 34.7] weeks in Caucasians, p = 0.031). Within the IMPACT cohort, TMB or presence of UV signature did not associate with PFS; patients with a Notch pathway gene alteration (n = 3) had a shorter PFS (median 7.9 [95% CI 5.1 – NR] vs. 17.9 weeks [10 – NR], p = 0.052). On multivariate analysis, ipilimumab plus nivolumab compared to other ICB regimens was associated with worse PFS, while Caucasian patients and those with a CHN site had a longer PFS (Table 2). Whole transcriptome sequencing was performed on 15 samples (8 pre- and 7 on-treatment) from 10 unique patients. There were 293 differentially expressed genes between samples with PFS ≥ 16 versus < 16 weeks. Gene set enrichment analysis noted upregulation of interferon alpha and gamma, UV response, and numerous metabolic pathways in the PFS ≥ 16 group. E2F targets, epithelial-mesenchymal transition, G2M checkpoint, mitotic spindle, TGF-beta signaling, and WNT/beta-catenin signaling pathways were upregulated in the PFS < 16 group. Analysis of tumor-infiltrating immune cell populations identified more dendritic cells and fewer non-regulatory CD4⁺ T cells in PFS high patients (p = 0.05, adjusted).

Conclusion: More than one-third of patients with AS treated with ICB derived clinical benefit, many of whom have CHN disease with a dominant UV signature. However, other primary disease sites also benefit despite a low TMB or lack of a UV signature. Additional research is needed to validate the above biomarkers of response and resistance.

Table 1: Patient characteristics

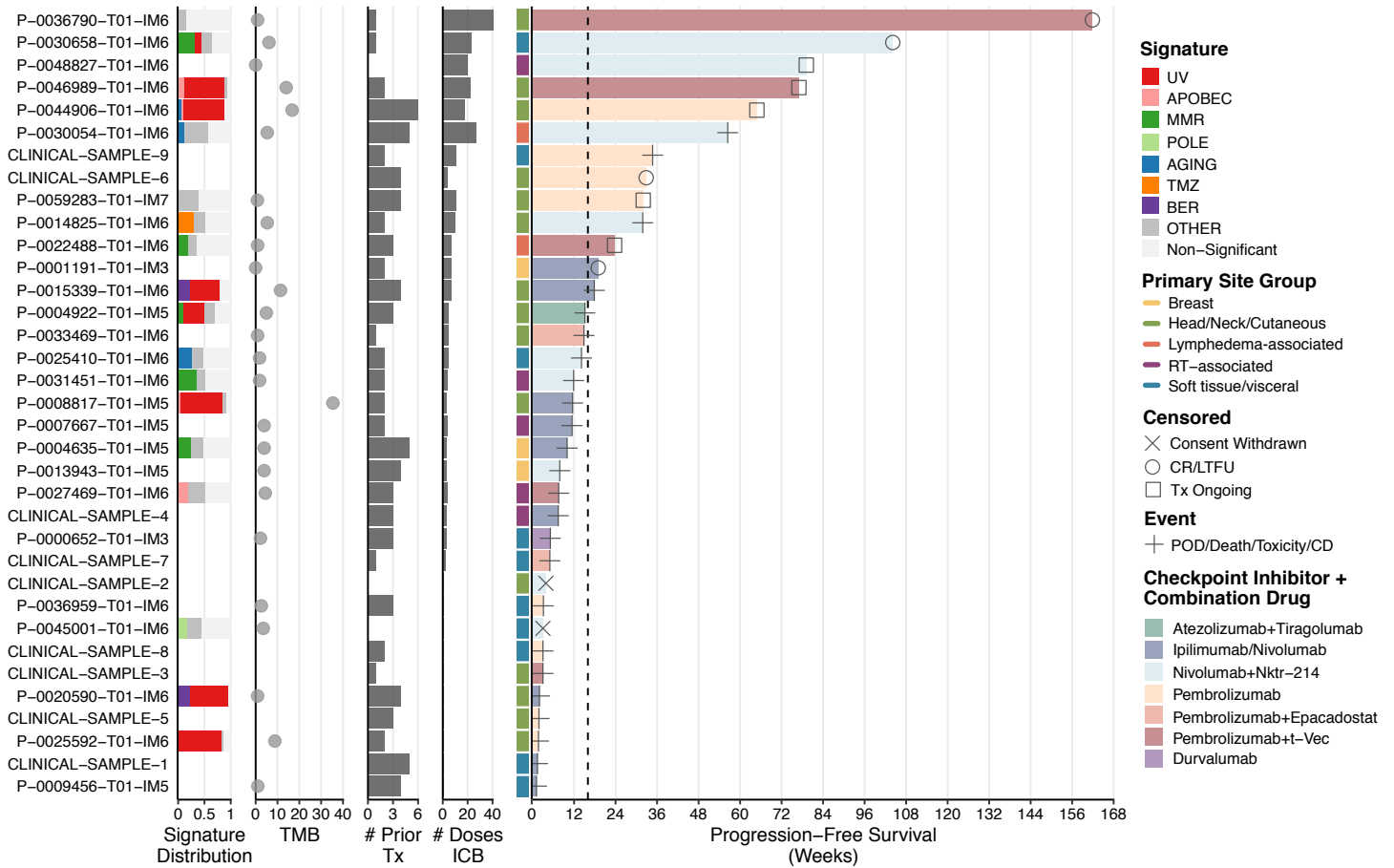
Clinical Variable	N = 35*
Age at diagnosis	69 (56-73)
Metastatic at diagnosis	11 (31%)
Sex	
Female	19 (54%)
Male	16 (46%)
Race	
Caucasian	29 (83%)
Asian/Indian	5 (14%)
Other	1 (2.9%)
Primary site	
Head/Neck/Cutaneous	14 (43%)
Soft tissue/visceral	10 (29%)
RT-associated	5 (14%)
Breast	3 (8.6%)
Lymphedema-associated	2 (5.7%)
ICB	
Ipi/nivo	9 (26%)
Nivo+NKTR-214	9 (26%)
Pembrolizumab	8 (23%)
Pembrolizumab + T-VEC	5 (14%)
Pembrolizumab + Epacadostat	2 (5.7%)
Durvalumab	1 (2.9%)
Atezolizumab + Tiragolumab	1 (2.9%)

*Median (IQR); n (%)

Table 2: Multivariate Analysis of PFS after ICB

Category	Variable	Reference	Hazard Ratio	95% CI	P value
Race	Caucasian	Other	0.179	0.049 - 0.663	0.010*
Metastases at diagnosis	Yes	No	0.399	0.129 - 1.227	0.109
ICB regimen	Anti-PD-1 Monotherapy	Anti-PD-1 plus other	2.153	0.613 - 7.557	0.231
	Ipilimumab plus nivolumab	Anti-PD-1 plus other	5.326	1.77 - 16.045	0.003*
Primary site	Head/Neck/Cutaneous	Soft tissue/visceral	0.164	0.042 - 0.638	0.009*
	Other	Soft tissue/visceral	0.284	0.066 - 1.221	0.091

*Statistically significant at P < 0.05





Poster #141 #1818900

TRABECTEDIN + NIVOLUMAB IN PRETREATED PATIENTS WITH ADVANCED LIPO- AND LEIOMYOSARCOMAS: FIRST RESULTS OF THE "L-GROUP" FROM THE NITRASARC-TRIAL OF THE GERMAN INTERDISCIPLINARY SARCOMA GROUP (GISG-15)

Daniel Pink, MD, PhD¹; Dimosthenis Andreou, MD, PhD²; Anne Flörcken, MD³; Alexander Golf, MD⁴; Stephan Richter, MD, PhD⁵; Torsten Kessler, MD⁶; Martin Kortüm, MD⁷; Christian Andreas Schmidt, MD⁸; Bernd Kasper, MD, PhD⁹; Eva Wardelmann, MD¹⁰; Jeanette Bahr⁸; Daniel W. Müller, MD¹¹; Disorn Sookthai¹¹; Marcin Ostrzyzek, MD¹¹; Salah-Eddin Al-Batran, MD¹¹; Peter Reichardt, MD¹²

¹Helios Klinikum Bad Saarow, Universitätsmedizin Greifswald, Bad Saarow, Brandenburg, GERMANY, ²Helios Klinikum Bad Saarow, Bad Saarow, Brandenburg, GERMANY, ³Charité-Universitätsmedizin Berlin, Berlin, GERMANY, ⁴Universitätsklinikum Tübingen, Tübingen, Baden-Württemberg, GERMANY, ⁵University Hospital Carl Gustav Carus, University Cancer Center/Medical Department I, Dresden, Dresden, Sachsen, GERMANY, ⁶University Hospital Muenster, Münster, Nordrhein-Westfalen, GERMANY, ⁷Universitätsklinikum Würzburg, Würzburg, Bayern, GERMANY, ⁸Universitätsmedizin Greifswald, Greifswald, Mecklenburg-Vorpommern, GERMANY, ⁹University of Heidelberg, Mannheim University Medical Center, Mannheim Cancer Center, Sarcoma Unit, Mannheim, Germany, Mannheim, Baden-Württemberg, GERMANY, ¹⁰Universitätsklinikum Münster, Münster, Nordrhein-Westfalen, GERMANY, ¹¹Institut für Klinische Krebsforschung IKF GmbH at Krankenhaus Nordwest, Frankfurt, Hessen, GERMANY, ¹²Oncology and Palliative Care, Sarcoma Center, Helios Klinikum Berlin-Buch, Berlin, Berlin, GERMANY

Objective: Single-agent programmed death-1 (PD-1) inhibitors have modest activity in the treatment of most soft tissue sarcomas (STS). Potential strategies to increase efficacy include combination therapies targeting the tumor microenvironment. Trabectedin (Tr) is approved for the treatment of adult patients (pt) with advanced STS after failure of anthracyclines and ifosfamide, or pt who are unsuited to receive these agents. Apart from direct growth inhibition and death of malignant cells, Tr induces macrophage depletion and/or other immunologic effects, suggesting a possible synergistic effect of combined Tr plus an anti-PD-1 agent. We therefore aimed to evaluate the efficacy and safety of combined Tr and nivolumab (Ni) in pt with anthracycline-pretreated metastatic or inoperable STS.

Methods: This prospective, explorative, two group, non-randomized phase II NiTraSarc trial enrolled pretreated pt with advanced STS (Group A: lipo- or leiomyosarcomas, Group B: non-L-sarcomas). Pt were initially treated with three cycles of Tr 1.5 mg/m², followed by the combination of Tr 1.5 mg/m² + Ni 240 mg ("late combination cohort" (LCC)) for up to 16 cycles. After positive results of a preplanned interim analysis, pt received the combination therapy starting with cycle 2 ("early combination cohort" (ECC)). Overall, 92 pt were recruited to the trial (55 in Group A, 37 in Group B). Primary efficacy endpoint was progression-free survival rate after 6 months (PFSR₆) according to RECIST v.1.1. Secondary endpoints comprised overall response rate (ORR), overall survival (OS), progression-free survival (PFS) and duration of disease stabilization (DoDS). Herein we present first analyses of the primary and most secondary efficacy endpoints as well as safety analyses in Group A based on a modified intention-to-treat (mITT) population of 54 evaluable pt (28 and 26 pt from the LCC and ECC, respectively).

Results: While the Group A's ECC cohort enrolled evenly 13 pt with leiomyosarcoma and 13 pt with liposarcoma, most pt in the LCC cohort had a leiomyosarcoma (22/28 pt). After a median follow-up of 11.2 months (m), the overall PFSR₆ in the mITTT population was 37.0%. There were no relevant differences in the PFSR₆ of pt with leiomyosarcoma and liposarcoma (37.1% vs. 36.8%). The median PFS amounted to 4.4 m for all patients, 4.7 m for leiomyosarcoma and 4.1 m for liposarcoma pt. The best overall responses (BOR) in the overall population and in the subgroups of pt with leiomyosarcoma and pt with liposarcoma were as follows: partial response (PR) in 9.3%, 14.3% and 0.0%; SD in 44.4%, 40.0% and 52.6%; progressive disease (PD) was 37.0%, 37.1% and 36.8%, respectively (data were missing in 9.3%, 8.6% and 10.5% of pt). Median duration of response (DoR) and median duration of stable disease (DoS) for mITT were 9.6 m and 7.9 m, respectively, with a resulting duration of disease stabilization (DoDS) of 8.1 m. We found no relevant differences in PFSR₆, PFS and ORR between LCC and ECC cohorts. Considering that this is an ongoing study with most pt being still alive, OS data were immature to be properly analyzed. All 54 pt experienced at least one adverse event (AE) with a total of 1315 AEs, 226 (17.2%) of which were considered to be grade ≥3 treatment-related AEs. The main grade ≥3 AEs were anemia (59.3% of pt), leukopenia (59.3% of pt), neutropenia (57.4% of pt), nausea (55.6% of pt) and fatigue (46.3% of pt).

Conclusion: Tr plus Ni showed activity in some pt, mostly with leiomyosarcoma, and had a manageable safety profile. However, the preliminary analyses of this cohort suggest no relevant improvement with the combination of Tr plus Ni compared to published outcomes of Tr monotherapy (Demetri et al. J Clin Oncol. 2016;34:786-93) regarding PFSR6 (37% vs 37%), PFS (4.40m vs 4.20m) and ORR (9.3% vs 9.9%). As compared with Tr alone, a slight improvement of DoR (9.6 m vs 6.5 m) and DoS (7.9m vs 6.0 m) of the combination should be interpreted with caution due to the small pt population, the nature of post-hoc analysis, and the retrospective comparison. Analyses of the collected data, including PD-L1 expression profile, to establish whether Tr plus Ni should be further pursued in these patients, are ongoing. ClinicalTrials.gov Identifier: NCT03590210; EudraCT: 2017-001083-38



Poster #142 #1819006

SAINT: AN EXPANDED PHASE 2 STUDY USING SAFE AMOUNTS OF IPILIMUMAB (I), NIVOLUMAB (N), AND TRABECTEDIN (T) AS FIRST-LINE TREATMENT OF ADVANCED SOFT TISSUE SARCOMA [NCT03138161]

Erlinda M. Gordon, MD¹; Ted T. Kim, BS²; Noufil Adnan, MD¹; Victoria Chua, MD³; Ishrat Bhuiyan, BS³; Sonu Thomas, MD⁴; Simranjit Sekhon, MD⁵; Don A. Brigham, PhD³; Victoria T. Chua-Alcala, MD⁵

¹Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES, ²Sarcoma Oncology Center, Santa Monica, California, UNITED STATES, ³Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES, ⁴Sarcoma Oncology Research Center, Santa Monica, CA, ⁵Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES

Objective: Background: Sarcoma cells are most immunogenic earlier in the disease course and before treatment when the immune system can recognize and destroy them. Hypothesis: Immune checkpoint inhibitors would be most effective when given as first-line therapy. Objectives: ¹To evaluate best objective response rate by RECIST v1.1 via CT scan or MRI, ²To assess progression-free survival (PFS) at 6 months, and ³To evaluate overall survival.

Methods: Eligible patients for this expanded Phase 2 study are males or females ≥ 18 years of age with locally advanced unresectable or metastatic soft tissue sarcoma, previously untreated, with measurable disease by RECIST v1.1.

Results: Seventy-nine subjects were evaluable for efficacy analysis. There were 7CR (2 surgical CR), 9PR, 51SD, 12PD. Overall response rate was 20.2%, Disease Control Rate, 85%. The median PFS was >6.7 (range:1-32) months, median OS, >17.6 (range: 0-36) months. Six-month PFS rate: 58.3%, 6-month OS rate: 79.3%. Grade 3 TRAEs include fatigue (n = 8), adrenal insufficiency (n = 1), dehydration (n = 1), hyponatremia (n = 2), increased AST (n = 8), increased ALT (n = 24), increased ALP (n = 2), port site infection (n = 2), psoriasis exacerbation (n = 1), anemia (n = 9), thrombocytopenia (n = 2), and neutropenia (n = 5). Grade 4 TRAEs include anemia (n = 1), neutropenia (n = 1), thrombocytopenia (n = 2), increased AST (n = 2), increased ALT (n = 2), and increased CPK (n = 2). Grade 5 TRAEs include rhabdomyolysis (n = 1). There was no incidence of alopecia nor cardiac toxicity reported.

Conclusion: Taken together, these data suggest that first-line combinatorial therapy with ipilimumab, nivolumab, and trabectedin: ¹have synergistic activities with no additive toxicities, and no alopecia nor cardiotoxicity, and ²may be equal or superior to, and safer than, standard first line therapy (doxorubicin/ifosfamide/mesna) for metastatic soft tissue sarcoma.



Poster #143 #1818895

CHARACTERIZATION OF MECA-79, CD1A, STAT1, AND LAMP3 IN THE INFLAMMATORY MICROENVIRONMENT IN MYXOFIBROSARCOMA AND UNDIFFERENTIATED PLEOMORPHIC SARCOMA

Ashley N. Flaman, MD, FRCPC¹; Elizabeth G. Demicco, MD PhD²; Brendan C. Dickson, MD MSc³; Nalan Gokgoz, PhD⁴; Jay S. Wunder, MSc., MD⁴; Irene L. Andrulis, PhD⁴

¹University of Toronto / Mount Sinai Hospital, Toronto, Ontario, CANADA, ²Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, Ontario, CANADA, ³Mount Sinai Hospital, Toronto, Ontario, CANADA,

⁴The Lunenfeld-Tanenbaum Research Institute, Toronto, Ontario, CANADA

Objective: Wide local excision ± radiation is the mainstay of therapy for myxofibrosarcoma (MFS) and undifferentiated pleomorphic sarcoma (UPS), with chemotherapy typically used in the metastatic setting, often with limited benefit. Immunotherapy is an emerging therapeutic approach in sarcoma; however, it is important to first understand the tumour inflammatory microenvironment, particularly because sarcomas are so multifarious. Prior studies have shown the presence of high endothelial venules (HEV) to be associated with tertiary lymphoid structures, tumour-infiltrating lymphocytes and possibly a more favourable tumour microenvironment in the context of carcinomas and melanoma. Increased LAMP3+ mature antigen-presenting dendritic cells, believed to play a role in adaptive immunity, have been reported in tumours with higher expression of PD-L1 and higher density of HEVs. We previously conducted transcriptome profiling on UPS and MFS and identified Th1 pathway activation in a subset of tumors; LAMP3 and a number of immunoglobulin genes were also differentially expressed. A group of Th1 genes including STAT1 are known to distinguish tumors with high versus low endothelial venules. We aim to characterize the prevalence of dendritic cells and their association with tertiary lymphoid structures and HEV in MFS and UPS.

Methods: Archival formalin-fixed paraffin-embedded tissue blocks from 25 MFS and 25 UPS resections or incisional biopsies without neoadjuvant therapy were selected. 4 µm thick sections were stained with H&E, and qualitatively scored for the presence of peripheral lymphoid aggregates with or without germinal centres. Immunohistochemistry (IHC) was performed for MECA-79 (a marker of HEVs), STAT-1, CD1a, and LAMP3. CD1a and MECA-79 were scored as positive vs negative. STAT1+ cells were scored semi-quantitatively as absent, low (1-10/HPF) or high >10/HPF. The number of LAMP3 positive cells was counted and averaged over 1 mm² in both random and hotspot areas. The location and distribution of staining (within peripheral lymphoid aggregates, intratumoural lymphocytic condensation, or diffuse / even intratumoural distribution) were also recorded. Immune counts were scored as high if greater than the average of all cases.

Results: Only 8% of cases showed germinal centres on H&E. MECA-79 staining highlighted rare HEV-like vessels associated with peripheral lymphoid aggregates in 6 cases (p=0.0003), including 2 with germinal centres (p=0.066), but also showed focal staining in tumour vessels not associated with lymphoid structures in an additional 2 cases. CD1a+ immature dendritic cells were only present in 1 MFS. LAMP3+ mature dendritic cells were seen in 92% of UPS and 96% of MFS. The average positive cell count was 25/mm² in UPS and 40/mm² in MFS in hotspots, and 2/mm² in UPS and 5/mm² in MFS in random representative areas. Average STAT1+ cell counts were low in UPS and high in MFS. In most cases (68% UPS and 76% MFS), LAMP3+ cells showed higher density in areas of intratumoural lymphocytic condensation or clustered in peripheral lymphoid aggregates; there were significantly higher hotspot counts in cases with peripheral lymphoid aggregates compared to those without (61/mm² vs 25/mm², MFS and UPS combined, p=0.0045). Tumours with high STAT 1 correlated with high expression of LAMP3 (>9/mm²), p=0.016.

Conclusion: MECA-79+ HEVs were only rarely present, and usually seen in conjunction with peripheral lymphoid aggregates with or without germinal centres, consistent with tertiary lymphoid structures. MFS trends to associate with a slightly more prominent LAMP3+ mature dendritic cell infiltrate, and increased STAT1+ cells, which may have implications for the immune response in MFS. Studies with additional cases and clinical correlation are needed to determine if these immune features have prognostic or theranostic significance.



Poster #144 #1819044

PERIPHERAL IMMUNE LANDSCAPE OF SOFT TISSUE SARCOMA: CELLULAR, PROTEOMIC AND TRANSCRIPTOMIC ANALYSIS

Jani Sofia J. Almeida, MSc¹; Paulo Rodrigues Santos²; Patrícia Couceiro³; Luana Madalena Sousa³; Tânia Fortes Andrade³; Ruben Fonseca⁴; Manuel Santos Rosa¹; Paulo Freitas Tavares⁴; José Manuel Casanova⁴

¹Institute of Immunology, Fac Medicine Univ Coimbra, Portugal, Coimbra, Coimbra, PORTUGAL, ²Immunology and Oncology Laboratory, Center for Neurosciences and Cell Biology & Institute of Immunology, Fac Medicine Univ Coimbra, Portugal, Coimbra, Coimbra, PORTUGAL, ³Immunology and Oncology Laboratory, Center for Neurosciences and Cell Biology, Univ Coimbra, Portugal, Coimbra, Coimbra, PORTUGAL, ⁴Bone and Soft Tumor Unit, Coimbra Hospital and University Centre, Coimbra, Portugal, Coimbra, Coimbra, PORTUGAL

Objective: Given the current limitations in STS treatment management, the lack of information about the immunological status of STS patients and the accessibility of the peripheral blood samples, the aim of this study was to perform a comprehensive analysis of the peripheral immune landscape of STS patients to identify potential indicators of disease evolution or therapy response.

Methods: The present study groups consisted of 31 STS patients and 37 age-matched control peripheral blood samples. Extended immunophenotyping was performed by flow cytometry for major lymphocyte populations, including markers of maturation, memory, activation and functional differentiation. An xMAP/Luminex® comprehensive approach was used for the analysis of the soluble proteome based in a 4-panel containing 103 cytokines, chemokines, growth factors and soluble immune checkpoints. A transcriptomic analysis of peripheral blood using a panel of 106 immune-related genes was performed by quantitative PCR.

Results: In general, STS was characterized by a significant granulocytosis, lymphopenia and decrease of total dendritic cells, associated with poor survival. Low counts of T, B and NK cell were also detected, and the proportion of B cells within the lymphocyte compartment was found markedly reduced. Low count of T cells and CD4 T cells was correlated with shorter survival and CD4 T and CD8 T cells were found significantly decreased and increased, respectively. We found higher proportions of effector memory CD4 T (CCR7-CD45RA-) and Th17 (CXCR3-CCR6+) cells and higher expression of the activation marker HLA-DR. Regarding B cells, high frequency of plasmablasts (CD24-CD38+) was detected and higher frequency of exhausted B cells (IgD-CD27-) was associated with poorer survival. The frequency of regulatory T cells (Tregs) and monocytic-myeloid derived suppressor cells (M-MDSCs) were found increased and the higher frequency of Tregs was correlated with prolonged survival. Through the plasma transcriptomic analysis, we observed a downregulation of the genes CD3D, CD3E, LTA, NCAM1, GZMB, PRF1, TNF, TNFRSF1B, IL23A, CD27, ICOSLG and TIGIT, which correlates with shorter lifetimes. Moreover, the lower expression of CD47, CD48 and IL18 genes and the higher expression of the LAG-3, SLAMF7, TNFSF12 and TNFSF13 genes were associated with prolonged survival. Plasma proteomic analysis revealed increased levels of IFN γ , IL-18, MCP-2, sIL-2R, sCD30 and sTIMD-4 and these elevated levels were associated with shorter survival as well as increased levels of MIP-1a, MIP-1b and Fractalkine, although they have been found reduced in patients. Furthermore, high plasma levels of ICOS-L were associated with prolonged survival and high plasma levels of MCP-1, MMP-1, TNFR2, CTLA4, BCL and IL-2 were associated with reduced survival.

Conclusion: The data obtained in this group of STS patients disclosed significant alterations in several immune populations, immune-related genes and soluble plasmatic factors. STS patients present low lymphocyte counts, with decreased T, B and NK cells, and downregulation of genes related to immune cytotoxic function compromising the effective anti-tumoral immune response. Likewise, the process of antigen presentation seems to be defective given the decrease in B cells and DCs, the downregulation of related-genes and the low plasmatic levels of cytokines linked to cell signaling. Furthermore, immune suppressor cells and soluble immune checkpoints inhibitors were found increased in STS patients. Taken together, these findings point out the importance of study the peripheral immune landscape of STS patients and the correlation with patients' survival could be useful to predict the outcome of the disease and adjust the therapeutical strategies.



Poster #145 #1818982

NY-ESO-1 EXPRESSION PROFILING AND PREVALENCE ASSESSMENT OF TUMOR BIOPSIES FROM PHASE I/II TCR T CELL THERAPY CLINICAL TRIALS IN ADVANCED SYNOVIAL SARCOMA OR MYXOID ROUND CELL LIPOSARCOMA

Erika Klohe, BS, MBA; Alexandra Gyurdieva, MS; Gurpreet Kapoor, PhD; Jaegil Kim, PhD; Ellie Corigliano, PhD, GlaxoSmithKline, Collegeville, Pennsylvania, UNITED STATES

Objective: In two early Phase I/II clinical trials (NCT02992743 and NCT01343043) assessing NY-ESO-1 TCR T cell therapy in patients with advanced synovial sarcoma (SS) and myxoid round cell liposarcoma (MRCLS), an investigational use only (IUO) immunohistochemical (IHC) clinical trial assay was used to determine NY-ESO-1 protein expression levels for patient screening and identification. Here we aim to assess the distribution of NY-ESO-1 protein expression levels and observed prevalence in these two clinical patient cohorts. We further describe the staining characteristics and similarities in SS and MRCLS indications and evaluate how an NY-ESO-1 IHC assay can aid in the identification of patients who may be eligible for NY-ESO-1 specific T cells [letecresgene autoleucel (lete-cel); GSK3377794] TCR targeted therapy.

Methods: An IUO IHC clinical trial assay was developed to detect NY-ESO-1 expression in formalin-fixed paraffin-embedded (FFPE) tissue specimens utilizing a commercially available anti-NY-ESO-1 monoclonal antibody, clone E978. Patient samples were predominantly archival tumor biopsies and NY-ESO-1 status was determined by pathological evaluation of stained tumor samples under light microscopy using the semi-quantitative histoscore (H-Score) method to capture percent tumor cell staining at each stain intensity of 0: null, 1+ (weak), 2+ (moderate) and 3+ (strong). NY-ESO-1 expression data were assessed descriptively for intensity distribution, dynamic range of percent tumor cell staining, and positive prevalence to observe expression patterns in SS and MRCLS clinical trial populations using a base assessment tumor proportion score (TPS) of $\geq 1\%$, irrespective of stain intensity.

Results: SS and MRCLS tumor samples tested demonstrated similar NY-ESO-1 expression patterns across a dynamic range of intensities (0, 1+, 2+, 3+) in the screened population. NY-ESO-1 overall prevalence (any positive staining, $\geq 1\%$, $\geq 1+$) was observed to be higher in MRCLS (34/35) than SS (72/102), at 97% vs. 71% of samples tested, respectively. The NY-ESO-1 IHC assay detected varying levels of NY-ESO-1 expression within and across tumor samples, with the primary expression mode of moderate/strong staining (2+/3+) at greater than 50% tumor cell staining in both indications. NY-ESO-1 expression was primarily localized in the cell nucleus and surrounding cytoplasm.

Conclusion: NY-ESO-1 expression across SS and MRCLS indications express highly similar IHC intensity levels inclusive of 1+, 2+ and 3+ and demonstrated a high prevalence of 71% and 97%, respectively at $\text{TPS} \geq 1\%$. As such, NY-ESO-1 strong staining in both SS and MRCLS indications, in a high percentage of patients evaluated supports the tests' utility as an aid in the identification of patients who may be eligible for NY-ESO-1 specific T cells (lete-cel) TCR targeted therapy. NY-ESO-1 expression levels and positive prevalence using a clinical trial IHC assay is consistent with what has been reported in the literature (1,2) and demonstrated consistent nuclear and cytoplasmic staining localization in tumor cells in SS and MRCLS sub-types, which are morphologically distinct forms of cancers arising from soft tissues. Funding: GSK and Adaptimmune [208469, NCT02992743; 208466, NCT01343043]. References 1. Hemminger JA, et al. *Mod Pathol.* 2013;26(2):282–288 2. Thomas R, et al. *Front Immunol.* 2018;9:947. Conflicts of interest: EC is a current employee of GSK and owns stocks/shares in GSK, Merck, Agilent Technologies, CRISPR Therapeutics, Thermo Fisher, and Healthcare electronic funds transfer for ARKG, XLV, IHF, IHI. EK, GK and JK are current employees of and owns stocks/shares in GSK. AG is a current employee of GSK and owns stock/shares in GSK and Amgen.



Poster #146 #1818968

SPEARHEAD-1: PRELIMINARY TRANSLATIONAL INSIGHTS FROM A PHASE 2 TRIAL OF AFAMITRESGENE AUTOLEUCEL (FORMERLY ADP-A2M4) IN PATIENTS WITH ADVANCED SYNOVIAL SARCOMA OR MYXOID/ROUND CELL LIPOSARCOMA

Sandra P. D'Angelo, MD¹; Steven Attia, DO²; Jean-Yves Blay, MD, PhD³; Kristen N. Ganjoo, MD⁴; Axel Le Cesne, MD⁵; Claudia Maria Valverde Morales, MD⁶; Albiruni Ryan Abdul Razak, MD, MB, MRCPI⁷; Sandra Strauss, BA, MBBS, MRCP (UK), PhD⁸; Brian A. Van Tine, MD, PhD⁹; Michael J. Wagner, MD¹⁰; Natalie Bath, MSc¹¹; Gareth Betts, PhD¹¹; Robyn Broad, PhD¹¹; Ian Donaldson, PhD¹¹; Chris Evans, DPhil¹²; Alasdair Gunn, PhD¹¹; Ashley Liddle, MSc¹¹; Cheryl McAlpine, PhD¹¹; Karen Miller, PhD¹¹; Jean-Marc Navenot, PhD¹²; Paul Noto, PhD¹²; Stavros Rafail, PhD¹²; William Spinner, PhD¹¹; Alex Tipping, PhD¹³; Erin Van Winkle, BS¹²; Ruoxi Wang, PhD¹¹; Swethajit Biswas, ChB (Hons), MRCP (UK), DPhil (Oxon)¹¹; Elliot Norry, MD¹²; Dennis Williams, PharmD¹²; Dejka M. Araujo, MD¹⁴

¹Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES, ²The Mayo Clinic, Jacksonville, Florida, UNITED STATES, ³Centre Léon Bérard, Lyon, Auvergne, FRANCE, ⁴Stanford Cancer Center, Stanford, California, UNITED STATES, ⁵Institut Gustave Roussy-Gustave Roussy Cancer Center-DITEP, Villejuif, Ile-de-France, FRANCE, ⁶Vall D'Hebron University Hospital, Barcelona, Catalonia, SPAIN, ⁷Division of Medical Oncology, Princess Margaret Cancer Centre, University Health Network, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, CANADA, ⁸University College London Hospital, London, England, UNITED KINGDOM, ⁹Washington University School of Medicine, St. Louis, Missouri, UNITED STATES, ¹⁰University of Washington/Fred Hutch/Seattle Cancer Care Alliance, Seattle, Washington, UNITED STATES, ¹¹Adaptimmune, Abingdon, England, UNITED KINGDOM, ¹²Adaptimmune, Philadelphia, Pennsylvania, UNITED STATES, ¹³Adaptimmune, Philadelphia, England, UNITED KINGDOM, ¹⁴The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES

Objective: Afamitresgene autoleucel (afami-cel; formerly ADP-A2M4) is a therapeutically active HLA-A2 restricted and MAGE-A4 targeted TCR T-cell therapy for the treatment of synovial sarcoma (SS) and myxoid/round cell liposarcoma (MRCLS) and has demonstrated a preliminary overall response rate (ORR) of 39.4% in this SPEARHEAD-1 trial [1]. To support the continued investigation of potential mechanisms of response and acquired resistance in SS and MRCLS patients, ongoing translational analyses, described in more detail below, are being performed. A comprehensive understanding of the potential mechanisms underpinning afami-cel therapeutic activity may enable future strategies to enhance responses.

Methods: Characterization of patient manufactured product (MP), peripheral blood, and tumor-derived samples obtained pre- and post-infusion are being performed. This includes profiling of MP and peripheral blood mononuclear cell (PBMC) samples for determination of transduced T-cell persistence (qPCR), immunophenotyping, in vitro cytotoxicity, and multiplex serum immune marker measurements. Tumor biopsy sample analyses includes duplexed TCR RNAscope, anti-CD3 IHC analysis, and multiplex immunofluorescence for spatial analyses of T-cell infiltration in context with tumor microenvironment (TME) molecular profiling.

Results: Following afami-cel infusion, all Cohort 1 patients evaluated (n = 37) had measurable, although variable, persistence of transduced cells throughout the interventional phase of the trial with some maintaining high levels of persistence (i.e., > 20,000 vector copies/ug DNA) beyond 6 months post infusion. Median time to peak persistence was 1.1 weeks (95% CI: 0.571, 1.143) and median peak persistence was 218,827.9 copies/ug DNA (range: 16775.8, 635,824.4). Preliminary evaluation of in vitro cellular cytotoxicity of the afami-cel MP from 10 patients in this pivotal Phase 2 trial was consistent with the MP in the prior Phase 1 trial [2]. Following afami-cel infusion, transient increases in multiple peripheral immune markers were observed and the most marked increases were in levels of IFN γ in both SS and MRCLS patients.

Conclusion: Preliminary translational findings appear to demonstrate a potent and functionally active afami-cel MP which aligns with the promising clinical activity of afami-cel in the SPEARHEAD-1 trial to be presented at this congress. Ongoing detailed evaluation of translational datasets, including potential relationships between cell kinetics and pharmacodynamic effects (IFN γ signaling), and sarcoma TME profiling, aim to provide a deeper translational understanding of the mechanisms of afami-cel response. An update will be available at the time of the congress. [1] D'Angelo et al. ASCO; June 4-7, 2021; Virtual [2] Van Tine BA, et al. CTOS; November 18-21, 2020; Virtual This study was sponsored by Adaptimmune (Philadelphia, PA, USA).



Poster #147 #1819007

GALLANT: A PHASE 2 STUDY USING METRONOMIC GEMCITABINE, DOXORUBICIN, NIVOLUMAB AND DOCETAXEL AS SECOND/THIRD LINE THERAPY FOR ADVANCED SARCOMA: TRIAL IN PROGRESS [NCT04535713]

Sant P. Chawla, MD¹; Noufil Adnan, MD²; Ted T. Kim, BS³; Victoria T. Chua-Alcala, MD¹; Simranjit Sekhon, MD¹; Ishrat Bhuiyan, BS⁴; Ania Moradkhani, NP¹; Erlinda M. Gordon, MD²

¹Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES, ²Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES, ³Sarcoma Oncology Center, Santa Monica, California, UNITED STATES,

⁴Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES

Objective: Background: In our experience, combinatorial therapy with lower doses of doxorubicin, gemcitabine and docetaxel has been effective with a manageable toxicity profile in patients with advanced soft tissue sarcomas. Hypothesis: The addition of nivolumab to this regimen will have synergistic effects and will improve treatment outcome. The primary objective is to evaluate progression-free survival (PFS). Secondary objectives are ¹To evaluate the best overall response (BOR) and duration of response (DOR) by RECIST v1.1 via CT scan or MRI during the treatment period; ²To determine progression-free survival rate at 6 and 12 months; and ³To determine overall survival rate at 6 and 12 months.

Methods: Two hundred sixty patients (40 LMS, 40 LPS, 40 UPS, 40 osteosarcoma, 40 Ewing, 20 synovial sarcoma, and 40 other histologic subtypes) will be enrolled. Inclusion criteria: Previously treated male and female subjects, > 18 years of age, of any ethnicity with pathologically confirmed diagnosis of locally advanced, unresectable or metastatic sarcoma, measurable disease by RECIST v1.1, and acceptable hematologic and organ functions. Exclusion Criteria: History of autoimmune disorder. Treatment schedule: Metronomic doses of gemcitabine (600 mg/m² max:1000 mg), doxorubicin (18 mg/m²; max: 32 mg), docetaxel (25 mg/m²; max:42 mg) on Day 1 and Day 8, and nivolumab (240 mg) on Day 1 only. Repeat treatment cycles may be given every 3 weeks if toxicity grade is <1. Statistical Plan: Analysis of Primary Endpoint: Progression-free survival (PFS) at 6 and 12 months will be obtained. Median PFS will be estimated, along with its two-sided 95% confidence interval. Analysis of Secondary Endpoints: Response will be classified as complete response (CR), partial response (PR), stable disease (SD), or progressive disease (PD) based on RECIST v1.1. Point estimates for efficacy endpoint incidences will be accompanied by a 2-sided 95% exact binomial CI (Clopper and Pearson, 1934). Overall survival and time to event endpoints will be summarized descriptively using the KM method. Safety (incidence and severity of adverse events and significant laboratory abnormalities) will be reported for all patients (ITT population). Patient incidence of all treatment-related and unrelated AEs will be tabulated by system organ class and preferred term using NIH CTCAE v5.0. Summary statistics will be provided for total number of doses, average dose administered, and duration of each treatment.

Results: This Phase 2 clinical trial is in progress. To date, 31 patients have been enrolled.

Conclusion: This Phase 2 clinical trial is in progress. To date, 31 patients have been enrolled.



Poster #148 #1818858

T-REGULATORY CELLS PREDICT CLINICAL OUTCOME IN SOFT TISSUE SARCOMA PATIENTS

Joanna Szkandera, MD¹; Maria Anna Smolle, MD²; Laurin Herbsthofer, PhD³; Mark Goda, Student⁴; Iva Brcic, MD⁴; Marko Bergovec, MD⁴; Susanne Scheipl, MD⁴; Barbara Prietl, PhD³; Martin Pichler, Prof.⁴; Armin Gerger, Prof.⁴; Christopher Rossmann, MD⁴; Jakob Riedl, MD⁴; Martina Tomberger, Technical assistant³; Pablo Lopez-Garcia, Dr.³; Amin El-Heliebi, PhD⁴; Andreas Leithner, Prof.⁴; Bernadette Liegl-Atzwanger, Prof.⁴

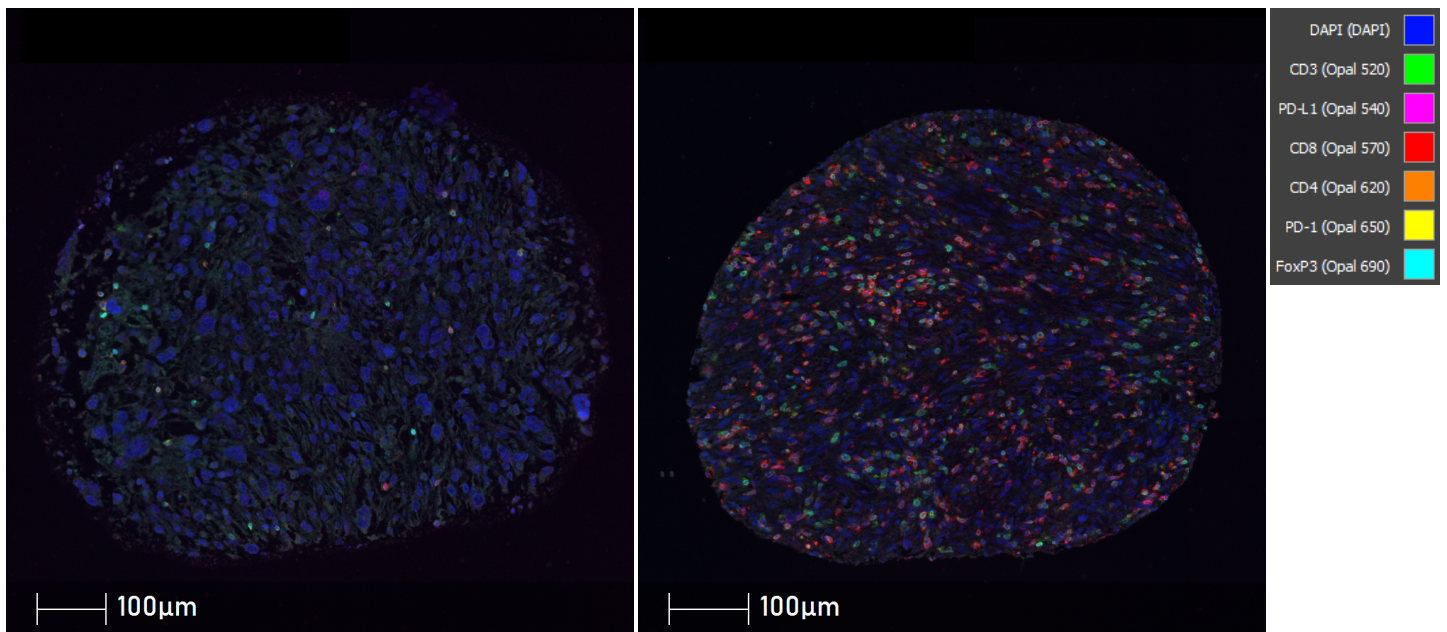
¹Medical University of Graz, Graz, Steiermark, AUSTRIA, ²Department of Orthopaedics and Trauma, Medical University Graz, Graz, Steiermark, AUSTRIA, ³CBmed GmbH, Graz, Steiermark, AUSTRIA, ⁴Medical University Graz, Graz, Steiermark, AUSTRIA

Objective: Soft tissue sarcomas (STS) are generally considered non-immunogenic, although specific subtypes respond to immunotherapy. Anti-tumour response within the tumour microenvironment relies on a balance between inhibitory and activating signals for tumour infiltrating lymphocytes (TILs). This study analysed TILs and immune checkpoint molecules in STS, and assessed their prognostic impact regarding local recurrence (LR), distant metastasis (DM), and overall survival (OS).

Methods: One-hundred-ninety-two surgically treated STS-patients (median age: 63.5 years; 103 males [53.6%]) were retrospectively included. Tissue microarrays were constructed, immunohistochemistry for PD-1, PD-L1, FOXP3, CD3, CD4, and CD8 performed, and staining assessed with multispectral imaging. TIL-phenotype abundance and immune checkpoint markers were correlated with clinical and outcome parameters (LR, DM, OS).

Results: PD-L1-expression was positively correlated with all T-cell subtypes. Significant differences between histology and all immune checkpoint markers except for FOXP3+ and CD3- PD-L1+ cell subpopulations were found. Higher levels of PD-L1, PD-1, and any TIL-phenotype were found in myxofibrosarcoma as compared to leiomyosarcoma (all p<0.05). Presence of Tregs was associated with increased LR-risk (p=0.006), irrespective of margins. Other TILs or immune checkpoint markers had no significant impact on outcome parameters.

Conclusion: TIL- and immune checkpoint marker-levels are most abundant in myxofibrosarcoma. High Treg-levels are independently associated with increased LR-risk, irrespective of margins.



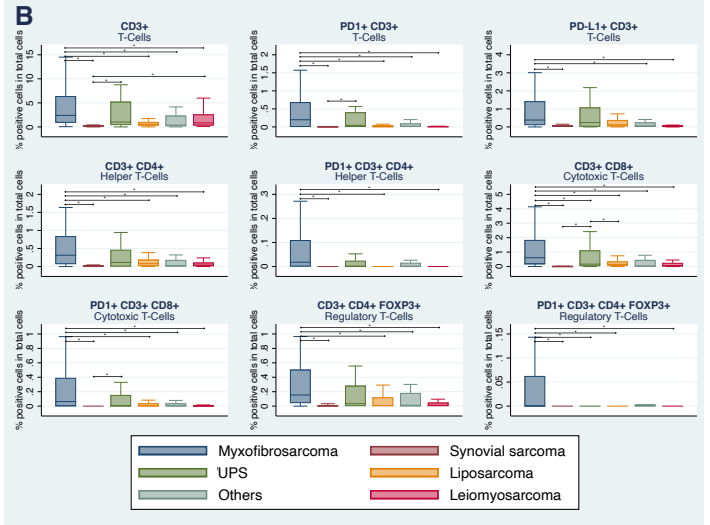
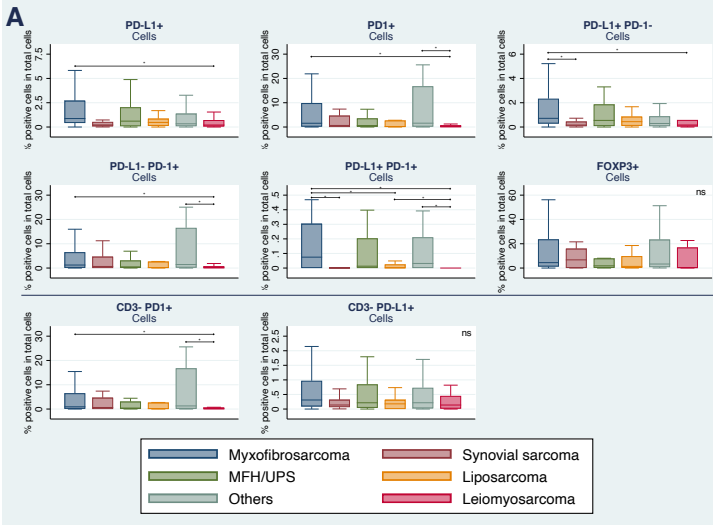


Table 2. Univariate competing risk regression analysis for local recurrence, and distant metastasis, with death as competing event. Univariate Cox-regression analysis for overall survival.

Univariate Analysis	Local Recurrence		Distant Metastasis		Overall Survival	
	HR (95%CI)	p-value	HR (95%CI)	p-value	HR (95%CI)	p-value
Female (vs. Male as ref.)	0.91 (0.40-2.07)	0.817	1.01 (0.62-1.67)	0.962	0.90 (0.56-1.45)	0.667
Age at Surgery (in years)	1.01 (0.99-1.03)	0.251	1.01 (0.91-1.02)	0.403	1.04 (1.02-1.05)	<0.001
R1/2 Margins (vs. R0 as ref.)	2.21 (0.96-5.10)	0.063	0.75 (0.41-1.37)	0.347	0.68 (0.37-1.25)	0.215
Upper limb (Ref.)	1		1		1	
Lower Limb	0.87 (0.35-2.22)	0.772	1.36 (0.73-2.53)	0.332	0.95 (0.55-1.69)	0.873
Trunk	0.94 (0.19-4.65)	0.935	1.23 (0.44-3.40)	0.695	1.35 (0.55-3.29)	0.511
Superficial (Ref.)	1		1		1	
Deep	0.40 (0.16-1.04)	0.059	1.23 (0.68-2.22)	0.497	0.97 (0.55-1.70)	0.907
Superficial + Deep	1.35 (0.48-3.81)	0.566	1.41 (0.63-3.17)	0.405	1.56 (0.76-3.19)	0.223
G1 (Ref.)	1		1		1	
G2	3.12 (0.39-24.86)	0.282	3.08 (0.73-12.92)	0.124	1.40 (0.45-4.40)	0.566
G3	2.10 (0.28-15.53)	0.468	4.08 (1.05-15.77)	0.042	2.11 (0.76-5.85)	0.149
Tumour size (in cm)	0.96 (0.88-1.05)	0.343	1.05 (1.01-1.09)	0.010	1.04 (1.00-1.08)	0.051
MF (Ref.)	1		1		1	
SS	N/A	N/A	1.93 (0.75-4.96)	0.173	1.70 (0.70-4.13)	0.239
UPS	0.93 (0.25-3.41)	0.907	2.32 (1.15-4.71)	0.020	1.73 (0.89-4.49)	0.108
LPS	0.66 (0.15-2.85)	0.580	0.55 (0.19-1.55)	0.256	0.39 (0.15-1.12)	0.080
Other	1.82 (0.62-5.33)	0.273	1.31 (0.60-2.86)	0.499	1.41 (0.68-2.93)	0.356
LMS	1.76 (0.53-5.86)	0.358	2.08 (0.98-4.44)	0.058	1.42 (0.62-2.81)	0.476
Adjuvant RTX (vs. no Adjuvant RTX as ref.)	1.23 (0.51-2.98)	0.653	0.95 (0.56-1.64)	0.894	0.68 (0.42-1.12)	0.132
Adjuvant CTX (vs. no Adjuvant CTX as ref.)	0.31 (0.03-2.29)	0.249	1.58 (0.78-3.23)	0.204	0.89 (0.43-1.86)	0.751
PD-L1+ Cells	1.07 (0.97-1.19)	0.248	1.02 (0.98-1.07)	0.323	1.02 (0.98-1.07)	0.355
PD-1+ Cells	1.02 (0.99-1.03)	0.070	1.01 (0.99-1.02)	0.449	1.01 (0.99-1.02)	0.481
PD-L1+ PD-1- Cells	1.10 (0.96-1.26)	0.178	1.04 (0.98-1.10)	0.194	1.03 (0.96-1.09)	0.446
PD-L1- PD-1+ Cells	1.02 (0.99-1.03)	0.070	1.01 (0.99-1.02)	0.431	1.01 (0.99-1.02)	0.536
PD-L1+ PD1+ Cells	1.03 (0.86-1.24)	0.728	0.99 (0.88-1.13)	0.974	1.06 (0.94-1.19)	0.357
FOXP3+ Cells	1.00 (0.98-1.02)	0.823	0.99 (0.98-1.01)	0.417	0.98 (0.96-0.99)	0.023
CD3+ T-Cells	1.02 (0.96-1.10)	0.503	1.02 (0.99-1.05)	0.161	0.99 (0.96-1.04)	0.857
PD1+ CD3+ T-Cells	1.07 (0.89-1.28)	0.473	1.01 (0.86-1.14)	0.877	1.04 (0.92-1.18)	0.525
PD-L1+ CD3+ T-Cells	1.09 (0.93-1.28)	0.293	1.02 (0.97-1.08)	0.408	1.01 (0.93-1.08)	0.960
CD3+ CD4+ Helper T-Cells	1.24 (0.99-1.55)	0.062	0.99 (0.86-1.14)	0.911	1.01 (0.88-1.15)	0.920
PD1+ CD3+ CD4+ Helper T-Cells	1.28 (0.79-2.05)	0.319	0.98 (0.69-1.38)	0.904	1.12 (0.81-1.56)	0.496
CD3+ CD8+ Cytotoxic T-Cells	0.91 (0.75-1.09)	0.300	0.98 (0.89-1.08)	0.659	1.01 (0.91-1.01)	0.991
PD1+ CD3+ CD8+ Cytotoxic T-Cells	0.77 (0.42-1.53)	0.493	0.94 (0.78-1.14)	0.541	1.08 (0.94-1.25)	0.258
CD3+ CD4+ FOXP3+ Tregs	1.33 (1.05-1.68)	0.016	0.99 (0.84-1.18)	0.966	0.99 (0.83-1.18)	0.888
PD-1+ CD3+ CD4+ FOXP3+ Tregs	8.91 (0.90-87.81)	0.061	0.78 (0.09-6.62)	0.820	0.86 (0.05-16.29)	0.921
CD3- PD1+ Cells	1.02 (0.99-1.03)	0.078	1.01 (0.99-1.02)	0.440	1.01 (0.99-1.02)	0.514
CD3- PD-L1+ Cells	1.09 (0.93-1.28)	0.312	1.08 (0.89-1.31)	0.458	1.15 (1.02-1.29)	0.021

Legend: p-values in bold and grey-shaded fields highlight significant results. N/A – not applicable as too few variables in group; TILs – tumour infiltrating lymphocytes; MFS – myxofibrosarcoma; SS – synovial sarcoma; UPS – undifferentiated pleomorphic sarcoma; LPS – liposarcoma; LMS – leiomyosarcoma

Table 3. Multivariate competing risk regression analysis for local recurrence, and distant metastasis, with death as competing event. Multivariate Cox-regression analysis for overall survival.

Multivariate Analysis	Local Recurrence		Distant Metastasis		Overall Survival	
	HR (95%CI)	p-value	HR (95%CI)	p-value	HR (95%CI)	p-value
Age at Surgery (in years)					1.03 (1.02-1.05)	<0.001
R1/2 Margins (vs. R0 as ref.)	2.14 (0.94-4.89)	0.072				
G1 (Ref.)			1			
G2			2.69 (0.66-11.03)	0.169		
G3			2.68 (0.69-10.39)	0.153		
Tumour size (in cm)			1.06 (1.02-1.11)	0.003	1.04 (0.99-1.08)	0.076
MF (Ref.)			1			
SS			1.72 (0.59-5.01)	0.321		
UPS			2.69 (1.29-5.62)	0.008		
LPS			0.48 (0.17-1.35)	0.163		
Other			1.57 (0.66-3.75)	0.307		
LMS			2.16 (1.07-4.33)	0.031		
CD3+ CD4+ FOXP3+ Tregs	1.41 (1.08-1.59)	0.006				
FOXP3+ Cells					0.98 (0.96-1.01)	0.076
CD3- PD-L1+ Cells					1.12 (0.98-1.27)	0.087

Legend: p-values in bold and grey-shaded fields highlight significant results. TILs – tumour infiltrating lymphocytes; MFS – myxofibrosarcoma; SS – synovial sarcoma; UPS – undifferentiated pleomorphic sarcoma; LPS – liposarcoma; LMS – leiomyosarcoma



Poster #149 #1818955

NATURAL KILLER AND CYTOTOXIC T CELL IMMUNE INFILTRATES ARE ASSOCIATED WITH SUPERIOR OUTCOMES IN SOFT TISSUE SARCOMAS

Sylvia M. Cruz¹; Sean J. Judge, MD²; Morgan A. Darrow, MD³; Cordelia Dunai, PhD⁴; Shuai Chen, PhD⁵; Steven W. Thorpe, MD²; Robert J. Canter, MD²

¹Division of Surgical Oncology, Department of Surgery, University of California Davis School of Medicine, Sacramento, California, UNITED STATES, ²University of California Davis, Sacramento, California, UNITED STATES, ³Pathology and Laboratory Medicine, University of California Davis School of Medicine, Sacramento, California, UNITED STATES,

⁴Dermatology, University of California Davis School of Medicine, Sacramento, California, UNITED STATES, ⁵Public Health Sciences, University of California Davis, Sacramento, California, UNITED STATES

Objective: Tumor infiltrating lymphocytes (TILs) have been shown to predict survival in soft tissue sarcomas (STS); however, the contribution of specific lymphocyte subsets such as natural killer (NK) and memory T cells to STS outcomes is undefined. We sought to characterize the extent of NK and memory T cell infiltration in STS to determine the correlation of these cytotoxic immune cells to patient outcomes.

Methods: Archived tumor tissue from 90 STS patients collected from 2008-2020 was evaluated. Tissue microarrays (TMAs) were constructed, and immunohistochemical analyses were performed by an STS pathologist for CD3, CD8, CD45RO, NKp46, TIGIT, and MHC-I. TIL scores of H&E slides were calculated. Metastasis-free survival (MFS) and overall survival (OS) were analyzed by Kaplan-Meier method.

Results: Among our cohort (mean age 62, 58% male), the mean tumor size was 13.2 cm, consistent with a high-risk population. Majority of tumors (58%) were located on the extremity, 23% were retroperitoneal, and 16% trunk. The most common histologies were liposarcoma (29%), myxofibrosarcoma (23%), and pleomorphic sarcoma (20%) with 84% high grade. With a median follow up of 46 months, MFS and OS were 25 and 91 months, respectively. We confirmed a positive correlation between CD8+ T cell infiltration and significantly improved MFS ($P < 0.05$), and a trend of improved MFS. Overall, NK cell infiltrates were low (median H score 0, range 0-66.5). However, we observed a trend for improved OS among patients with higher NKp46 scores (OS 68 months for NKp46 scores below median versus not reached for scores above median, $P = 0.07$). The expression of TIGIT and MHC-I correlated with T cell infiltration ($P < 0.05$). MHC-I correlated with T cell infiltration ($P < 0.05$), but TIGIT did not.

Conclusion: Infiltration of cytotoxic lymphocyte subsets, including NK cells, is associated with superior OS in STS patients undergoing surgery. Further characterization of the immune infiltrate in STS may yield better biomarkers of prognosis and immune targeting.



Poster #150 #1818918

PHASE 2 STUDY OF ATEZOLIZUMAB IN ADVANCED CLEAR CELL SARCOMA (CCS)

Alice P. Chen, MD¹; Abdul Rafah Naqash, MD²; Geraldine O'Sullivan Coyne, MD²; Nancy Moore, RN²; Elad Sharon, MD, MPH²; Anthony P. Conley, MD³; Elizabeth J. Davis, MD⁴; Priscilla Merriam, MD⁵; Jared Foster, PhD⁶; Naoko Takebe, MD PhD²; Kristin K. Fino, PhD⁷; Katherine V. Ferry-Galow, PhD⁷; Ralph E. Parchment, PhD⁷; James H. Doroshow, MD¹

¹NCI/NIH, Bethesda, Maryland, UNITED STATES, ²NCI, Bethesda, Maryland, UNITED STATES, ³MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁴Vanderbilt University Cancer Center, Nashville, Tennessee, UNITED STATES, ⁵Dana Farber Cancer Institute, Boston, Massachusetts, UNITED STATES, ⁶NCI CTEP, Bethesda, Maryland, UNITED STATES, ⁷Frederick National Laboratory for Cancer Research, Fredrick, Maryland, UNITED STATES

Objective: Clear cell sarcoma (CCS) constitutes <1% of all sarcomas and frequently presents in adolescents and young adults. There is no standard of care therapy approved for CCS. We are currently evaluating the clinical activity of atezolizumab (atezo), an anti-PD-L1 antibody, in patients (pts) with advanced CCS and grade 2 or 3 chondrosarcomas (NCT04458922). Herein we report on interim results from the CCS cohort.

Methods: This is a multicenter, open-label, single-arm phase 2 study in pts with documented EWSR1/ATF1 or EWSR1/CREB1 translocation or histologically confirmed CCS. Atezo is administered at a fixed dose of 1200 mg in adult pts (≥ 18 years of age) or 15 mg/kg (1200 mg max) in pediatric pts age ≥ 2 , once every 21 days. Tumor biopsies (mandatory) are being collected from adult patients at baseline and prior to cycle 3 day 1 (± 3 days). The primary objective of this study is to determine the objective response rate (ORR) using RECIST 1.1. Secondary clinical objectives are to determine the duration of response and progression-free survival. Pharmacodynamic assessments of treatment-induced changes in the number of activated CD8+ T cells infiltrating the tumor are planned to correlate these changes with clinical response. The study employs a Simon 2-stage design. Accrual will be halted at 9 patients for interim response evaluation; if at least one response is observed, accrual will continue for a total of 17 pts. The regimen will be considered worthy of further testing if an ORR of $\geq 17.6\%$ is achieved among 17 evaluable pts.

Results: As of June 4, 2021, 8 CCS pts have been enrolled in the first stage of this trial (5 females, 3 males). The median pt age was 36 years (range, 26-46). Race distribution was: 6 Caucasian, 1 Black, and 1 Asian. All pts had baseline ECOG scores ≤ 1 . The median time on treatment was 2.0 months (range, 0.8 -7.9). The median number of cycles was 3. At data cutoff, response evaluation was available for 6 pts: 2 had stable disease (SD), for 5.1 and 7.9 months, respectively, and 4 had a best response of progressive disease (PD). Two pts went off study before being evaluated for response: 1 pt due to clinical progression and 1 due to toxicity. The most common treatment-related adverse events (AEs) included: fatigue (5 pts), anorexia (3 pts), fever (2 pts), nausea (2 pts), and weight loss (2 pts). Potential immune-related AEs included transaminitis, acneiform rash, hypophysitis, hyperhidrosis, and hypothyroidism (n=1 patient each). G3 treatment-related AEs were systemic immune activation and vomiting, each observed within the first 2 cycles in 2 distinct pts, both of whom required hospitalization. The pt with systemic immune activation had permanent treatment discontinuation for toxicity and the pt with vomiting came off for clinical progression. G3 lymphopenia was also observed in 1 pt, who recovered and did not require treatment discontinuation. No G4/5 AEs were observed.

Conclusion: The single-agent activity of atezo will be better elucidated following completion of enrollment and response evaluations for the first stage of the trial. Evaluation of PD-1/PD-L1 immune checkpoint (IC) biomarkers and changes in CD8 T-cell counts in paired biopsies is planned. Funded by NCI Contract No HHSN261200800001E.



Poster #151 #1818880

PHASE II STUDY OF THE ANTIBODY-CYTOKINE FUSION PROTEIN L19TNF PLUS DACARBAZINE FOR PRETREATED PATIENTS WITH ADVANCED OR METASTATIC SOFT TISSUE SARCOMA: RESULTS OF THE RUN-IN PART

Torsten Kessler, MD¹; Daniel Pink, MD, PhD²; Peter Reichardt, MD³; Emanuela Palmerini, MD⁴; Piotr Rutkowski, MD, PhD⁵; Teresa Hemmerle, PhD⁶; Dario Neri, Prof.⁷; Christoph Schliemann, MD¹

¹University Hospital Muenster, Münster, Nordrhein-Westfalen, GERMANY, ²Helios Klinikum Bad Saarow, Universitätsmedizin Greifswald, Bad Saarow, Brandenburg, GERMANY, ³Oncology and Palliative Care, Sarcoma Center, Helios Klinikum Berlin-Buch, Berlin, Berlin, GERMANY, ⁴IRCCS Istituto Ortopedico Rizzoli, Bologna, Emilia-Romagna, ITALY,

⁵Department of Soft Tissue/Bone Sarcoma and Melanoma; Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Mazowieckie, POLAND, ⁶Philgogen S.p.A., Siena, Toscana, ITALY, ⁷Philogen S.p.A., Siena, Toscana, ITALY

Objective: L19TNF (onfekafusk alfa) is a recombinant fully human antibody-cytokine fusion protein consisting of the antibody fragment L19 directed against the neovasculature and tumor necrosis factor (TNF). Although TNF is one of the most potent antitumor cytokines, the considerable therapeutic potential of natural TNF cannot be fully exploited due to severe side effects, which preclude achievement of therapeutically active concentrations in the tumor. To circumvent these issues, the fully human antibody-cytokine fusion protein L19TNF, composed of the vascular targeting antibody fragment scFv(L19) fused to human recombinant TNF, has been designed to selectively deliver TNF to the tumor tissue while sparing normal organs. L19TNF has demonstrated substantial therapeutic activity in preclinical models of sarcoma when administered alone or in combination with dacarbazine. Here we report the initial findings from the run-in part of the phase II study PH-L19TNFSARC-03/18 (NCT04733183). This study investigates the combination of L19TNF plus dacarbazine in patients with advanced or metastatic soft tissue sarcoma that received at least two prior lines of therapy.

Methods: This is a phase II, multi-center, open-label, randomized trial of L19TNF (13µg/kg, days 1, 3, and 5, q3w) in combination with dacarbazine (day 1) versus dacarbazine alone (1000 mg/m²) in patients with advanced unresectable or metastatic soft tissue sarcoma, who received at least two prior systemic therapies including at least one prior therapy based on anthracyclines. The dose of dacarbazine in combination with L19TNF is explored in a run-in part of the study. The primary endpoint is progression-free survival (PFS). The study is powered to detect an improvement of median PFS from 2.6 months to 5.2 months in combination-treated patients, with a sample size of 86 patients in the randomized part of the study. Eligibility criteria include grade 2-3 advanced or metastatic soft tissue sarcoma, measurable disease according to RECIST 1.1, age 18 - 80 years, ECOG performance status of ≤ 2, and adequate organ function.

Results: The combination was safely applicable. Five patients were treated in the run-in part of the study at 13 µg/kg L19TNF and 1000 mg/m² dacarbazine and no unacceptable toxicities occurred. The most common treatment related (L19TNF, dacarbazine or the combination) adverse events were chills, pyrexia, hypotension and GGT increased, anaemia, nausea, ALT increased, AST increased and WBC decreased. No serious adverse events occurred. So far, one partial remission and two stable diseases out of 4 patients were observed.

Conclusion: L19TNF can be safely applied in combination with dacarbazine and induces tumor responses in patients with previously pretreated advanced or metastatic soft tissue sarcomas.



Poster #152 #1819008

PHASE 1 STUDY OF ESCALATING DOSES OF EX VIVO EXPANDED, AUTOLOGOUS NATURAL KILLER CELLS IN PATIENTS WITH PATHOLOGICALLY CONFIRMED CANCER REFRACTORY TO CONVENTIONAL THERAPY [NCT03941262]

Sant P. Chawla, MD¹; Simranjit Sekhon, MD¹; Noufil Adnan, MD²; Ted T. Kim, BS³; Victoria T. Chua-Alcala, MD¹; Ania Moradkhani, NP¹; Steven Cha, MD⁴; Erlinda M. Gordon, MD²

¹Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES, ²Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES, ³Sarcoma Oncology Center, Santa Monica, California, UNITED STATES, ⁴NK-Gen Biotech, Santa Ana, California, UNITED STATES

Objective: Background and Rationale: SNK01 is an autologous natural killer (NK) cell-derived adopted cellular immunotherapy being developed as a single agent and in combination with targeted therapies to treat advanced and metastatic solid tumors. NK cells are an essential class of innate immune cells that play a critical role in mediating antitumor response. NK cells can directly kill tumor cells and rapidly secrete proinflammatory cytokines to potentiate the adaptive immune response. SNK01 is the first-in-kind, autologous non-genetically modified NK cell therapy with highly enhanced cytotoxicity and near 100 % expression of CD16, NKG2D, NKp46, and DNAM-1, which can be consistently produced from healthy subjects, and heavily treated cancer patients alike. Objectives: Primary : To investigate the safety of SNK01 using NIH CT CAE vs 5.0 Secondary: To assess objective response rate (ORR), progression-free survival (PFS) using RECIST v1.1 and overall survival (OS).

Methods: In this single-arm Phase I study to investigate the safety and potential anti-tumor activity of SNK01, eleven patients (Cohorts 1-3) with refractory metastatic solid tumors were treated in a 3+3 monotherapy dose escalation study with five weekly infusions of SNK01 (Dose Level 1: 1×10^9 , Dose Level 2: 2×10^9 , and Dose Level 3: 4×10^9 cells/infusion). After completing the 3 Cohorts of single dose escalation of SNK01, the protocol was amended to include Cohort 4 (n=18) wherein SNK01 is given in combination with an immune checkpoint inhibitor (avelumab or pembrolizumab). Patients with PD-L1 negative or low PD-L1+ tumors who have failed conventional therapy and who have measurable disease by RECIST 1.1 are being enrolled to receive either SNK01 (4×10^9 cells) + pembrolizumab 200 mg q 3 weeks or avelumab 800 mg q 2 weeks. Patients will be treated until disease progression or unacceptable toxicity. Primary end point is safety. Secondary endpoints are objective response rate (ORR), progression-free survival (PFS) and overall survival (OS). The trial is currently in progress and 16/18 patients have been enrolled to date.

Results: The trial is currently in progress and 16/18 patients have been enrolled to date.

Conclusion: The trial is currently in progress and 16/18 patients have been enrolled to date.



Poster #153 #1818863

RADIATION-INDUCED SARCOMAS RESPONDING TO PEMBROLIZUMAB

Benjamin C. Powers, MD¹; Julie Hamlin, APRN²; Dana Smith, RN²; Tiffany Verhulst, RN²

¹The University of Kansas Health System, Leawood, Kansas, UNITED STATES, ²The University of Kansas Health System, Overland Park, Kansas, UNITED STATES

Objective: As we continue to do a better job of long-term survivorship in treating primary cancers, the incidence of radiation-induced tumors seems to be increasing, although still considered rare (less than 1% of adults exposed to definitive radiation treatment). Radiation-induced sarcomas account for about 1 in every 20 new sarcoma cases, with risk factors being higher the dose of radiation, longer latency period since radiation, and younger age at time of initial radiation exposure. Almost all are thought to be high-grade tumors, suggesting local aggressiveness and high risk for metastatic disease. Here, we present two separate cases of radiation-induced sarcomas responding deeply and quickly to pembrolizumab monotherapy, hopefully suggesting a shift in treatment paradigms.

First patient is a 67 year old male with right tonsillar squamous cell carcinoma status post chemoradiation in 2006 noticed growing right jaw mass in Summer 2020, causing pain with mastication, right sided otalgia, and tenderness to palpation over the right temporomandibular joint. He was requiring fentanyl patches and short-acting opiates as needed. Steroids and antibiotics did not help. CT 10/19/20 showed destructive 6cm right mandibular mass. Second attempt at biopsy on 11/18/20 diagnosed undifferentiated pleomorphic sarcoma (UPS), radiation-induced. ENT deemed this surgically unresectable. Notably, radiation was thought to have caused right internal carotid artery occlusion in 2014 with ongoing residual left sided weakness.

Outside medical oncology opinion suggested doxorubicin-based chemo with concurrent radiation. He got a second opinion at The University of Kansas Health System, suggesting front-line immunotherapy as the most thoughtful strategy due to previous insults and reduced performance status from stroke.

Methods: The second case is a 85 year old female with early stage right sided breast cancer treated with lumpectomy and radiation in 1999. In 2017, she noticed bruising on her right breast. By August 2018, mammogram showed 1.5cm mass. Needle biopsy confirmed radiation-induced angiosarcoma (AS). September 2018, she had mastectomy: 1.8cm high grade angiosarcoma with negative margins. Staging CT October 2018 noted multiple bilateral lung nodules up to 13mm. She opted to hold on any therapy over the holidays, but repeat CT January 2019 showed progression in lungs with recurrences along chest wall clinically. She started on sunitinib January 2019, with dose adjustments made due to poor appetite, acid reflux. Her lung metastases completely resolved within the first few months of therapy (image 2). By May 2020, she had recurrences along chest wall, with no obvious recurrence in lungs. She switched to paclitaxel 135mg/m² IV q3wks May 2020, after salvage surgery was considered.

Re-biopsy of palpable mass 7/24/20 showed tP53 alteration and a FLT4 mutation, as well as 3 other VUS. After 3 cycles of paclitaxel, CT 8/10/20 showed progression of chest wall masses as well as increase in a 5mm subpleural nodule. Therefore, we decided on pembrolizumab as next step.

I purposefully did not check PDL-1 status via IHC in either circumstance, as immunotherapy seemed to be the only reasonable option. I did not want confounding results to potentially influence the availability of trying the drug for each of the respective patients.

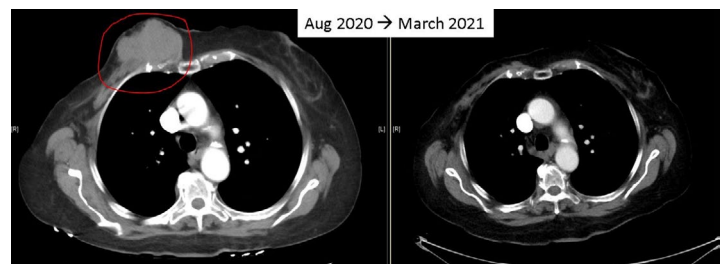
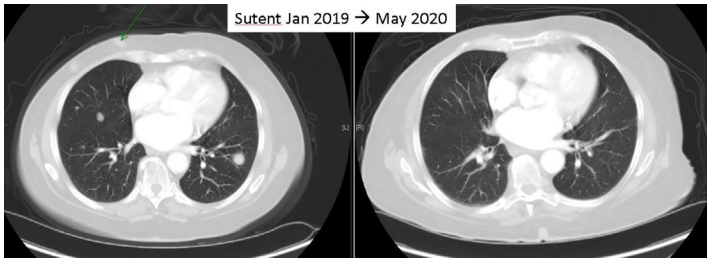
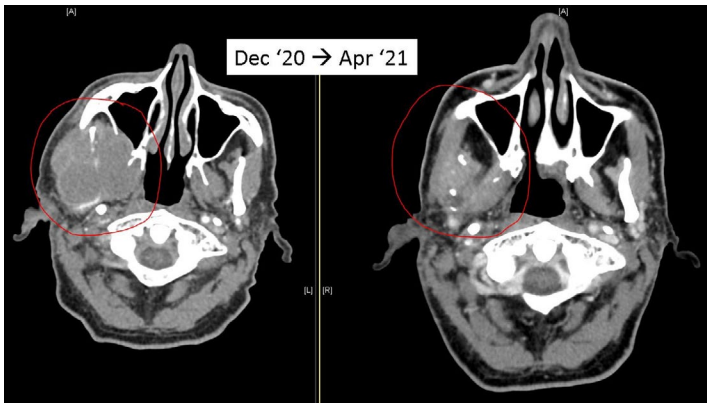
Results: For the man with the radiation-induced UPS, he received first dose of single-agent pembrolizumab 12/21/2020. Quickly, he was showing a really nice response clinically. First restaging scan in early April 2021 showed same response radiologically with a marked decrease in the R masticator mass (image 1). Pain, swelling, and trouble chewing are much better; in fact, he is totally off all opiates now. He has no major side effects; he has dry skin/rash that he uses steroid cream on with relief. We plan to switch him to every 6 week dosing as he is doing so well.

For the woman with radiation-induced AS, we switched therapy to pembrolizumab 200 mg IV every 3 weeks, first dose 9/2/2020. Within a week and a half of first dose, her medial chest wall mass erupted out of the skin, oozing and bleeding consistently (image 3). By second cycle, she revisited with radiation oncology and breast surgery to see if anything local could be done for palliation. She agreed to stereotactic body radiotherapy to the fungating mass, but even before she could get started, the mass started shrinking rapidly with more immunotherapy.

She "feels great", and despite getting COVID in the midst of this treatment, she has had no major complications from

either immunotherapy or virus. She does not need to keep any bandage or gauze on this area anymore, as there is really no visible/palpable mass left. We converted to every 6 week dosing of pembrolizumab in December 2020. She has no new masses on exam or on follow up CT scans (image 4).

Conclusion: We present deep responses from pembrolizumab in two radiation-induced sarcoma cases: one as front-line therapy in a male with UPS and borderline performance status due to stroke, second in the relapsed/refractory setting after an older woman failed anti-VEGF therapy and conventional taxane chemotherapy for her angiosarcoma. There is excitement amongst the sarcoma community to pursue an actual trial utilizing immunotherapy for these radiation-induced sarcomas (irregardless of subtype). No matter, we are already seeing the positive responses and improvement in quality of life utilizing pembrolizumab in these situations, and would encourage trying pembrolizumab for any of the radiation-induced sarcomas you may encounter.





Poster #154 #1818855

INTERIM SAFETY AND EFFICACY RESULTS FROM A PHASE 1/2 STUDY OF BA3011, A CAB-AXL-ADC, IN PATIENTS WITH ADVANCED SARCOMA OR OTHER SOLID TUMORS

Breelyn A. Wilky, MD¹; Mihaela Druta, MD²; Jordi Rodón, MD³; Anthony P. Conley, MD³; Gerald Falchook, MD⁴; Howard Burriss, MD⁵; Matthew Ingham, MD⁶; Inderjit Mehmi, MD⁷; Eric Sievers, MD⁸

¹University of Colorado School of Medicine, Aurora, CO, ²H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida, UNITED STATES, ³MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁴Sarah Cannon Research Institute at HealthONE, Denver, Colorado, UNITED STATES, ⁵Sarah Cannon Research, Nashville, Tennessee, UNITED STATES, ⁶New York Presbyterian Hospital/Columbia University Medical Center, New York, New York, UNITED STATES, ⁷The Angeles Clinic and Research Institute, A Cedars-Sinai Affiliate, Los Angeles, California, UNITED STATES, ⁸BioAtla, Inc., San Diego, California, UNITED STATES

Objective: BA3011 is a conditionally active biologic anti-AXL antibody-drug conjugate (CAB-AXL-ADC) being developed as an anticancer therapy for patients with advanced solid tumors. Conditional and reversible binding by CABs is designed to reduce off-tumor toxicity and immunogenicity, avoid tissue-mediated drug deposition, and improve pharmacokinetics (PK). AXL is a cell-surface transmembrane receptor protein tyrosine kinase highly expressed in several tumor types including sarcoma. Increased AXL expression has been associated with tumor resistance to chemotherapy, programmed death-1 (PD-1) inhibitors, molecular targeted therapy, and radiation therapy. In the current study, we sought to identify the safety profile, recommended Phase 2 dose (RP2D), and preliminary evidence of antitumor activity of BA3011 in patients with advanced sarcoma or other solid tumors.

Methods: Study BA3011-001 is an ongoing, multi-center, open-label, Phase 1/2 first-in-human trial of BA3011. In Phase 1, BA3011 is administered once (Q3W) or twice (2Q3W) every 3 weeks via intravenous (IV) infusion. Phase 2 is an open label assessment of the efficacy and safety of BA3011 alone and in combination with a PD-1 inhibitor in patients with AXL-expressing tumor membrane percent score (TmPS) ≥ 50 with advanced refractory sarcoma who have measurable disease and documented progression. Interim Phase 1 data from this study are described here.

Results: In Phase 1, a total of 60 subjects have received BA3011 at dose levels from 0.3 to 3.0 mg/kg Q3W, and 1.2 to 1.8 mg/kg 2Q3W, including 22 subjects with sarcoma. Of the first 75 sarcoma patients screened for AXL tumor membrane expression, approximately 50% had a TmPS ≥ 70 . No clinically meaningful on-target toxicity was observed, with a low rate of constipation. Dose-limiting toxicities were limited to monomethyl auristatin E (MMAE) conjugate-associated toxicity at the highest dose tested, including reversible neutropenia. In Phase 1 sarcoma subjects, treatment-emergent adverse events (TEAEs) in 2 (9.1%) subjects led to treatment discontinuation (Table 1). Eight subjects had grade 3 related TEAEs and 1 subject had grade 4, which generally were MMAE related, including reversible myelosuppression, transient liver enzyme elevations, and some metabolic disturbances (hypokalemia, hyponatremia) (Table 2). Transient grade 1-2 liver enzyme elevations seen during cycle 1 treatment generally did not re-occur upon re-treatment. The RP2D was determined to be 1.8 mg/kg Q2W based on an integrated evaluation of Phase 1 data, including PK modeling. The PK profile of BA3011 was approximately dose proportional; in Phase 1 the half-life was determined to be approximately 4 days. BA3011 antitumor activity that correlated with AXL tumor membrane expression was observed in sarcoma subjects. Confirmed partial responses were demonstrated in 4 sarcoma subjects (2 with undifferentiated pleomorphic sarcoma, 1 with leiomyosarcoma, and 1 with Ewing sarcoma) treated with BA3011 at the RP2D dose of 1.8 mg/kg (Q3W; 2Q3W), with all having TmPS ≥ 70 (Figure 1). Phase 1 sarcoma subjects had on average failed 4 prior lines of therapy. Durability of response in sarcoma subjects at the RP2D dose in this ongoing study is demonstrated in Figure 2.

Conclusion: Based on preliminary efficacy and safety results from this study, the benefit-risk profile of BA3011 monotherapy appears to be favorable in subjects with sarcoma. No clinically meaningful on-target toxicity was observed. In Phase 1 sarcoma subjects, evidence of antitumor activity was observed, with higher AXL tumor membrane expression correlating with response. These results suggest focused enrollment of patients with high levels of AXL tumor membrane expression may result in increased clinical benefit. AXL appears to be expressed at a consistent rate throughout all sarcoma subtypes tested; a larger sample size for some subtypes is required to confirm these findings. Phase 2 is ongoing in subjects with AXL-expressing advanced refractory sarcoma.

Table 1: Overview of Adverse Events – Sarcoma Subjects in Phase 1

Characteristic	BA3011 0.3 mg/kg (Q3W) (N=1)	BA3011 1.8 mg/kg (Q3W) (N=2)	BA3011 2.4 mg/kg (Q3W) (N=2)	BA3011A 1.2 mg/kg (2Q3W) (N=2)	BA3011A 1.8 mg/kg (2Q3W) (N=15)	Total (N=22)
Any TEAE	1 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	15 (100.0)	22 (100.0)
TEAE with CTCAE grade 3 or 4	0	1 (50.0)	1 (50.0)	2 (100.0)	10 (66.7)	14 (63.6)
Related TEAEs with CTCAE grade 3 or 4	0	0	1 (50.0)	0	8 (53.3)	9 (40.9)
Any serious TEAE	0	1 (50.0)	1 (50.0)	0	7 (46.7)	9 (40.9)
Any related serious TEAE ^a	0	0	0	0	2 (13.3)	2 (9.1)
TEAE leading to treatment discontinuation	0	0	0	0	2 (13.3)	2 (9.1)
Related TEAE leading to treatment discontinuation ^b	0	0	0	0	2 (13.3)	2 (9.1)
Death related to TEAE	0	0	0	0	0	0

Abbreviations: CTCAE = Common Terminology Criteria for Adverse Events; Q3W = every 3 weeks; TEAE = treatment-emergent adverse event

^a Related serious TEAE: Gastritis, CTCAE Grade 2; Hepatic encephalopathy, CTCAE Grade 2

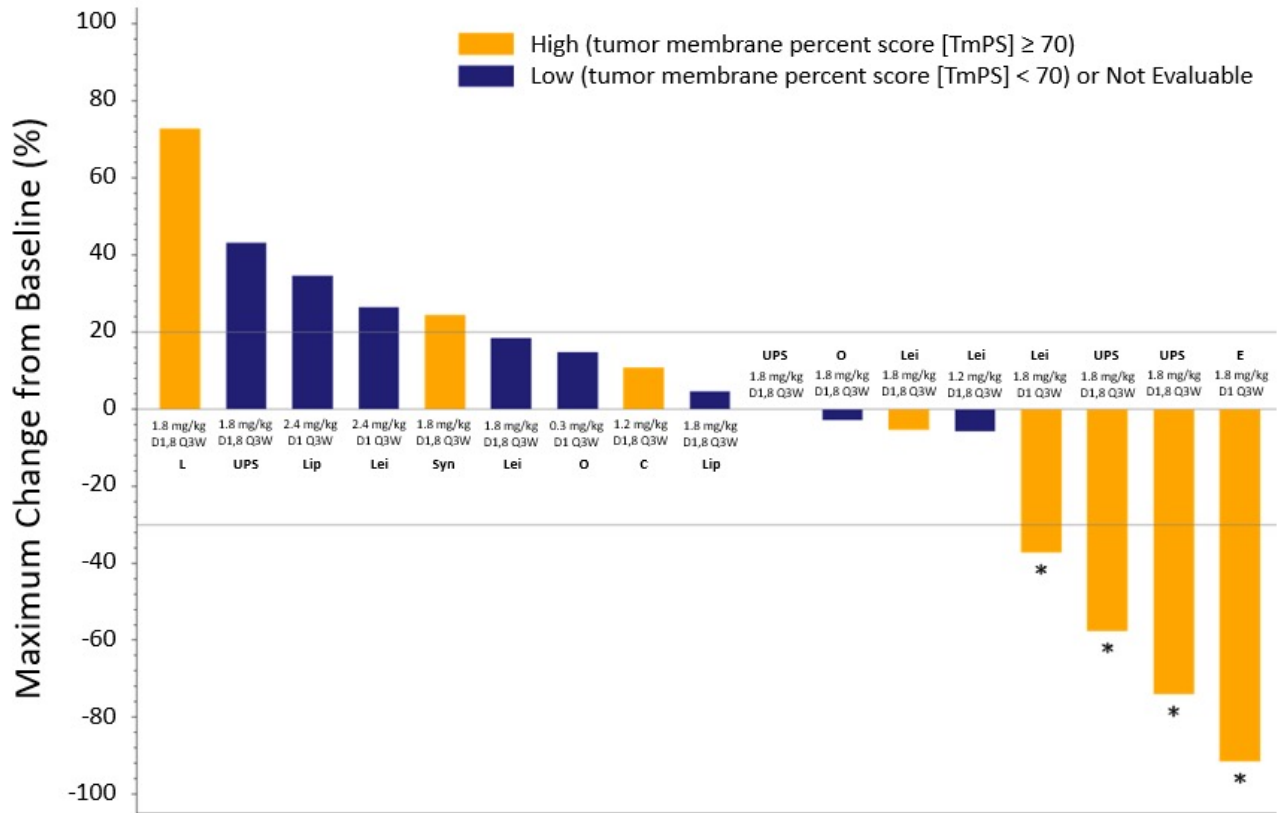
^b Neuropathy peripheral, CTCAE grade 2; fatigue, CTCAE grade 2

Table 2: Most Frequent Related Treatment-Emergent Adverse Events (≥ 20%, All Grades) or Any Related Grade 3/4 Events – Sarcoma Subjects in Phase 1

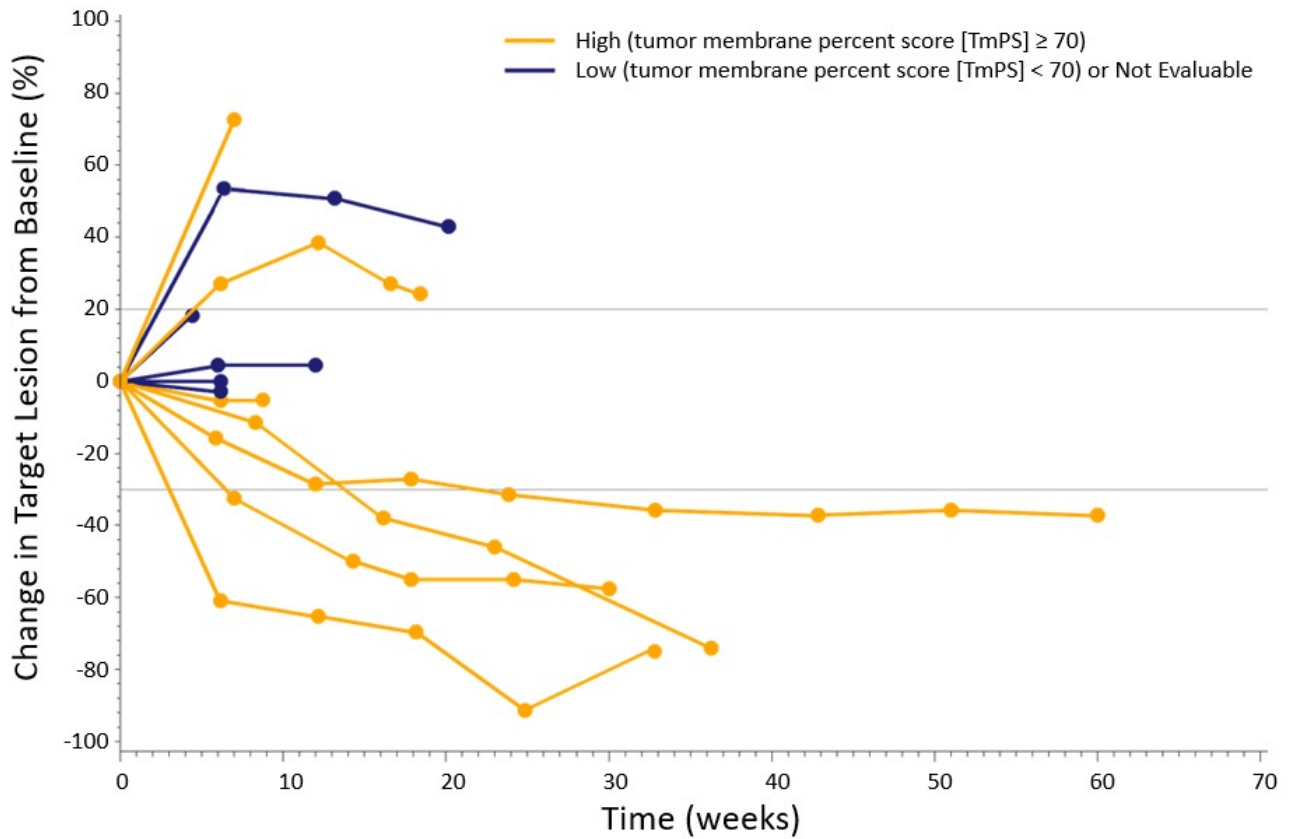
Preferred Term	Related TEAEs		
	All Grades n (%)	Grade 3 n (%)	Grade 4 n (%)
Number of subjects with at least one TEAE (N=22)	19 (86.4)	8 (36.4)	1 (4.5)
Fatigue	9 (40.9)	0	0
Nausea	9 (40.9)	1 (4.5)	0
Alanine aminotransferase increased	8 (36.4)	0	0
Aspartate aminotransferase increased	10 (45.5)	1 (4.5)	0
Diarrhoea	5 (22.7)	0	0
Vomiting	5 (22.7)	1 (4.5)	0
Alopecia	5 (22.7)	0	0
Neuropathy Peripheral ^a	5 (22.7)	0	0
Anemia	1 (4.5)	1 (4.5)	0
Hypokalaemia	2 (9.1)	2 (9.1)	0
Neutropenia	2 (9.1)	1 (4.5)	1 (4.5)
Blood bilirubin increased	1 (4.5)	1 (4.5)	0
Febrile neutropenia	1 (4.5)	1 (4.5)	0
Neutrophil count decreased	1 (4.5)	1 (4.5)	0
Stomatitis	1 (4.5)	1 (4.5)	0

^a All events Grade 1-2, related

Abbreviations: CTCAE = Common Terminology Criteria for Adverse Events; Q3W = every 3 weeks; TEAE = treatment-emergent adverse event



* = confirmed Partial Response/Complete Response
 Q3W = Day 1 every 3 weeks; 2Q3W = Days 1,8 every 3 weeks
Sarcoma type: C = chondrosarcoma; E = Ewing sarcoma; Lei = leiomyosarcoma; Lip = liposarcoma; O = osteosarcoma; Syn = synovial sarcoma;
 UPS = undifferentiated pleomorphic sarcoma





Poster #155 #1818902

METHODS FOR EXTRACTION AND EXPANSION OF TUMOR-INFILTRATING LYMPHOCYTES FROM HUMAN SARCOMA CORE NEEDLE BIOPSIES AND RESECTED TISSUE

Cristiam Moreno Tellez, MD¹; Kyle Powers, BS²; Allison Christians, BA²; Jing Liu, PhD²; Brian A. Van Tine, MD, PhD³; Jacqui Toeniskoetter⁴; Eduardo Davila, PhD²; Breelyn A. Wilky, MD²

¹University of Colorado School of Medicine, Parker, Colorado, UNITED STATES, ²University of Colorado School of Medicine, Aurora, Colorado, UNITED STATES, ³Washington University School of Medicine, St. Louis, Missouri, UNITED STATES, ⁴Washington University, St. Louis, Missouri, UNITED STATES

Objective: Immunotherapies, including chemotherapy combinations with immune checkpoint inhibitors (ICIs), are increasingly being studied in sarcomas with a subset of patients achieving meaningful and durable responses. However, biomarkers of response and resistance are still under investigation. The presence of tumor-infiltrating lymphocytes (TIL), including T cells, B cells and natural killer cells, have been associated with improved responses to ICIs. However, most trials utilize small core needle biopsies which limits our ability to perform in-depth TIL phenotyping and functional assays. Additionally, the requirement for fresh tissue and viable TIL creates a logistical challenge for multi-institution trials shipping correlative samples. The ability to expand TIL populations would allow for multiplex flow cytometry, single cell RNA sequencing, and functional assays to better understand the inflammatory and suppressive TIL phenotypes that may dictate response and resistance mechanisms to immunotherapy combinations. We sought to establish an efficient protocol to extract and expand TILs from sarcoma tissue samples with minimum surface protein modification, even when biopsies were obtained from other centers and shipped to our laboratory. We aimed to optimize TIL numbers and viability to permit downstream phenotyping assays.

Methods: Core needle biopsies were obtained from soft tissue sarcoma patients participating on two IRB-approved clinical trials, NCT04028063, and NCT04551430. Additional fresh tissue was obtained from patients undergoing routine surgical procedures on our IRB-approved tumor banking protocol. Tissue specimens obtained at University of Colorado were transferred to our laboratory from the operating room (OR) or biopsy suite in RPMI media plus 10% fetal bovine serum (FBS) with antibiotics and antifungals for OR specimens. Subjects on NCT04551430 were biopsied at Washington University with samples shipped overnight in RPMI/10% FBS, with the average time from collection to culture of 20 hours. Single biopsy cores or 3 mm³ sections of bulk tumor were plated in individual wells of a 24 well plate with 1.2 mL of TIL media, consisting of AIMV media, 10% human serum, 1% Penicillin/Streptomycin, 1X Glutamaxx, Normocin 50ug/ml plus 6000 IU of human interleukin-2 (IL-2). Samples were incubated at 37 degrees Celsius with 5% CO₂ with media changes every 2-3 days and fresh IL-2 added every other day. Visual inspection was performed daily, and once samples were 80% confluent, the TIL and any adherent tumor cells were resuspended and split into additional wells. Once the TIL were maximally expanded (day 15-20), they were counted and cryopreserved in liquid nitrogen. For later analysis, samples were thawed, revived for 24 hours in TIL media, and then used for downstream assays including flow cytometry.

Results: To date, we have attempted TIL culture and expansion on 23 core needle biopsies and 8 fresh tumors from surgical resections, with successful TIL cultures for 20 core biopsies (86.9%) and 6 fresh tumors (75%). TIL culture was successful from a variety of sarcoma subtypes (Table 1). After approximately 20 days of culture, the average number of TIL obtained from core biopsies was 8.8 million (range 100,000 to 30 million), and from surgical specimens the average number of TIL was 9.8 million (range 5-40 million). While yields were better with freshly obtained tissues from our institution, which were processed within 2 hours, the majority of samples shipped overnight from an outside center still yielded sufficient TIL for downstream assays. Phenotyping by multiplex flow cytometry to compare initial vs. expanded TIL populations is ongoing, and representative results will be presented at the meeting.

Conclusion: We have demonstrated an effective method to expand TIL from small amounts of tumor tissue, even with delayed processing in a variety of soft tissue sarcomas. This approach will facilitate critical correlative studies to better understand the immune microenvironment in sarcomas treated with immunotherapy.

Table 1. Expansion of tumor-infiltrating lymphocytes.

SAMPLE ID	SARCOMA SUBTYPE	NUMBER OF TIL AT CRYOPRESERVATION (MILLIONS)
NCT04028063 (Doxorubicin + PD1/CTLA4), core needle biopsies		
DCI 010-TX	Pleomorphic liposarcoma	20
DCI 011-BL	Leiomyosarcoma	15
DCI 012-TX	Angiosarcoma	30
DCI 013-BL	Leiomyosarcoma	30
DCI 013-TX	Leiomyosarcoma	25
DCI 014-BL	Dedifferentiated liposarcoma	0
DCI 014-TX	Dedifferentiated liposarcoma	6
DCI 015-BL	Dedifferentiated liposarcoma	0
DCI 015-TX	Dedifferentiated liposarcoma	2
DCI 016-BL	Angiosarcoma	30
DCI 016-TX	Angiosarcoma	1
DCI 017-BL	Leiomyosarcoma	4
DCI 018-BL	Endometrial stromal sarcoma	0.5
NCT04551430 (Cabozantinib with or without ipilimumab/nivolumab), core needle biopsies, shipped from Washington University)		
WUI-002 - TX	blinded	15
WUI-003- TX	blinded	0.1
WUI-004- TX	blinded	0.1
WUI-005- TX	blinded	0
WUI-006- TX	blinded	1
WUI-007- TX	blinded	1
WUI-008- TX	blinded	1
WUI-009- TX	blinded	6
WUI-013- TX	blinded	8
WUI-015- TX	blinded	8
Fresh tumor specimens obtained from surgical resections (University of Colorado Hospital)		
CU SARC 01	UPS	0
CU SARC 06	Dedifferentiated liposarcoma	6
CU SARC 07	GIST	10
CU SARC 14	Myxofibrosarcoma	5
CU SARC 16	DSRCT	0
CU SARC 17	Low grade myxofibrosarcoma	9
CU SARC 18	UPS	8.5
CU SARC 39	MPNST	40

Abbreviations: TX, (on treatment); BL, (baseline); UPS, (undifferentiated pleomorphic sarcoma); DSRCT (desmoplastic small round cell tumor); GIST, (gastrointestinal stromal tumor), MPNST (Malignant peripheral nerve sheath tumor).



Poster #156 #1818934

CHARACTERIZATION OF TUMOR INFILTRATING IMMUNE CELLS FROM ADULT SOFT TISSUE SARCOMAS

Jacky H.K Chen, HBSc¹; Jay S. Wunder, MSc., MD²; Kim M. Tsoi, MD, PhD³; Nalan Gokgoz, PhD²; Irene L. Andrulis, PhD²,
¹Lunenfeld Tanenbaum Research Institute, Mount Sinai Hospital, Toronto, Ontario, CANADA, ²The Lunenfeld-Tanenbaum Research Institute, Toronto, Ontario, CANADA, ³University of Toronto, Mount Sinai Hospital, Toronto, Ontario, CANADA

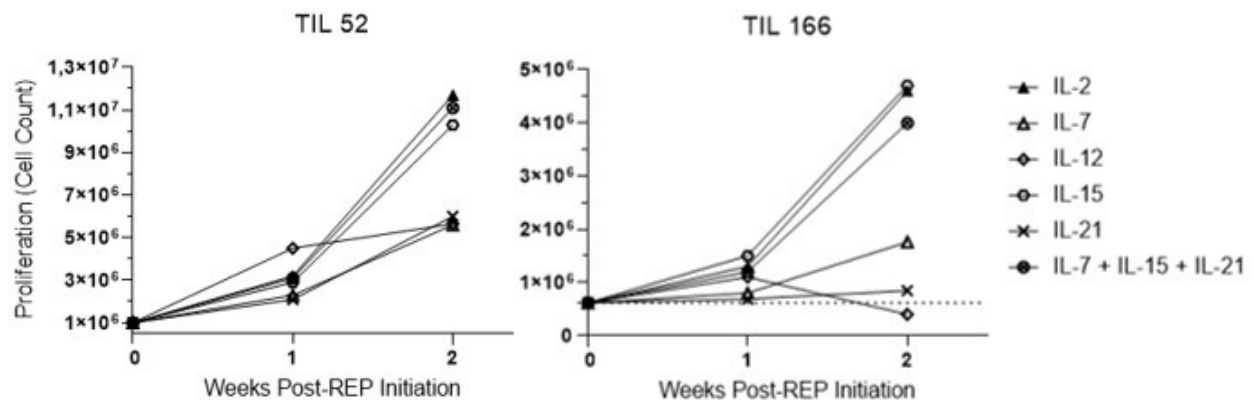
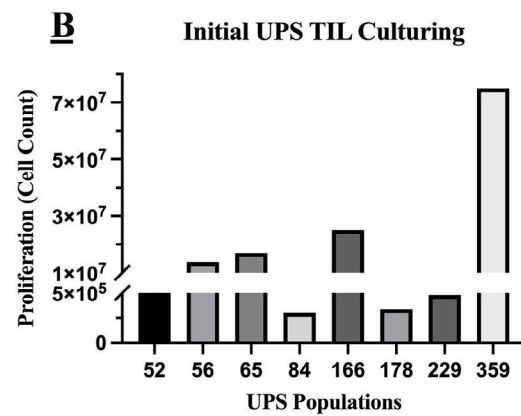
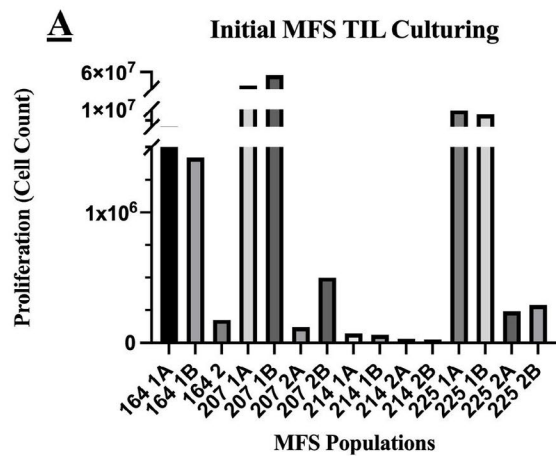
Objective: Sarcoma is a group of rare soft tissue and bone tumors with over 50 distinct subtypes. The survival rate ranges widely due to the lack of efficacious treatments. Immunotherapy, such as adoptive cell therapy (ACT), has drawn profound interest due to its minimal toxicities. In ACT, tumor infiltrating lymphocytes (TILs) are isolated from patients, expanded, and autologously infused back. Clinical responses vary across patients and subtypes, and further research is necessary to improve ACT. We recently observed TILs in Undifferentiated Pleomorphic Sarcoma (UPS) and Myxofibrosarcoma (MFS), and that PD-L1 overexpression is correlated with better clinical outcomes in UPS but not MFS. The Th1 anti-tumoral inflammatory pathway was identified to be highly activated in the former cohort, which may explain the favorable outcome. These results illustrate the differences where TILs may play a critical role. We hypothesize that there are phenotypic and functional differences between TILs of UPS with differential PD-L1 expression that may be related to clinical outcomes. However, sarcoma TILs are rare and challenging to culture, which significantly impedes their studies. We first aim to robustly expand sarcoma TILs to sufficient numbers.

Methods: TILs were expanded and cultured from 4 MFS and 8 UPS primary tumors with various PD-L1 expression, determined by RT-qPCR (Fig 1). We optimized the traditional tumor fragment (TF) protocol, initially developed by the Rosenberg group, to expand rare sarcoma TILs. Cryopreserved bulk tumors were revitalized, fragmented into 1mm³, and seeded at one fragment per well in 2 mL of complete media (CM; IMDM with 6000 IU/mL of IL-2) for two weeks. TILs were maintained in their individual wells to promote the diversity of TCR clones. The rapid expansion protocol (REP), integral step in ACT following the TF protocol, was modified to use anti-CD3/CD28 magnetic Dynabeads to expand TILs further. During REP, TILs were co-treated with gamma-chain cytokines (IL-2, 7, 15, 21). Flow cytometry panels were developed to evaluate TIL phenotype, cytotoxicity, and intracellular cytokine production.

Results: We previously expanded TILs from the four MFS cases via the original TF protocol with four weeks of culturing in CM. Of the 15 MFS TIL populations derived, only 40% achieved sufficient cells (1x10⁶) for analysis (Fig 2A). Our optimized TF protocol expanded TILs from 8 UPS cases with a 62.5% success rate (Fig 2B), further enhanced to 87.5% with our modified Dynabead REP treatment (data not shown). UPS TILs were further stimulated with REP and various gamma-chain cytokine treatments (Fig 3). In traditional ACT, IL-2 is used to promote TIL proliferation. However, prolonged culturing with IL-2 is known to cause activation-induced cell death, problematic in clinical treatments. We demonstrated that alternative treatments with a cocktail (IL-7, 15, and 21) or IL-15 alone could achieve TIL proliferation comparable to that of IL-2. Additionally, we previously performed an unbiased large-scale cytokine screening of TILs and detected proteins of interest, including CXCL9, Angiogenin, and TGF-Beta (data not shown). To identify the cellular sources of cytokines amongst heterogeneous TILs, we developed flow panels to extensively characterize the phenotype and function of our expanded TILs (Fig 4).

Conclusion: Sarcoma infiltrates are difficult to culture and their roles remain largely unstudied. By optimizing the TF protocol in conjunction with anti-CD3/CD28 treatments, we developed a robust in vitro pipeline to expand rare sarcoma TILs for downstream characterization. We also demonstrated that alternate gamma chain cytokines may effectively replace IL-2 during TIL expansion. Future phenotypic and functional evaluation of UPS TILs, with our customized flow panels, would elucidate the role of differential tumor-PD-L1 expression on UPS patient's pathology. These findings would inform the implementation of ACT for sarcoma treatments.

MFS Cases	PD-L1/STAM2	UPS Cases	PD-L1/STAM2
TIL164	0.43	TIL 52	0.1
TIL207	0.094	TIL 56	0.81
TIL214	0.37	TIL 65	0.52
TIL225	0.143	TIL 84	0.16
		TIL 166	3.25
		TIL 178	2.49
		TIL 229	0.26
		TIL 359	n/a



Fluorophore	Panel #1	Panel #2	Panel #3	Panel #4
FITC	FOXP3	CD163	FOXP3	CD163
PerCP-Cy5.5	CD62L	GATA3	IL-8	IL-8
PE	Ly108/CD352	CD206	IL-5	Osteopontin
PE-CF594	CD69	CD45	IL-6	CD45
PE-Cy7	CTLA-4	CD11c	GATA3	CD68
APC	CD25	LFA-1	CXCL9	CXCL9
Alexa700	CD4	CD4	TGF-B1,2,3	TGF-B1,2,3
APC-Cy7	CD45	CD14	CD45	CD45
BV421	T-bet	HLA-DR	CCL4	CD86
eF506	viability	viability	viability	viability
BV605	PD-1	VLA-4	CD4	Angiogenin
BV711	TIM3	CD40	T-bet	IL-13
BV711	CD45RO	CD56	IL-13	n/a
BV786	CCR7	CD68	IL-10	IL-10
BUV395	CD3	CD3	CD3	CD3
BUV496	CD8	CD8	CD8	CD56
BUV737	CD45RA	CD86	IFN- γ	IFN- γ



Poster #157 #1818910

DETERMINING THE CONTRIBUTIONS OF PD-L1 AND CO-EXPRESSED GENES TO THE UPS ANTI-TUMOUR MICROENVIRONMENT

Victoria S. Coward¹; Maisha Syed, MSc²; Nalan Gokgoz, Ph.D²; Jay S. Wunder, MSc., MD²; Irene L. Andrulis, PhD²
¹The Lunenfeld-Tanenbaum Research Institute, Toronto, Ontario, CANADA, ²The Lunenfeld-Tanenbaum Research Institute, Toronto, Ontario, CANADA

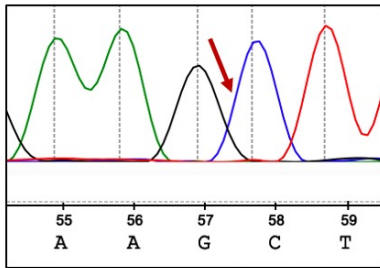
Objective: Sarcoma is arguably the most heterogeneous group of cancers with over 50 subtypes and as a result, survival rates have remained relatively stagnant in recent decades. Sarcoma treatment strategies rely on surgical resection, meaning immunotherapy interventions applied to other malignancies are largely underutilized. Some adult soft tissue sarcoma cases showed positive results in a clinical trial of the Programmed Cell Death 1 Receptor (PD-1) inhibitor, Pembrolizumab, but it is unknown why some patient did not show a response¹. Wunder et al. demonstrated that a subset of Undifferentiated Pleiomorphic Sarcoma (UPS) cases harboured tumour-infiltrating lymphocytes (TILs), expressed high levels of PD-1 ligand (PD-L1) RNA and had positive clinical outcomes². This was not found in the Myxofibrosarcoma (MFS) subtype. Through RNA-sequencing, a list of differentially expressed genes between UPS cases with high and low PD-L1 expression was determined. Genes in the Th1 and dendritic cell (DC) maturation pathway were significantly active within this list. We hypothesize that tumour-related genes from the Th1 and DC maturation pathway may be related to an anti-tumour microenvironment. Our aims are to create and characterize patient-derived cell cultures to identify the potential roles of Th1 and DC maturation pathway genes in tumour-immune interactions by examining the functional differences in cytokine and chemokine output.

Methods: Sarcoma specimens from untreated patients undergoing open biopsy or surgical resection have been collected for the isolation of both tumour cells and the respective TILs. Various dissociation and tumour culturing protocols were optimized for each case, and methods were tested on multiple subtypes. Cultured UPS cells were validated as tumor cells using whole exome sequencing (WES) to confirm that the cells reflected the patient samples. The gene expression of PD-L1 and genes of interest in bulk tumour and cultured cells were investigated using qPCR. An exploratory cytokine blot was used to identify what chemical messengers may be secreted by UPS cell lines. After further quantification, the functional differences in the tumour-secreted cytokines will be determined via immune cell migration assays that use cell line-conditioned media and CD3+ cells. Migration of immune cells will be analyzed through enumeration and flow cytometry.

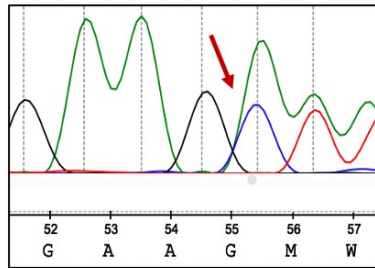
Results: Due to the heterogeneity of sarcoma the optimal culturing conditions were variable, therefore techniques were optimized on a case-specific basis. This project utilizes viably-preserved tumour samples dissociated into small fragments. The fragments are plated in various culture conditions and the systems that yield a successful culture used going forward. Of 27 attempted cases (UPS n=14 and MFS n=13), 21 showed growth beyond passage 5. WES of bulk tumour, patient blood and cell line DNA confirmed that the cultured cells reflected the patient sample (Figure 1). In accordance with Wunder et al. 2020, bulk tumours had Th1 pathway genes co-expressed with PD-L1 when assayed by qPCR. Finally, differences in cytokine secretion between different UPS cell lines were identified and are currently being quantified using a Luminex assay (Figure 2).

Conclusion: A subset of resected patient samples can form successful cell cultures and reflect molecular characteristics of the original patient sample. Bulk UPS tumours co-express PD-L1 and Th1 pathway genes in both RNA-sequencing and qPCR experiments. Further, UPS cell lines have unique cytokine secretion profiles. Future experiments will explore if PD-L1 and co-expressed genes in UPS cells contribute to these different cytokine profiles, which could suggest tumour-driven microenvironment conditions. By creating a model, characterizing it, and assessing the functional consequences of tumour-derived cytokine secretions, we aim to illustrate how tumour-directed interactions may shape the UPS microenvironment.

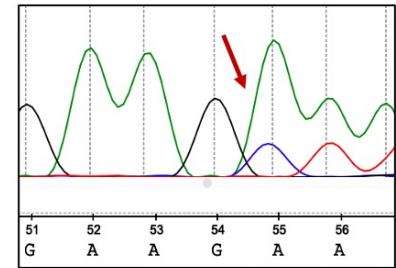
(RT#) Case	Subtype & PD-L1 Status	Gene Symbol	Variation	VAF	Tumour AD (Ref/Alt)	Effect
(RT-3220) TIL 18	UPS PD-L1 High	ATRX	4837_4842	0.467	9/11	nonframeshift deletion



ATRX from Patient Blood



ATRX from Patient Bulk Tumour



ATRX from Cultured Cell Line

Cytokines	24hrs			48hrs		
	PD-L1 low		PD-L1 high	PD-L1 low		PD-L1 high
	STS148	TIL 84	STS162	STS148	TIL 84	STS162
Osteoprotegerin	6.27	2.21	0.71	10.06	3.46	1.02
IL-10	1.62	2.47	0.46	2.73	-1.82	0.52
TNF-b	1.21	2.99	0.65	0.83	4.32	0.74
CCL24	1.12	3.68	0.95	0.65	0.72	1.15
IL-5	1.35	0.44	2.28	-0.01	1.21	3.05
PDGF-BB	0.94	2.03	2.84	0.61	2.35	2.76
EGF	1.25	2.35	0.76	0.70	2.30	0.77
CXCL7	1.42	2.13	0.78	0.63	0.92	0.76
CXCL1	1.48	2.73	1.35	1.62	6.41	1.74
IL-2	0.70	0.59	1.36	0.88	0.88	1.92
FGF-6	0.58	0.03	1.02	0.40	1.06	1.57
IGFBP-2	1.31	1.50	0.73	0.70	0.69	0.89
CCL7	1.45	0.92	0.56	1.62	0.76	1.10
NT-3	1.63	1.19	0.78	1.30	0.49	0.77
Oncostatin M	0.88	2.06	0.84	0.53	2.81	1.13
IGFBP-4	1.41	1.70	0.99	0.74	1.56	1.29
CCL13	0.57	0.52	1.11	0.28	0.19	0.97
Flt-3L	0.37	0.87	1.17	0.22	0.61	1.45
CCL23	0.87	1.71	0.76	0.66	0.64	1.08
HGF	0.61	2.06	0.83	0.22	1.20	1.30
CXCL9	0.89	1.52	0.70	0.48	3.16	1.23



Poster #158 #1818970

DESMOID TUMOR AND MOLECULAR TESTING FROM PATIENT REPORTED DATA IN AN INTERNATIONAL NATURAL HISTORY STUDY

Maneesh Kumar, MD, PhD¹; Danielle Braggio, PhD, BCMAS²; Amanda L. Lucas³; Lynne Hernandez⁴; Kelly Mercier, PhD⁵
¹Desmoid Tumor Research Foundation, Cedar Rapids, Iowa, UNITED STATES, ²Desmoid Tumor Research Foundation, Houston, Texas, UNITED STATES, ³Desmoid Tumor Research Foundation, Jacksonville Beach, Florida, UNITED STATES, ⁴Desmoid Tumor Research Foundation, Philadelphia, Pennsylvania, UNITED STATES, ⁵Desmoid Tumor Research Foundation, Cary, North Carolina, UNITED STATES

Objective: Desmoid tumors (DTs) are commonly associated with mutations in the CTNNB1 gene (sporadic DTs) or the APC gene (Familial adenomatous polyposis (FAP)-related DTs). Although mutational testing is recommended to confirm diagnosis and guide treatment by a consensus of DT experts, it is not clear to what extent testing is performed. Patient reported data are described here for those participants who have reported receiving mutational testing.

Methods: The web-based natural history study launched September 2017 in collaboration with the National Organization of Rare Disorders. It contains 15 surveys covering diagnostics, disease, treatment, care management, and quality of life. Independence testing was performed using Pearson's chi squared test.

Results: Of the 696 participants that have consented and started surveys, 302 have completed the surveys pertaining to molecular testing. Ninety-five (31%) report mutational testing and 188 report not having had mutational testing (62%), Male participants tended to have had molecular testing more often than female participants (38% of male vs. 28% of female) but was not statistically significant. American Indian or Alaska Natives had the lowest rate of molecular testing (0/3). Seventy percent (7/10) of Black or African American participants did not have molecular testing, while 167/261 (64%) of White participants did not have molecular testing. Although not reaching statistical significance, this data suggests that molecular testing is low across all races but may be disproportionately lower in American Indian or Alaska Native and Black or African American populations. This may be attributed to an unbalanced race population in the study, along with access to testing. Chest wall and abdominal wall tumors were the least likely to have mutational testing performed (28% for each) while intra-abdominal tumors the most likely (43%). Molecular testing for intra-abdominal tumors may be higher than others because they are more commonly associated with FAP-related DTs. Misdiagnosis rates were similar across those with mutational testing and those without. It is not clear, however, if the mutation information assisted in the eventual DT diagnosis. Taken together, it does not appear that mutational testing is used heavily in diagnosis at this time. Specific mutations of the CTNNB1 have been identified in DTs (include 41A, 45F, and 45P mutations). In this data, 28 participants reported the status of the CTNNB1 gene: five were wildtype and 23 had a mutation. The specific mutation did not correlate with recurrence or with response to surgery. However, it appears that a mutation in the CTNNB1 gene does increase recurrence as compared to wildtype and continued growth following surgery.

Conclusion: DTs are most common in women with a median incidence of 30-40 years. They are associated with mutations in the CTNNB1 and APC genes but mutational testing is not often provided, although it is the current recommendation. Natural history studies are an important tool to assess this rare tumor population. American Indian or Alaska Native and Black or African Americans may receive fewer mutational testing than white participants. However, due to lack of diversity in the study population this difference is not statistically significant. Similarly, due to a small sample size, CTNNB1 mutations may indicate poor response to surgery and increased recurrence, but more data is needed.

		Has the Participant had any genetic or molecular testing?		
		Yes	No	Unknown or No Response
Gender (n = 302)				
	Male	35 (38%)	49 (54%)	7 (8%)
	Female	58 (28%)	139 (67%)	12 (6%)
	Transexual	2 (100%)	0 (0%)	0 (0%)
Race (n = 302)				
	American Indian or Alaska Native	0 (0%)	3 (100%)	0 (0%)
	Asian	3 (75%)	0 (0%)	1 (25%)
	Black or African American	2 (20%)	7 (70%)	1 (10%)
	Other	2 (40%)	3 (60%)	0 (0%)
	Refused or No Response	4 (21%)	8 (42%)	7 (37%)
	White	84 (32%)	167 (64%)	10 (4%)
Misdiagnosed (n = 284)				
	Yes	40 (35%)	70 (61%)	4 (4%)
	No	52 (31%)	107 (64%)	7 (4%)
	Unknown or No Response	0 (0%)	2 (50%)	2 (50%)

Table 1. Demographics of participants who have responded to the molecular diagnostics questions. There are no significant differences between the sexes or races of those who have reported receiving molecular testing of their tumors. However, men and white participants tend to have higher rates of molecular testing. Additionally, there are no significant differences in the participants who reported being misdiagnosed initially to those who received a correct diagnosis.



Poster #159 #1818874

IS MOH'S MICROGRAPHIC SUGERY REALLY SUPERIOR TO WIDE LOCAL EXCISION FOR DERMATOFIBROSARCOMA PROTUBERANS (DFSP)? A MULTICENTER INTERNATIONAL STUDY

Matthew T. Houdek, MD¹; Kim M. Tsoi, MD, PhD²; Katerine Mallett, MD¹; Matthew R. Claxton, BS¹; Sarah Almubarak, BS²; Peter C. Ferguson, MD²; Peter S. Rose, MD¹; Jay S. Wunder, MD²

¹Mayo Clinic, Rochester, Minnesota, UNITED STATES, ²University of Toronto, Mount Sinai Hospital, Toronto, Ontario, CANADA

Objective: Dermatofibrosarcoma protuberans (DFSP) is a rare soft tissue sarcoma. It has been found to be a locally aggressive tumor, with a very low rate of metastatic disease. Previous series have shown a potential superiority of Moh's micrographic surgery (MMS) compared to wide local excision (WLE), however those series were flawed in their study design by including patients with locally recurrent DFSP and those with fibrosarcomatous transformation into a single group. As such the purpose of the current series was to compare the outcome of patients undergoing WLE to MMS presenting with primary DFSP.

Methods: We reviewed 233 (113 female, 120 male, mean age of 41±15) patients undergoing Mohs micrographic surgery (n=80, 34%) or traditional excision (n=153, 66%) to treat a primary DFSP of the trunk (n=97, 42%), upper extremity (n=71, 30%), or lower extremity (n=65, 28%) at two tertiary sarcoma centers between 1991 and 2018. Eight (3%) received radiotherapy, either preoperative (n=6), postoperative (n=1), and intraoperatively (n=1). 178 (76%) patients had a history of a previously inadvertently excised primary tumor. Mean tumor size was 4±2 cm. Mean postoperative follow up was 6 (range 2-28 years). In the WLE group, margins were negative in 144 (94%) and microscopically positive in 9 (6%). In the Moh's group, 1 patient had a residual microscopically positive margin which needed to be cleared with a WLE. In addition it the Moh's group required a mean of 2±1 layers to reach a negative margin.

Results: There was no difference (p>0.05) in the baseline characteristics in terms of patient age, gender, tumor size or history of a previous inadvertent excision between patients who underwent an WLE and those who underwent a MMS. Following excision there was 1 local recurrence occurring at 4-years postoperative which occurred in the MMS group, while there were 2 cases of distant disease recurrence occurring in WLE group at 2- and 3-years postoperative. The 5-year local recurrence free survival was 100% in the WLE group and 98% in the MMS group (p=0.16). The 5-year metastatic free survival was 98% in the WLE group and 100% in the MMS group (p=0.29). There was 1 death due to disease in the WLE group at 4-years postoperative.

Complications occurred in 25 (11%) patients, with no difference (p=0.37) in the incidence of complications between patients treated with a WLE (n=14, 9%) and MMS (n=11, 14%). The most common complications were wound complications (n=14, 6%), with no difference (p=0.77) in the incidence of wound complications between WLE (n=10, 7%) and MMS (n=4, 5%). In the Moh's group 7 (9%) patients required an additional surgical procedure for wound closure or coverage which required a separate anesthetic.

Conclusion: Contrary to previous series, there was no difference in oncologic outcome comparing MMS or WLE. The goal of treatment for DFSP is to achieve a negative margin and with this local recurrence is very low.

Table 1

Preoperative Characteristic	Wide Local Excision (n=153)	Moh's (n=80)	P Value
Patient Age	41±15 years	43±16 years	0.63
Male Gender	81 (53%)	39 (49%)	0.58
Female Gender	72 (47%)	41 (51%)	0.58
Tumor Size	4±2 cm	4±2 cm	0.77
Previous Inadvertent Excision	117 (76%)	61 (76%)	1.0



Poster #160 #1818990

DESMOID TUMOURS IN FAMILIAL ADENOMATOUS POLYPOSIS PATIENTS: FAVOURABLE OUTCOMES WITH MULTIDISCIPLINARY MANAGEMENT

Eisar Al-Sukhni, MD¹; Harini Suraweera, MSc²; Kara Semotiuk, MS, (C)CGC³; Carol J. Swallow, MD PhD FRCSC FACS²; Savtaj Brar, MD MSc FRCSC⁴; Albiruni Ryan Abdul Abdul Razak, MD, MB, MRCPI⁵; Abha A A. Gupta, MD, M.Sc., FRCPC⁶; Rebecca A. Gladdy, MD PhD FRCSC FACS²

¹Mount Sinai Hospital, Toronto, Ontario, CANADA, ²Department of Surgical Oncology, Princess Margaret Hospital, University Health Network and Mount Sinai Hospital, Toronto; Lunenfeld Tanenbaum Research Institute, Sinai Health System, Toronto, Ontario, CANADA, ³Zane Cohen Centre for Digestive Diseases/Mount Sinai Hospital, Toronto, Ontario, CANADA, ⁴Department of Surgical Oncology, Princess Margaret Hospital, University Health Network and Mount Sinai Hospital, Toronto, Ontario, CANADA, ⁵Division of Medical Oncology, Princess Margaret Cancer Centre, University Health Network, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, CANADA, ⁶Hospital for Sick Children and Princess Margaret Cancer Center and University of Toronto, Toronto, Ontario, CANADA

Objective: To describe the outcomes and multimodality treatment required for the management of desmoid tumours (DT) in familial adenomatous polyposis (FAP) patients treated at an expert sarcoma centre.

Methods: Consecutive patients with FAP and a diagnosis of DT managed at our centre from 2000-2021 were identified from institutional databases. Data was collected regarding demographics, diagnosis, treatment, and outcomes. When multiple tumours were present, these were grouped and analyzed by body site: mesenteric/retroperitoneal (M/RP), abdominal wall (AW), extremity, back, and breast. Institutional REB approval was obtained.

Results: Of 45 patients with 67 DTs, 25 (56%) were female. All but 4 (8.9%) were diagnosed with FAP before DT diagnosis; all but 2 underwent surgery for FAP. Median time from age at colectomy to DT diagnosis was 3.0 years (range 0-41). DTs were distributed as follows: 39 (58%) M/RP, 17 (25%) AW, 4 (6%) extremity, 3 (5%) back, 4 (6%) breast. M/RP tumours were present in 39 (87%) patients. Symptoms secondary to DT developed in 32 patients (71%) and were severe in 12 (27%) (recurrent SBO requiring hospitalization, abscess/fistula, ureteric obstruction requiring intervention). Initial treatment on a per tumour basis was as follows: observation, 30 (46%); chemotherapy (CTX), 15 (23%); surgery, 10 (15%); and other drugs (sorafenib, tamoxifen, or sulindac), 10 (15%). Best response to initial intervention including observation was: no evidence of disease in 8 (13%); residual disease, 43 (71%); and progressive disease, 10 DT (16%). DTs were controlled with <1 intervention in 78% of patients. In 34 patients with stable or regressed disease after initial intervention, median PFS was 23.4 years (95%CI 7.6-39.2). At some point, 19/45 (42%) patients received CTX. CTX included methotrexate and vinorelbine/vinblastine (1 doxorubicin). Following CTX, 83% of DTs remained stable with no further intervention at a median follow up of 2.7 years (range 0.1-15). In the 12 severely symptomatic patients, 4 required 2-4 interventions for DT control (one of these continued to progress after latest therapy). Additional treatments after progression on chemotherapy included further chemotherapy (3 patients), other systemic agents (3 patients), and radiation (1 patient). At a median follow up of 6.0 years (range 0.7-35.8), 33 (73%) patients were alive with disease, 7 (16%) were alive without disease, and 5 (11%) were dead of non-DT-related causes. No patients died of complications related to their DT during the follow up period.

Conclusion: The majority of DT in FAP remained stable with observation alone or a single intervention. Vinca-alkaloid based chemotherapy was the most common individual intervention and produced a durable response in most DTs. While no deaths occurred directly as a result of DT, over a quarter of patients experienced significant morbidity related to their tumours and required a greater number of interventions and a multidisciplinary approach to achieve disease and symptom control.



Poster #161 #1818890

EVALUATION OF PRIMARY SPORADIC DESMOID TYPE FIBROMATOSIS MANAGEMENT AND THE UNDERLYING FACTORS INFLUENCING VARIED OUTCOMES, A SINGLE SOFT TISSUE SARCOMA UNIT SERIES.Misbah Khan¹; Anant Desai, MD²¹University Hospitals Birmingham, London, England, UNITED KINGDOM, ²University Hospital Birmingham NHS Foundation Trust, Birmingham, England, UNITED KINGDOM

Objective: Desmoids are rare fibroblastic tumours. They present with a persistent challenge in selecting the best individual treatment option on account of their known unpredictable biological behaviour. Appropriately, we endeavoured to evaluate various clinicopathological attributes towards tumour behaviour in our series of fibromatosis at a single large soft tissue sarcoma unit.

Methods: This is a retrospective review of 95 diagnosed cases of primary truncal sporadic fibromatosis managed at the centre between 1st March 2011 and 29th February 2020. Disease course was recorded clinically as well as radiologically, with all significant events documented in accordance with the RECIST criteria. We studied the rate of progression for patients managed with active surveillance, and the rate of recurrence for surgically treated group. Additionally, the relevant event-free survivals and potential risk factors predicting disease behaviour were analysed over a median length of follow-up of 27months (IQR of 10-47).

Results: 69.5% of the patients (n= 66) were offered an initial period of conservative management. The rest received treatment upfront, which essentially comprised surgery (n=28). Overall, 2-year adverse event-free survival was 83.8%. 2-year PFS was higher in the WW group (88.9%) than RFS in the surgical group (77.1%) p=0.02. Adverse event rate in both groups compared favourably, 28.8% in W&W and 28.6% in the surgical group. At final follow-up, rate of stable disease in WW group was 47% (n=31) and regression rate was 24.2 % (n=16). On Cox regression analysis, the mean time to progress was 14 +2.0 months (95%CI 7.22-12.75) with larger tumour size as the only significant prognostic indicator (p= 0.05). Meantime to recurrence in the surgical group was 13.8 + 2.76 (95% CI 10.28-19.38) with tumour location a significant factor correlated with recurrence(p=0.05).

Conclusion: This study confirms the safety of both treatment approaches in primary sporadic desmoids. The adverse event rate remained comparable for two groups but event-free survival in our study was better for the active surveillance group than the surgical group.

Table-1 Demographic and clinical characteristics of studied population

Variable	N (%)	WW	Surgery
		N (%)	N (%)
Age at time of diagnosis years mean (SD; range)	<u>39.4 (16.3; 16-90)</u>	<u>38.9(16.7;13-90)</u>	<u>40.8(15.4;18-74)</u>
Gender			
Male	30(31.6%)	17(25.8%)	12(42.9%)
Female	65(68.4%)	49(74.2%)	16(57.1%)
Hormonal association (pregnancy)			
Yes	29(30.5%) *	25(37.9%)	4(14.3%)
Tumour Location			
Abdominal wall	47(49.5%)	40(60.6%)	7(25%)
Superficial trunk**	21(22.1%)	17(25.8%)	4(14.3%)
Intra-abdominal	26(27.4%)	9(13.6%)	17(60.7%)
Beta Catenin on IHC			
+ve	67(70.5%)	43(65.2%)	23(34.8%)
-ve	11(11.6%)	10(15.2%)	1(3.6%)
Incomplete/No record	17(17.9%)		
Tumour size			
<5cm	33(34.7%)	23(34.8%)	10(35.7%)
5-10cm	47(49.5%)	35(53.0%)	11(39.3%)
>10cm	15(15.8%)	8(12.1%)	7(25%)

Table-2 Predicting factors for overall survival

	Univariate analysis		Multivariate Analysis		
	p-value	Odds Ratio	p-value	Hazard ratio	95% CI
Age	0.92	1.16	0.23	0.38	0.79-1.82
Hormonal association +ve	0.35	1.70	0.60	1.65	0.26-10.40
Tumour Location	0.92		0.09		
Abdominal wall	0.99	1.01	0.96	0.96	0.21-4.44
Extra-abdominal Trunk	0.74	0.77	0.04	0.05	0.003-0.93
Beta Catenin	0.36	2.69	0.72	0.65	0.06-7.08
Tumour size	0.11		0.26		
5-10cm	0.03	5.47	0.32	2.99	0.35-25.61
>10cm	0.16	3.88	0.89	0.84	0.07-10.40
Upfront treatment					
Surgery	0.26	1.87	0.02	0.03	0.002-0.55

Table-3 Predicting factors for Progression in patients managed with active Surveillance

	Univariate analysis		Multivariate Analysis		
	p-value	Odds ratio	p-value	Odds ratio	95% CI
Age <50	0.82	1.21	0.39	2.04	0.39-10.58
Hormonal association	0.05	4.20	0.53	1.51	0.42-5.45
Tumour Location	0.39		0.38		
Abdominal wall	0.98	0.99	0.58	0.72	0.22-2.33
Extra-abdominal Trunk	0.99	0.00	0.17	0.21	0.02-1.92
Beta Catenin	0.89	0.77	0.10	5.44	0.71-41.94
Tumour size	0.04		0.05		
5-10cm	0.99	19.99	0.02	6.71	1.43-31.36
>10cm	0.99	20.10	0.11	4.26	0.71-25.70

Table-4 Predicting factors for recurrence in surgically managed subjects

	Univariate analysis		Multivariate Analysis		
	p-value	Odds Ratio	p-value	Hazard ratio	95%CI
Age	1.00	1.00	0.92	0.91	0.14-5.93
<50					
Hormonal association	0.78	0.71	0.32	2.55	0.40-16.03
Tumour Location	0.97		0.05		
Intra-abdominal	0.89	1.20	0.27	0.28	0.03-2.69
Extra-abdominal Trunk	0.95	0.92	0.02	0.03	0.00-0.51
Beta Catenin +ve	0.12	0.13	0.32	0.23	0.01-4.11
Tumour size	0.53		0.46		
5-10cm	0.41	2.29	0.23	3.69	0.44-31.32
>10cm	0.76	0.67	0.55	2.15	0.17-26.28
Margins +ve	0.38	2.17	0.32	2.54	0.40-16.03
Type of Surgical resection					
Complex*	0.85	1.15	0.27	0.36	0.06-2.19

Figure-1: Overall adverse event free survival

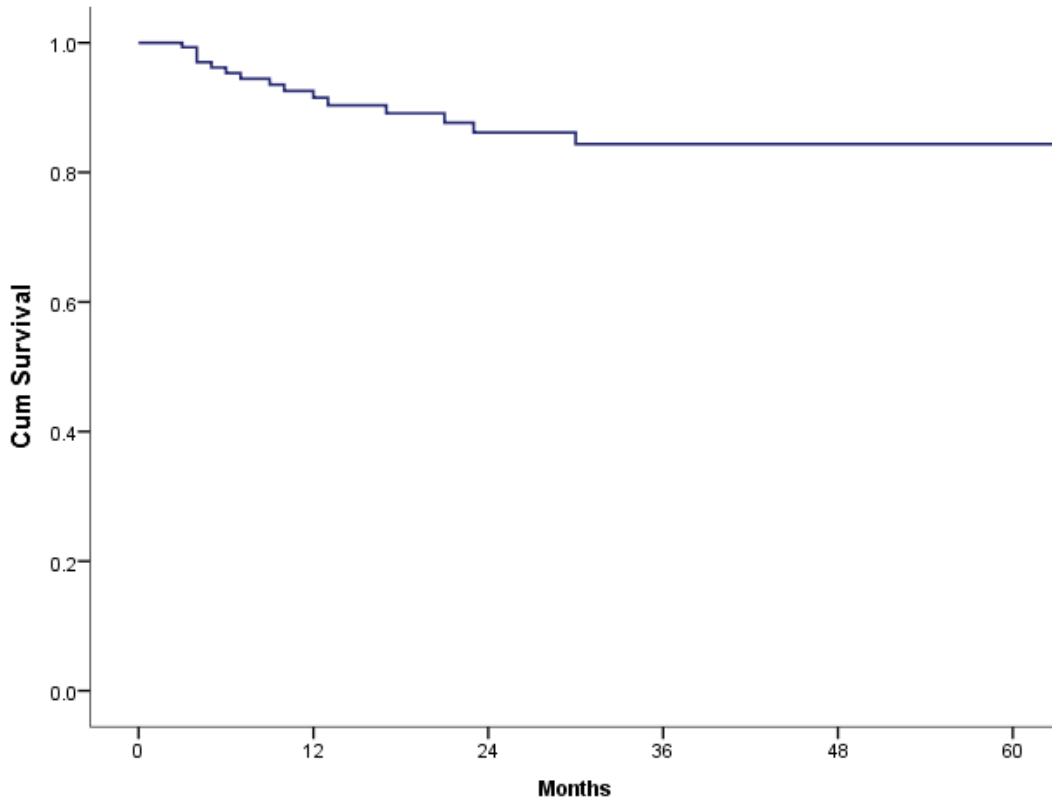


Figure-2: Adverse event-free survival according to the upfront treatment approach

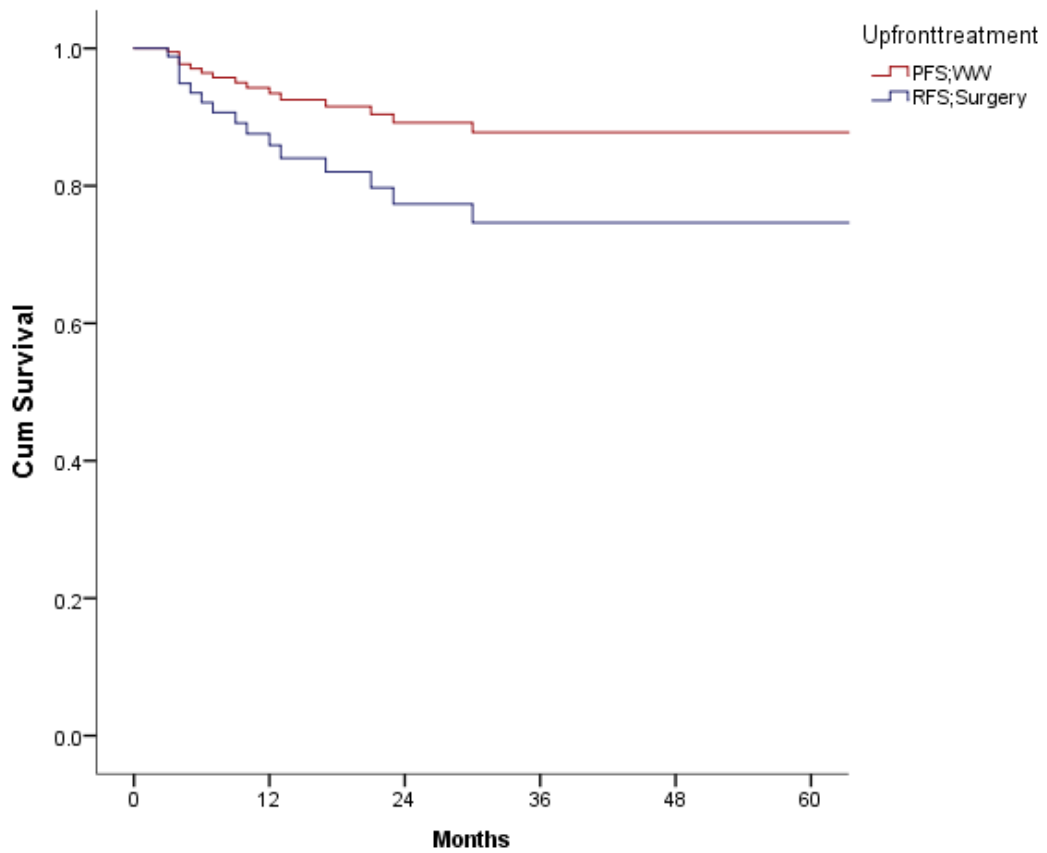


Figure-3: Survival function; Time to Progress. a) Overall, b) according to tumour size

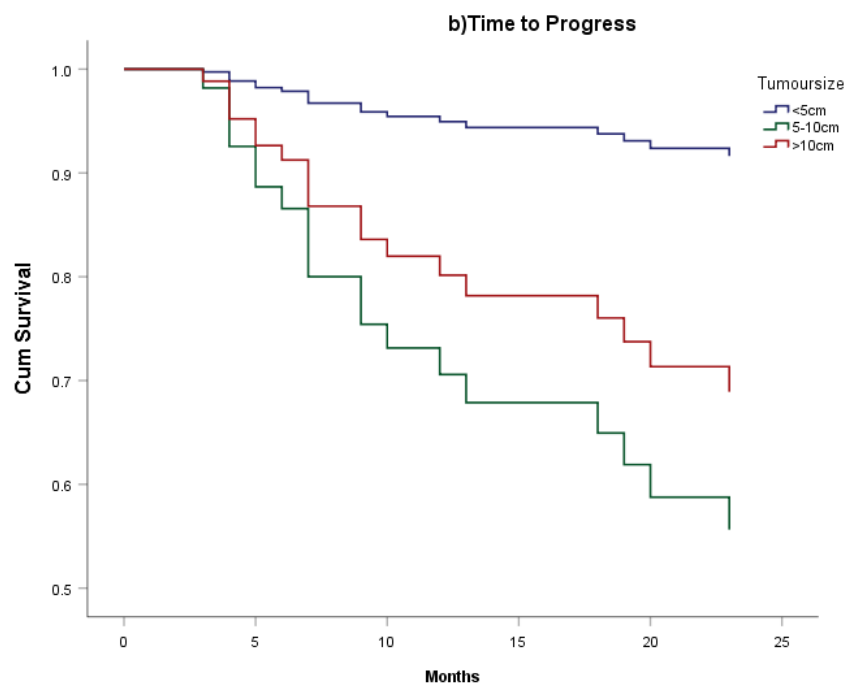
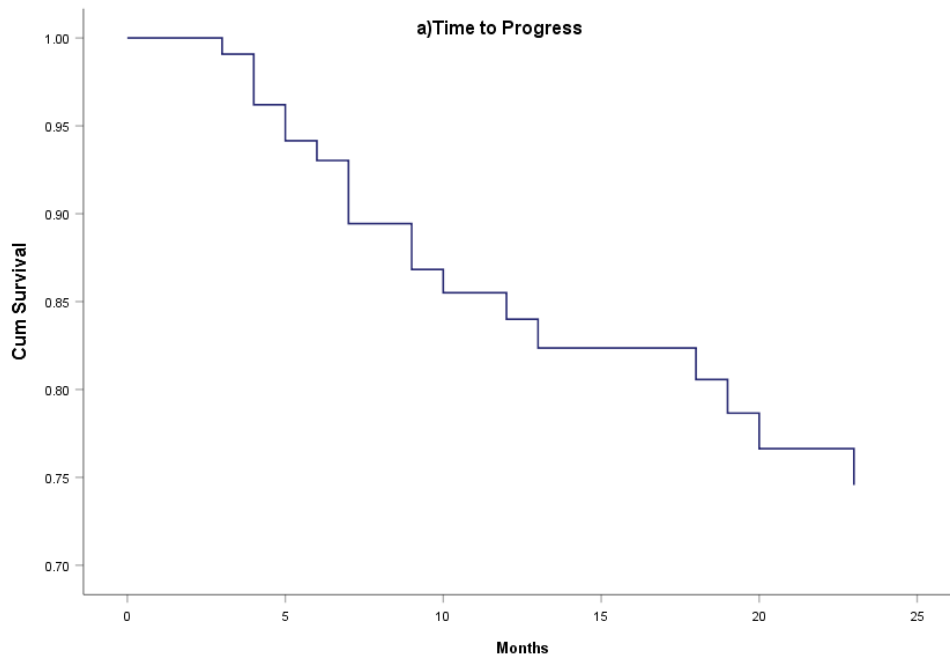
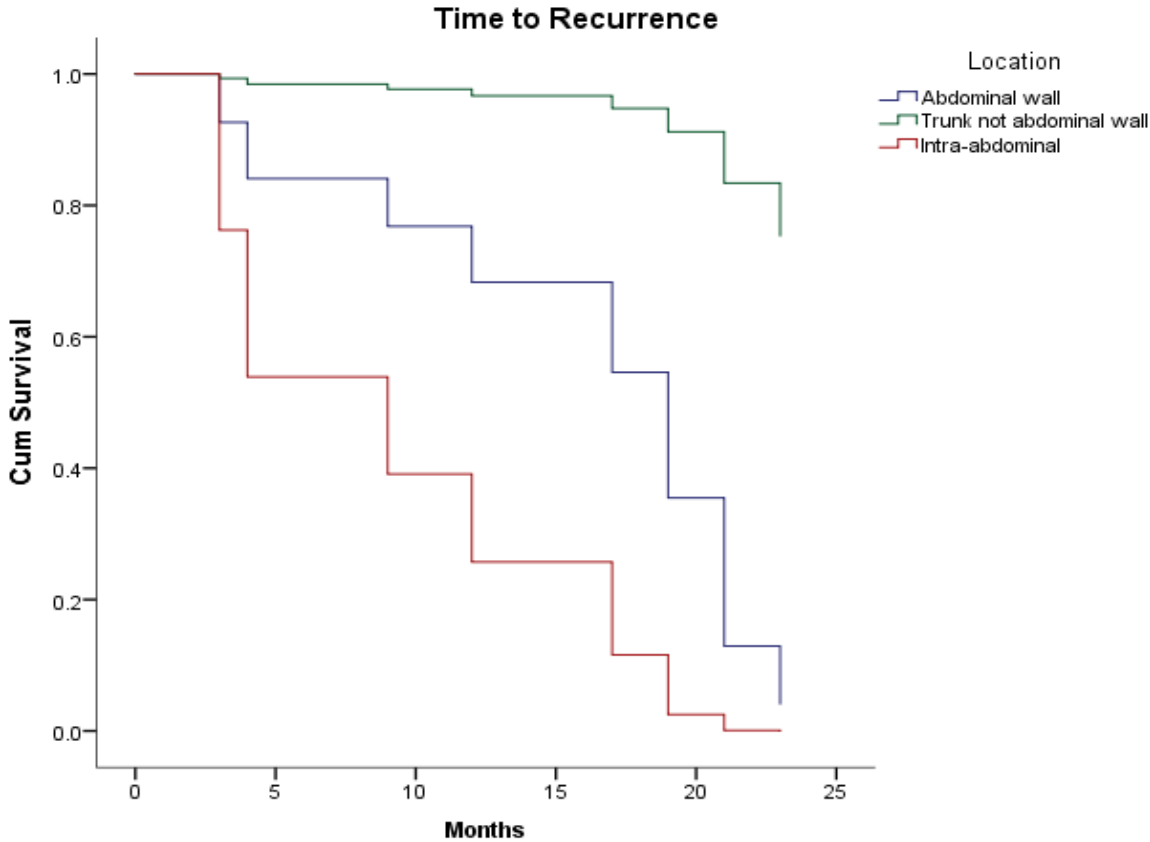
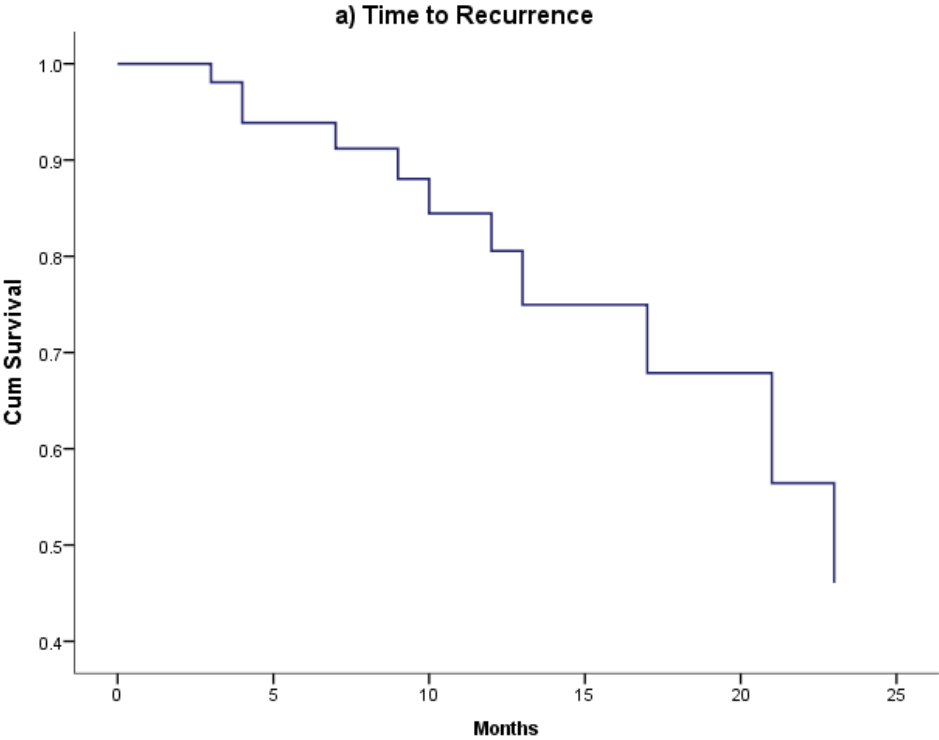


Figure-4: Survival function; Time to Recurrence. a) Overall, b) according to tumour location





Poster #162 #1819042

MARGINAL RESECTION OF NON-COELOMIC ATYPICAL LIPOMATOUS TUMOURS/WELL-DIFFERENTIATED LIPOSARCOMAS IS ASSOCIATED WITH A LOW RATE OF LATE LOCAL RELAPSE: IMPLICATIONS FOR FOLLOW UP PROTOCOLS

Gausihi Sivarajah, MBBS FRACS¹; Andrew J. Hayes, PhD²; Hayden Snow, MBBS, FRACS³; Myles Smith, PhD²; Dirk Strauss, MD²

¹Royal Marsden NHS Trust, London, England, UNITED KINGDOM, ²The Royal Marsden Hospital NHS Foundation Trust, London, England, UNITED KINGDOM, ³Peter MacCallum Cancer Centre, Melbourne, Victoria, AUSTRALIA

Objective: Historical case series of surgical resections of extremity Atypical Lipomatous tumours/Well-differentiated liposarcomas (ALT) have suggested high rates of local recurrence (LR). However, these series are not homogenous cohorts of patients undergoing planned oncological resections in a specialist sarcoma unit, with many series including patients in whom the diagnosis of ALT was made postoperatively or on relapse. In this study we analysed a large cohort of patients with extended follow up almost all of whom underwent function-preserving planned marginal resections (as contrasted with a radical wide resection with the aim of gaining widely clear histopathological margins) of primary deep extremity / trunk ALTs at a specialist sarcoma centre. We assessed both surgical morbidity and rates of local and distant relapse with the overall aim of identifying whether there was a cohort of patients that could be considered for less intensive follow up.

Methods: After institutional ethical approval, a retrospective analysis of all patients with a preoperative diagnosis, either on imaging or histopathology, of a primary non coelomic ALT undergoing surgery in a specialist sarcoma unit between 2000 and 2015 was performed. Only patients with a histologically confirmed diagnosis of ALT on final histopathological analysis either by immuno-histochemistry for CDK4/P16 and/or MDM2 positivity by fluorescence in-situ hybridisation were included in the study. Patients with tumours located predominantly in the groin but with a component of the tumour passing from the groin into the retroperitoneum were included in the study but patients with principally retroperitoneal tumours with extension into the groin were excluded. To review a homogeneous cohort of patients with purely low-grade disease, any tumour with known high risk features (sclerosing/inflammatory features; myxoid, pleomorphic, and spindle cell subtypes; and de-differentiated components) was excluded from the analysis.

Oncological endpoints were LR, local Disease Free Survival (DFS) and distant DFS. Margin status was classified as R0 if margin clearance was >1mm on histo-pathology, R1 if the histo-pathological margins were positive but the surgeon described complete macroscopic removal of the tumour, and R2 if the surgeon described residual tumour in situ or if the surgeon divided the tumour to preserve a neurovascular structure or at the inguinal ligament. Prognostic variables potentially influencing LR (age, size, site, margin status, and histological findings) were analysed by univariable and multivariable analysis. Statistical analyses were performed using STATA[®] v.15

Results: 127 patients were identified, with a median follow-up of 54 months (0-235). Median Age was 61 yrs. (15-91) Median maximal tumour size was 17.5 cm (5-36) with 85.0% in the lower limb or limb girdle, 10% in the upper limb or limb girdle and 5% in the trunk or head and neck. 93.7% of patients underwent a marginal resection as described by the operating surgeon. Median hospital length of stay was 3 days (0-16) with 7.9% of patients returned to theatre for evacuation of a haematoma and 18.1% of patients underwent outpatient seroma aspiration. No patients had radiotherapy or chemotherapy. Margin status was R0 in 33 patients (26%) R1 in 86 patients (68%) and R2 in 8 patients (6%).

16 patients (12.6%) had LR, occurring at median time of 54.5 months. 4 of these 16 patients had no intervention and remain under surveillance. The remaining underwent surgery. 1- and 5-year LDFS was 100% and 87.2%, respectively. Only one patient with pleomorphic liposarcomatous transformation in a recurrent tumour developed distant metastases. No patients died of this disease. Tumour factors significantly associated with increased LR were younger age, upper limb / limb girdle location and an R2 resection (Table 1). In patients with an ALT confined to the lower limb who underwent complete excision (R0/R1) the local relapse rate was 8%. In the 8 patients with an R2 resection the LR rate was 75%.

Conclusion: Resection of non-coelomic ALTs by function-preserving marginal resection has a low morbidity, a low rate of LR and extremely low rate of distant relapse. Patients undergoing a complete marginal excision of a lower limb ALT, irrespective of size, should be considered for a less intensive follow up protocol than is currently advised for standard extremity sarcomas.

Table 1 Univariable and Multivariable analyses of factors associated with Local Recurrence.

	Univariable Analysis		Multivariable Analysis	
	HR (95% CI)	p value	HR (95% CI)	p value
Gender	1.00 (reference)		1.00 (reference)	
Female	1.67 (0.58-4.80)	0.35	*	*
Age (years)				
≤ 40	1.00 (reference)		1.00 (reference)	
41-65	0.29 (0.08-1.13)	0.08	0.24 (0.05-1.07)	0.06
≥ 65	0.26 (0.06-1.13)	0.07	0.10 (0.02-0.62)	<0.05
Site of tumour				
Lower limb	1.00 (reference)		1.00 (reference)	
Upper limb	4.97 (1.33-18.5)	<0.05	4.57 (1.01-20.5)	<0.05
Truncal wall	5.18 x 10 ⁻¹⁷	.	3.08 x 10 ⁸	.
Tumour size (cm)*				
≤ 12.5	1.00 (reference)		1.00 (reference)	
12.6-23.9	2.53 (0.30-21.2)	0.39	*	*
≥ 24	3.59 (0.44-29.0)	0.23	*	*
Margins				
R0	1.00 (reference)		1.00 (reference)	
R1	5.39 (0.67-44.3)	0.12	5.04 (0.54-46.9)	0.16
R2	25.9 (2.85-237)	<0.05	55.1 (4.72-644)	<0.001
Histological findings†				
None	1.00 (reference)		1.00 (reference)	
Evidence of necrosis	1.01 (0.36-2.83)	0.99	*	*
Evidence of nuclear atypia	1.75 x 10 ¹⁵	.	*	*
Presence of septations	0.82 (0.26-2.59)	0.73	*	*
Presence of lipoblasts	1.83 (0.61-5.42)	0.28	*	*
IHC: CDK4 [^]	1.84 (0.48-7.04)	0.37	*	*
IHC: p16‡	0.66 (0.16-2.76)	0.57	*	*
MDM2 amplification‡	0.52 (0.12-2.19)	0.37	*	*

*Tumour size divided into subgroup based on interquartile range and median.

†Histological findings based on biopsy and/or final specimen.

[^]Only representative of patients operated on from 2007-2016.

‡Only representative of patients operated on from 2009-2016.



Poster #163 #1818920

SURGICAL MARGIN FOR PHOSPHATURIC MESENCHYMAL TUMORS IN SOFT TISSUES: AN ANALYSIS OF THE RADIOLOGICAL-HISTOPATHOLOGICAL CORRELATION

Hiroshi Kobayashi, MD, PhD¹; Noahiro Makise, MD, PhD¹; Nobuaki Ito, MD, PhD¹; Liuzhe Zhang, MD¹; Yuki Ishibashi, MD¹; Masachika Ikegami, MD, PhD¹; Yusuke Shinoda, MD, PhD¹; Toru Akiyama, MD, PhD²; Tetsuo Ushiku, MD, PhD¹; Sakae Tanaka, MD, PhD¹

¹The University of Tokyo Hospital, Bunkyo-ku, Tokyo, JAPAN, ²Jichi Medical Center, Omiya-shi, Saitama, JAPAN

Objective: Phosphaturic mesenchymal tumors primarily cause tumor-induced osteomalacia, a rare paraneoplastic syndrome, and half occur in soft tissues. There are few reports about the surgical margins of these tumors. This study aimed to clarify the optimal surgical margin for phosphaturic mesenchymal tumors by analyzing radiological and histopathological features.

Methods: This study included eight cases, seven primary and one recurrent, of tumor-induced osteomalacia caused by soft-tissue phosphaturic mesenchymal tumors that were surgically treated between January 2000 and January 2019. We evaluated the radiological and histopathological features of all tumors and investigated the correlation of these features, the surgical margin, and recurrence of hypophosphatemia.

Results: The tumors were located in superficial (n=5) and deep (n=3) tissues. Six of the eight tumors had a clear boundary, but five had an irregular margin. Three tumors had a hypointense rim on T2-weighted images, indicating fibrous tumor encapsulation. Histopathological analysis revealed infiltrative growth in six of the eight tumors, which correlated with an irregular margin seen on imaging. Although there was no recurrence in patients treated with wide surgical margins, one of the three patients treated with marginal tumor resection experienced a recurrence of hypophosphatemia, with histopathological analysis showing infiltration of subcutaneous fat. In contrast, two tumors with clear boundaries, regular margins, and fibrous capsule seen on imaging, had no infiltrative growth and were cured by marginal resection. In one recurrent case, tumor infiltration was observed in the previous surgical scar, which was not detected on preoperative imaging.

Conclusion: Soft-tissue phosphaturic mesenchymal tumors with an irregular boundary seen on imaging tend to be infiltrative, especially into subcutaneous fat, and should be treated by wide margin resection. Tumors with a fibrous capsule with clear and regular margins are cured by marginal margin resection. These findings could inform surgeons' decisions regarding the resection of soft-tissue phosphaturic mesenchymal tumors.



Poster #165 #1819029

MANAGEMENT OF DESMOID-TYPE FIBROMATOSIS IN TWO CENTERS FROM ARGENTINA

Sergio Quildrian, MD¹; Anabella Daffinoti, MD²; Francisco Colazo, MD³; Diego Prost, MD²; Walter Nardi, MD³; Sonia Patron Costas, MD²; Nahir Queiro, MD³; Gonzalo Cervelo, MD²; Julieta Gerino, MD²; Fernando Carrizo, MD²; Julieta Arbat, MD²; Pablo Desanzo, MD³; Luciana Bella Quero, MD³; Cintia Novas, MD³; Carlos Silva, MD³; Gabriela Cinat, MD²; Jorge Chapela, MD⁴

¹Buenos Aires British Hospital; Angel Roffo Institute of Oncology, University of Buenos Aires, Buenos Aires, Buenos Aires, ARGENTINA, ²Angel H Roffo Institute of Oncology, Buenos Aires, Ciudad Autonoma de Buenos Aires, ARGENTINA, ³Buenos Aires British Hospital, Buenos Aires, Ciudad Autonoma de Buenos Aires, ARGENTINA, ⁴Angel H Roffo Institute of Oncology, Buenos Aires, Buenos Aires, ARGENTINA

Objective: To evaluate the management and results in patients with limb and truncal desmoid-type fibromatosis treated in two referral centers.

Methods: Patients with confirmed desmoid-type fibromatosis treated 2006 and 2021 were retrospectively evaluated. Demographic and tumor characteristics, primary site, front-line treatment, response and evolution were evaluated. According to actual recommendations, we evaluated type of front-line treatment (active treatment versus observation) dividing the series in two groups: G1 (2006-2013) and G2 (2014-2021). Fisher Exact Test was used to compare groups.

Results: We evaluated 49 patients with desmoid-type fibromatosis, median age 35(IQR, 25-45) years and 36(73%) patients were females. The tumor was located in the limbs in 18(36.7%) patients, abdominal wall in 15(30.6%) patients, superficial trunk in 10(20.4%) patients, retroperitoneal/pelvis in 5(10.2%) patients and intraabdominal in 1 patient. At initial consultation primary disease was observed in 30(61%) patients. Median duration of symptoms was 12(IQR, 5-38) months and the most common initial symptoms were related to indolent growth of the tumor (39 patients, 73%). Of patients with previous treatment it was surgery in 18(90%) and systemic treatment in 2(10%). Active treatment was delivered in 35 cases as follows: surgery (33), systemic therapy (2). Observation without active treatment was indicated in 14 cases (28.5%) as follows: 7 patients with primary tumor, 5 patients with recurrent tumor and 2 patients with previous R1. With a median follow-up of 55(IQR, 14-94) months 19 patients have stable disease, 1 remission, 4 progression and 25 remain without evidence of disease. In patients treated with front-line surgery recurrence was observed in 14 cases (42%). In patients with observation as front-line approach and primary or recurrent tumor at initial consultation we observed 11(91.6%) stable disease and 1 progression disease. In Group 1 (n=24) active treatment was indicated in 22 patients and observation in 2 patients, in Group 2 (n=25) active treatment was indicated in 13 patients and observation in 12 patients (p=0.0036).

Conclusion: The most common sites of primary tumors were limbs and abdominal wall. The surgical treatment had a high proportion of recurrence (>40% in the present series). Observation without active treatment was associated with >90% of stable disease in patients consulting with primary or recurrent tumors. Front-line conservative approach was preferred in most recent years.



Poster #166 #1818924

RANDOMIZED PLACEBO-CONTROLLED DOUBLE BLIND PHASE II STUDY OF ZALTOPROFEN FOR PATIENT WITH DIFFUSE-TYPE AND UNRESECTABLE LOCALIZED TENOSYNOVIAL GIANT CELL TUMORS

Akihiko Takeuchi, MD, PhD¹; Makoto Endo²; Akira Kawai, MD³; Yoshihiro Nishida⁴; Ryu Terauchi⁵; Akihiko Matsumine⁶; Hisaki Aiba, MD⁷; Tomoki Nakamura⁸; Susumu Tandai⁹; Toshifumi Ozaki¹⁰; Manabu Hoshi¹¹; Kenichi Yoshimura¹²; Akihiro Nomura¹³; Toshinori Murayama¹³; Hiroyuki Tsuchiya¹, ¹Department of Orthopedic Surgery, Kanazawa University School of Medicine, Kanazawa, Ishikawa, JAPAN, ²Department of Orthopaedic Surgery, Kyushu University, Fukuoka, Fukuoka, JAPAN, ³National Cancer Center Hospital, Chuo-ku, Tokyo, JAPAN, ⁴Department of Orthopedic Surgery, Nagoya University Graduate School of Medicine, Nagoya, Aichi, JAPAN, ⁵Department of Orthopaedics, Kyoto Prefectural University of Medicine Graduate School of Medicine, Kyoto, Kyoto, JAPAN, ⁶Department of Orthopaedics and Rehabilitation Medicine, University of Fukui, Fukui, Fukui, JAPAN, ⁷Department of Orthopaedic Surgery, Nagoya City University Graduate School of Medical Sciences, Nagoya, Aichi, JAPAN, ⁸Department of Orthopaedic Surgery, Mie University Graduate School of Medicine, Tsu, Mie, JAPAN, ⁹Department of Orthopaedic Surgery, Asahikawa Medical University, Asahikawa, Hokkaido, JAPAN, ¹⁰Department of Orthopaedic Surgery, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Science, Okayama, Okayama, JAPAN, ¹¹Department of Orthopaedic Surgery, Osaka City University Graduate School of Medicine, Osaka, Japan, Osaka, Osaka, JAPAN, ¹²Future Medical Center, Hiroshima University Hospital, Hiroshima, Hiroshima, JAPAN, ¹³Innovative Clinical Research Center (iCREK), Kanazawa University Hospital, Kanazawa, Ishikawa, JAPAN

Objective: A tenosynovial giant cell tumor (TGCT) is a locally aggressive benign neoplasm arising from intra- or extra-articular tissue. Diffuse TGCT (D-TGCT) most commonly develops in the knee, followed by the hip, ankle, elbow, and shoulder. Surgical removal is the only effective treatment option for patients. However, a local recurrence rate of up to approximately 50% has been reported. We revealed that zaltoprofen, a nonsteroidal anti-inflammatory drug possessing the ability to activate peroxisome proliferator-activated receptor gamma (PPAR γ), can inhibit the proliferation of TGCT stromal cells via PPAR γ . PPAR γ is a ligand-activated transcription factor that belongs to the nuclear hormone receptor superfamily. It plays an important role in the differentiation of adipocytes from precursor cells and exhibits antitumorigenic effects on certain malignancies. Therefore, we conducted an investigator-initiated clinical trial to evaluate whether zaltoprofen is safe and effective for patients with D-TGCT or unresectable localized TGCT (L-TGCT).

Methods: This study was a randomized, placebo-controlled, double-blind, multicenter trial to evaluate the safety and efficacy of zaltoprofen for patients with D-TGCT or L-TGCT. For the treatment group, zaltoprofen 480 mg/day was administered for 48 weeks; the placebo group received similar dosages of sugar pills without zaltoprofen. Twenty participants in each group were needed in this trial (40 participants total). The primary outcome was the progression-free rate (PFR) at 48 weeks after treatment administration. "Progression" was defined as any of the following requiring surgical interventions: 1) repetitive joint swelling due to hemorrhage; 2) limited range of joint motion; 3) invasion of adjacent cartilage or bone; 4) severe joint space narrowing; 5) increase in tumor size. This study was registered at the University Hospital Medical Information Network (UMIN) Clinical Trials Registry (UMIN000025901).

Results: Forty-one patients were enrolled and randomly assigned to either zaltoprofen (n=21) or placebo (n=20). The mean age was 44 years (range, 26 to 66 years) in zaltoprofen and 47 years (range, 24 to 69 years) in placebo. Tumor locations were a knee in 26 and an ankle in 15 patients. Progression events occurred in seven patients (4 for zaltoprofen and 3 for placebo). Specifically, severe joint space narrowing in two, increase in tumor size in one, and repetitive joint swelling in one patient for zaltoprofen and severe joint space narrowing, increase in tumor size, and repetitive joint swelling each in one patient for placebo. PFR after 48 weeks were 80.7% (95% confidence interval (CI), 56.31-92.28) for zaltoprofen versus 85% (95% CI, 60.38-94.90) for placebo (p=0.712). The objective tumor response was graded as PR in 1, SD in 18, and PD in 1 at 24 weeks and PR in 1 and SD in 16 at 48 weeks for zaltoprofen and the grades for placebo were SD in 18 and PD in 1 at 24 weeks; and SD in 15 and PD in 3 at 48 weeks for placebo. There was no significant difference between zaltoprofen and placebo tumor grades at 48 weeks (p=0.229). The tumor gradually grew larger with placebo (0.94% at 24, 3.97% at 36, and 4.79% at 48 weeks) in a time-dependent manner, whereas it only changed slightly with zaltoprofen (1.61% at 24, 0.10% at 36, and -1.55% at 48 weeks), however, there was no significant difference (p=0.860 at 24, p=0.349 at 36, and p=0.887 at 48 weeks) at any time points. No adverse effects (> Grade 3) were observed.

Conclusion: This was the first study to evaluate the efficacy of zaltoprofen in patients with D-TGCT or unresectable L-TGCT. Zaltoprofen was well tolerated and there were no incidents of safety issues with zaltoprofen; however, both groups presented with a stable disease course for 48 weeks. The long-term clinical course of TGCT should be clarified. Zaltoprofen did not appear to improve PFR in this limited period. Further analysis with long-term administration of zaltoprofen is considered a possibility for the future.



Poster #167 #1818851

A PROSPECTIVE REAL-WORLD STUDY OF THE DIFFUSE-TYPE TENOSYNOVIAL GIANT CELL TUMOR PATIENT JOURNEY: A 2-YEAR OBSERVATIONAL ANALYSIS

Nicholas M. Bernthal, MD¹; Geert Spierenburg, MD²; John H. Healey, MD, FACS³; Silvia Stacchiotti, MD⁴; Emanuela Palmerini, MD⁵; Sebastian Bauer, MD⁶; Erik J. Geiger, MD¹; Zachary Burke, MD¹; Bart Schreuder, MD, PhD⁷; Andreas Leithner, MD, PhD⁸; Javier Martin-Broto, MD, PhD⁹; Francois Gouin, MD, PhD¹⁰; Hans Gelderblom, MD, PhD²; Eric L. Staats, MD⁵; Julio Lopez-Bastida, MSc, PhD¹¹; Elisabeth Beyerlein, MSc¹²; Xin Ye, PhD¹³; Petra Laeis, PhD¹²; Michiel van de Sande, MD PhD²

¹David Geffen School of Medicine at UCLA, Santa Monica, California, UNITED STATES, ²Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ³Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES, ⁴Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY, ⁵IRCCS Istituto Ortopedico Rizzoli, Bologna, Emilia-Romagna, ITALY, ⁶West German Cancer Center, University of Duisburg-Essen, Essen, Nordrhein-Westfalen, GERMANY, ⁷Radboud University, Nijmegen, Gelderland, NETHERLANDS, ⁸Medical University of Graz, Graz, Steiermark, AUSTRIA, ⁹Fundacion Jimenez Diaz University Hospital, Madrid, Madrid, SPAIN, ¹⁰Center Leon Berard, Lyon, Rhone-Alpes, FRANCE, ¹¹University Castilla-La Mancha, Talavera de la Reina, Castilla-La Mancha, SPAIN, ¹²Daiichi Sankyo Europe GmbH, Munich, Bayern, GERMANY, ¹³Daiichi Sankyo, Inc., Basking Ridge, New Jersey, UNITED STATES

Objective: Diffuse-type tenosynovial giant cell tumor (D-TGCT) is a rare, locally aggressive neoplasm. The existing literature on D-TGCT is largely limited to retrospective case series. The natural history of the disease and patient experience are not well described. The TGCT Observational Platform Project (TOPP) is a prospective international registry aimed at describing the clinical behavior of the disease and various treatment patterns. This analysis provides a picture of the treatment journey of D-TGCT patients as a 2-year observational follow-up.

Methods: TOPP is an observational prospective study conducted at 12 sites (7 European countries and at 2 US sites). Patients with histologically confirmed D-TGCT were followed prospectively and data were collected on the type of treatment course (No current/planned treatment [wait-and-see] or Current/planned treatment [surgery, systemic, future surgery] selected at each time point. The treatment course (ie, type of treatment) was collected at baseline (BL) (at the time of enrollment in the registry), and at 1 year (Y1) and 2 years (Y2). Patients were categorized as those who remained on the initial treatment course and those who changed treatment course with specific changes noted (ie, systemic treatment to surgery) during the 2-year observation period. However, patients who received treatment intervention at BL, followed by no specific treatment at Y1 and/or Y2, were documented as remaining on the same treatment course/no treatment intervention.

Results: Of the 183 total patients (BL analysis set) who entered the study, 176 patients (108 female, 61.4%) were included in the full analysis set (FAS; mean age: 43.5 years; range 18-77), and patients with no post baseline data were excluded. Of the FAS, 165 patients (93.8%) had a follow-up visit at Y1 and 168 (95.5%) had a follow-up visit at Y2. At BL, the majority of tumors were located in the knee (n=120/176, 68.2%). At BL, the most common number of prior surgeries received was 1 (n=71/176, 40.3%). Of the 176 patients, 79 (44.9%) were not being treated at BL, nor did they have planned treatment, 45 (25.6%) had current/planned systemic therapy only, 39 (22.1%) had surgery only, 5 (2.8%) had radiotherapy, 4 (2.3%) had future surgery planned, 2 (1.1%) had both surgery and systemic treatment, 1 (0.6%) had surgery + 90Yttrium, and 1 (0.6%) had systemic treatment + future surgery required. Of the 79 patients not treated at BL, 60 (75.9%) remained without treatment/planned treatment at Y1, 54 (90%) of whom continued without treatment at Y2 (Figure 1). Eleven of the 79 patients (13.9%) changed treatment course (6 systemic, 4 surgery, 1 future surgery) at Y1, with 2/11 (18.2%) deciding to change their treatment course to surgery (1 systemic to surgery, 1 future surgery to surgery) at Y2. Of the 45 patients with systemic treatment at BL, 38 (84.4%) did not change course at Y1, and 30 (78.9%) of the 38 patients did not change course at Y2 (Figure 2). From BL to Y1, 6/45 patients (13.3%) changed from systemic to surgery (n=5) and future surgery (n=1), none of whom changed treatment course at Y2. Thirty-two (82%) of the 39 BL patients treated with only surgery did not change treatment at Y1, 30/32 patients (93.8%) did not change at Y2. Four patients at BL had planned future surgery, and 3 had surgery at Y1.

Conclusion: During the 2-year observation period, the majority of patients remained on the same treatment course. Those who changed treatment course, utilized multimodal treatment options. This is the first analysis to describe D-TGCT patient

treatment through longitudinal assessment, demonstrating the need for multidisciplinary teams in the treatment of this chronic disease in order to present patients with all treatment options.

Figure 1. Flow chart of treatment during 2-year observation period with no current/planned treatment at baseline

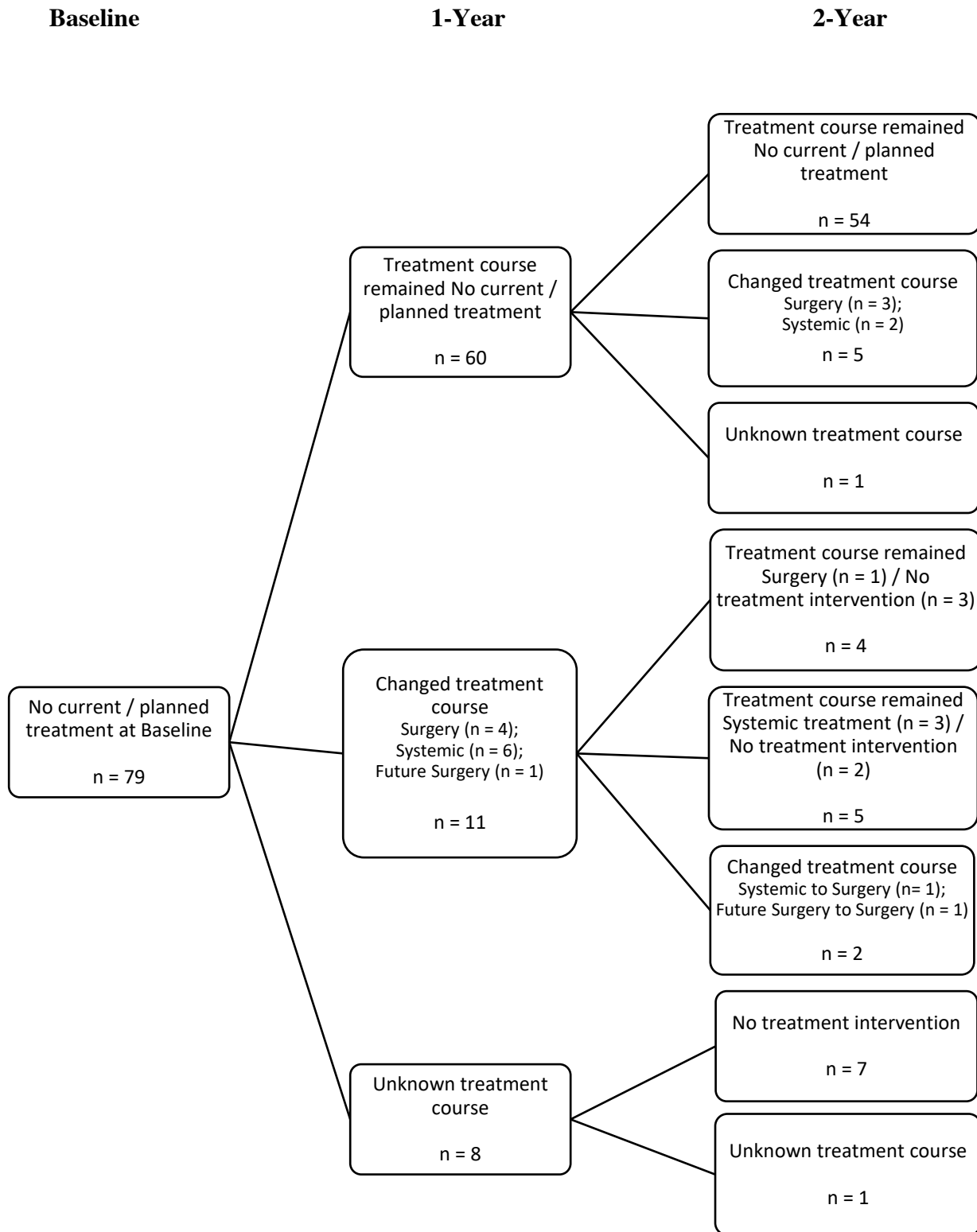
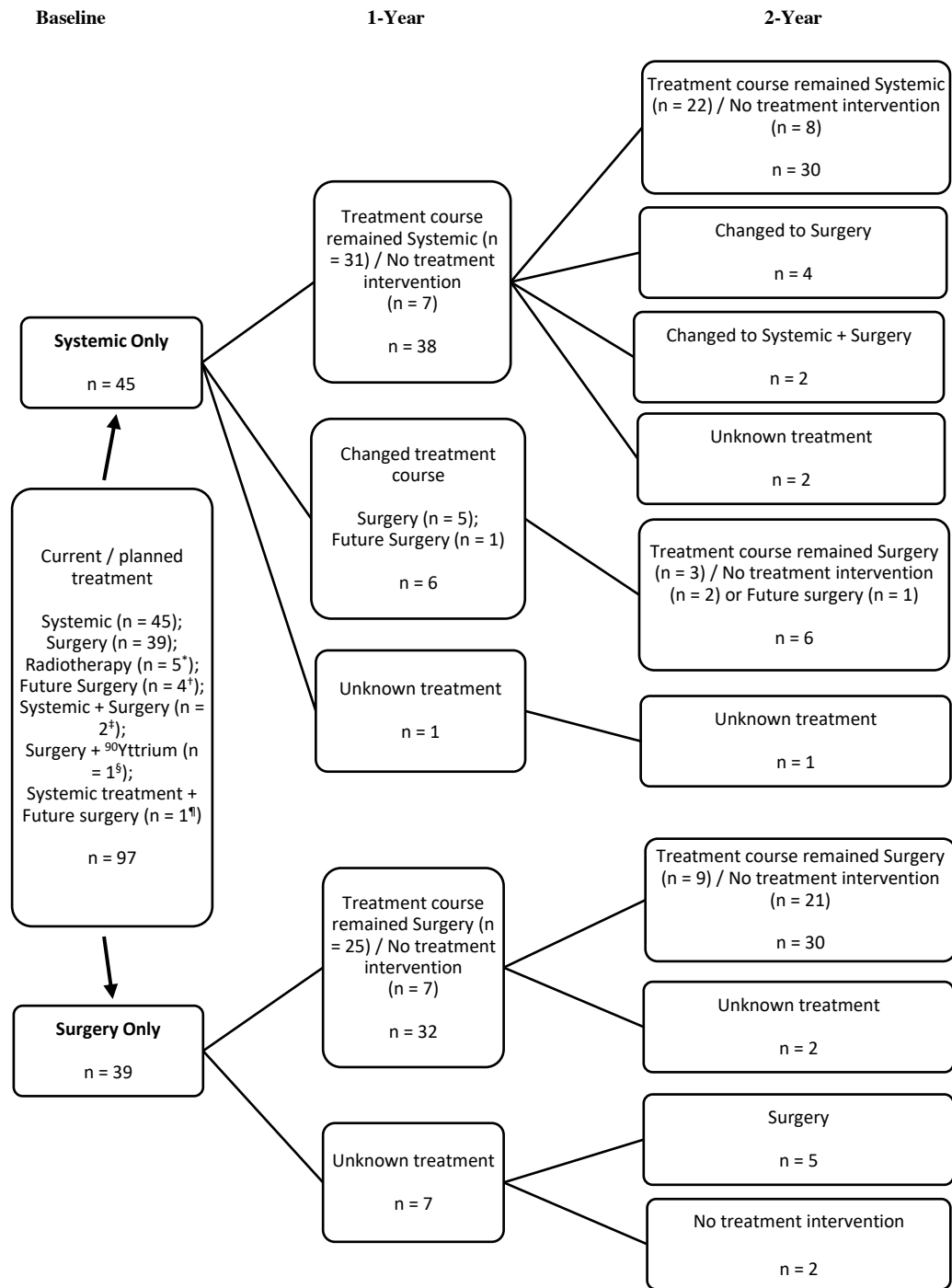


Figure 2. Flow chart of treatment during 2-year observation period with current/planned treatment at baseline



*By Year 2, 1 patient remained on Radiotherapy, 1 had surgery at Year 1, 2 were No treatment intervention and 1 had Unknown treatment.

[†]By Year 1, 3 of the 4 patients had Surgery and 1 patient remained as Future Surgery through Year 2.

[‡]One patient switched to Systemic only, and 1 patient switched to Surgery only by Year 1.

[§]Changed treatment course (systemic + surgery) at Year 1 and switched to systemic only at Year 2.

[¶]Changed treatment course to surgery at Year 1 and switched to No treatment intervention at Year 2.



Poster #168 #1819071

CLINICAL RECOGNITION AND LOCAL RECURRENCE RATES OF ABC SECONDARY TO GCT

 Ahmet Salduz, MD, PhD candidate¹; Michael Russel, MD²; Benjamin J. Miller, MD MS²
¹Istanbul University, Istanbul, Istanbul, TURKEY, ²University of Iowa, Iowa City, Iowa, UNITED STATES

Objective: Aneurysmal bone cyst (ABC) is a benign cystic bony lesion that is composed of blood-filled cavernous spaces separated by septa containing osteoclast-type giant cells, fibroblasts and reactive woven bone. ABC can arise de novo as a primary lesion or arise secondarily within a pre-existing bone lesion. Approximately 30–50% of the ABC is secondary, which developed from a pre-existing lesion. Although several studies have described the radiologic, pathologic, and clinical characteristics of primary ABCs, there is a paucity of this information in the literature regarding secondary ABCs. Our goal was to describe the local recurrence rates and risk factors for recurrence of primary ABC, secondary ABC in GCT, and GCT. Specifically, we questioned if the behavior of ABC secondary to GCT more closely aligned with a primary ABC or GCT (Figure 1).

Methods: Between 2010-2020, 44 consecutive patients who had at least 2-year follow-up with a histologically confirmed primary ABC, ABC secondary to GCT, and GCT were identified. The mean age of the patients was 24.4 years old (range 6-81 years old). The mean follow-up was 49.4 months (range 24-124 months). ABC, GCT, and ABC secondary to GCT were diagnosed in 24 (54%), 12 (27%), and 8 (18%) patients, respectively. Most of the cases were in the femur ¹⁶and tibia (10). Surgery was performed by a single surgeon (BJM) using adjuvants of high-speed burr, cauterization, and hydrogen peroxide. Our preference was to use cancellous allograft in younger patients with ABC and cementation in older patients with GCT. The tumor size was calculated by using volume formula by $V = \pi/6 \times L \times W \times H$ and largest dimension of the lesion and the tumors were staged based on the Enneking/MSTS benign bone tumor classification system. Descriptive statistics, Chi-square test and Kaplan-Meier survival analysis were used in SPSS 20 statistic program.

Results: We found a recurrence rate of 5/44 (11%) for the entire cohort with 5-year recurrence free survival of 89%. There was not a significant difference between ABC, GCT and ABC secondary to GCT recurrence free survival rate which are 92%, 92% and 75% at 5 years respectively ($p=0.46$) (Figure 2).

In the ABC group, the mean age was 14 years old (range 6-40 years old). The local recurrence rate was 8.3% (2/24). No variables (age, sex, size, cystic component, presence of pathologic fracture and stage), significantly affected the recurrence rate, except for soft tissue extension ($p=0.037$) (Figure 3).

In the GCT group, the mean age was 36 years old (range 15-81 years old). The local recurrence rate was 15% (3/20). We did not find clear associations with any of the investigated variables (age, sex, size, fracture, soft tissue extension, stage). Recurrence was observed in 1/12 patient in the classic GCT group and 2/8 patients in the ABC secondary to GCT group. Pathologic diagnosis was not significant in terms of recurrence ($p=0.31$). However, MRI appearance was significantly affecting the recurrence rate. The bone lesions show pure solid (11/20), pure cystic (5/20), and mixed (4/20) component on the MRI. Recurrences occurred in 0/11 patient with pure solid appearance, 1/5 patient with pure cystic appearance and 2/4 patient with mixed appearance ($p=0.033$) (Figure 4).

Primary ABC and secondary ABC can look very similar on preoperative imaging, so we investigated clinical and radiographic factors that could help distinguish at the time of presentation. The mean age of primary ABC was 14.9 years old, compared to secondary ABC of 25.1 years old ($p=0.003$). There were no statistical differences between ABC and ABC to secondary GCT groups regarding sex, MRI appearance (cystic or mixed), pathologic fracture, soft tissue extension, and tumor volume.

Conclusion: In our cohort, we found that the local recurrence rate was similar in ABC, ABC secondary to GCT, and GCT groups. Secondary ABC demonstrated a higher rate of local recurrence, potentially explained by a higher use of bone graft rather than cement. An older age at the time of presentation, in particular in patients with a solid component on MRI, may suggest a secondary ABC rather than primary. Surgeons should anticipate that patients with a radiographic appearance consistent with ABC in the third decade of life and beyond are likely to be secondary to GCT and should manage using diligent curettage, surgical adjuvants, and cementation in anticipation of this final diagnosis.

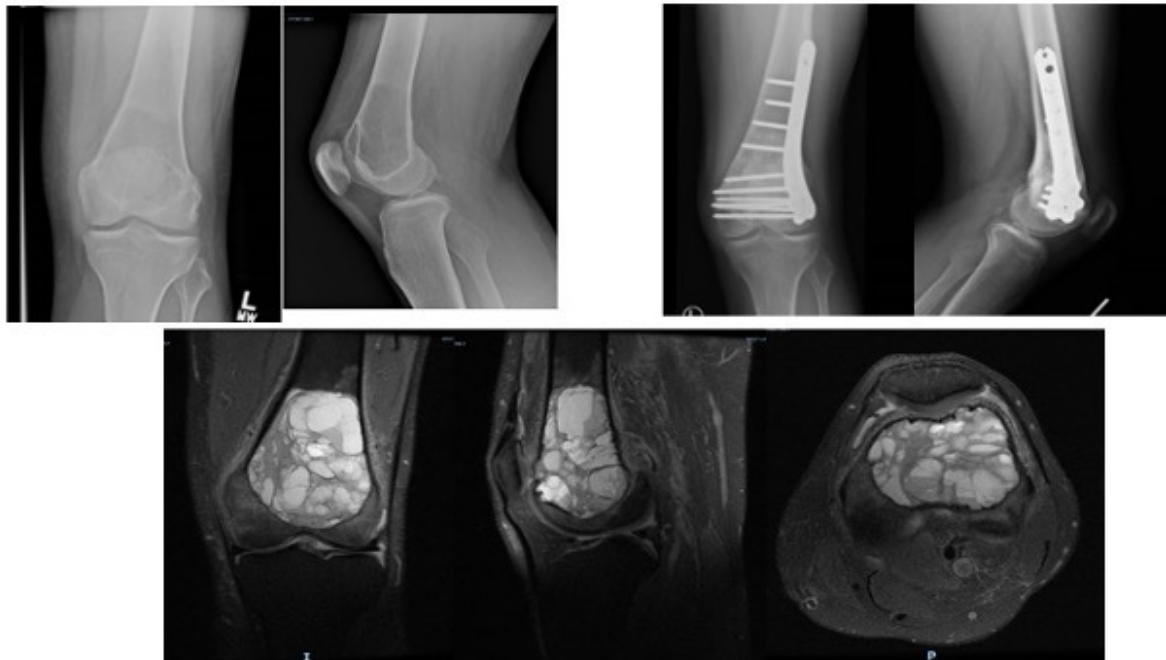


Figure 1. 29 years old male patient with ABC secondary to GCT in distal femur treated curettage, bone grafting and plating. MRI shows pure cystic changes.

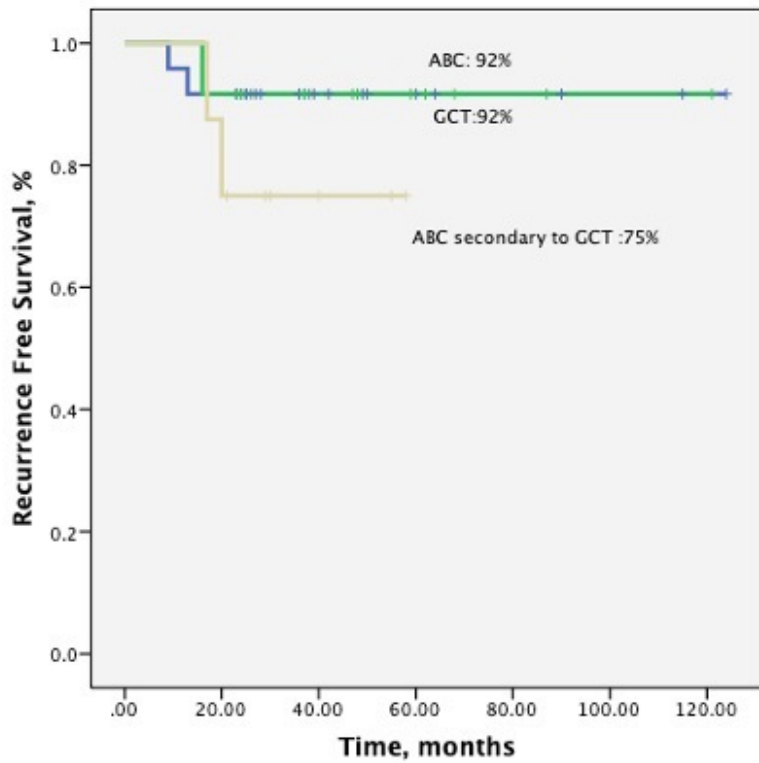


Figure 2: Recurrence free survival rate of the three groups with no significant differences ($p=0.46$).

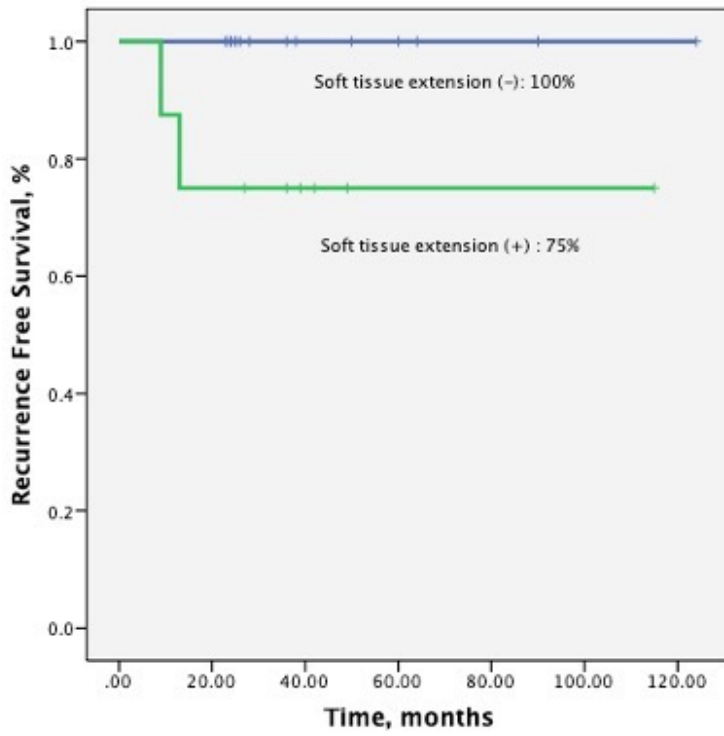


Figure 3. Recurrence free survival rate of ABC subgroups regarding soft tissue extension. Presence of the soft tissue extension has significantly worse recurrence free survival ($p=0.037$).

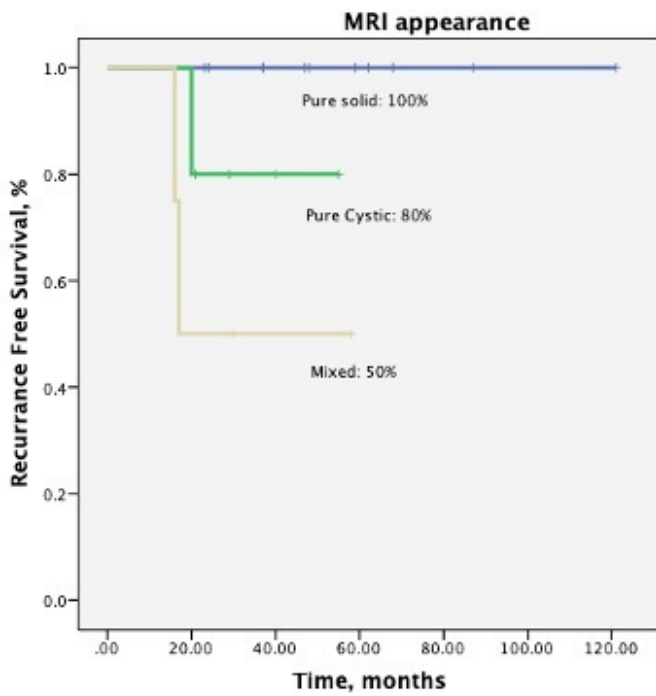


Figure 4: Recurrence free survival rate was significantly different among three GCT subgroups regarding MRI appearance ($p=0.033$).



Poster #169 #1819034

THE RECURRENCE RATE OF DIFFUSE TENOSYNOVIAL GIANT CELL TUMOUR OF THE KNEE FOLLOWING STAGED OPEN SYNOVECTOMY

Stefan A. St George, MD; Paul Clarkson, MB ChB, University of British Columbia, Vancouver, British Columbia, CANADA

Objective: Diffuse-type Tenosynovial Giant-Cell Tumour (d-TGCT) of large joints is a rare, locally aggressive, soft tissue tumour affecting predominantly the knee. Previously classified as Pigmented Villonodular Synovitis (PVNS), this monoarticular disease arises from the synovial lining and is more common in younger adults. Given the diffuse and aggressive nature of this tumour, local control is often difficult and recurrence rates are high. Current literature is comprised primarily of small, and a few larger but heterogeneous, observational studies. Both arthroscopic and open synovectomy techniques, or combinations thereof, have been described for treatment of d-TGCT of the knee.

There is, however, no consensus on the best approach to minimize recurrence of d-TGCT of the knee. Some limited evidence would suggest that a staged, open anterior and posterior synovectomy might be of benefit in reducing recurrence. To our knowledge, no case series has specifically looked at the recurrence rate of d-TGCT of the knee following a staged, open, posterior and anterior approach. We hypothesized that this approach may provide better recurrence rates as suggested by larger more heterogeneous series.

Methods: A retrospective review of the local pathology database was performed to identify all cases of d-TGCT or PVNS of the knee treated surgically at our institution over the past 15 years. All cases were treated by a single fellowship-trained orthopaedic oncology surgeon, using a consistent, staged, open, posterior and anterior approach for synovectomy. All cases were confirmed by histopathology and followed-up with regular repeat MRI to monitor for recurrence. Medical records of these patients were reviewed to extract demographic information, as well as outcomes data, specifically recurrence rate and complications. Any adjuvant treatments or subsequent surgical interventions were noted.

Results: 23 patients with a minimum follow up of 2 years were identified. Mean age was 36.3 at time of treatment. There were 10 females and 13 males. Mean follow up was 7.5 years. 14/23 (60.9%) had no previous treatment. 5/23 had a previous arthroscopic synovectomy, 1/23 had a previous combined anterior arthroscopic and posterior open synovectomy, and 3/23 had a previous open synovectomy. Mean time between stages was 87 days (2.9 months). 7/23 (30.4%) patients had a recurrence. Of these, 3/7 (42.9%) were treated with Imatinib and 4/7 (57.1%) were treated with repeat surgery (3/4 arthroscopic and 1/4 open).

Conclusion: Recurrence rates of diffuse type TGCT in the literature vary widely but tend to be high. In our retrospective study, a staged, open, anterior and posterior synovectomy provides recurrence rates that are lower than rates previously reported in the literature. These findings support prior data suggesting this approach may result in better rates of recurrence for this highly recurrent difficult to treat tumour.



July 9, 2020

To Whom It May Concern:

This letter is to confirm that Dr. Stefan St. George is currently enrolled as a PGY-IV resident in the Department of Orthopaedics at the University of British Columbia. His residency training started July 01, 2017, and will complete on June 30, 2022. Dr. St. George is in good standing in the residency program.

If you require any other information, please do not hesitate to contact me.

Sincerely,

A handwritten signature in black ink, appearing to read 'H. Broekhuysen'.

Henry Broekhuysen, MD, FRCSC
Director of Postgraduate Education
Department of Orthopaedics
University of British Columbia

HMB/vw



Poster #171 #1818882

A PHASE 4, MULTICENTER STUDY TO EVALUATE DISCONTINUATION AND RE-TREATMENT IN SUBJECTS WITH TENOSYNOVIAL GIANT CELL TUMOR PREVIOUSLY TREATED WITH PEXIDARTINIB

Silvia Stacchiotti, MD¹; Jason Jiang, MD, PhD²; Florence Mercier, MSc³; Hamim Zahir, PhD²; Margaret Wooddell, PhD, MPH, MBA²

¹Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY,

²Daiichi Sankyo, Inc., Basking Ridge, New Jersey, UNITED STATES, ³Daiichi Sankyo Europe GmbH, Munich, Bayern, GERMANY

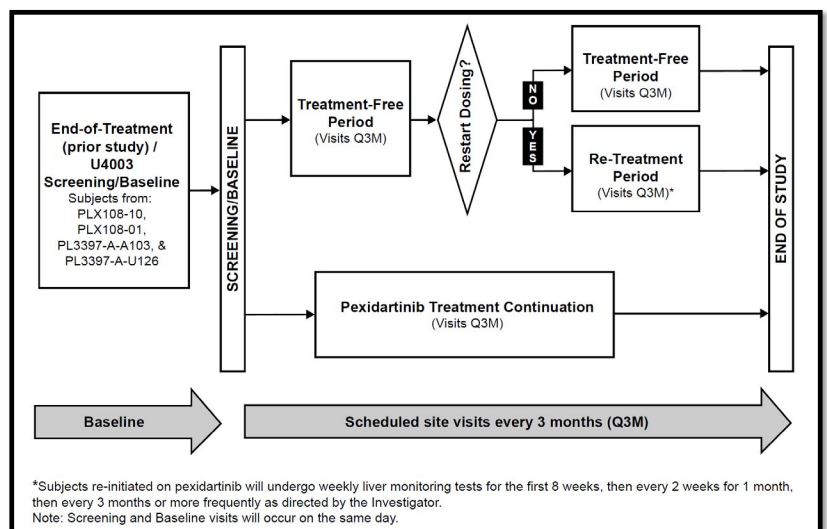
Objective: Tenosynovial giant cell tumor (TGCT) is a rare, locally aggressive neoplasm of the synovium, bursae, or tendon sheaths driven by overexpression of colony-stimulating factor-1 (CSF-1). Pexidartinib is an oral small-molecule tyrosine kinase inhibitor that targets CSF-1 receptor (CSF-1R), proto-oncogene receptor tyrosine kinase (c-Kit), and FMS-like tyrosine kinase 3 harboring an internal tandem duplication mutation, and approved by the United States Food and Drug Administration (US FDA) for the treatment of adult patients with symptomatic TGCT associated with severe morbidity or functional limitations and not amenable to improvement with surgery. Pexidartinib is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) because of the risk of hepatotoxicity. Over the long-term, most patients treated with pexidartinib achieved a clinically relevant tumor response. The objective of this study is to fully understand the impact of pexidartinib treatment discontinuation in patients who benefited from the drug.

Methods: This is a phase 4, multicenter study in subjects with TGCT treated with pexidartinib from one of 4 prior studies: (PLX108-10 [ENLIVEN; NCT02371369], PLX108-01 [NCT01004861], PL3397-A-A103 [NCT02734433], and PL3397-A-U126 [NCT03291288]), at sites located in the US, EU, Australia, and Taiwan. At their End of Treatment (EOT) visit from these prior studies, subjects were enrolled into the phase 4 study (PL3397-A-U4003). The study subjects were offered the choice to enroll into one of two cohorts: ¹Pexidartinib Treatment Continuation Cohort in which subjects continue uninterrupted pexidartinib treatment at the same dose level as the prior EOT visit, or ²Treatment Free/Re-Treatment Cohort in which subjects discontinue pexidartinib treatment with the possibility to re-initiate treatment based on the Investigator's and subject's discretion. Considerations are given to tumor response, subjective and/or functional measures, and safety parameters in the decision-making process. The rationale for re-treatment with pexidartinib, dose modification or interruption will be recorded accordingly. Eligible subjects in the Treatment Continuation Cohort undergo clinical assessments at 3-month intervals for the duration of the study. Subjects in the Treatment-Free/Re-treatment Cohort will undergo clinical assessments at 1- and 3-months following enrollment, and at 3-month intervals thereafter (Figure). The primary objective is the proportion of subjects who remain treatment-free at 12 and 24 months after entering the Treatment-Free period of the Treatment-Free/Re-treatment Cohort. The secondary objectives pertaining to patient reported outcome (PRO) measures (Patient-Reported Outcomes Measurement Information System – Physical Function [PROMIS PF], and European Quality of Life Five Dimension Five Level Scale [EQ-5D-5L]) will be summarized descriptively over time by period and Cohort. The mean change from Baseline for these measures will also be reported over time. Qualitative tumor assessments will be summarized descriptively for all subjects in both Cohorts. Safety analyses (Adverse Events [AE], serious AE, electrocardiogram, and laboratory assessments [serum chemistry, hematology, and urinalysis]) will be performed, and subjects analyzed by Cohort separately. (NCT04526704; EudraCT #: 2020-000192-20)

Results: This is a clinical trial in progress; no results are available.

Conclusion: This is a clinical trial in progress; no conclusions are available.

Figure: Study level flow diagram





Poster #172 #1818889

AL102, ORAL GAMMA-SECRETASE INHIBITOR FOR THE TREATMENT OF DESMOID TUMORS

 Bernd Kasper, MD, PhD¹; Jason Kaplan, MD²; Gary Gordon, MD, PhD³; Mrinal M. Gounder, MD⁴

¹University of Heidelberg, Mannheim University Medical Center, Mannheim Cancer Center, Sarcoma Unit, Mannheim, Germany, Mannheim, Baden-Wuerttemberg, GERMANY, ²Ayala Pharmaceuticals, Highland Park, Illinois, UNITED STATES, ³Ayala Pharmaceuticals, Northbrook, Illinois, UNITED STATES, ⁴Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES

Objective: AL102, a potent, orally available, selective inhibitor of gamma secretase-mediated Notch signaling, is currently under development as an antineoplastic agent. Evidence supports the causal role of Notch pathway deregulation in tumorigenesis (Previs, 2015; Wang, 2015; Braune, 2016; Vinson, 2016; Xiao, 2016; Zhao, 2017). Multiple studies have demonstrated cross talk between Notch signaling and the Wnt/ β -catenin pathways which is a crucial player in the pathogenesis of desmoid tumors (DT). Along with overexpression of β -catenin, desmoid tumors express Notch and its downstream transcription factor hairy and enhancer of split 1 (HES1) (Shang, 2015; Bui, 2017).

Gamma secretase inhibitors (GSI) have significant antitumor activity against DT. An oral GSI (PF-03084014) was effective in treating desmoid tumors with an objective response rate (ORR) of 71.4% in a Phase 1 study with 7 patients (Villalobos, 2018). In a Phase 2 study with PF-03084014, 5 out of 17 patients (29%) experienced a confirmed partial response (PR) and another 5 patients had prolonged stable disease (Kummar, 2017). In a Phase 1 study with AL101 (formerly known BMS-906024; study CA216001), another GSI developed by Ayala, 2 participants with DT had confirmed partial response (PR) lasting either >3.5 years or >1 year; and an additional participant with extremity DT had stable disease lasting 1 year before discontinuing treatment (El-Khoueiry, 2018).

RINGSIDE is a Phase 2/3, randomized study in patients with progressive DT. Part A (Phase 2) is an open-label, dose regimen finding study; Part B (Phase 3) is a double blind, placebo-controlled study utilizing the dose regimen selected in Part A with the primary objective of assessing progression free survival (PFS).

Methods: Part A of RINGSIDE is open label and is enrolling up to 36 patients randomized among three dosing regimen arms: 1.2 mg daily (total of 8.4 mg weekly), 2 mg twice weekly (total of 4 mg weekly), and 4mg twice weekly (total of 8 mg weekly), with initial follow up of safety, tolerability, and tumor volume by MRI after 16 weeks in order to determine the optimal dose. The study will also be closely assessing quality of life (QOL) measures by using Patient Reported Outcome (PRO) tools. At the end of Part A, all patients who are benefiting from and tolerating AL102 will be eligible to enroll into an open label extension study at the selected dose where long-term efficacy and safety will be monitored. Part B of the study will start immediately after dose selection from Part A and will be a double-blind placebo-controlled study enrolling up to 156 patients with progressive disease, randomized 2:1 between AL102 or placebo. The study's primary endpoint will be PFS, with secondary endpoints including objective response rate, duration of response, and QOL measures derived from the GODDESS, PROMIS, EQ-5D, and Brief Pain Inventory PROs.

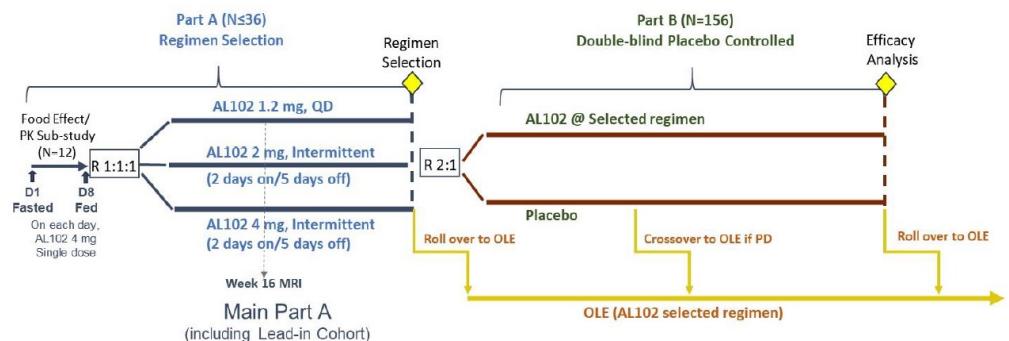
An open-label extension study will be designed to enroll participants from 3 sources: (a) roll-over participants who complete Part A (post regimen selection), (b) crossover Part B placebo-treated participants with centrally reviewed radiographic progression, and (c) roll-over participants who completed Part B (post efficacy analysis) (refer to Figure 1).

An Independent Data Monitoring Committee will review safety and efficacy data from both study parts. RINGSIDE is currently open for enrollment.

Results: There are no results to present at this time.

Results: There are no results to present at this time.

Conclusion: There are no results or conclusions to present at this time.

Figure 1 Study Schema


Abbreviations: CT, computed tomography; D, day; MRI, magnetic resonance imaging; OLE, open-label extension; PK, pharmacokinetics; QD, once daily; R, randomization



Poster #173 #1818930

PHASE 2 BASKET STUDY TO EVALUATE THE ANTITUMOR ACTIVITY AND SAFETY OF LENVATINIB IN CHILDREN, ADOLESCENTS, AND YOUNG ADULTS WITH RELAPSED OR REFRACTORY SOLID MALIGNANCIES

Samuel Abbou, MD¹; Nicolas André, MD, PhD²; Alba Rubio San-Simón, MD³; Edita Kabickova, MD, PhD⁴; Peter Múdry, PhD⁵; Wayne Nicholls, FRACP⁶; Kyung-Nam Koh, MD, PhD⁷; Alexey Maschan, MD⁸; Tezer Kutluk, MD, PhD⁹; Mercedes García Lombardi, MD¹⁰; Isabelle Aerts, MD¹¹; Nadège Corradini, MD¹²; Michela Casanova, MD¹³; Csongor Kiss, MD, PhD, DSc¹⁴; Nicholas G. Gottardo, MBChB, FRACP, PhD¹⁵; Jodi McKenzie, PhD¹⁶; Xuan Deng, PhD¹⁷; Rohini Singh, MD¹⁷; Behzad Bidadi, MD¹⁸; Hyoung Jin Kang, MD, PhD¹⁹

¹Gustave Roussy, Villejuif, Ile-de-France, FRANCE, ²Hôpital de la Timone, Aix-Marseille University, Marseille, Provence-Alpes-Cote d'Azur, FRANCE, ³Hospital Universitario Niño Jesús, Madrid, Madrid, SPAIN, ⁴Pediatric Hematology and Oncology, University Hospital Motol and Charles University, 2nd Medical School, Prague, Stredocesky kraj, CZECH REPUBLIC, ⁵Univeristy Hospital Brno – Children's Hospital, Brno, Moravskoslezsky kraj, CZECH REPUBLIC, ⁶Queensland Children's Hospital and University of Queensland, Brisbane, Queensland, AUSTRALIA, ⁷Asan Medical Center Children's Hospital, University of Ulsan College of Medicine, Seoul, Seoul-t'ukpyolsi, REPUBLIC OF KOREA, ⁸Federal Research and Clinical Centre of Pediatric Hematology, Oncology and Immunology, Moscow, Moskva, RUSSIA, ⁹Hacettepe University Faculty of Medicine & Cancer Institute, Ankara, Ankara, TURKEY, ¹⁰Hospital de Niños Ricardo Gutierrez, Buenos Aires, Buenos Aires, ARGENTINA, ¹¹Institut Curie, Paris, Ile-de-France, FRANCE, ¹²Institute of Pediatric Hematology and Oncology (IHOPE), Lyon, Auvergne, FRANCE, ¹³Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ¹⁴University of Debrecen, Debrecen, Hajdu-Bihar, HUNGARY, ¹⁵Perth Children's Hospital, Perth, Western Australia, AUSTRALIA, ¹⁶Eisai Inc., Woodcliff Lake, New Jersey, UNITED STATES, ¹⁷Merck & Co., Inc., Kenilworth, New Jersey, UNITED STATES, Kenilworth, NJ, ¹⁸Merck & Co., Inc., Kenilworth, New Jersey, UNITED STATES, ¹⁹Seoul National University College of Medicine, Seoul National University Cancer Research Institute, Wide River Institute of Immunology, Seoul National University Children's Hospital, Seoul, Seoul-t'ukpyolsi, REPUBLIC OF KOREA

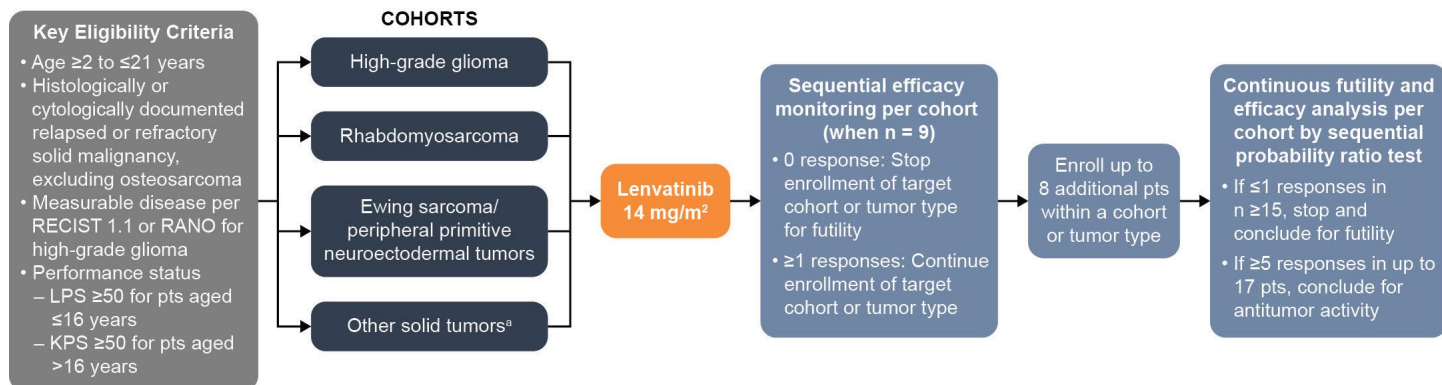
Objective: Currently, survival outcomes for pediatric patients (pts) with relapsed or refractory (R/R) solid tumors are poor because of limited available treatment options. Given that efficacy outcomes have plateaued with traditional cytotoxic chemotherapy, there remains a great unmet need for improved and targeted therapies for this population. Lenvatinib, a multiple receptor tyrosine kinase (RTK) inhibitor, selectively inhibits VEGF receptors 1-3, in addition to other proangiogenic and oncogenic pathway-related RTKs, including FGFR 1-4, PDGFR-alpha, KIT, and RET. These RTKs are thought to play a substantial role in the growth and metastasis of various pediatric solid tumors, which tend to be highly vascularized. Lenvatinib has shown antitumor activity in xenograft models of pediatric solid tumors and has demonstrated efficacy and manageable safety in various adult malignancies. An open-label phase 1b/2 study (NCT02432274) evaluating lenvatinib in children and adolescents with R/R solid tumors identified a recommended phase 2 dose of 14 mg/m² daily and showed a manageable safety profile consistent with the safety profile in adults; there were no significant differences in pharmacokinetics among children, adolescents, and adults (Gaspar N et al. J Clin Oncol. 2017;35:10544). Here we describe the design of a trial that will investigate the antitumor activity and safety of lenvatinib in children, adolescents, and young adults with R/R solid malignancies (NCT04447755). Of particular interest for this study are tumor types that are among the most common types of solid tumors in children and which have poor outcomes in the recurrent or metastatic setting, including high-grade glioma, rhabdomyosarcoma, and Ewing sarcoma.

Methods: In this open-label, multicenter, phase 2 basket study, eligible pts are aged ≥2 to ≤21 years and have histologically or cytologically documented R/R solid malignancy, excluding osteosarcoma; measurable disease per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1) or Response Assessment in Neuro-Oncology (RANO) for high-grade glioma; and a Lansky play score (LPS) ≥50 for pts aged ≤16 years or a Karnofsky performance status (KPS) scale score ≥50 for pts aged >16 years. Pts will be enrolled in 4 cohorts: high-grade glioma, rhabdomyosarcoma, Ewing sarcoma, and any other solid tumors excluding osteosarcoma. At least 36 pts will be enrolled in the study (9 in each of the 4 cohorts), with a maximum enrollment of 17 pts for each tumor type. All pts will receive lenvatinib 14 mg/m² orally once daily (adjusted for body surface area) up to a maximum daily dose of 24 mg. Treatment will continue until disease progression is verified by the investigator per RECIST 1.1 or RANO for high-grade glioma, initiation of another anticancer therapy, unacceptable toxicity, or withdrawal of consent. The study will use a sequential monitoring procedure to evaluate for futility and efficacy (Figure). A total enrollment of approximately 150 pts is expected. The primary end point is objective response rate (ORR)

at week 16 for each tumor type by investigator review per RECIST 1.1 or RANO for high-grade glioma. Secondary end points are ORR and progression-free survival for each tumor type by investigator per RECIST 1.1 or RANO for high-grade glioma; best objective response, duration of response, disease control rate, and clinical benefit rate for each tumor type; and the safety, palatability, acceptability, and pharmacokinetics of lenvatinib. Exploratory end points are the relationship between lenvatinib exposure, adverse events, and efficacy; overall survival for each tumor type; and molecular biomarkers. Recruitment is underway.

Results: Not applicable.

Conclusion: Not applicable.



^aIf $n < 9$ for a given tumor type in the other solid tumors cohort, the data will be summarized by descriptive analysis



Poster #174 #1819017

TRABECTEDIN CLINICAL ACTIVITY AND IMPACT ON SYMPTOM BURDEN AND QUALITY OF LIFE IN PATIENTS WITH ADVANCED SOFT TISSUE SARCOMA: RESULTS OF THE GREEK REAL-WORLD BEYOND-STTS STUDY

Stefania Kokkali, MD, MSc¹; Ioannis Boukovinas, MD, PhD, PharmaD²; Epaminondas Samantas, MD, PhD³; Pavlos Papakotoulas, MD, PhD⁴; Ilias Athanasiadis, MD, PhD⁵; Charalampos Andreadis, MD, PhD⁶; Parisis Makrantonakis, MD, PhD⁷; George Samelis, MD, PhD⁸; Eleni Timotheadou, MD, PhD⁹; George Vassilopoulos, MD, PhD¹⁰; Christos Papadimitriou, MD, PhD¹¹; Dimitrios Tzanninis, MD¹²; Ioannis Kotsantis, MD, PhD¹³; Kiki Karvounis-Marolachakis, BSc¹⁴; Theodora Theodoropoulou, BSc, MSc¹⁴; Amanda Psyrris, MD, PhD¹³

¹Saint-Savvas Cancer Hospital, Athens, Athens, Attiki, GREECE, ²Medical Oncology, Bioclinic of Thessaloniki, Thessaloniki, Thessaloniki, GREECE, ³Third Oncology Clinic, AgioiAnargiroi Athens General Hospital, Athens, Attiki, GREECE, ⁴First Chemotherapeutic Oncology Department, Theagenion Anti-Cancer Hospital of Thessaloniki, Thessaloniki, Thessaloniki, GREECE, ⁵Oncology Department, Hygeia Athens Private Hospital, Athens, Attiki, GREECE, ⁶Third Department of Clinical Oncology and Chemotherapy, Theagenion Anti-Cancer Hospital of Thessaloniki, Thessaloniki, Thessaloniki, GREECE, ⁷Second Department of Clinical Oncology and Chemotherapy, Theagenion Anti-Cancer Hospital of Thessaloniki, Thessaloniki, Thessaloniki, GREECE, ⁸Oncology Department at Hippocraton General Hospital of Athens, Athens, Attiki, GREECE, ⁹Department of Medical Oncology, Papageorgiou Hospital, Aristotle University of Thessaloniki, Thessaloniki, Thessaloniki, GREECE, ¹⁰Department of Hematology, Larissa University Hospital, Larissa, Larisa, GREECE, ¹¹Oncology Unit, Aretaieion University Hospital, National and Kapodistrian University of Athens, Athens, Attiki, GREECE, ¹²Medical Oncology Unit of Athens Medical Center, Athens, Attiki, GREECE, ¹³Division Medical Oncology, Attikon University General Hospital of Athens, Haidari, Attiki, GREECE, ¹⁴Medical Department, Genesis Pharma SA, Athens, Chalandri, Attiki, GREECE

Objective: Advanced soft tissue sarcomas (aSTS) represent a heterogeneous group of neoplasms with limited treatment options. Trabectedin is indicated in EU for the treatment of aSTS patients who have failed or are unfit to receive anthracycline/ifosfamide. The study aims to generate real-world evidence on trabectedin effectiveness in aSTS and its impact on symptom burden and quality of life in routine clinical practice in Greece.

Methods: This prospective study consecutively enrolled consented patients with histologically confirmed aSTS initiated on trabectedin per local label. Data were collected through routine assessments and patient-reported outcomes [MD Anderson Symptom Inventory (MDASI) and EuroQol-5 Dimensions-3-Levels (EQ-5D-3L) instrument] at 6-week intervals during the first 24 weeks and every 12 weeks thereafter for a maximum of 182 weeks.

Results: Between 21-Dec-2015 and 06-Jun-2018, 64 eligible patients (median age: 58.3 years; 62.5% females; median disease duration: 15.3 months; 67.2% metastatic) were enrolled by 13 hospital sites in Greece. At baseline, 93.8% had ECOG performance status ≤ 1 and 53.1% had ≥ 1 comorbidity. Disease histological subtypes included leiomyosarcoma (32.8%), pleomorphic undifferentiated sarcoma (15.6%), and liposarcoma (10.9%). Of the patients, 17.2%, 53.1% and 29.7% had received none, 1, and ≥ 2 prior treatment lines, respectively. A median of 3.0 (interquartile range: 2.0-6.0) trabectedin cycles were received. The median progression-free survival (PFS) and overall survival were 6.6 and 13.1 months, respectively. The 3- and 6-month PFS rates were 67.9% and 51.2%, respectively; the disease control rate was 21.9%. Baseline MDASI and EQ-5D index scores did not significantly change at post-baseline visits. The treatment discontinuation rate due to toxicity was 9.4%. The adverse drug reaction rate was 46.9% (serious: 17.2%; grade 3/4: 31.3%).

Conclusion: In a real-world setting, trabectedin demonstrated clinically meaningful benefits in aSTS patients who have failed or are unsuited to receive anthracycline/ifosfamide, with no new emerging safety signals, and without imposing additional burden on patients' quality of life.



ctos[®]

2021 *Virtual* Annual Meeting

Poster Presentations

Poster Session 2



Poster #175 #1818869

THE SURVEILLANCE AFTER EXTREMITY TUMOR SURGERY (SAFETY) TRIAL: RESULTS OF THE PILOT STUDY AND SUCCESSFUL INTERNATIONAL EXPANSION

Michelle Ghert, MD, FRCSC¹; The SAFETY, Investigators²

¹McMaster University, Oakville, Ontario, CANADA, ²McMaster University, Hamilton, Ontario, CANADA

Objective: Following surgical resection of a high-grade extremity soft-tissue sarcoma (STS), 40-50% of all patients will develop a local or distant recurrence. Therefore, intensive post-operative surveillance is routine practice. However, the adverse effects of intensive surveillance must be considered, particularly in light of the fact that the majority of patients that develop distant metastases cannot be cured.

Methods: The Surveillance After Extremity Tumor Surgery (SAFETY) trial, is an international multi-center randomized controlled trial (RCT) aimed to identify the optimal post-operative surveillance strategy in the STS population. Patients are randomized into one of 4 surveillance groups for the first 2 years of follow-up: ¹CXR every 3 months, ²CT every 3 months, ³CXR every 6 months, or ⁴CT every 6 months. The primary outcome is overall survival at 5 years, and secondary outcomes include quality of life and healthcare costs.

Results: At the time of abstract submission, STS patients have been randomized across 14 open clinical sites in five countries. An additional 12 clinical sites are in the active start-up phase. Patient interest in the trial has matched or exceeded expectations and multi-site collaborative experience has led to important protocol refinements.

Conclusion: STS patient surveillance has been identified by consensus as a top research priority in the field. The SAFETY investigators have successfully demonstrated the ability to coordinate international RCTs through the PARITY trial and continue to do so in the SAFETY trial. Further expansion of the SAFETY collaborative network will be important for the recruitment of the SAFETY target sample size, and CTOS members are encouraged to visit the study website at www.SAFETYrct.com to register as an investigator.



Poster #176 #1818941

OUTCOMES RELATED TO THE TREATMENT OF SARCOMAS WITH ANTHRACYCLINES AND/OR IFOSFAMIDE DURING PREGNANCY

Amanda Parkes, MD¹; Yeonhee Park, PhD²; Kristi Posey, PA³; Sonia Godbole, MD⁴; Keith Skubitz, MD⁵; Steven I. Robinson, MD⁶; Mark Agulnik, MD⁷; Brian A. Van Tine, MD, PhD⁴; Angela C. Hirbe, MD, PhD⁴; J Andrew Livingston, MD³

¹University of Wisconsin Carbone Cancer Center, Madison, Wisconsin, UNITED STATES, ²University of Wisconsin-Madison Department of Biostatistics and Medical Informatics, Madison, Wisconsin, UNITED STATES, ³MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁴Washington University School of Medicine, St. Louis, Missouri, UNITED STATES, ⁵University of Minnesota, Minneapolis, Minnesota, UNITED STATES, ⁶Mayo Clinic, Rochester, Minnesota, UNITED STATES, ⁷City of Hope, Duarte, California, UNITED STATES

Objective: Sarcomas are rare diagnoses, however they are seen with relative frequency in adolescents and young adults and thus can present in pregnancy. While a sarcoma diagnosis during pregnancy represents a vulnerable time for mother and fetus, there is limited sarcoma-specific data to support safety of commonly used sarcoma chemotherapy regimens in pregnancy. We sought to study the administration of anthracyclines and/or Ifosfamide in pregnancy, characterizing the largest group of sarcomas receiving such treatment in pregnancy thus far reported.

Methods: We conducted a multi-institutional retrospective study, identifying patients with bone or soft tissue sarcoma who received anthracyclines and/or Ifosfamide during pregnancy at six institutions. Retrospective chart review identified variables related to demographics, cancer diagnosis, therapies including those received during pregnancy, and outcome of the patient and fetus. Data was summarized numerically using descriptive statistics such as proportion for categorical variables and mean (standard deviation) or median (range with minimum and maximum) for continuous variables. We performed Wilcoxon rank sum test to compare two independent samples (i.e., patients with pregnancy loss and patients with live birth). Survival times were displayed graphically using Kaplan-Meier curves with median survivals.

Results: We identified 12 patients with sarcoma who received anthracyclines and/or Ifosfamide during pregnancy, including 4 bone sarcomas and 8 soft tissue sarcomas diagnosed at a mean gestational age of 17.4 +/- 5.6 weeks. Details of chemotherapy administered in pregnancy are seen in Table 1. Two patients also underwent surgery during pregnancy, both with R0 resection of extremity tumors occurring at 19- and 36-weeks gestational age.

Pregnancy outcomes are seen in Table 2; 8/12 patients (66.7%) had live births. Of the 8 live births, the mean gestational age at time of delivery was 30.5 +/- 3.9 weeks and 62.5% (5/8) of infants required a stay in the neonatal intensive care unit (NICU). Mean infant post-delivery hospitalization was 66.5 +/- 53.6 days. Median birth weight was 690.0 grams (range: 660.5-1535.0 grams) and 50% of infants with available birth weights were below the 10th percentile for birth weight for gestational age. The Kaplan-Meier estimate of disease-free survival (DFS) is seen in figure 3, with median DFS of 62 months. Three patients in our study died, all due to progressive disease, with median time from pregnancy to death of 9 months.

Conclusion: In this multi-institutional study of sarcoma chemotherapy regimens administered during pregnancy, we found a higher rate of pregnancy complications and fetal demise than reported for better studied cancers during pregnancy such as breast cancer and Hodgkin lymphoma. While all patients in our study received chemotherapy in the second trimester or later, 33.3% of patients (4/12) had pregnancy loss at a mean of 20.8 +/- 3.6 weeks and all but two patients had pregnancy complications. Fetal growth restriction was frequently identified and all deliveries were preterm leading to high NICU needs and long infant post-delivery hospitalizations. Of the 4 patients with pregnancy loss, all received both Doxorubicin and Ifosfamide during pregnancy with chemotherapy initiated at a mean of 15.5 weeks of gestation, as compared with chemotherapy initiation at a mean of 21.6 weeks of gestation for those patients with live births. Gestational age at time of chemotherapy initiation was statistically significant between patients with live birth versus pregnancy loss (p=0.021). While limited by a small sample size, our study represents the largest study of patients with sarcomas that received anthracyclines and/or Ifosfamide in pregnancy thus far reported and suggests that there may be increased risk of combination Doxorubicin and Ifosfamide administration in pregnancy, particularly when given at an earlier gestational age.

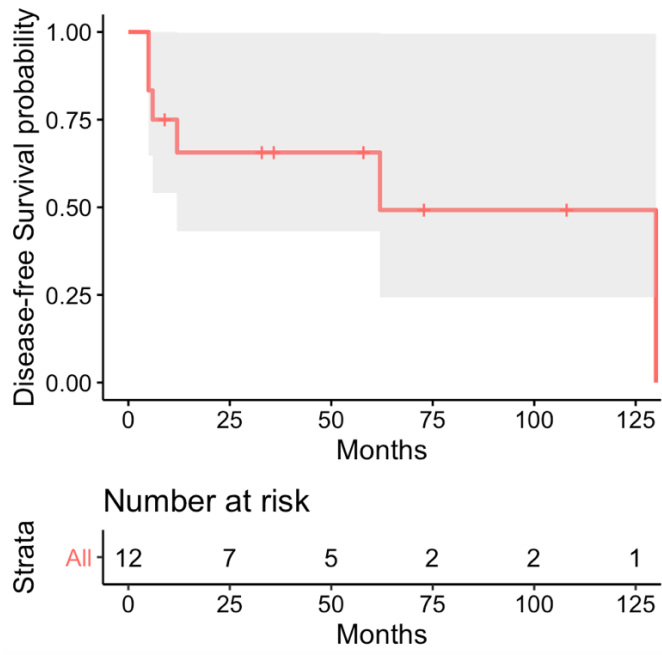
Table 1. Chemotherapy Administered During Pregnancy (n = 12).

Chemotherapy regimens administered during pregnancy	n (%)
Epirubicin/Ifosfamide	1 (8.3)
Doxorubicin/Ifosfamide	6 (50.0)
Doxorubicin/Cyclophosphamide → Doxorubicin/Ifosfamide	1 (8.3)
Doxorubicin/Cisplatin	2 (16.7)
Doxorubicin → Doxorubicin/Dacarbazine	1 (8.3)
Vincristine, Doxorubicin, Cyclophosphamide alternating with Ifosfamide and Etoposide	1 (8.3)
Gestational week chemotherapy initiated (week)	Mean (SD) 19.6 (4.2)
Number of chemotherapy cycles during pregnancy	Mean (SD) 3.2 (1.7)
Type of chemotherapy	n (%)
Neoadjuvant	7 (58.3)
Adjuvant	2 (16.7)
Palliative	3 (25.0)
Intent of therapy given during pregnancy	n (%)
Curative	8 (66.7)
Palliative	4 (33.3)
Chemotherapy best response during pregnancy	n (%)
Complete response	1 (8.3)
Partial response	5 (41.7)
Stable disease	2 (16.7)
Progression of disease	2 (16.7)
Remained as no evidence of disease	2 (16.7)

Table 2. Characteristics and Pregnancy Outcomes (n = 12).

Patient No.	Histology	Type of Pregnancy	Systemic Therapy During Pregnancy	Gestational Week Systemic Therapy Started (weeks)	Pregnancy Complications	Live Fetal Birth?	Gesta-tional Age at Birth or Fetal Demise (weeks)
1	Malignant peripheral nerve sheath tumor	Natural	Epirubicin/ Ifosfamide	24	Fetal growth restriction	Yes	26
2	Osteo-sarcoma	Natural	Doxorubicin/ Ifosfamide	22	Fetal growth restriction, anhydramnios, maternal hemoperitoneum	Yes	27
3	Synovial sarcoma	In vitro fertilization	Doxorubicin/ Ifosfamide	16	Fetal growth restriction, anhydramnios, intrauterine fetal demise	No	20
4	Osteo-sarcoma	Natural	Doxorubicin/ Cisplatin	21	None	Yes	36
5	Ewing sarcoma	Natural	Vincristine, Doxorubicin, Cyclophosphamide alternating with Ifosfamide and Etoposide	16	Fetal growth restriction, fetal demise found at time of induction for abnormal umbilical artery Doppler study	No	24
6	Myxofibro-sarcoma	Natural	Doxorubicin/ Ifosfamide	22	Reduced fetal movements, abnormal intrauterine fetal heart rates	Yes	26
7	High grade spindle cell sarcoma	Natural	Doxorubicin/ Ifosfamide	13	Intrauterine stillbirth	No	16
8	Osteo-sarcoma	Natural	Doxorubicin/ Cisplatin	23	None	Yes	34
9	Desmoid	Natural	Doxorubicin; Doxorubicin/ Dacarbazine	16	Fetal growth restriction	Yes	33
10	High grade spindle cell sarcoma	Natural	Doxorubicin/ Cyclophosphamide; Doxorubicin/ Ifosfamide	18	Fetal growth restriction, asymmetric growth restriction	Yes	32
11	High grade spindle cell sarcoma	Natural	Doxorubicin/ Ifosfamide	27	Oligohydramnios	Yes	30
12	High grade spindle cell sarcoma	Intrauterine insemination	Doxorubicin/ Ifosfamide	17	Fetal demise	No	23

Figure 3. Kaplan-Meier Estimate of Disease-Free Survival Time Curve (n = 12).





Poster #177 #1818864

SIX+ YEARS OF BENEFIT WITH SINGLE AGENT PAZOPANIB IN UNRESECTABLE METASTATIC UNDIFFERENTIATED PLEOMORPHIC SARCOMA

Benjamin C. Powers, MD¹; Mark Myron, MD²; Julie Hamlin, APRN²; Tiffany Verhulst, RN²; Dana Smith, RN²

¹The University of Kansas Health System, Leawood, Kansas, UNITED STATES, ²The University of Kansas Health System, Overland Park, Kansas, UNITED STATES

Objective: When looking at clinical trials utilizing pazopanib for metastatic sarcomas, there tends to be very select cases that have much different, much better progression free survival benefit from the drug. Here we present a case of a gentleman with unresectable undifferentiated pleomorphic sarcoma with presumed metastatic disease to lungs and liver at time of diagnosis. Based on initial presentation, his overall prognosis was very poor.

After trying doxorubicin/ifosfamide, gemcitabine/docetaxel and trabectedin, he had over six years of clinical benefit from single agent pazopanib, and is alive and well 8.5 years into this diagnosis, although still with metastatic disease.

Methods: At age 61, a practicing attorney was referred for a 12.4cm x 7.8cm undifferentiated pleomorphic sarcoma of the retroperitoneum encasing the right ureter, diagnosed in December 2012 via percutaneous biopsy of the retroperitoneal mass. Tumor was diffusely positive for vimentin and desmin, negative for CD57, collagen4, S-100, CD34, EMA, MyoD1, pancytokeratin. FISH study for CPM amplification was negative. KIT and PDGFRA analysis showed no activating mutations. Staging CT chest December 2012 showed multiple subcentimeter bilateral lung nodules, and MRI abdomen January 2013 confirmed numerous liver lesions (largest 2.2cm) most consistent with metastatic disease. It was deemed nonsurgical, due to ureteral encasement and metastatic burden.

He received standard adriamycin/ ifosfamide but did not respond. The patient then proceeded to gemcitabine/docetaxel. He had severe skin reaction, so it had to be discontinued. In October 2013, the patient was treated with trabectedin on a compassionate use trial. He completed 16 cycles of treatment, and although the primary retroperitoneal sarcoma was responding, he was progressing in the liver (image 1). The patient then elected to try pazopanib in November 2014.

Results: He continued for 6+ yrs on pazopanib with relatively stable disease in lungs/liver, despite a slowly growing retroperitoneal sarcoma.

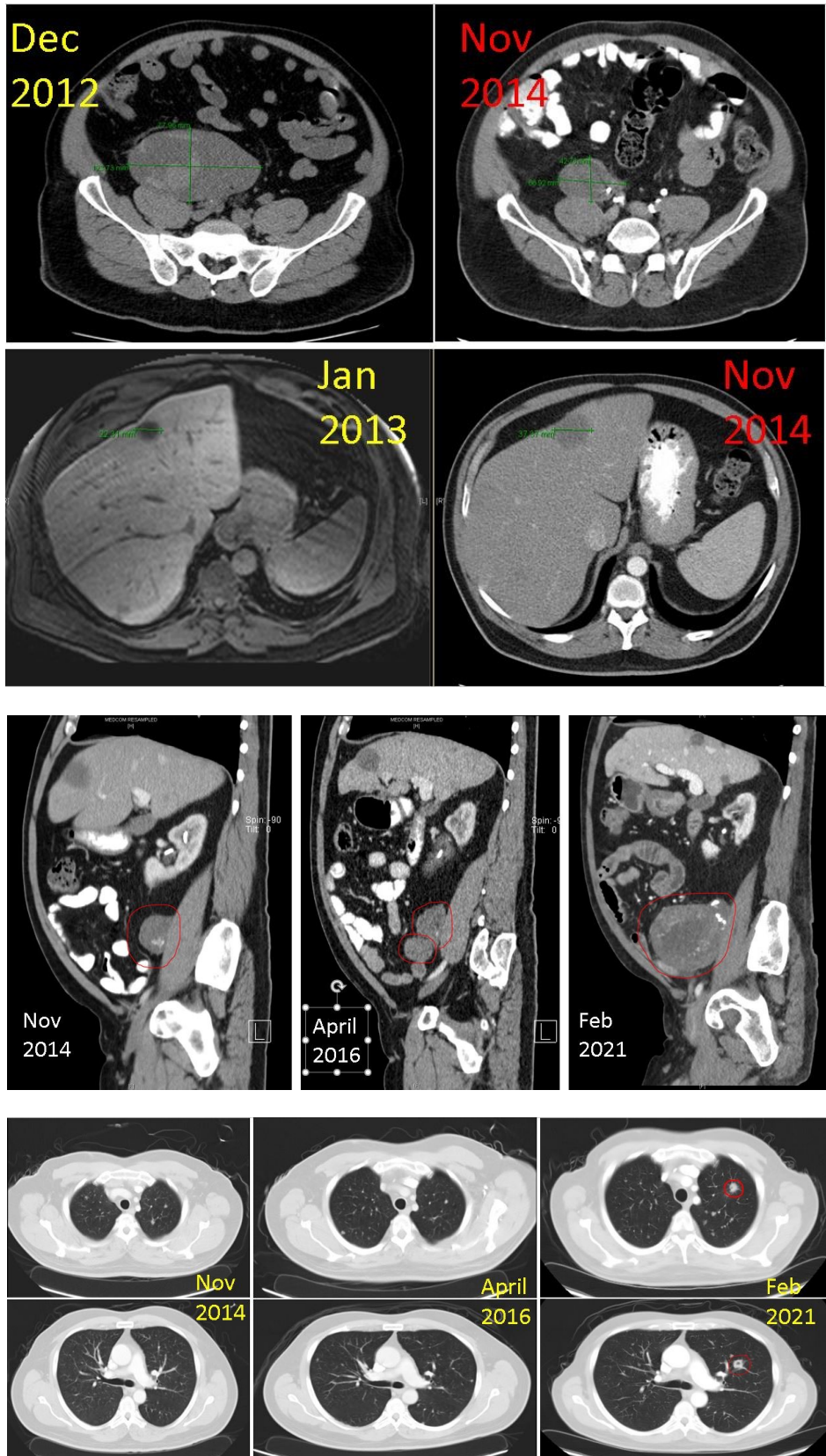
The patient had significant, sometimes uncontrollable, diarrhea (requiring adult diapers while sleeping) with 800mg dose, so he maintained on 600 mg daily for years. Interestingly, in April 2016, CT scan showed development of a 4.5cm mass inferior to the previously described retroperitoneal sarcoma; this eventually fused into a bilobed mass over time (image 2). Due to good tolerance of 600mg daily dose and lack of great options otherwise in Spring 2016, it was decided to keep him on such for palliative sake.

Over the six-plus years he was on the medicine, he was able to continue to practice law full-time, and he and his wife travelled the world. In December 2020, he was found to have multi-vessel coronary artery disease. Due to ongoing use of pazopanib, we were worried about healing properties if he were to undergo open heart surgery, so he underwent stents to the blockages.

On surveillance CT February 2021, there was finally two growing nodules in left lung concerning for progressive disease, while the retroperitoneal sarcoma continued to change slowly (image 3). Therefore, he has been switched to pembrolizumab Spring 2021, based on SARC028. We will know how he is responding to such by the time of CTOS in November 2021. If he had been on a clinical trial (i.e. PALETTE), where RECIST criteria was used to determine effectiveness, he would have needed to stop the medicine in April 2016, after 17 months of therapy, due to development of new inferior portion of the mass. But clearly, by keeping him on such, he had ongoing long term clinical benefit from the medicine for nearly five years more until February 2021.

Conclusion: We wanted to highlight a case of six-plus years of clinical benefit using single-agent pazopanib in an unresectable undifferentiated pleomorphic sarcoma of the retroperitoneum with lung and liver lesions at diagnosis in 2012. There are two main treatment-related points with this case. First is the fact that his primary undifferentiated sarcoma in the retroperitoneum was responding well to compassionate use trabectedin, although the mixed/progressive disease in the liver caused the switch to pazopanib. In the US, trabectedin is only FDA-approved for lipo- and leiomyo-sarcomas, but this shows yet another positive response to this drug, despite the lack of indication in this tumor type.

Second, and really the reason for this poster, this case has brought to question how we should use this drug clinically, experientially. We certainly will consider keeping people on pazopanib (irregardless of RECIST criteria), if they are tolerating decently and there is no clinical deterioration from their cancer burden. In our case, he is still practicing law full time and enjoying life for over eight and a half years since original diagnosis, with much of that good time related to the clinical benefit from pazopanib. I would encourage other oncology providers to have that same mindset before abandoning a drug too soon.





Poster #178 #1819013

FRAGILITY INDEX OF CLINICAL TRIALS FOR SYSTEMIC TREATMENT OF SOFT TISSUE SARCOMA

Abdulazeez Salawu, MBBS, PhD, MRCP(UK)¹; Brooke Wilson, MD²; Albiruni Ryan Abdul Abdul Razak, MD, MB, MRCP¹,
¹Division of Medical Oncology, Princess Margaret Cancer Centre, University Health Network, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, CANADA, ²Princess Margaret Cancer Centre, Toronto, Ontario, CANADA

Objective: The Fragility Index (FI) is a measure of the robustness of randomized clinical trials (RCTs) with positive statistically significant endpoints, based on threshold p-values. It estimates the minimum number of events that would have to change in order to switch the trial results from significant to non-significant. Here, we perform a FI evaluation of comparative RCTs of systemic treatments for STS.

Methods: A systematic search of Medline, Embase and Cochrane databases for adult randomized phase II and III drug trials in advanced STS, excluding non-malignant and gastrointestinal stromal tumors (January 1998 to December 2020) was carried out. Studies that performed non-comparative analysis and subgroup analyses of previously reported studies were excluded. Data on positive primary and/or secondary time-to-event (TTE) outcomes – progression free survival (PFS), overall survival (OS) and time to Progression (TTP) were abstracted for reconstruction of survival tables using the Parmar Toolkit (Parmar et al. Stat Med 1998). Adaptation of the FI framework to allow the use of TTE outcomes was performed as previously described (Desnoyers et al, Cancer Treat Rev 2021) and the number of additional events in the experimental group that would result in a non-significant effect for the positive endpoint of each trial was calculated. The FI was then compared quantitatively to the number of patients in each trial who withdrew consent or were lost to follow-up. Data abstraction and analysis was independently performed by at least 2 co-authors for consensus.

Results: We identified 55 RCTs in advanced STS, among which 6 phase II (median sample size of 128; range 73 - 270) and 6 phase III (median sample size of 454; range 355 - 711) trials with positive TTE endpoints were eligible for inclusion in the FI analysis (summarized on Table 1). These include 4 studies that led to FDA approval for trabectedin, eribulin, pazopanib and olaratumab. The primary endpoint was used for FI analysis in 9 of the 12 trials (75%). Randomization was 1:1 in 9 (75%) studies with and the rest had 2:1 randomization. PFS was the most common TTE outcome evaluated in 9 (75%) studies. OS was evaluated in 2 studies and TTP in one study. Only one study had positive results for both PFS and OS (both secondary endpoints) with similar observed hazard ratio and calculated FI (Table 1). For this study, only the FI based on OS (the more clinically meaningful endpoint) was selected for inclusion in the summarized FI evaluation data below. The median FI was 8 (range 3-52). Seven trials (58%) had FI < 10, and 2 studies had FI between 10 and 20. Two of the remaining 3 trials (with FI ≥ 20) led to FDA drug approval (Table 1). Among 11 studies that reported data, the median number of patients who withdrew consent or were lost to follow up (WCLFU) was 12 (range 1-25). WCLFU was ≥ FI in 5 studies (45%), all of which also had FI < 10 and included 2 studies that led to FDA approval for eribulin and olaratumab. It is notable that licensing for olaratumab has since been withdrawn following negative phase III data.

Conclusion: This FI evaluation of positive STS trials suggests that their statistical significance is often dependent upon a small number of events (<10) and that FI is exceeded by WCLFU in many such studies. These results emphasize the importance of real-world analyses and confirmatory randomized trials following registration trials in soft tissue sarcoma. The FI can serve to complement internationally agreed value scales such as ESMO Magnitude of Clinical Benefit scale (MCBS) or ASCO value framework for the evaluation of clinical benefit of systemic treatments in advanced STS.

Table1: Fragility Index of Randomized Clinical Trials in advanced STS

Study	Treatment	Control	Randomization	Outcome Measured	Total Sample size	Reported HR	Withdrew consent or lost to follow up (n)	Fragility Index
Phase III Trials								
van der Graaf et al, 2012 ^a	Pazopanib	Placebo	2:1	PFS ^c	369	0.31	12	38
Demetri et al, 2013	Ridaforolimus	Placebo	1:1	PFS ^c	711	0.72	17	11
Judson et al, 2014	Doxorubicin + Ifosfamide	Doxorubicin	1:1	PFS	455	0.74	14	7
Blay et al, 2015	Cisplatin + Ombrabulin	Cisplatin+ Placebo	1:1	PFS ^c	355	0.76	n/r	8
Demetri et al, 2016 ^a	Trabectedin	Dacarbazine	2:1	PFS ^c	518	0.55	22	52
Schoffski et al, 2016 ^a	Eribulin	Dacarbazine	1:1	OS ^c	452	0.77	16	3
Phase II Trials								
Chawla et al, 2015	Aldoxorubicin	Doxorubicin	2:1	PFS ^c	123	n/r	9	13
Kawai, et al 2015	Trabectedin	Best Supportive Care	1:1	PFS ^c	73	0.07	1	22
Brodowicz et al, 2018	Regorafenib	Placebo	1:1	PFS ^c	139	0.5	2	6
Garcia del Muro et al, 2011	Gemcitabine + Dacarbazine	Dacarbazine	1:1	PFS	113	0.58	1	5
				OS	113	0.56	1	4
Tap et al, 2016 ^{a, b}	Doxorubicin + Olaratumab	Doxorubicin	1:1	OS	133	0.46	7	7
Demetri et al, 2009	Trabectedin 3-weekly	Trabectedin weekly	1:1	TTP ^c	270	0.734	25	5

^a – trial led to FDA approval

^b – FDA approval subsequently withdrawn

^c - Outcome was primary endpoint of the trial

TTP – Time to progression; PFS – Progression free survival; OS – overall survival; HR – Hazard ratio; n/r – not reported



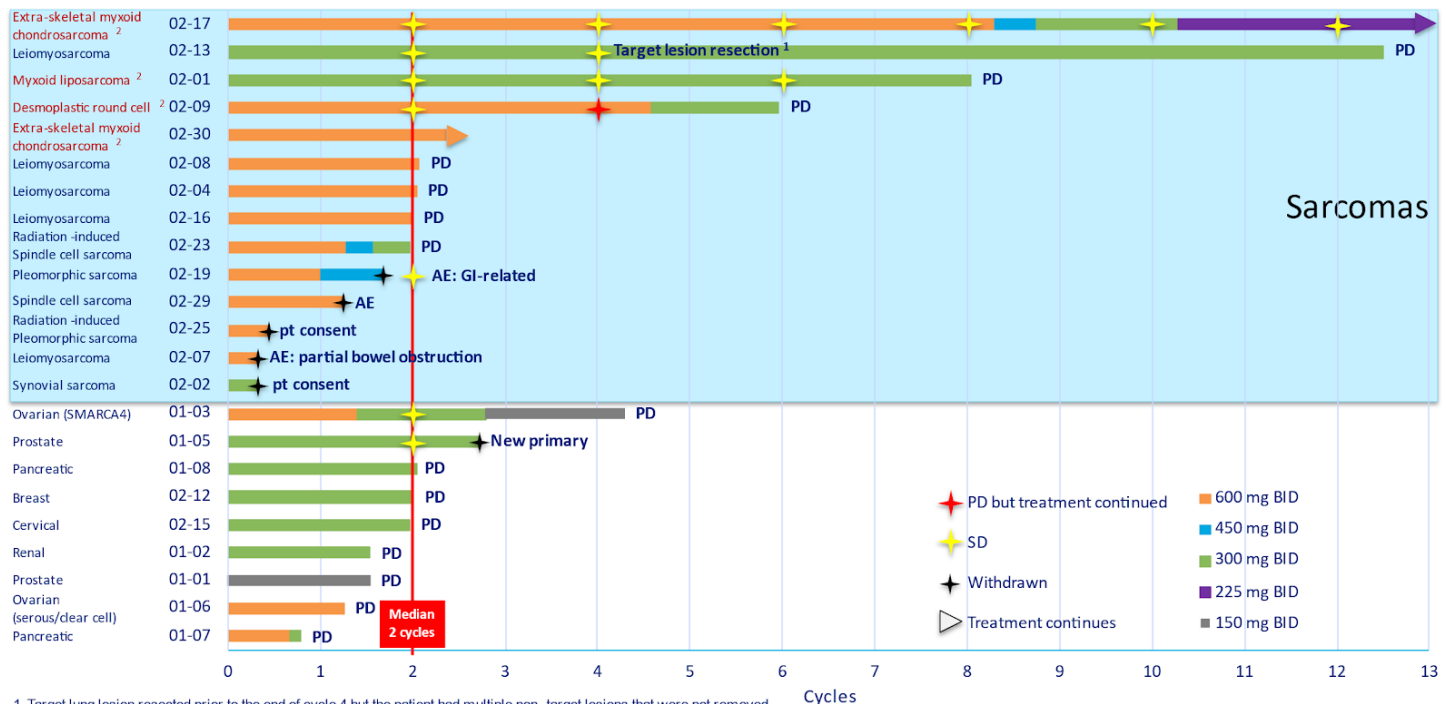
Poster #179 #1819078

PRELIMINARY EFFICACY FROM AN ONGOING PHASE 1 DOSE ESCALATION STUDY OF SECLIDEMSTAT (SP-2577) IN ADVANCED SARCOMAS AND OTHER SOLID TUMORS

Sant P. Chawla, MD¹; Victoria T. Chua-Alcala, MD¹; Jasgit Sachdev, MD²; David Wages, MD³; David Stenehjelm, MD⁴; Daniela Santiesteban⁵; Nadeem Mirza, MD,MPH⁵; Simranjit Sekhon, MD⁶; Erlinda M. Gordon, MD⁷; Michael Gordon, MD²
¹Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES, ²HonorHealth Research Institute, Scottsdale, Arizona, UNITED STATES, ³Doc Wages LLC, Southborough, Massachusetts, UNITED STATES, ⁴University of Minnesota, Duluth, Minnesot, UNITED STATES, ⁵Salarius Pharma, Houston, Texas, UNITED STATES, ⁶Sarcoma Oncology Center, Tracy, California, UNITED STATES, ⁷Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES

Objective: Background: Lysine-specific demethylase 1 (LSD1) is an epigenetic enzyme aberrantly expressed in many sarcomas and other solid tumors. High levels of LSD1 expression are often correlated with poor patient prognosis due to LSD1’s role in cancer cell proliferation, metastasis, and chemoresistance. LSD1 has been shown to associate with over 60 regulatory proteins to drive cancer progression. For instance, in sarcomas driven by FET translocations, LSD1 associates with the resulting FET oncoprotein to promote cancer cell growth. Seclidemstat is a novel, selective, reversible, and oral LSD1 inhibitor capable of inhibiting both LSD1’s catalytic and scaffolding functions. In FET-translocated sarcomas, SP-2577 disrupts FET oncoprotein-driven tumorigenesis via inhibition of LSD1’s enzymatic and scaffolding functions. We report the preliminary efficacy of seclidemstat from an ongoing Phase 1 trial enrolling patients with advanced sarcomas and other solid tumors. Objectives: Primary Objective: To evaluate the safety and tolerability of SP-2577 in patients with advanced solid tumors. Secondary Objectives: determine the maximum tolerated dose(MTD), characterize pharmacokinetics, evaluate the effect of food on pharmacokinetics, evaluate antitumor activity.\

Methods: SALA-003-AC19 (NCT03895684) is a Phase 1 trial of single-agent SP-2577 in patients with advanced sarcoma and other solid tumors. All patients had progressive disease (PD) at the time of study entry. Patients received oral SP-2577 twice a day under fasting conditions, in 28-day cycles (C). The primary objective is safety and tolerability. Secondary objectives are to determine maximum-tolerated dose, preliminary efficacy, pharmacokinetics, and pharmacodynamics.



1. Target lung lesion resected prior to the end of cycle 4 but the patient had multiple non-target lesions that were not removed
 2. FET-translocated sarcomas are shown in red

Data as of 25 June 2021

Results: As of January 31, 2021; 21 patients were enrolled (12 sarcomas, 2 prostate, 2 ovarian, 2 pancreatic, 1 renal, 1 cervical, 1 breast). Patients received escalating doses of SP-2577 from 150 to 600 mg BID and the dose escalation is ongoing. The median age was 63 years (range, 21–79). 43% were male, and patients had received a median of 4 (range, 1–8) prior systemic therapies. The most common treatment-related AEs (TEAEs) were fatigue (24% all grades) and GI-related (24% decreased appetite; 24% diarrhea; all grades). Only one grade 3 TEAE occurred in more than one patient (dehydration, n=2). No grade 4 events were reported and there were no treatment-related deaths. Full safety data will be presented after the completion of Phase 1. Two patients had at least one dose reduction. Among the 14 patients who were evaluable for response at end of C2, 7 patients (50%) had the best response of stable disease (SD) with a median time to progression (TTP) of 4.3 months (range, 2.1–11.5); this group contained 5 sarcoma patients (Figure). All 3 FET-translocated patients enrolled in the study showed a TTP (Table) that suggests single-agent activity, and 2 of these patients had prolonged SD > 6 months.

Conclusion: Seclidemstat has shown encouraging activity among advanced sarcoma patients with a manageable safety profile. Preliminary clinical data supports further exploration in FET-translocated sarcoma as a single agent in an ongoing phase 2 trial (ClinicalTrials.gov Identifier: NCT03600649)

Table. Subset of patients who showed SD at cycle 2 restaging assessment as of June 25, 2021.

Diagnosis	Genetic Abnormality	# prior systemic treatments	Dose level ¹ (mg BID)	TTP (months)
Extra-skeletal myxoid chondrosarcoma ²	FET-translocation: TAF15-CHN	1	600	11.9+
Myxoid liposarcoma	FET-translocation: FUS-DDIT3	5	300	7.2
Desmoplastic small round cell tumor	FET-translocation: EWSR1-WT1	5	600	4.3
Leiomyosarcoma ³	-	2	300	11.5
Pleomorphic sarcoma ⁴	-	1	600	2.1
Ovarian	Mutation in SMARCA4	5	600	3.9
Prostate	-	5	300	2.6

1. Entry dose level
2. Patient remains on study drug (stable disease)
3. Underwent wedge resection of target lung lesion after C2 and other residual lung lesions did not progress until 11.5 months
4. No PD, discontinued SP-2577 due to adverse events



Poster #180 #1818913

SAFETY AND RECOMMENDED PHASE 2 DOSE OF NEXT GENERATION NY-ESO-1-SPECIFIC TCR T-CELLS IN HLA-A*02 PATIENTS WITH SYNOVIAL SARCOMA OR NON-SMALL CELL LUNG CANCER: MASTER PROTOCOL (SUBSTUDIES 1 AND 2)

Adam J. Schoenfeld, MD¹; Mehmet Altan, MD²; Taofeek K. Owonikoko, MD, PhD, MSCR³; Sandra P. D'Angelo, MD¹; Brian H. Ladle, MD, PhD⁴; Jonathan Noujaim, MD⁵; Kai He, MD, PhD⁶; David Liebner, MD⁶; Adrian G. Sacher, MD⁷; John B.A.G. Haanen, PhD⁸; Jeffrey Yachnin, MD, PhD⁹; Chao Huang, MD¹⁰; Brian A. Van Tine, MD, PhD¹¹; Aisha N. Hasan, MD¹²; Thomas Faitg, PhD¹³; Emily Butler, PhD¹³; Aiman Shalabi, PharmD¹³; Steven Attia, DO¹⁴; Dejka M. Araujo, MD¹⁵

¹Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES, ²MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ³Winship Cancer Institute of Emory University, Atlanta, Georgia, UNITED STATES, ⁴Johns Hopkins University, Baltimore, Maryland, UNITED STATES, ⁵Institut D'Hématologie-Oncologie, Hôpital Maisonneuve-Rosemont, Montreal, Province du Québec, CANADA, ⁶The Ohio State University, Columbus, Ohio, UNITED STATES, ⁷Princess Margaret Cancer Centre, Toronto, Ontario, CANADA, ⁸Antoni van Leeuwenhoek Ziekenhuis, Amsterdam, Noord-Holland, NETHERLANDS, ⁹Karolinska Institutet, Stockholm, Uppsala Lan, SWEDEN, ¹⁰University of Kansas Medical Center, Kansas City, Kansas, UNITED STATES, ¹¹Washington University School of Medicine, St. Louis, Missouri, UNITED STATES, ¹²GlaxoSmithKline, Collegeville, Pennsylvania, UNITED STATES, ¹³GlaxoSmithKline, Philadelphia, Pennsylvania, UNITED STATES, ¹⁴The Mayo Clinic, Jacksonville, Florida, UNITED STATES, ¹⁵The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES

Objective: Letetresgene autoleucel (lete-cel; GSK3377794) is an autologous T-cell therapy using a genetically modified T-cell receptor (TCR) to improve recognition of cancer cells expressing NY-ESO-1/LAGE-1a. Next generation NY-ESO-1 TCR T-cell therapies, such as GSK3901961 and GSK3845097, integrate added genetic modifications to enhance anticancer activity. GSK3901961 co-expresses the CD8 α chain to stabilize TCR-human leukocyte A (HLA) class I interactions on CD4+ T cells, improving T-cell persistence and helper functions such as Type 1 T-helper antitumor responses. GSK3845097 co-expresses a dominant negative transforming growth factor- β (TGF- β) type II receptor to reduce TGF- β pathway activation and maintain T-cell proliferation, cytokine production, and cytotoxicity in the tumor microenvironment. A first-time-in-human master protocol (NCT04526509) will evaluate safety, tolerability, and recommended Phase 2 dose (RP2D) of these and possible subsequent therapies. Substudy 1 will assess GSK3901961 in patients with advanced non-small cell lung cancer (NSCLC) or synovial sarcoma (SS). Substudy 2 will assess GSK3845097 in patients with advanced SS.

Methods: Each substudy includes a dose confirmation stage to assess RP2D and a dose expansion stage. Key inclusion criteria are age ≥ 18 years; measurable disease per RECIST v1.1; HLA-A*02:01, A*02:05, or A*02:06 positivity; NY-ESO-1/LAGE-1a tumor expression; advanced (metastatic/unresectable) SS with t(X;18) translocation and anthracycline-based therapy receipt/completion/intolerance (SS only); and Stage IV NSCLC, receipt of ≥ 1 prior line(s) of standard of care (SOC) therapy including programmed death receptor- or ligand-1 inhibitors, and SOC chemotherapy receipt/intolerance (Substudy 1 only). Key exclusion criteria are prior malignancy that is not in complete remission or clinically significant systemic illness; prior receipt of gene/NY-ESO-1-specific therapy or allogeneic stem cell/solid organ transplant; central nervous system metastases (SS only); and actionable genetic aberration and receipt/failure of ≥ 3 systemic therapy lines (Substudy 1 only). Primary endpoints are safety (adverse events) and tolerability (dose-limiting toxicities). Secondary endpoints include investigator-assessed overall response rate, duration of response, and maximum expansion/persistence and phenotype of infiltrating transduced T cells. Exploratory endpoints include laboratory parameters, overall survival, and anti-GSK3901961 or -GSK3845097 titers as applicable. Analyses will be descriptive.

Results: The substudies are enrolling.

Conclusion: This study was funded by GSK (209012; NCT04526509). Editorial support was provided by Eithne Maguire, PhD and Katie Crossland, PhD of Fishawack Indicia, part of Fishawack Health, UK; funded by GSK. This abstract was previously presented at the American Association for Cancer Research (April 10–15 and May 17–21, 2021) and the American Society of Clinical Oncology Annual Meeting (June 4–8, 2021).



Poster #181 #1818922

EMACTUZUMAB: TARGET MEDIATED DRUG DISPOSITION

David J. Kerr, MD DSc¹; Jean-Pierre Delord, MD²; Carlos Gomez Roca, MD²; Antonine Italiano, MD³; Sandra P. D'Angelo, MD⁴; Michael Cannarile⁵; Georgina Meneses-Lorente⁵; Christophe Le Tourneau⁶; Jean-Yves Blay, MD, PhD⁷; Axel Mescheder, MD⁸

¹University of Oxford, Oxford, England, UNITED KINGDOM, ²IUCT-Oncopole, Toulouse, Provence-Alpes-Cote d'Azur, FRANCE, ³Institute Bergonié, Bordeaux, Aquitaine, FRANCE, ⁴Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES, ⁵F. Hoffmann-La Roche, SWITZERLAND; ⁶Institut Curie, Paris, FRANCE ⁷Centre Léon Bérard, Lyon, Auvergne, FRANCE, ⁸SynOx Therapeutics, Dublin 1, Dublin, IRELAND

Objective: The objective of this pharmacokinetic (PK) and pharmacodynamic (PD) study was to develop a concentration effect model to determine the biologically optimal dose of emactuzumab.

Methods: This was an open-label, multicentre, dose-escalation Phase Ia/b trial in patients with advanced solid tumours and TGCT. The single-agent emactuzumab dose was escalated from 100 mg up to 3000 mg and administered as intravenous infusion in different dosing regimen (twice a week, thrice a week, and biweekly or monthly).

Blood samples for safety and PK assessments were taken both at baseline, on Day 1 of each 2-week cycle, and five additional timepoints during Cycle 1 (Days 2, 4, 8, 10, and 12), and one additional timepoint during Cycle 2 (Day 8). For analysis of emactuzumab in human serum, an adapted ELISA was developed using human CSF-1R as capture reagent and an anti-idiotypic antibody against emactuzumab applied as detection reagent. The PK parameters were estimated using non-compartmental analysis.

For PD assessment, tumour biopsies were taken at baseline and around 4 weeks on treatment. Samples were analysed for CD68, CD163, and CSF-1R expression with immunohistochemical (IHC) staining. Furthermore, fluorescence-activated cell sorting was used to monitor peripheral blood monocyte subsets over time. Specifically, we assessed the number of CD45+/CD14+ and CD14Dim/CD16High monocytes; the latter express high levels of CSF-1R and represent about 5 – 10% of all monocytes. The tissue biopsies (skin and TGCT) were immediately subjected to fixation in 10% neutral-buffered formalin, and were transferred to tissue processing and paraffin embedding according to standard protocols. The following antibodies were obtained from Ventana Medical Systems (Tucson, AZ, USA): CD68 (clone KP-1) and CD 163 (clone MRQ-26). An in-house-generated anti-human-CSF-1R monoclonal mouse antibody (clone 29; Roche Diagnostics GmbH, Germany) was used for IHC detection of CSF-1R. Sections were subjected to automated staining on a Benchmark XT instrument (Ventana Medical Systems).

Results: The PK of emactuzumab in patients with TGCT and advanced solid tumours after single IV administration (Cycle 1) is non-linear. The PK of emactuzumab was shown to be non-linear across the doses 100 - 900 mg. Both C_{max} and AUC showed a greater than dose proportional increase, accompanied by a decline in clearance over the same dose range, indicating that the elimination of emactuzumab across this dose range is predominantly target-mediated (indicative data are shown in Table 1). For doses above 900 mg, exposure increased approximately dose-proportionally and little change in total clearance was seen (Table 1; Figure 1). Terminal t_{1/2} estimates increased with increasing dose ranging from approximately 1.5 - 9 days. The apparent volume of distribution ranged from 3.7 – 6.2 L, which is consistent with the majority of the drug residing within the confines of the central compartment.

Results (ongoing): A decrease in CD163/CD68 and CSF-1R expressing macrophage levels (% change from baseline) in a dose/exposure manner was observed following four weeks of emactuzumab therapy in both surrogate skin (dermal macrophages; Figure 2) and tumour (tumour associated macrophages) samples. A plateau in macrophage depletion was observed from an approximate C_{avg} of 100 µg/mL (approximately corresponding to a 900 mg dose) in the dose escalation parts. A trend for peripheral blood levels of CD14+/CD16+ monocytes to decrease from pre infusion baseline levels, concomitantly with emactuzumab average concentration, was observed during Day 1 of Cycle 1, as was a rapid and sustained exposure-dependent increase of CSF-1, consistent with a positive feedback loop.

Conclusions: Target mediated drug disposition (TMDD) corresponds to a special case⁴ wherein a significant proportion of a drug (relative to dose) is bound with high affinity to a pharmacological target (CSF 1R), such that this interaction is reflect-

ed in the PK properties of the drug eg. dose-dependent effects on steady-state volume of distribution and total systemic clearance. It was apparent that TMDD was operating in these clinical studies, leading us to develop a concentration-effect model to define the optimal biological dose of 1000 mg every 2 weeks^{2,3}. This dose achieved the required 90% or more target saturation resulting in depletion of macrophages (both in the tumour and the skin)^{1,5} and was supported by further PD markers such as peripheral monocyte subsets and circulating CSF-1 levels¹.

References

¹F. Hoffmann-La Roche Ltd, Investigator's Brochure (RO5509554) Emactuzumab, Version 12, March 2021.

²Cassier PA, Italiano A, Gomez-Roca CA, Le Tourneau C, Toulmonde M, Cannarile MA, et al. CSF1R inhibition with emactuzumab in locally advanced diffuse-type tenosynovial giant cell tumours of the soft tissue: a dose-escalation and dose-expansion phase 1 study. *Lancet Oncol* 2015;16:949e56.

³Cassier PA, Italiano A, Gomez-Roca CA, Le Tourneau C, Toulmonde M, D'Angelo SP, et al. Long-term clinical activity, safety and patient-reported quality of life for emactuzumab-treated patients with diffuse-type tenosynovial giant-cell tumour. *Eur J Cancer*. 2020;141:162-170

⁴Mager DE. Target-mediated drug disposition dynamics. *Biochem Pharmacol*. 2006; 72(1):1-10

⁵Bissinger S, Hage C, Wagner V, Maser IP, Brand V, Schmittnaegel M, et al. Macrophage depletion induces edema through release of matrix-degrading proteases and proteoglycan deposition. *Sci Transl Med*. 2021;13:eabd4550

Table 1 Clinical Pharmacokinetics (Mean [% CV]) of Emactuzumab Following Single IV Infusion (100 - 3000 mg, q2w) during Cycle 1 (Emactuzumab Monotherapy)

Dose (mg)	Mean (CV%) ^a	C _{max} (µg/mL)	AUC _{last} (d × µg/mL)	V _d (L)	CL (L/day)	t _{1/2} (day)
100 n=2 ^b	Individual value	21.6, 37.2	54.0, 64.7	3.68, 2.55	1.78, 1.16	1.55, 1.53
200 n=1	Individual value	24.9	65.2	6.87	2.89	1.79
400 n=6	Mean (CV%)	123 (20.8)	587 (27.5)	4.50 (17.4)	0.610 (46.4)	6.68 (58.7)
600 n=5	Mean (CV%)	207 (9.1)	929 (19.0)	4.53 (10.9)	0.518 (26.6)	6.84 (30.9)
900 n=6	Mean (CV%)	298 (14.8)	1880 (26.5)	3.79 (19.0)	0.369 (49.9)	8.60 (32.1)
1350 ^c n=4	Mean (CV%)	501 (25.1)	2270 (67.5)	4.07 (52.2)	0.361 (37.8)	7.69 (15.6)
2000 n=6	Mean (CV%)	638 (20.9)	3330 (30.0)	4.64 (26.7)	0.452 (43.1)	8.29 (34.7)
3000 n=6	Mean (CV%)	980 (39.6)	4180 (37.9)	6.24 (46.4)	0.635 (50.7)	7.92 (21.7)

AUC_{last} = area under the concentration-time curve from 0 to time when drug was undetectable; CL = clearance; C_{max} = maximum concentration of drug; CV = coefficient of variation; d = day; IV = intravenous; q2w = every 2 weeks; t_{1/2} = half-life; t_{last} = time when drug was undetectable; V_d = volume of distribution.

^a Individual values are reported when N ≤ 2.

^b All patients received an initial dose of 100 mg emactuzumab. Data are included from one patient that received 100 mg emactuzumab q2w following the run-in dose of 100 mg.

^c Lambda z was not calculated for one patient therefore t_{1/2}, V_d and CL not calculated for that patient. Patient 2006 was excluded for most calculations since t_{last} was 24 hours.

Figure 1 Total Clearance of Emactuzumab on Cycle 1 Emactuzumab Monotherapy

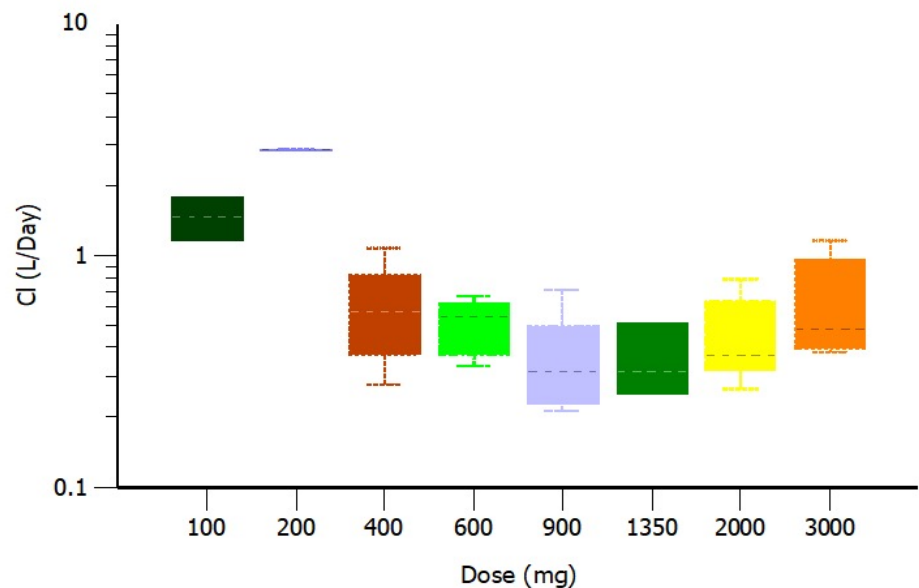
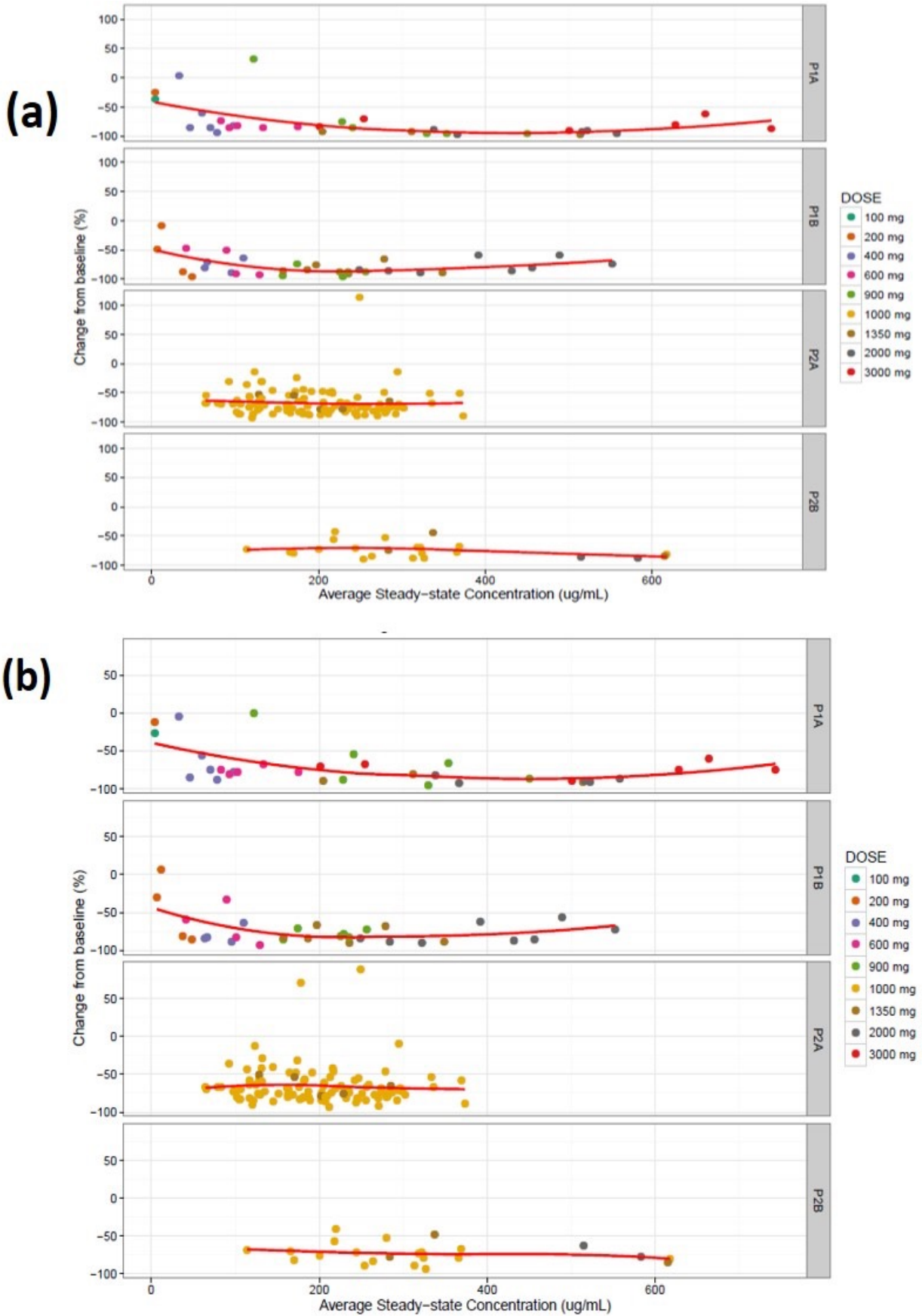


Figure 2 Systemic Exposure versus (a) CD163+/CD68+ Macrophage Levels (b) CSF-1R+ Macrophage Levels in Paired Skin Biopsy Samples





Poster #182 #1819001

FIRST-IN-HUMAN TRIAL OF SQ3370 IN RELAPSED OR REFRACTORY SOFT TISSUE SARCOMA AND OTHER SOLID TUMORS: PROOF-OF-CONCEPT FOR CLICK CHEMISTRY-BASED CAPAC PLATFORM

 Alexander Guminski, MD/PhD¹; Vivek Bhadri, MD²; Nam Bui, MD³; James Strauss, MD⁴; Robert Steffner, MD⁵; Kathleen Batty, MD¹; Madeline Strach, MD⁶; Michael Zakharian, MS⁷; Steven Smith, PhD⁷; Sangeetha Srinivasan, PhD⁷; Wayne M. Saville, MD⁷; Jose M. Mejia Oneto, MD/PhD⁷; Nathan Yee, PhD⁷; Vivek Subbiah, MD⁸
¹Royal North Shore Hospital, St Leonards, New South Wales, AUSTRALIA, ²Chris O'Brien Lifehouse, Camperdown, New South Wales, AUSTRALIA, ³Stanford University Department of Oncology, Stanford, California, UNITED STATES, ⁴Mary Crowley Cancer Research, Dallas, Texas, UNITED STATES, ⁵Stanford Cancer Institute, Palo Alto, California, UNITED STATES, ⁶Chris O'Brien Lifehouse, Camperdown, New South Wales, AUSTRALIA, ⁷Shasqi, Inc., San Francisco, California, UNITED STATES, ⁸The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES

Objective: While cancer immunotherapies and targeted therapies have been very successful in treating a wide variety types of tumors, the diverse histologies and tumor microenvironment of most soft tissue sarcomas (STS) limit their use and efficacy in this patient population. Instead, older chemotherapies such as anthracyclines (doxorubicin (Dox)) are regarded as the systemic treatment of choice for STS. Unfortunately, objective tumor responses are uncommon and risks of serious adverse events such as cardiotoxicity limit treatment to a maximum of 4-5 months. Shasqi's lead candidate, SQ3370, represents a new therapeutic modality to treat STS and other solid tumors by using a drug with known efficacy, Dox, and expanding its pharmacological capabilities while minimizing its systemic toxicity. SQ3370 utilizes Shasqi's proprietary Click Activated Protodrugs Against Cancer (CAPACTM) platform, a click chemistry-based approach that activates cancer drugs at a specific tumor site. The treatment consists of a local intratumoral injection of a prodrug-capturing biomaterial (SQL70) followed by 5 daily systemic infusions of an attenuated prodrug of Dox (SQP33). Complementary chemical groups in the 2 components allow the local capture and release of active Dox in situ. In pre-clinical models, this approach allowed an 8.95-fold increase in Dox dose level with minimal systemic adverse events and no evidence of cardiotoxicity. Tumor regression in non-injected distal lesions was also observed, suggesting a systemic anti-tumor, or abscopal, effect. The activity of SQ3370 is solely based on chemistry and is independent of tumor biomarkers or local factors such as enzymatic activity, pH, or oxygen levels. In this first-in-human (FIH) Phase 1 study, we are evaluating the safety and tolerability of the novel CAPAC based SQ3370. The trial is currently ongoing and is actively accruing patients.

Methods: SQ3370-001 (NCT04106492), the first-in-human Phase 1 study, is currently open to patients with advanced solid tumors in the US and Australia. The trial follows a conventional 3+3 design. Eligible patients are ≥18 years old with an injectable local or metastatic lesion for which published data indicates responsiveness to anthracyclines. Patients must be relapsed/refractory after standard of care therapy and must not have received > 300 mg/m² of Dox (or equivalent anthracycline). The cycle length is 21 days with no limit on total cycles. Primary objectives include safety, tolerability, and determination of the recommended Phase 2 dose. Additional objectives include assessment of pharmacokinetics in plasma and tumor biopsies, preliminary efficacy per RECIST v1.1, and immune response as assessed by mass cytometry and tumor IHC.

Results: As of June 2021, nine patients have been enrolled. SQ3370 treatment has been generally well-tolerated with no dose-limiting toxicities observed. Plasma PK data from patients appears consistent with preclinical data; the plasma concentration of SQP33 protodrug increases while that of active Dox decreases as the residence time of the injected biopolymer lengthens. Plasma exposure to active Dox peaks at Days 1-2 post SQL70 injection, followed by a decline on Days 3-5. Plasma Dox exposure has not exceeded levels reported with IV Dox, even at an SQP33 dose of 2.7 times the molar equivalent of the IV Dox maximum dose of 75 mg/m². Preliminary tumor analysis suggests substantial local exposure to Dox continues 2 weeks after the last SQP33 dose.

Conclusion: SQ3370 appears to be well tolerated and demonstrates proof-of-concept for the first click-chemistry-based therapy in the clinic. Preclinical and clinical PK data are consistent, indicating that high tumor levels can be achieved while limiting systemic exposure. Data supports further development of SQ3370 and dose escalation continues.



Poster #183 #1818911

IGNYTE-ESO: LETETRESGENE AUTOLEUCEL (LETE-CEL; GSK3377794) SAFETY AND ACTIVITY IN HLA-A*02+ PATIENTS WITH SYNOVIAL SARCOMA OR MYXOID/ROUND CELL LIPOSARCOMA (SUBSTUDIES 1 AND 2): A MASTER PROTOCOL

Sandra P. D'Angelo, MD¹; Jonathan Noujaim, MD²; Fiona Thistlethwaite, MD, PhD³; Albiruni Ryan Abdul Abdul Razak, MD, MB, MRCP⁴; Silvia Stacchiotti, MD⁵; Warren Chow, MD⁶; John B.A.G. Haanen, PhD⁷; Anna Chalmers, MD⁸; Steven I. Robinson, MD⁹; Brian A. Van Tine, MD, PhD¹⁰; Kristen N. Ganjoo, MD¹¹; Melissa L. Johnson, MD¹²; Victoria L. Chiou, MD¹³; Thomas Faitg, PhD¹³; Mary Woessner, MD¹³; Laura Pearce, MS¹³; Aiman Shalabi, PharmD¹³; Jean-Yves Blay, MD, PhD¹⁴; George D. Demetri, MD¹⁵

¹Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES, ²Institut D'Hématologie-Oncologie, Hôpital Maisonneuve-Rosemont, Montreal, Province du Québec, CANADA, ³The Christie NHS Foundation Trust and University of Manchester, Manchester, England, UNITED KINGDOM, ⁴Division of Medical Oncology, Princess Margaret Cancer Centre, University Health Network, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, CANADA, ⁵Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY, ⁶City of Hope Comprehensive Cancer Center, Duarte, California, UNITED STATES, ⁷Antoni van Leeuwenhoek Ziekenhuis, Amsterdam, Noord-Holland, NETHERLANDS, ⁸Huntsman Cancer Institute, University of Utah, Salt Lake City, Utah, UNITED STATES, ⁹Mayo Clinic, Rochester, Minnesota, UNITED STATES, ¹⁰Washington University School of Medicine, St. Louis, Missouri, UNITED STATES, ¹¹Stanford Cancer Center, Stanford, California, UNITED STATES, ¹²Sarah Cannon Research Institute, Nashville, Tennessee, UNITED STATES, ¹³GlaxoSmithKline, Philadelphia, Pennsylvania, UNITED STATES, ¹⁴Centre Léon Bérard, Lyon, Auvergne, FRANCE, ¹⁵Dana-Farber Cancer Institute and Ludwig Center at Harvard University, Boston, Massachusetts, UNITED STATES

Objective: Letetresgene autoleucel (lete-cel; GSK3377794) is an autologous T-cell product using a genetically modified T-cell receptor to target cancer cells expressing the cancer testis antigen New-York esophageal squamous cell carcinoma 1 (NY-ESO-1). Lete-cel is currently being investigated alone and in combination in multiple tumor types [1,2]. NY-ESO-1 is expressed in 70–80% of synovial sarcoma (SS) and 80–90% of myxoid/round cell liposarcoma (MRCLS) tumors [3,4], suggesting these tumors may be prime lete-cel targets. This master protocol design (IGNYTE-ESO; NCT03967223) enables evaluation of multiple cell therapies in multiple tumor types and treatment stages in separate substudies, beginning with lete-cel in substudies 1 and 2 for SS and MRCLS.

Methods: Substudy 1 is a single-arm study assessing lete-cel in treatment-naïve patients (ie, anthracycline therapy-naïve for metastatic disease) with advanced (metastatic/unresectable) NY-ESO-1+ SS or MRCLS as a first line of therapy (n=10 planned). Substudy 2 is a pivotal, single-arm study assessing lete-cel in patients with NY-ESO-1+ SS or MRCLS who progressed after anthracycline therapy (n=70 planned). Key eligibility criteria are age ≥10 years and NY-ESO-1 and HLA-A*02 positivity. Exclusion criteria include prior NY-ESO-1-specific/gene therapy, allogeneic stem cell transplant, and central nervous system metastases. Screened patients undergo leukapheresis for lete-cel manufacture, lymphodepletion, lete-cel infusion, and follow-up (FU). Long-term FU (15 years) may be done under a separate protocol. The substudy 2 primary endpoint is overall response rate (ORR) per RECIST v1.1 assessed by central independent review. Substudy 1 is not testing any formal hypotheses; statistical analysis will be descriptive. Substudy 2 is comparing ORR with the historical control assuming at least 90% power with 0.025 one-sided type I error. Secondary endpoints include efficacy (time to/duration of response, disease control rate, progression-free survival), safety (adverse event [AE] frequency/severity, serious AEs, AEs of special interest), and pharmacokinetic (maximum transgene expansion [C_{max}], time to C_{max}, area under the time curve from zero to time t as data permit).

Results: Enrollment began in December 2019.

Conclusion: This study was funded by GSK (208467; NCT03967223). Editorial support was provided by Eithne Maguire, PhD, and Katie Crossland, PhD, of Fishawack Indicia, part of Fishawack Health, UK, and funded by GSK. This abstract was first presented at American Society of Clinical Oncology Annual Meeting on June 4–8, 2021. References 1. Reckamp KL, et al. *Ann Oncol* 2019;30(Suppl_5):v602–v660. 2. Rapoport A, et al. *J Clin Oncol* 2020;38:15_suppl, TPS8555. 3. D'Angelo SP, et al. *Cancer Discov* 2018;8(8):944–957. 4. D'Angelo SP, et al. *J Clin Oncol* 2018 36:15_suppl, 3005.



Poster #184 #1818975

TRIAL IN PROGRESS: NIVOLUMAB AND RELATLIMAB IN PATIENTS WITH ADVANCED CHORDOMA

Arun Singh, MD¹; Bartosz Chmielowski, MD PhD²; Sandra Brackert, NP²; Anahis Hagopian²; John Glaspy, MD²; Noah C. Federman, MD³; Brooke Crawford, MD⁴; Nicholas M. Bernthal, MD⁵

¹University of California, Los Angeles, Santa Monica, California, UNITED STATES, ²University of California, Los Angeles, Santa Monica, California, UNITED STATES, ³UCLA Medical Center, Los Angeles, California, UNITED STATES,

⁴University of California, Los Angeles, Los Angeles, California, UNITED STATES, ⁵David Geffen School of Medicine at UCLA, Santa Monica, California, UNITED STATES

Objective: Chordomas are derived from notochordal remnants and are typically treated with surgery and radiation therapy. For advanced chordomas, there are no approved systemic therapies. Preclinical evidence and anecdotal reports have indicated that the immune system is active in chordomas and that there may be a role for immunomodulation in treating this disease.

Methods: This study is a single arm, signal finding trial that will evaluate the response rate by RECIST 1.1 criteria in patients with advanced chordoma treated with nivolumab (480 mg Q4 weeks up to 2 years) and relatlimab (160 mg Q4 weeks up to 2 years). The primary objective of this study is to assess the safety of nivolumab and relatlimab in subjects with metastatic or locally advanced/unresectable chordoma. Secondary objectives are to ascertain the RR, and the 4 and 6 month PFS by RECIST 1.1. The main inclusion criteria for the study include age >12, ECOG of 0-1, unresectable, progressive disease with measurable disease by RECIST 1.1, and standard bone marrow, hepatic and renal parameters. Main exclusion criteria include any palliative surgery or XRT 28 days prior to enrollment, immunosuppressive therapy 28 days prior to enrollment, active autoimmune disease within the past 3 years or uncontrolled or significant cardiovascular disease. Blood and pretreatment and on-treatment biopsies for PD-L1 and immune microenvironmental analysis is also being collected.

Results: To date, 10/20 patients with conventional chordoma have signed consent and 8 have started on trial: 5 clival/Cspine, 4 sacral, 1 thoracic. 50 AEs (Grades 1-4) have been noted to date, with 2 events being grade 3-4: nausea. 3 SAEs have been noted: 2 episodes of headache and 1 episode of sepsis. The median PFS of the first 7 evaluable patients was 20.3 weeks. Pretreatment biopsies have been obtained in 9/10 patients and blood has been collected on all patients.

Conclusion: The trial is ongoing and accruing patients.



Poster #185 #1818883

PHASE 1 STUDY OF CABOZANTINIB IN COMBINATION WITH TOPOTECAN-CYCLOPHOSPHAMIDE FOR PATIENTS WITH RELAPSED EWING SARCOMA OR OSTEOSARCOMA

Kevin Campbell, MD¹; Wendy London, PhD²; David S. Shulman, MD³; Brian Crompton, MD²; Kelly Klega, PhD²; Kerri Cavanaugh, RN²; Natalie Collins, MD²; Suzanne Shusterman, MD²; Katherine A. Janeway, MD³; Steven G. DuBois, MD³

¹Dana-Farber Cancer Institute, Brookline, Massachusetts, UNITED STATES, ²Dana-Farber Cancer Institute, Boston, Massachusetts, UNITED STATES, ³Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, Massachusetts, UNITED STATES

Objective: Ewing sarcoma (ES) and osteosarcoma are aggressive malignancies that most commonly affect adolescents and young adults. The poor overall survival for patients with relapsed or refractory ES and osteosarcoma presents a significant challenge and opportunity for development of novel treatment approaches.

Cabozantinib, an oral tyrosine kinase inhibitor (TKI), inhibits VEGFR-2 and MET, important mediators of tumor growth and angiogenesis. A recent phase 2 single agent study of cabozantinib in patients with advanced ES or osteosarcoma demonstrated efficacy in each cohort, yielding a 6-month objective response rate of 25.6% in patients with ES and 6-month non-progression in 33.3% of patients with osteosarcoma.

Preclinical studies in solid tumor models have demonstrated that targeting proangiogenic mechanisms in combination with cytotoxic chemotherapy can overcome chemoresistance and inhibit sarcoma growth. The combination of cyclophosphamide and topotecan was active in phase 1 and phase 2 trials for patients with ES and osteosarcoma.

Methods: We present this trial in progress abstract that describes the design of our ongoing trial. The primary objective of this prospective, open-label, single arm, phase 1 clinical trial is to determine the maximum tolerated dose of cabozantinib in a novel combination with topotecan and cyclophosphamide in patients with relapsed or refractory ES and osteosarcoma. Using a 3+3 dose escalation design, 6-24 patients will be accrued to dose levels in cohorts of 3. Key eligibility criteria include age ≥6 and ≤30 years, BSA ≥1.25m² and <2m² and ability to swallow intact pills. Prior cabozantinib is not allowed, though prior topotecan and cyclophosphamide are allowed in specific circumstances. Patients may have either measurable or evaluable disease.

As cabozantinib will be given in combination with chemotherapy agents, the dose will begin at 62.5% of the recommended phase 2 pediatric dose (see table). Topotecan and cyclophosphamide will begin at standard doses. Given that TKIs may be better tolerated when started at a modest dose and then increased over time, pre-defined inpatient dose escalation will be allowed. Recent data suggest combining TKIs in series with chemotherapy (rather than concomitant) may improve tolerability. A contingency dose level (-1B) is included to allow evaluation of a discontinuous dosing strategy if dose levels with concomitant dosing are tolerable.

Correlative biology endpoints include circulating tumor DNA (ctDNA) and circulating tumor cells (CTCs).

Results: The trial opened to enrollment at the Dana-Farber Cancer Institute in December 2020 (NCT04661852) and remains ongoing.

Conclusion: No conclusions are able to drawn at this time.

Dose Escalation Schema

Dose Level	Cabozantinib 25 mg/m ² /day, PO Days 8-21	Topotecan 0.75 mg/m ² /day, IV Days 1-5	Cyclophosphamide 250 mg/m ² /day, IV Days 1-5
-1B		Days 1-5	Days 1-5
-1A	Days 1-21	Days 1-4	Days 1-4
1*	Days 1-21	Days 1-5	Days 1-5
2	40 mg/m ² /day Days 1-21	Days 1-5	Days 1-5

*Will begin at dose level 1. If deemed intolerable, dose level -1A or -1B will be evaluated, with decision based upon toxicities observed at dose level 1.



Poster #186 #1819077

A PHASE 1B/2 STUDY OF LIPOSOMAL ANNAMYCIN (ANN) IN PATIENTS WITH PREVIOUSLY TREATED SOFT-TISSUE SARCOMAS (STS) WITH PULMONARY METASTASES

Sant P. Chawla, MD¹; Robert Shepard, MD²; Cynthia Abbate²; Simranjit Sekhon, MD³; Victoria T. Chua-Alcala, MD¹; Ted Kim⁴; Noufil Adnan, MD⁵; Waldemar Priebe, MD⁶; Sandra Silberman, MD²; J. Paul Waymack, MD⁷; Erlinda M. Gordon, MD⁵

¹Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES, ²Moleculin, Houston, Texas, UNITED STATES, ³Sarcoma Oncology Center, Tracy, California, UNITED STATES, ⁴Sarcoma Oncology Center, Santa Monica, California, UNITED STATES, ⁵Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES, ⁶University Of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁷Moleculin Biotech, Houston, Texas, UNITED STATES

Objective: Background: The lungs are the most common site of STS metastases, and although the anthracycline doxorubicin (DOX) is usually utilized for treatment, results are markedly suboptimal. ANN is a multilamellar liposomal-formulation of Annamycin (ANN) active against multidrug-resistant tumors and has shown no cardiotoxicity compared to doxorubicin. Furthermore, in preclinical studies, ANN has been found to localize high concentrations in pulmonary tissues that significantly exceeded DOX and prolonged survival in animal sarcoma models. Objectives: Primary Endpoint: To determine the safety, maximum tolerated dose (MTD), and recommended Phase 2 (RP2D) of ANN. Safety will be evaluated based on adverse events (AEs) according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v5.0. Secondary Objectives: To determine the preliminary efficacy of L-Annamycin through Overall Response Rate (ORR), ORR targeted to pulmonary metastases, Clinical Benefit rate, PFS, OS, potential for surgical resectability after L-Annamycin administration, duration of response per RECIST v1.1.

Methods: Methods: ANN will be administered on Day 1, followed by 20 days off, before starting the next 21-day cycle. Patients will have safety monitoring to include evaluation of cardiac function by echocardiogram and biomarkers. Treatment will continue every 21 days, provided the Investigator considers that the benefits of treatment with ANN continue to outweigh the risks or until tumor progression is observed, or unacceptable toxicity occurs. Tumor response will be monitored every 6 weeks during treatment and every 3 months following completion of therapy. During Phase 1b, dose escalation will proceed according to a standard 3 + 3 design. During the Phase 2 portion of the study, a maximum of 25 subjects will be enrolled at the RP2D to evaluate efficacy further. Eligible patients for this study are males or females, ≥ 18 years of age, with a pathologically confirmed diagnosis of STS, and unresectable radiographically measurable disease in the lung that can be assessed using RECIST V.1.1; disease progression on prior anthracycline therapy with a cumulative dose of ≤ 450 mg/m²; and no significant comorbidities that preclude treatment in this study. Safety evaluations will take place in all patients receiving at least one dose of the study drug. Patients evaluable for efficacy will be assessed for response to treatment by radiologic studies, and primary efficacy endpoints will include complete and partial responses as per revised RECIST guidelines.

Results: This is a trial in progress.

Conclusion: This is a Phase 1B/2 clinical trial in patients with STS with pulmonary metastases to evaluate the safety and efficacy of an anthracycline derivative (ANN) that has a greater propensity for localization to the lungs, as well as activity in doxorubicin-resistant disease. Data will be provided for this study potentially to support the establishment of a new therapeutic option for these patients.



Poster #187 #1818897

A POST HOC ANALYSIS OF THE EPAZ TRIAL: THE ROLE OF GERIATRIC VARIABLES IN ELDERLY SOFT TISSUE SARCOMA (STS) PATIENTS ON TOXICITY

Rainer Hamacher, MD¹; Xiaofei Liu, PhD²; Markus K. Schuler, MD, PhD³; Leopold Hentschel, Dipl. Psych⁴; Patrick Schöffski, MD⁵; Hans-Georg Kopp, MD⁶; Sebastian Bauer, MD⁷; Bernd Kasper, MD, PhD⁸; Lars Lindner, MD⁹; Jens-Markus Chemnitz, MD¹⁰; Martina Crysandt, MD¹¹; Alexander Stein, MD¹²; Björn Steffen, MD¹³; Stephan Richter, MD, PhD⁴; Gerlinde Egerer, MD¹⁴; Philipp Ivanyi, MD¹⁵; Annegret Kunitz, MD¹⁶; Viktor Grünwald, MD¹⁷,
¹Department of Medical Oncology, Sarcoma Center, West German Cancer Center, University Hospital Essen, Essen, Nordrhein-Westfalen, GERMANY, ²Institute for Biostatistics, Hannover Medical School, Hannover, Niedersachsen, GERMANY, ³University Hospital Carl Gustav Carus/ Medical Department I, Dresden, Berlin, Berlin, GERMANY, ⁴University Hospital Carl Gustav Carus, University Cancer Center/Medical Department I, Dresden, Dresden, Sachsen, GERMANY, ⁵General Medical Oncology, University Hospitals Leuven – Campus Gasthuisberg, Leuven, Brabant Wallon, BELGIUM, ⁶Robert Bosch Centrum für Tumorerkrankungen Stuttgart, Stuttgart, Baden-Württemberg, GERMANY, ⁷Medical Oncology, University Hospital Essen Westdeutsches Tumorzentrum, Essen, Nordrhein-Westfalen, GERMANY, ⁸University of Heidelberg, Mannheim University Medical Center, Mannheim Cancer Center, Sarcoma Unit, Mannheim, Germany, Mannheim, Baden-Württemberg, GERMANY, ⁹Department of Medicine III, University Hospital, Ludwig Maximilian University Munich, Munich, Bayern, GERMANY, ¹⁰Community Hospital Middle Rine / Department of Hematology, Oncology, Clinical Infectious Diseases, Clinical Immunology, Hemostaseology and Medical Intensive Care, University Hospital Cologne, Koblenz, Rheinland-Pfalz, GERMANY, ¹¹University Hospital RWTH Aachen, Aachen, Nordrhein-Westfalen, GERMANY, ¹²University Hospital Hamburg-Eppendorf, Hamburg, Hamburg, GERMANY, ¹³University Hospital Frankfurt, Frankfurt, Hessen, GERMANY, ¹⁴University Hospital Heidelberg, Heidelberg, Baden-Württemberg, GERMANY, ¹⁵Clinic for Hematology, Hemostasis, Oncology and Stem Cell Transplantation, Medical School Hannover, Hannover, Niedersachsen, GERMANY, ¹⁶Vivantes Clinic Berlin-Spandau /Department of Hematology, Oncology and Tumor Immunology, University Hospital Charite Berlin, Berlin, Berlin, GERMANY, ¹⁷Interdisciplinary Genitourinary Oncology at the West-German Cancer Center, Clinic for Internal Medicine (Tumor Research) and Clinic for Urology, University Hospital Essen, Essen, Nordrhein-Westfalen, GERMANY

Objective: The EPAZ study (NCT01861951) recently showed that pazopanib was non-inferior to doxorubicin in patients ≥ 60 years treated in first line for advanced STS [1]. The current post hoc analysis aimed to assess the impact of frailty on toxicity and treatment discontinuation.

Methods: Patients ≥ 60 years with advanced STS were randomized for treatment with either pazopanib or doxorubicin [1]. Elderly minimal comprehensive geriatric assessment (GA) [consisted of G8 screening tool, Charlson Comorbidity Index (CCI), instrumental activities of daily living (IADL) and social situation] were assessed at baseline. Age > 75 years, liposarcoma, ECOG performance status = 2, $G8 \leq 14$, $IADL \geq 1$ and $CCI \geq 2$ were tested for their impact on occurrence of CTCAE grade 3/4 adverse events (AEs), serious adverse events (SAEs) and treatment discontinuation using Cox proportional hazards model. Treatment was always included as a covariate in the Cox model.

Results: Univariate analysis showed a reduced risk for CTCAE grade 3/4 AEs for treatment with pazopanib (HR 0.46; 95%-CI 0.25 – 0.86; $p = 0.015$). The risk was increased for ECOG = 2 (HR 4.20; 95%-CI 1.41 – 12.51; $p = 0.010$), $G8$ score ≤ 14 (HR 1.96; 95%-CI 1.09 – 3.50; $p = 0.024$) and $IADL \geq 1$ (HR 2.14; 95%-CI 1.12 – 4.09; $p = 0.021$) independent of treatment. The risk for SAEs was increased as well for ECOG = 2 (HR 5.49; 95%-CI 1.38 – 21.74; $p = 0.015$), $G8$ score ≤ 14 (HR 3.32; 95%-CI 1.67 – 6.63; $p = 0.001$) and $IADL \geq 1$ (HR 2.44; 95%-CI 1.10 – 5.43; $p = 0.029$). On multivariate analysis only pazopanib remained significant with reduced risk for CTCAE grade 3/4 AEs (HR 0.53; 95%-CI 0.29 – 0.95; $p = 0.033$) and $G8$ score ≤ 14 with increased risk for SAEs (HR 2.67; 95%-CI 1.26 – 5.69; $p = 0.011$). Neither age nor CCI showed any impact on CTCAE grade 3/4 AEs or SAEs. An influence on treatment discontinuation was not observed for any of the analyzed parameters.

Conclusion: This post hoc analysis of the EPAZ trial demonstrates that pazopanib has a reduced risk for CTCAE grade 3/4, but no difference for SAEs compared to doxorubicin. Moreover, age had no impact on CTCAE grade 3/4 AEs or SAEs. Instead, functional assessment such as ECOG PS, $G8$ and IADL are of predictive value with higher risk of AEs and SAEs in STS independent of the treatment. Therefore, functional assessment should be used to counsel patients and tailor therapy

to individual needs. Reference 1. Grünwald V, Karch A, Schuler M, Schöffski P, Kopp HG, Bauer S, et al. Randomized Comparison of Pazopanib and Doxorubicin as First-Line Treatment in Patients With Metastatic Soft Tissue Sarcoma Age 60 Years or Older: Results of a German Intergroup Study. *J Clin Oncol*. 2020;38(30):3555-64.



Poster #188 #1818994

A PHASE III, MULTI-CENTRE, RANDOMIZED, DOUBLE-BLIND, GROUP COMPARATOR TRIAL TO ASSESS THE SAFETY AND EFFICACY OF EMACTUZUMAB VS PLACEBO IN PATIENTS WITH TENOSYNOVIAL GIANT CELL TUMOURS (TANGENT)

Axel Mescheder, MD¹; Jean-Yves Blay, MD, PhD²; Nicole LeBoeuf, MD, MPH³; Hans Gelderblom, MD, PhD⁴; Michiel van de Sande, MD PhD⁴; David Kerr, CBE MD DSc FRCP FRCGP FACP FMedSci⁵; Simon Cook, CSci, MIMBS⁶; Rowena Abbey, BSc hons⁷; Ulrich Granzer, PhD⁸; Kevin Carroll, PhD⁹; Jerry Kenna, PhD¹⁰; Ray Barlow, PhD¹¹; Broes Naeye, PhD¹¹

¹SynOx Therapeutics, Dublin 1, Dublin, IRELAND, ²Centre Léon Bérard, Lyon, Auvergne, FRANCE, ³Harvard Medical School, Cambridge, Massachusetts, UNITED STATES, ⁴Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ⁵University of Oxford, Oxford, England, UNITED KINGDOM, ⁶Celleron Therapeutics, Oxford, England, UNITED KINGDOM, ⁷SynOx Therapeutics Ltd, Dublin, Dublin, IRELAND, ⁸Granzer Regulatory Consulting & Services, Munich, Bayern, GERMANY, ⁹KJC Statistics Ltd., Stoke on Trend, England, UNITED KINGDOM, ¹⁰Kenna Consulting, Macclesfield, England, UNITED KINGDOM, ¹¹SynOx Therapeutics, Dublin, Dublin, IRELAND

Objective: Tenosynovial giant cell tumors (TGCT) are rare, benign tumors, arising in synovial lining of joints, tendon sheaths, or bursae. 2 types are distinguished: localized, either digits or extremity, and diffuse lesions. A recent nationwide study in the Netherlands analyzed estimated a worldwide incidence rates in digits, localized-extremity and diffuse TGCT of 29, 10, and 4 per million person-years, respectively (Mastboom et al., 2017). TGCT is not in itself a life-threatening disease, but especially the diffuse type may result in important functional impairments, significant joint damage, and decline in quality of life for otherwise young and healthy individuals. The Primary Efficacy Objective of this study is to estimate the efficacy of emactuzumab by measuring the Objective Response Rate (ORR). Secondary Efficacy Objectives will include selected patient reported outcomes as well as Duration of Response (DoR), and the Surgical Intervention Rate. The Safety Objective of this study is to monitor subject wellbeing and assess treatment tolerability.

Methods: CSF-1 is a secreted cytokine/hematopoietic growth factor that plays an essential role in the proliferation, differentiation, and survival of monocytes, macrophages, and related cells. It is localized to the 1p13 breakpoint and appears to have a major oncogenic role in TGCT. Emactuzumab is a humanized monoclonal antibody which binds specifically to human CSF-1R and is selective for the receptor dimerization interface of the human CSF-1R extracellular domain. Systemic therapy of dTGCT patients with emactuzumab resulted in pronounced and durable responses associated with symptomatic improvement and a manageable safety profile (Cassier et al., 2020). Study Design: Eligible subjects will be double-blinded, randomised to receive either emactuzumab or placebo on a 1:1 ratio for a maximum of 10 weeks (5 cycles). Efficacy will be measured using Response Evaluation Criteria in Solid Tumours (RECIST 1.1) by Magnetic Resonance Imaging (MRI) imaging and secondary endpoints including patient reported outcome measures (PROM). The incidence and severity of AEs (evaluated according to Common Terminology Criteria for Adverse Events [CTCAE] version 5.0), physical examination, electrocardiogram (ECG) parameters, humanised anti-human antibody (HAHA), serum biochemistry, haematology, and urinalysis will be recorded to determine tolerability. Dermatological adverse drug reactions (ADRs) will be evaluated by a central dermatologist and managed where appropriate using standardized therapeutic measures. This is a multi-center study to be conducted at up to 50 sites across Europe, Canada, and the United States of America (USA). Up to 120 subjects will be randomized to treatment.

Results: Safety, efficacy, and QoL parameters will be followed every two weeks during treatment, post-treatment on a three-monthly basis for a year, and thereafter at 18 months and 2 years. Expected low grade ADRs associated with the emactuzumab mechanism of action will be managed in accordance with standardized therapeutic guidance set out in the protocol. Subjects who progress (with worsening symptoms and/or objective progressive disease on imaging) within 6-18 months will be eligible for emactuzumab retreatment in an open-label phase. A cross-over of the placebo group is allowed.

Conclusion: TGCT is a rare, localized neoplasia of the joints. Although non-lethal, it may cause important functional impairments, significant joint damage, and decline in quality of life for otherwise young and healthy individuals. The level and duration of the emactuzumab dose regimen has been selected based on the Phase I results to maximize the depletion of CSF-1R macrophages, whilst minimizing the potential for toxicity. Subjects will be closely monitored throughout the

study for safety, efficacy, and QoL. Liver safety monitoring and assessment will be undertaken in accordance with US FDA's guidance document: <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/drug-induced-liver-injury-premarketing-clinical-evaluation> It is therefore considered to be of benefit and justified to conduct a Phase II study of emactuzumab in subjects with TGCT. The risks identified to date for emactuzumab as monotherapy are considered to be acceptable for treatment in this subject population with the proposed study design. The risk-benefit ratio for a study drug for a limited treatment period in a dose that will induce limited toxicity in a setting of benign, yet invalidating disease, is the lesson learned from previous trials. The study design is currently under review with the competent authorities and will be finalized according to their guidance. Patient enrolment is expected to start by end of 2021/early 22 with a duration of 12-18 months. References: Mastboom J L et al; 2017. Higher incidence rates than previously known in tenosynovial giant cell tumors. *Acta Orthopaedica* 88 (6): 688–694. Cassier P A et al; 2020. Long-term clinical activity, safety and patient-reported quality of life for emactuzumab-treated patients with diffuse-type tenosynovial giant-cell tumour. *European Journal of Cancer* 141: 162-170.



Poster #189 #1819002

NEOADJUVANT THERAPY INCREASES BOTH MYELOID AND LYMPHOID CELLS IN THE SARCOMA TUMOR MICROENVIRONMENT

Laura Riobos, PhD¹; Peter Goff, MD PhD²; Teresa Kim, MD¹; Bonnie LaFleur, PhD³; Matthew B. Spraker, MD PhD⁴; Kimberly Smythe, BS⁵; Yuzheng Zhang, M.S.⁶; Qianchuan He, PhD⁶; Wendy M Blumenschein, PhD⁷; Natalie A. LaFranzo, PhD⁸; Seth M. Pollack, MD⁹

¹University of Washington, Seattle, Washington, UNITED STATES, ²Universtiy of Washington, Seattle, WA, ³University of Arizona, Tucson, Arizona, UNITED STATES, ⁴Washington University, St. Louis, Missouri, UNITED STATES, ⁵FHCRC, Seattle, Washington, UNITED STATES, ⁶Fred Hutchinson Cancer Research Center, Seattle, Washington, UNITED STATES, ⁷Merck & Co. Inc., Kenilworth, New Jersey, UNITED STATES, ⁸Cofactor Genomics, San Francisco, California, UNITED STATES, ⁹Northwestern University, Chicago, Illinois, UNITED STATES

Objective: Recent trials have shown efficacy of anti-PD-1 immunotherapy in some patients with advanced soft tissue sarcoma (STS). Neo-adjuvant radiation improves local control in STS patients and there are currently multiple trials looking at the combination of radiotherapy with checkpoint inhibitors in sarcoma patients. Understanding how neoadjuvant radiotherapy modulates the tumor microenvironment is critical to design new combination therapies. We have analyzed the changes in STS tumor microenvironment (TME) pre- to post neoadjuvant therapy both at the protein (multiplex immunohistochemistry, mIHC) and gene expression level (NanoString and CoFactor ImmunoPrism).

Methods: Thirty-two STS patients who underwent neoadjuvant radiation followed by curative intent resection from 2007-2014 were identified in a retrospective review of an institutional database. Tumor infiltrating leukocytes (TIL) were measured by mIHC. Slides were digitized using the PerkinElmer Vectra 3.0 and data was imported into FlowJo 10 for quantitative image cytometry analysis. Whole transcriptome RNA sequencing by CoFactor was performed using RNA extracted from FFPE sections, followed by ImmunoPrism analysis. Gene expression was measured using a custom multiplex, 800-gene Immune Profiling Panel. Quantile normalized data was analyzed with nCounter platform, log₂ transformed and Bonferroni correction was used for multiple testing. Significant genes up- or down-regulated by 1.5 fold change post- to pre- neoadjuvant therapy were analyzed in KEGG Mapper Pathway database (https://www.genome.jp/kegg/tool/map_pathway1.html).

Results: Thirty-two STS patients who received neoadjuvant radiation previous to surgery were included in the analysis. Notably, 66% of patients were also treated with chemotherapy prior to radiation and resection. Results were consistent across the 3 different technologies used in the analysis (mIHC, NanoString and ImmunoPrism). The most prevalent immune cells in the tumor before neoadjuvant therapy were myeloid cells (45% of all immune cells) and B-cells (37%). T- cells accounted for 13% of immune infiltrates and NK cells for 5%. Neoadjuvant therapy significantly increased ($p=0.0002$) the total immune cells infiltrating the tumor (mean±SD, pre: 24.0±12.4, post: 40.2±17.9), which was observed across all histologic subtypes analyzed. Both, lymphoid and myeloid cells increased with neoadjuvant therapy. An increase in the percentage of monocytes and macrophages was observed post- neoadjuvant therapy. Over 60% of the macrophages expressed the M2-type marker CD206. A significant increase in B-cells, NK-cells and CD4-T cells was also observed, accompanied by a significant decrease of T-regulatory (FoxP3+) cells. KEGG pathways analysis was performed on NanoString data. Sixty-five genes from the custom NanoString panel had significantly altered expression pre- vs. post- radiation, 43 genes were upregulated (FC>1.5) and 22 genes were down-regulated (FC <0.67). Multiple genes and cytokines related to antigen presentation and phagosome were highly enriched and upregulated, including HLA-II, as well as monocyte and macrophage related genes (CD14, MARCO, MRC1, CXCL2, S100A8/9). Genes associated with cell cycle progression were downregulated (ANXA2, BRAF, BIRC5, MKI67), suggesting that neoadjuvant therapy was effective in halting tumor cell replication. In addition, genes associated with B- and NK-cells were also enriched and upregulated in the analysis.

Conclusion: Preoperative radiation induces infiltration of both effector and suppressive immune cells into an already complex sarcoma microenvironment. Myeloid cells, and specially M2-macrophages, are the main component of the TME even after neoadjuvant therapy. In order to generate a more robust immune response that synergize with checkpoint inhibitors, one might consider other therapies that stimulate a potent Type-I immunity.



Poster #190 #1819012

OUTCOMES FOLLOWING DEFINITIVE TREATMENT OF LOCALIZED MALIGNANT PERIPHERAL NERVE SHEATH TUMOUR (MPNST) ARE SIGNIFICANTLY WORSE FOR PATIENTS WITH NF1

Abha A. Gupta, MD, MSc, FRCPC¹; Hagit Peretz Soroka, PhD²; Peter C. Ferguson, MD, PhD, FRCSC³; Jay S. Wunder, MSc., MD⁴; Kim M. Tsoi, MD, PhD⁵; Carol J. Swallow, MD PhD FRCSC FACS⁶; Rebecca A. Gladdy, MD PhD FRCSC FACS⁶; Savataj Brar, MD, MSc, FRCSC⁷; Peter Chung, MD⁸; Charles Catton, MD FRCPC⁸; Philip Wong, MD MSc MDCM FRCPC⁸; Elizabeth G. Demicco, MD PhD⁹; Brendan C. Dickson, MD MSc¹⁰; Albiruni Ryan Abdul Abdul Razak, MD, MB, MRCP¹¹; Anthony Griffin, MSc¹²; David Shultz, MD PhD¹³; Rachel Aubrey, BSc¹⁴

¹Division of Medical Oncology, Princess Margaret Cancer Centre, University Health Network, University of Toronto, The Hospital for Sick Children, Canadian Sarcoma Research and Clinical Collaboration (CanSaRCC), Toronto, Ontario, CANADA, ²Princess Margaret Cancer Center, Canadian Sarcoma Research and Clinical Collaboration (CanSaRCC), Toronto, Ontario, CANADA, ³Division of Orthopaedic Surgery, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, CANADA, ⁴The Lunenfeld-Tanenbaum Research Institute, Toronto, Ontario, CANADA, ⁵University of Toronto, Mount Sinai Hospital, Toronto, Ontario, CANADA, ⁶Department of Surgical Oncology, Princess Margaret Hospital, University Health Network and Mount Sinai Hospital, Toronto; Lunenfeld Tanenbaum Research Institute, Sinai Health System, Toronto, Toronto, Ontario, CANADA, ⁷Department of Surgical Oncology, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, CANADA, ⁸Department of Radiation Oncology, Princess Margaret Hospital, University Health Network, Toronto, Toronto, Ontario, CANADA, ⁹Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, Toronto, Ontario, CANADA, ¹⁰Mount Sinai Hospital, Toronto, Ontario, Canada, ¹¹Division of Medical Oncology, Princess Margaret Cancer Centre, University Health Network, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, CANADA, ¹²Division of Orthopaedic Surgery, Department of Surgery, Sinai Health System, Toronto, Ontario, CANADA, ¹³Department of Radiation Oncology, Princess Margaret Hospital, University Health Network, University of Toronto, Toronto, Ontario, CANADA, ¹⁴Princess Margaret Cancer Center, Canadian Sarcoma Research and Clinical Collaboration (CanSaRCC), McMaster University, Toronto, Ontario, CANADA

Objective: Malignant peripheral nerve sheath tumour (MPNST) is a soft tissue sarcoma associated with aggressive behaviour. It most frequently arises sporadically (NF0), in the setting of prior radiotherapy, or in patients with Neurofibromatosis Type 1 (NF1). We hypothesized, based on our clinical experience, that patients with NF1-associated MPNSTs experience more rapid disease progression and worse outcomes compared to NF0.

Methods: Data was collected on all patients with localized MPNST from August 1st, 1999 and May 1st, 2021 who presented to Princess Margaret Hospital and Mount Sinai Hospital (Toronto). Patient demographics, treatment, and outcomes were extracted from the CanSaRCC Database (Canadian Sarcoma Research and Clinical Collaboration). Overall survival (OS), from the date of diagnosis to the date of death, freedom from recurrence (FFR), and freedom from distant-metastasis (FFDM) were estimated using the Kaplan Meier method and differences in survival were evaluated using the log-rank test. Univariable (UVA) and multivariable (MVA) Cox regression models were computed to look for variables that correlated to clinical outcomes. T-test and Wilcoxon rank were used to compare means and medians between groups. Chi square test was used to compare demographic features. The statistical analysis was performed using SAS 9.4, SAS Institute Inc., Cary, NC.

Results: Of 186 MPNST (66 NF1), 175 were localized (60 NF1 and 115 NF0). Demographics are described in Table 1. NF1 patients were younger ($p=0.0001$) with larger tumours at presentation ($p=0.01$). NF1 patients were more likely to experience recurrence (63.3 % vs. 45.2%, $p=0.02$) with higher mortality rate (58.3 % vs. 40%, $p=0.02$). At 2 years, OS, FFR, and FFDM were decreased among NF1 patients (Figure 1). On UVA and MVA, both NF1 and tumor size were correlated to OS, FFR, and FFDM (Table 2).

Conclusion: There have been multiple studies, with conflicting results, on the impact of NF1 on the prognosis of MPNSTs. This study suggests patients with localized NF1-associated MPNST experience a significantly higher rate of death, disease progression, and distant metastasis compared to patients with sporadic MPNST. The reasons for our findings remain unclear but will be further investigated.

Table 1. Patient and Tumor Characteristics of 186 Patients With MPNST

		NF0 N (%)	NF1 N (%)
STAGE AT DIAGNOSIS	Localized	115 (95.8)	60 (90.9)
	Metastatic	5 (4.2)	6 (9.1)
LOCALIZED AT DIAGNOSIS			
SEX	Male	55 (47.8)	30 (50)
	Female	60 (52.2)	30 (50)
AGE AT DIAGNOSIS (Years)	Median	51	34.5
	Range	(17 - 86)	(11 - 84)
MAX DIAMETER OF PRIMARY (cm)	Median	6.5	10
	Range	(1.2 - 31)	(2.1 - 30)
SITE OF PRIMARY	Peritoneum	4 (3.5)	4 (6.6)
	Trunk	15 (13)	20 (33.3)
	Lower Extremity	32 (27.8)	11 (18.3)
	Pelvis	35 (30.4)	13 (21.7)
	Bowel	1 (0.8)	1 (1.7)
	Upper Extremity	28 (24.3)	11 (18.3)
SURGERY	No	7 (6.1)	9 (15)
	Yes -Not Amputation	102 (88.7)	46 (76.7)
	Amputation	6 (5.2)	5 (8.3)
RADIATION	No	38 (33)	16 (26.7)
	Preop	54 (46.9)	27 (45)
	Postop	17 (14.8)	14 (23.3)
	Palliative	6 (5.2)	3 (5)
CHEMOTHERAPY	No	97 (84.3)	47 (78.3)
	Neoadjuvant	9 (7.8)	2 (3.3)
	Adjuvant	9 (7.8)	11 (18.3)
RECURRENCE	No	63 (54.8)	22 (36.7)
	Yes	52 (45.2)	38 (63.3)
DECEASED	No	69 (60)	25 (41.7)
	Yes	46 (40)	35 (58.3)

Table 2. 2yr - Univariate and Multivariate Analysis of 175 MPNST Patients (Localized at Diagnosis)

		UVA			MVA		
		HR	95% CI	P	HR	95% CI	P
Overall Survival (OS)	NF1 (ref:NF0)	2.9	1.6 - 5.1	0.0004	2.2	1.2-4.1	0.001
	SEX	1.5	0.8 - 2.6	0.2			
	AGE AT DIAGNOSIS	0.99	0.98 - 1.012	0.16			
	MAX DIAMETER OF PRIMARY	1.07	1.03 - 1.12	0.001	1.07	1.019 - 1.12	0.005
Freedom from recurrence (FFR)	NF1 (ref:NF0)	2.2	1.4 - 3.5	0.0014	1.8	1.1 - 3	0.02
	SEX	1.5	0.9 - 2.4	0.1			
	AGE AT DIAGNOSIS	0.99	0.98- 1.006	0.3			
	MAX DIAMETER OF PRIMARY	1.06	1.02 - 1.1	0.001	1.05	1.016 - 1.094	0.006
Freedom from distant - metastasis (FFDM)	NF1 (ref:NF0)	2.5	1.3 - 4.6	0.005	1.95	1.02 - 3.7	0.04
	SEX	1.9	0.9 - 3.6	0.065			
	AGE AT DIAGNOSIS	0.99	0.97 - 1.006	0.2			
	MAX DIAMETER OF PRIMARY	1.09	1.04 - 1.14	0.0001	1.085	1.04 - 1.14	0.0004

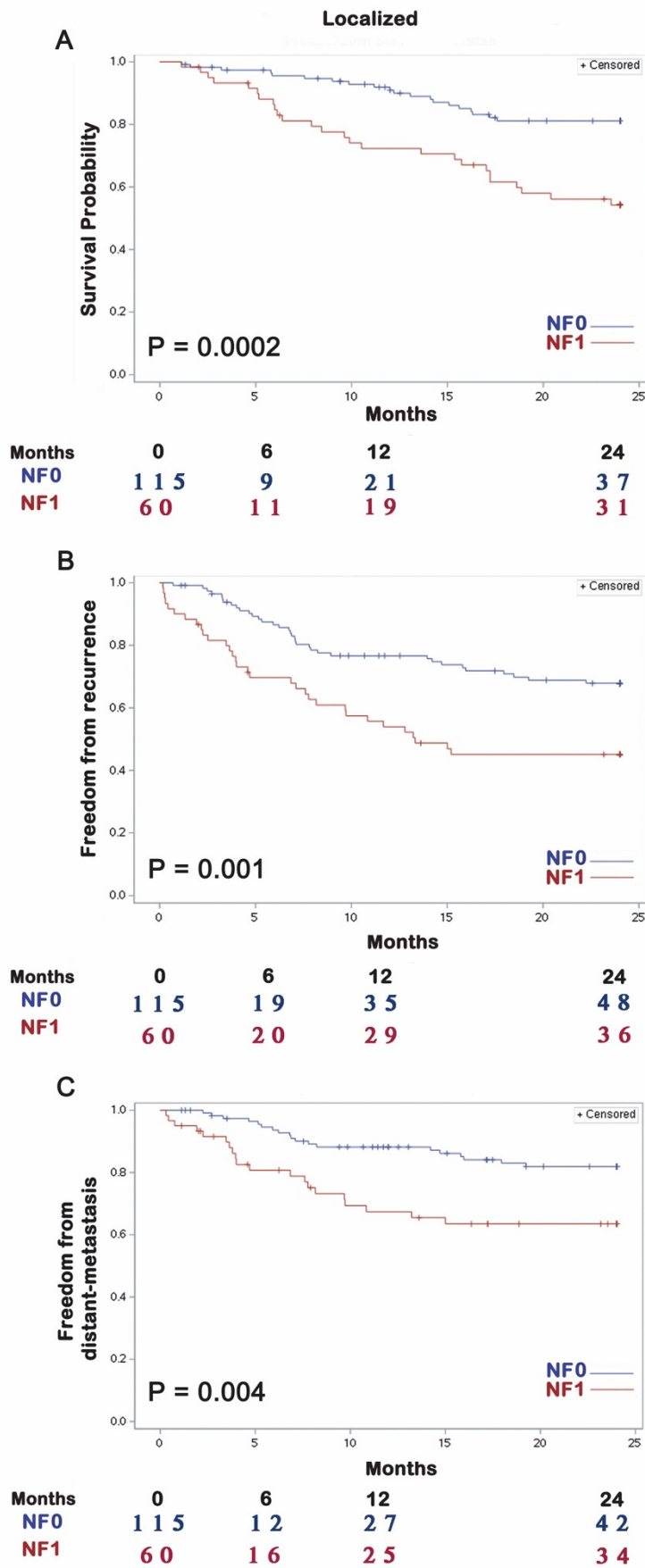


Figure 1. 2-year outcome of MPNST patients with Neurofibromatosis Type 1 (NF1) or sporadically (NF0).



Poster #191 #1818972

TRANSCUTANEOUS OXYGEN AS A PREDICTOR OF WOUND HEALING COMPLICATIONS IN PREOPERATIVELY RADIATED SOFT TISSUE SARCOMA

Lukas M. Nystrom, MD¹; Benjamin J. Miller, MD MS²; Yuxuan Jin, MS¹; Nathan Mesko, MD¹; Jeremy White, MD³; Andre Spiguel, MD⁴

¹Cleveland Clinic, Cleveland, Ohio, UNITED STATES, ²University of Iowa, Iowa City, Iowa, UNITED STATES, ³University of Oklahoma, Oklahoma City, Oklahoma, UNITED STATES, ⁴University of Florida, Gainesville, Florida, UNITED STATES

Objective: While there are clear advantages of preoperative radiation as an adjuvant to surgery in soft tissue sarcoma, there are well-demonstrated negative consequences with regard to surgical wound healing. An estimated 43% of patients with lower extremity tumors will experience wound complications. Currently there are no reliable clinical criteria to aid physicians in determining an individual patient's risk of developing a wound healing complication. We hypothesized that skin oxygenation, as measured by transcutaneous oxygen (TcO₂) at the proposed incision, would correlate with risk for development of wound complications after resection. Measurement of pre-operative TcO₂ represents a novel application of a simple, noninvasive method by which to assess skin oxygenation.

Questions/Purposes:

1. Does TcO₂ immediately prior to surgery predict wound healing complications?
2. Does TcO₂ recovery, or lack thereof, from end of radiation to the time of surgery predict a wound healing complication?
3. What effect does a wound healing complication have on patient reported and functional outcome measurements?

Methods: This study was designed as a prospective, multi-institutional observational study. Institutional review board approval was obtained at all participating sites. Inclusion criteria were a biopsy proven soft-tissue sarcoma of the lower extremity planned for preoperative radiation followed by curative intent limb-sparing surgical excision with a primary closure. TcO₂ measurements of the surgical field were obtained at three time points along the treatment course: prior to the start of radiation, immediately following radiation, and within 24 hours prior to the procedure. Five leads were placed based on the planned incision, with a control on the contralateral limb. The primary outcome was the presence of a wound healing complication within 6 months following surgical resection. Wound healing complications were defined as those requiring operative wound management (irrigation and debridement, wound closure, skin graft or flap), readmission for IV antibiotics, need for initiation of oral antibiotics, and need for dressing changes or wound packing for greater than 4 weeks after the operation, and need for aspiration (including serial aspiration) of a seroma. Additional data collected included patient, tumor and treatment variables, PROMIS Global Health and Musculoskeletal Tumor Society for the lower limb (MSTS) scores at 3 and 6 months post-surgery. Continuous variables were summarized using medians and interquartile ranges. Categorical variables were summarized using counts and percentages. Univariate logistic regression with TcO₂ as a single predictor was built to investigate the relationship between TcO₂ and wound healing at 6-month. Model results were represented using odds ratios and 95% confidence intervals. Data management and analysis were done in R software (Version 3.5; Vienna, Austria). All tests were two-sided, with an alpha level of 0.05.

Results: 43 patients were enrolled across 5 centers from 2017-2020. Four patients were ultimately excluded, leaving a total of 39 patients for analysis. There were 24 men, and 15 women with a mean age of 65.5 years. 18 of 39 patients (46.2%) experienced a wound healing complication, with some patients experiencing multiple complications. While trends were noted favoring higher skin oxygenation in patients without complications (Table 1a and 1b), these did not reach statistical significance. MSTS and PROMIS Physical Function T-scores, which were no different at baseline, were significantly decreased in the patients who had a wound healing complication at 3 months, but normalized and were no different at 6 months (Table 2) at the time most wound had healed.

Conclusion: Skin oxygenation was observed to be decreased, although statistically insignificant, in patients who had wound healing complications. Change in the skin oxygenation from end of radiation to the time of surgery did not correlate with wound healing outcomes. Surgeon (MSTS) and patient reported measurements (PROMIS Physical) of function were significantly decreased at 3 months in patients who had a wound healing complication. These were largely at the height of their complication and demonstrates the clinical relevance of this problem. We propose that while the TcO₂ may have utility, it lacked the ability to discern the patient at risk due to incomplete sampling of the surgical site.

Table 1a. Univariable logistic regression results using the lowest reading of TcO2 prior to surgery as a dichotomous variable as the single predictor in the model to evaluate the odds of having any complication.

Label	Odds Ratio (95% CI)	P-value
TcO2 Lowest Reading Prior to Surgery: \geq 25mmHg vs. $<$ 25mmHg	0.24 (0.04, 1.44)	0.12
TcO2 Mean Reading Prior to Surgery: \geq 25mmHg vs. $<$ 25mmHg	0.36 (0.03, 4.31)	0.42
TcO2 Mean Change: Increase vs. Decrease/Stable	1.05 (0.28, 3.92)	0.94

Table 1b. Univariable logistic regression results using the lowest reading of TcO2 prior to surgery as a continuous variable as the single predictor in the model. A 1-unit increase in TcO2 would lead to a 3% decrease in the odds of having any complication. When the mean reading of TcO2 is the single predictor in the model, a 1-unit increase in TcO2 would lead to a 2% decrease in the odds of having any complication. When the mean change of TcO2 is the single predictor in the model, a 1-unit increase in the mean change of TcO2 would lead to a 2% decrease in the odds of having any complication. However, none of these results showed statistical significance.

Factor	OR (95% CI)	p-value
TcO2 lowest reading prior to surgery	0.97 (0.93, 1)	0.08
TcO2 mean reading prior to surgery	0.98 (0.94, 1.02)	0.32
TcO2 mean change: Preop - After Radiation	0.98 (0.93, 1.03)	0.38

Table 2 MSTS and PROMIS Scores by Complication

Variable	Level	Total (N=39)	No (N=21)	Yes (N=18)	p.overall
MSTS 3 months		60.0 [50.0;83.3]	83.3 [56.7;93.3]	50.0 [43.3;60.0]	0.001
MSTS 6 months		83.3 [63.3;94.2]	83.3 [76.7;96.7]	73.3 [63.3;93.3]	0.345
Baseline PROMIS Physical T-Score		46.2 (8.79)	45.9 (7.50)	46.5 (10.3)	0.835
Baseline PROMIS Mental T-Score		51.8 (8.03)	51.6 (8.63)	52.0 (7.50)	0.880
3 months PROMIS Physical T-Score		47.2 (10.8)	50.3 (10.6)	43.4 (10.1)	0.045
3 months PROMIS Mental T-Score		50.7 (9.26)	52.8 (9.05)	48.3 (9.14)	0.127
6 months PROMIS Physical T-Score		54.1 (11.2)	52.2 (11.1)	56.3 (11.3)	0.256
6 months PROMIS Mental T-Score		56.5 (9.95)	55.6 (9.15)	57.6 (11.0)	0.542



Poster #192 #1818866

WHAT FACTORS DO NEW PATIENTS CONSIDER IMPORTANT WHEN SELECTING AN ORTHOPEDIC ONCOLOGIST?

 Linus Lee, BE¹; Charles A. Gusho, BS²; Vishal Patel, BS¹; Alan T. Blank, MD, MS¹
¹Rush University Medical Center, Chicago, Illinois, UNITED STATES, ²Rush University Medical Center, Milwaukee, Wisconsin, UNITED STATES

Objective: Consumer-driven healthcare plans have necessitated an even stronger focus on quality of care. An improved understanding of patients' rationale for selecting a physician may provide an opportunity to tailor the clinical practice to offer improved patient quality of care and improve patient satisfaction. This investigation sought to identify factors that new patients consider to be important when selecting an orthopedic oncologist.

Methods: Following Institutional Review Board approval, all new patients presenting to an orthopedic oncology clinic between January 2019 and August 2020 were invited to complete an anonymous survey. Prior to completion of the survey, each eligible patient received a short cover letter describing the study. The subsequent questionnaire was designed using REDCap and consisted of 27 survey items. The importance of each factor was scaled from least important ¹to unimportant (2), somewhat important (3), very important (4), and most important (5).

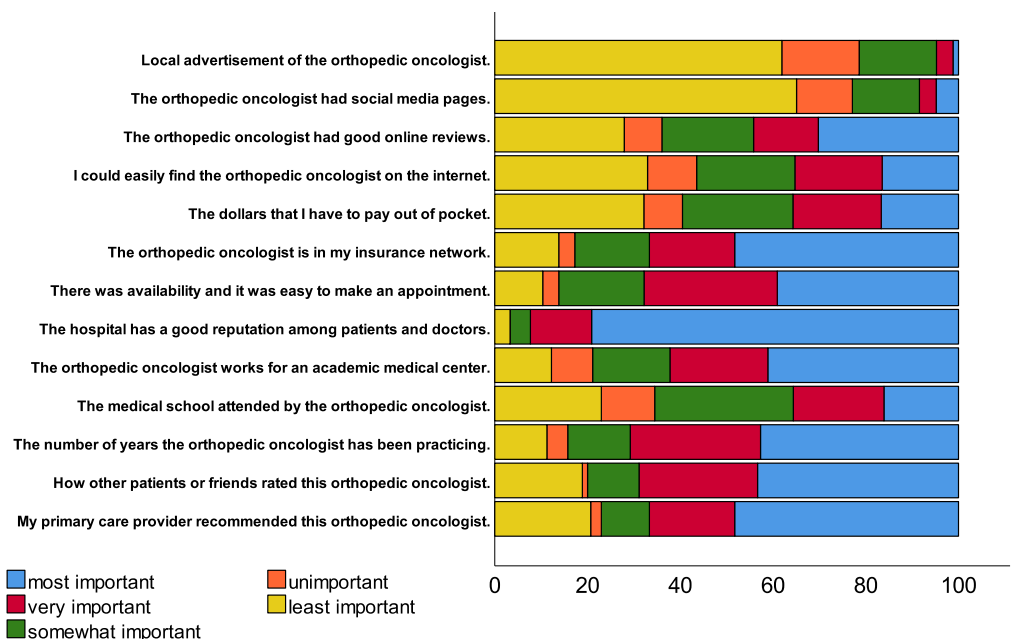
Results: A total of 101 new patients with a median age of 66 years (range, 14 years to 91 years) participated in the study. Most were referred by another doctor (n = 63, 62.4%), and of the referring providers, the most frequent specialty was orthopedic surgery (n = 32, 51%). Using a Likert-type scale with 1 representing 'least important' and 5 representing 'most important', the most important factor was the hospital reputation (mean, 4.65; SD, 0.85). Additional factors of importance were the number of years in practice (3.87 ± 1.3) and a primary care provider referral (3.71 ± 1.6). Patients younger than 40 years old found social media (p = 0.016) and Internet (p = 0.035) presence of their surgeon to be more important than older patients. In contrast, older patients considered care within an academic center to be of greater importance than younger patients (p = 0.014).

Table 1. Demographics of all responders.

	Frequency (n)	Percent (%)
Age (years)†	66	14 - 91
Female	61	60.4
Male	39	39.0
Health Insurance		
Governmental	46	45.5
Employee	39	38.6
Private	14	13.9
Other	2	2.0
Highest Schooling		
Graduate or Professional Degree	39	38.6
College Degree	36	35.6
Some College, No Degree	15	14.9
Highschool or GED	7	6.9
No Degree	3	3.0
Referral		
Yes	63	62.4
No	38	37.6

Sum may not represent total cumulative count (n = 101). † median (range).

Conclusion: This investigation suggests a primary care referral, as well as hospital and physician reputation, are among the most important factors when selecting an orthopedic oncologist. Furthermore, social media utilization appears to be more important for younger patients.





Poster #193 #1819020

BRAIN METASTASES FROM ADULT SARCOMA: THE EXPERIENCE OF THE HELLENIC GROUP OF SARCOMA AND RARE CANCERS (HGSRC).

Stefania Kokkali, MD, MSc¹; Louiza Vini, MD, PhD, FRCR²; Anastasia Stergioula, MD³; Anastasios Kyriazoglou, MD, PhD⁴; Nikolaos Vassos, MD, PhD, FACS, FICS, MHBA⁵; Ioannis Boukovinas, MD, PhD, PharmaD⁶

¹Saint-Savvas Cancer Hospital, Athens, Athens, Attiki, GREECE, ²"Iatriko" Hospital of Athens, Athens, Attiki, GREECE,

³Department of Radiation Oncology, "Iaso", Department of Tomotherapy-Stereotactic Radiosurgery "Iatropolis", Athens, Athens, Attiki, GREECE, ⁴Oncology Unit, Department of Clinical Therapeutics, General Hospital Alexandra, Athens, Athens, Attiki, GREECE, ⁵Division of Surgical Oncology, Mannheim University Medical Center, University of Heidelberg,

Mannheim, Baden-Wuerttemberg, GERMANY, ⁶Medical Oncology, Bioclinic of Thessaloniki, Thessaloniki, GREECE

Objective: Brain metastases are a rare occurrence in patients with sarcoma and the available information is relatively limited. We present our experience regarding patients with sarcoma brain metastases and their clinical presentation, define treatment modalities and examine prognostic factors associated with post-brain metastasis survival.

Methods: The study was conducted in five centers within the Hellenic Group of Sarcoma and Rare Cancers and one center in Germany. We performed a retrospective cohort study of patients with sarcoma who developed brain metastases from April 2002 to April 2020. We analyzed the clinical, radiological and histopathological data, as well as the treatment modalities and the long-term outcomes. The Kaplan-Meier method was used for survival analysis.

Results: Thirty-four adult patients were included (M:F = 16:18) with a median age at diagnosis of the primary sarcoma of 53 years (range; 15-76) and a median age at brain metastases diagnosis of 55.5 years (range; 18-75). The sarcomas originated either from soft tissue (n=27) or from bone (n=7) and the most common subtypes were leiomyosarcomas (n=8, of which 1 retroperitoneal and 4 uterine leiomyosarcomas), Ewing sarcomas/PNET (n=7), osteosarcomas (n=3). The primary tumor mostly located in the extremities (n=18) and in uterus (n=5), presenting with a median size of 8 cm (range; 2.7-25) and mostly with grade 3. The vast majority of patients had already extracranial metastatic disease [lung (n=28), bone (n=19), liver (n=7)]. Median time from sarcoma diagnosis to cerebral metastasis diagnosis was 16 months (range; 1-136). Cerebral metastases were classified as supratentorial (n=20), infratentorial (n=5), both supratentorial and infratentorial (n=5) and meningeal (n=1). A single brain metastasis was found in 42%, 2-4 metastatic lesions in 32% and more than 4 in 26% of the patients. The most common symptom was headache (n=18), followed by nausea (n=6), cranial nerve involvement (n=4), vertigo (n=4) and seizure (n=2). Treatment modalities of these patients included whole-brain radiation therapy (WBRT) (n=20), chemotherapy (n=17), exclusive palliative care (n=12), surgery (n=9), targeted therapy (n=6) or stereotactic radiosurgery (n=4). Despite these treatments, most patients experienced progression of brain metastases and at the last follow-up twenty-three patients were deceased. Median overall survival from brain metastasis diagnosis was 3 months (range; 0-80).

Conclusion: Sarcomatous brain metastases are a rare occurrence. Upon neurological symptoms shown in patients with sarcoma, a brain imaging should be performed. Patients with sarcoma brain metastases have a particularly poor prognosis and the appropriate therapeutic approach is yet to be defined.



Poster #194 #1819033

IMMUNE CORRELATES IN SOFT TISSUE SARCOMA UNDERGOING NEOADJUVANT RADIATION AND DUAL CHECKPOINT BLOCKADE

*Adrienne Victor, MD, MSc; Numbereye Numbere, MD, MBBS; Deepak Sahasrabudhe, MD
University of Rochester, Rochester, New York, UNITED STATES*

Objective: USAR17 is a pilot study on the safety of adding dual checkpoint inhibition (DCI) to neoadjuvant radiation in soft tissue sarcoma. Here we report initial correlative studies on patient samples before and after treatment.

Methods: Subjects undergoing standard of care radiation prior to surgery for resectable soft tissue sarcomas were eligible to participate. Participants could choose the control arm or interventional arm, adding ipilimumab 1mg/kg q6 weeks x2 and nivolumab 240mg IV q2 weeks x4 while undergoing radiation. Adverse event profile as well as exploratory biomarker samples were collected. Patients could receive adjuvant chemotherapy after surgery. Tumor samples were analyzed for percent necrosis and PD-1, PD-L1 (22c3 clone), and PD-L2 (B7-DC clone) expression by immunohistochemistry (IHC). Immune cell infiltrates examined for these as well as CD3 and CD163.

Results: The first 10 subjects on this study underwent analysis of tumor specimens, 6 in the DCI arm and 4 controls. 2 patients did not undergo surgery, both in the DCI arm, one due to metastasis and one due to physical decline without evidence of progression. Of the 8 patients with resection specimens, 4 had $\geq 95\%$ necrosis (three in control arm and one in DCI arm), one had 90% necrosis (DCI arm), and three had 50% or less necrosis (2 DCI and 1 control arm). All 4 patients with $\geq 95\%$ necrosis are alive without recurrence; two received adjuvant chemotherapy. Three of the 4 patients with less than 95% necrosis developed metastasis, and the fourth died from surgical site bleeding shortly after completing adjuvant chemotherapy. Six paired samples had enough tissue for further correlative IHC analysis. Three pretreatment samples had low level tumor expression of PD-1, PD-L1, or PD-L2; none expressed more than one marker. Five post-treatment samples had low-level expression of one or more markers, two had multiple markers, and expression of pretreatment markers increased. Immune cell infiltrates were positive for CD3 and CD163 in all but one pretreatment sample with no CD3 infiltration; some increased post radiation, some decreased, and some remained unchanged.

Conclusion: In this preliminary evaluation, all patients with $\geq 95\%$ necrosis on post-treatment samples are alive and disease free. There was a trend towards increased tumor expression PD-1 and ligands post radiation. There were no clear trends between immune marker expression and $\geq 95\%$ necrosis post-treatment or between control and DCI groups, but sample sizes were limited.



Poster #195 #1818951

NOVEL ACCELERATED HYPOFRACTIONATED RADIOTHERAPY IN SOFT TISSUE SARCOMA, UTILIZING SIMULTANEOUS INTEGRATED BOOST

*Matthew N. Mills, MD; Justin Miller, CMD, RT; Vladimir Feygelman, PhD; Arash Naghavi, MD
H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida, UNITED STATES*

Objective: There is a movement towards more hypofractionated radiotherapy (RT) for its benefit in number of treatments, cost, patient convenience, decreased population interaction during a pandemic, and to exploit the lower a/b of soft tissue sarcomas (STS). Therefore, we created an accelerated simultaneous integrated boost (SIB) regimen that replaced the standard adjuvant RT approach in STS. This study evaluates the acute toxicity of this SIB approach, along with the difference in expected long-term sequela by dosimetrically comparing each patient's plan against a standard sequential RT plan.

Methods: A prospectively maintained database was retrospectively reviewed for 31 patients with STS who underwent resection followed by adjuvant radiotherapy. Standard radiation dosing for R0/R1/R2 resections (sequential: 50 + 14/16/20Gy in 32-35 fractions) were replaced with an SIB plan treating to 50.4 and 63/64.4/70Gy in 28 fractions, respectively. Acute toxicity during and after radiation treatment were reported as per CTCAE (v5). A subset of 10 patients were subsequently planned with a standard sequential approach, utilizing the same treatment volume and planning system. These approaches were then compared for differences in dosimetry via Wilcoxon signed rank test. Field size was defined as the volume which received at least 50 Gy. Time-to-event outcomes were estimated with Kaplan-Meier analysis from the start of radiation and included local control (LC) and overall survival (OS).

Results: With a median follow up of 8.2 months (1.6-15.6), age of 68 years (20-83) and preoperative tumor diameter of 6cm (2-31), the majority of patients in this cohort were male (61%), high grade (67.7%), lower (39%) or upper extremity (26%) STS, and underwent gross total resection with either negative (45.2%) or microscopically positive (19.4%) margins. Five patients (16%) experienced grade 3 toxicity, all of which were acute radiation dermatitis that resolved by the 3-month follow up visit. Grade 3 toxicity was most common in patients treated to 70Gy ($p=0.023$), with no events observed in the 63Gy cohort. The 1-year LC and OS were 100 and 71%, respectively. In comparison to the sequential boost plan, the SIB approach had a significantly lower field size (mean difference 218cm³, $p=0.002$), bone V50 (mean difference 10%, $p=0.031$), and max dose to the skin (mean difference 4.1 Gy, $p=0.008$).

Conclusion: In addition to benefits in cost, convenience, population interaction, and improved biological effect in STS, the use of adjuvant radiotherapy with accelerated SIB hypofractionation offers a safe approach that can lower field size and dose to surrounding structures, which may translate to improved long-term toxicity (e.g. fracture, joint stiffness, fibrosis, lymphedema, etc.) when compared to standard sequential radiation. Longer follow up is required to determine if these dosimetric benefits translate to improved long-term toxicity benefit.



Poster #196 #1819081

THE UTILIZATION OF STEREOTACTIC BODY RADIOTHERAPY IN THE MANAGEMENT OF SOFT TISSUE SARCOMA LIVER AND PULMONARY METASTASIS

Aqeel Ashraf, B.Med.Sc., BMBCh; Nasra AlBusaidi, MD; Paul Ramia, MD; Simon Gauvin, MD; Neil Kopek, MD; Sinziana Dumitra, MD, MSc (Epi), FRCS(C)
McGill University, Montreal, Province du Québec, CANADA

Objective: A multimodality treatment strategy is essential to achieve optimal outcomes and prolong survival in metastatic soft tissue sarcoma (STS) patients. Among the several available treatment options, stereotactic body radiotherapy (SBRT) is gaining interest in treating metastatic hepatic and pulmonary lesions. Nevertheless, the data regarding the safety and efficacy of SBRT in such population is quite limited. The aim of this study is to assess the efficacy and safety SBRT in the management metastatic STS to the liver and lungs.

Methods: The medical records of patients who underwent SBRT for unresectable hepatic and pulmonary metastasis between January 2008 – January 2021 at a sarcoma referral center were identified and retrospectively reviewed. Outcomes, including local control, local relapse, disease free interval (DFI), overall survival (OS) as well as radiotherapy characteristics and treatment toxicity were extracted and analyzed. A log rank test was performed comparing liver and no liver metastases survival.

Results: A total of 31 patients (male = 17; female = 14) with 9 liver and 44 pulmonary metastatic lesions were identified and included in the analysis. The most frequent pathology was leiomyosarcoma followed by myxofibrosarcoma and the most common primary sites were the extremities and abdominal viscera. The median time to liver metastasis was 34.9 months, while it was 8.8 months for pulmonary metastasis. The median gross tumor volume (GTV) for liver and pulmonary lesions were 9.95cm³ and 2.4cm³, respectively; the planned target volumes (PTV) were 23cm³ and 5.6cm³. Most patients with metastatic liver lesions were managed with a total dose of 48 Gy divided in 4 fractions; pulmonary metastases were commonly treated with 50 Gy divided in 5 fractions. Local control was achieved in 42 metastatic lesions (91%) and local relapse occurred in 5. Overall survival post SBRT was 56 months and was higher in those patients treated for non-liver metastasis (62 mo) compared to those treated for liver metastasis (46 mo) with local recurrence being significantly higher in the liver group (p=0.03). Most patients did not experience acute adverse effects, though three patients developed mild dermatological symptoms that were managed conservatively with topical medication. Most of the patients (77.5%) also received systemic treatment in addition to the local treatment.

Conclusion: SBRT is effective in the management of soft tissue sarcoma liver and pulmonary metastasis (STSLPM) with high local control rates. This type of therapy was tolerable in most patients and is a good treatment option in patients with unresectable metastatic disease with curative intent.



Poster #197 #1819055

CIVASHEET® USE FOR RECURRENT SOFT TISSUE SARCOMA: A SINGLE INSTITUTION EXPERIENCE

Crystal S. Seldon, MD¹; Julie Grossman, MD²; Gautam Shrivastava, ScM³; Melanie Fernandez, BA²; Sheila Conway, MD⁴; Andrew Rosenberg, MD PhD⁵; Alan Livingstone, MD⁵; Dido Franceschi, MD²; Jonathan C. Trent, MD, PhD⁶; Matthew Studenski, PhD²; Raphael Yechieli, MD²

¹University of Miami, Homestead, Florida, UNITED STATES, ²University of Miami, Miami, Florida, UNITED STATES, ³University of Miami, Miami, Georgia, UNITED STATES, ⁴University of Miami/Jackson Memorial Hospital, Miami, Florida, UNITED STATES, ⁵University of Miami, University of Miami, Florida, UNITED STATES, ⁶Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES

Objective: Treatment options for recurrent soft tissue sarcoma (STS) are limited. Postoperative brachytherapy or IMRT are favored to reduce risk of late radiation-associated toxicity, however, local control rates vary from 47-83%, with complication rates of 12-80% (1-3). CivaSheet® is a palladium-103, implantable, intra-operative radiation therapy device which emits unidirectional radiation that enables boost doses in patients who have otherwise received the maximum radiation dose. Here, we present our initial clinical experience with the first 10 cases using this new technology to provide additional radiation to the tumor bed after surgery and prior RT treatment. We aim to determine rates of local and distant recurrence as well as to assess adverse events following CivaSheet® placement.

Methods: 9 patients received CivaSheet® implants from March 2018 to November 2019 for a total of 10 cases at our institution (one patient received 2 implants). 40% of cases were of tumors of the retroperitoneum, 20% of the lower extremity and 40% of the trunk. Adjuvant radiation was administered by a palladium-103 implant, which delivered an average of 47 Gy (35-55).

Results: After an average follow-up of 22.1 months (5-38), the local recurrence rate was 30% with affected patients having primaries of the retroperitoneum (67%) and trunk (33%). The distant recurrence rate was 20% with sites of distant recurrence being the lungs from primaries of the retroperitoneum (50%) and trunk (50%). Both patients who experienced distant recurrences were 2 of the 3 patients that experienced local recurrences. 33% of patients (3/9) experienced Grade 3 and Grade 4 adverse events. 1 patient with a tumor of the trunk experienced Grade 3 wound dehiscence requiring operation and CivaSheet® removal. 2 patients with lower extremity tumors developed Grade 4 wound dehiscence requiring major reconstruction with flap resection and CivaSheet® removal. (Table 1)

Conclusion: At the time of analysis, the local recurrence rate was 30% with complication rates of 33%, which is consistent with previously published data following adjuvant brachytherapy after STS recurrence. Patients with extremity tumors unanimously developed Grade 4 adverse events. This treatment should be further validated in future clinical trials.

Table 1: Treatment details and outcomes by tumor site

Tumor site	Number of cases	Adverse events	Implant dose	Local recurrence rate	Distant recurrence rate
Extremity	2	2 Grade 4 events	40 Gy (35-45)		
Trunk	4	1 Grade 3 events	45 Gy (35-55)	25% (1/4)	25% (1/4)
Retroperitoneum	4		45 Gy (40-50)	50% (2/4)	25% (1/4)
Total	10		47 Gy (35-55)	30 % (3/10)	20% (2/10)

Gy = Gray



Poster #198 #1818977

ASSESSING RADIOGRAPHIC AND PATHOLOGICAL RESPONSE IN MYXOID LIPOSARCOMA PATIENTS TREATED WITH PREOPERATIVE RADIOTHERAPY

Robert Gao, MD; Ivy A. Petersen, MD; Michael Haddock, MD; Andrew Folpe, MD; William Harmsen, MS; Safia Ahmed, MD

Mayo Clinic, Rochester, Minnesota, UNITED STATES

Objective: The goal of this retrospective, single institution study was to assess the degree of radiographic and pathological response in myxoid liposarcoma (MLPS) patients treated with preoperative radiotherapy (RT). We also sought to identify disease and treatment characteristics associated with response.

Methods: Following IRB approval, we used a prospectively maintained institutional database to identify all patients with a histologic diagnosis of MLPS from 1992 to 2021. Patients who received preoperative RT at our institution were included. We used cone beam computed tomography (CBCT) to assess changes in tumor volume and greatest dimension during treatment. Patients without CBCT images available were excluded from analysis. Tumors were contoured on CBCT images prior to treatment and at the end of each week of RT. Percentage change in tumor volume and greatest dimension were calculated based on the pre-treatment and final week contours. Patients with tumors incompletely visualized on CBCT were excluded from volume analysis but included on greatest dimension analysis. Surgical pathology reports were reviewed to determine degree of pathological response, with extensive pathological treatment response considered as <50% viable tumor remaining, as defined in the DoReMy trial. Tumors were "low-grade" (<5% round cell) or "high-grade" (>5% round cell).

Results: Twenty patients met inclusion criteria. Patients received RT between 2013 and 2021. Median age at diagnosis was 51 years (IQR: 39-60). A majority (15, 83.3%) of patients had low-grade tumors. Patients were most commonly treated using three-dimensional conformal RT (11, 55%). The most frequent dose/fractionation scheme was 50 Gy in 25 fractions (16, 80%), with 3 patients (15%) receiving 36 Gy in 18 fractions. Median pre-RT volume and greatest dimension were 120 cc (IQR: 56-399) and 11.2 cm (IQR: 8.4-14.1), respectively. Median percentage change in volume was -37% (IQR: -46 to -29), and median percentage change in greatest dimension was -10% (IQR: -20 to -7). Pathologic evaluation showed 10 (50%) specimens to have extensive treatment response; the median viable tumor percentage was 40% (IQR: 10-80%). There was no relationship between either change in volume or greatest dimension with pathological response. No disease or treatment factors, including grade, RT modality, RT dose, or pre-RT volume or dimension were associated with pathological response. At a median follow-up of 3.2 years, 1- and 3-year risk of local failure was 0% and 16.2% (95% CI: 4.5-57.7%), respectively.

Conclusion: In this analysis of MLPS patients treated with preoperative RT, we report significant decreases in tumor volume and greatest dimension during RT. There may be a role for adaptive RT planning to reduce target volumes and minimize RT-associated morbidity, particularly during more protracted 25-fraction courses. There was no relationship between radiographic and pathological response. In our limited cohort, we observed a lower rate of extensive pathological treatment response compared to that reported in the DoReMy trial, despite a majority of patients having received 50 Gy.



Poster #199 #1819009

MANAGEMENT OF MYXOFIBROSARCOMA: IMPACT OF TUMOR DEPTH AND ROLE OF PREOPERATIVE RADIATION IN LOCAL CONTROL

Maya Abdou; Ivy A. Petersen, MD; William Harmsen, MS; Matthew T. Houdek, MD; Brittany A. Looker, PA-C, MS; Michael Haddock, MD; Safia Ahmed, MD
Mayo Clinic, Rochester, Minnesota, UNITED STATES

Objective: Myxofibrosarcomas (MFS) are highly infiltrative with a tendency for local recurrence. In extremity and truncal soft tissue sarcomas preoperative external beam radiation (EBRT) is generally preferred, but due to difficulties with defining surgical margins in MFS the appropriate timing of EBRT in these patients is unclear with some institutions preferring to use radiation postoperatively. The purpose of this study is to evaluate local control and patterns of recurrence in MFS treated with preoperative radiation and surgery.

Methods: An institutional radiation oncology database was searched for patients with MFS who received radiotherapy and definitive surgery between 2013-2021. Out of these, only patients who had neoadjuvant radiotherapy with definitive surgery were included. Frozen section analysis of surgical margins was standardly performed on all patients at the time of definitive surgery.

Results: A total of 43 patients were identified, (28 male, 65%) with median age at diagnosis of 67 years (range 42-89). 77% of the patients presented with MFS in the extremities, and 23.3% in the trunk. 30 patients had tumors superficial to fascia, while 13 had tumors deep to the fascia. Median tumor size was 6.5 cm (Table 1). All but 4 patients had intermediate/high grade tumors. Out of the 43 patients, 21 (49%) had undergone inadvertent excision (IE) of the tumor prior to their definitive treatment. Of these inadvertent excisions 95% were tumors in the subcutaneous compartment. Only 1 patient with a deep tumor location underwent inadvertent surgery. Mean EBRT was 50 Gy. Four patients received intraoperative radiation (2), perioperative brachytherapy (1), or postoperative EBRT for close surgical margins. 11 patients received chemotherapy (7 neoadjuvant, 9 concurrent with radiation, 0 postoperative). Margins at definitive surgery were negative in all patients with 10 having no residual after IE. Reconstruction was performed in all but 2 patients (Table 2). Follow-up and survival rates were calculated from the date of definitive surgery. With a median follow-up of 4 yrs., 2 patients had local recurrence (LR) at 1.25, and 3.0 yrs., and 6 developed distant metastases (DM). One local recurrence was at the margin of the EBRT field and the other was centrally located: both alive at last evaluation. Most common site of DM was lung followed by bone. None of the patients with no residual tumor at definitive surgery had LR. The 5-year progression free survival was 75%. Overall, 5-year survival rate was 97 %.

Conclusion: Preoperative radiation in MFS in the setting of frozen section margin analysis is associated with excellent local control. Subcutaneous location of MFS is associated with a high rate of IE.

Table 1

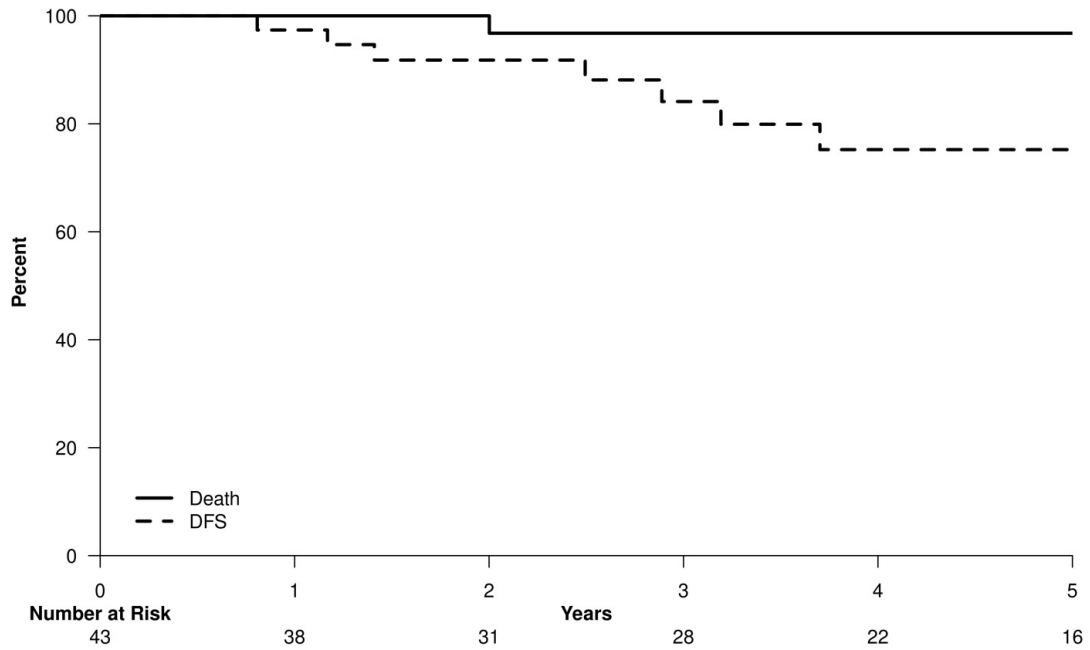
	Inadvertent Excision+		Non-inadvertent Excision	
	sub	deep	sub	deep
Number of Pts	20	1	10	12
Median tumor size at Dx (cm)	5.85	4	5.15	9.45
Local recurrence	0	0	1	1
Distant metastases	0	0	0	6
Median closest margin (cm)+	1.3	N/A	0.3	0.5

+ For those with residual disease

Table 2

Type of reconstructive surgery+	Inadvertent Excision		Non-inadvertent Excision	
	Sub	Deep	Sub	Deep
Complex wound closure	1	0	0	7
Split thickness skin graft	16	1	8	1
Fasciocutaneous and/or muscle flap	19	1	8	6

+some patients had a combination of these procedures for their reconstructive surgery





Poster #200 #1818921

EFFICACY OF VMAT RADIOTHERAPY FOR SOFT TISSUE SARCOMA OF THE EXTREMITIES

Anna K. Lawless, BSc, MPH, MBBS¹; Nonga Fangupo, MRadTher, BMedHlthSc²; Reuben Patrick Estoesta, MHSc(MRS), BAppSc(RT)²; Gino Perez, BAppSc(RT), BSc(Nurs)²; Samara Alzaidi, PhD³; Robin Hill, PhD, MSc, BSc(Hons)⁴; Angela Hong, MBBS, MMed, PhD, FRANZCR⁵

¹Chris O'Brien Lifehouse, Sydney, Australia, Sydney, NSW, New South Wales, AUSTRALIA, ²Chris O'Brien Lifehouse, Sydney, Australia, Sydney, New South Wales, AUSTRALIA, ³Department of Radiation Oncology, Chris O'Brien Lifehouse, Sydney, Australia, Sydney, New South Wales, AUSTRALIA, ⁴Department of Radiation Oncology, Chris O'Brien Lifehouse, Sydney, Australia, Institute of Medical Physics, School of Physics, University of Sydney, Sydney, Australia, Sydney, New South Wales, AUSTRALIA, ⁵Department of Radiation Oncology, Chris O'Brien Lifehouse, Sydney, Australia, Faculty of Medicine and Health, The University of Sydney, Sydney, Australia, Camperdown, Victoria, AUSTRALIA

Objective: Radiotherapy is a standard part of limb conserving therapy for extremity soft tissue sarcoma (STS) at high risk of recurrence. Toxicities increase with radiation dose and volume of normal tissue irradiated. This study sought to compare dosimetry of intensity modulated radiotherapy (IMRT) and volumetric modulated arc radiotherapy (VMAT) to investigate the optimal planning technique.

Methods: Twenty patients with extremity STS who underwent preoperative radiotherapy (50 Gy in 25 fractions) between 2016 and 2020 at a sarcoma specialist centre were included. The original treatment techniques were IMRT or 3D conformal. VMAT plans were retrospectively generated according to the original tumour and organ at risk constraints. Quality assurance was performed as per departmental protocol. Wilcoxon signed-rank test was used to compare dosimetric parameters (for planning target volume, in-field bone and soft tissue structures), monitor units (MU) and treatment time.

Results: Median patient age was 65 years and majority were male (n=14, 70%). Commonest subtype was undifferentiated pleomorphic sarcoma (n=14, 70%) and most tumours were located on the thigh (n=12, 60%). Median PTV volume was 1110 cm³ and median volume of in-field bone 236 cm³.

PTV coverage was subtly favoured VMAT, although differences were not statistically significant. VMAT plans had slightly higher mean dose (50.5 vs 50.4 Gy, p=0.218), and minimum dose (38.7 vs 42.1 Gy, p=0.014), with lower maximum dose (53.6 vs 53.3 Gy, p=0.218), and higher Conformity Index (1 vs 0.99, p=0.03) and V95% (1422 vs 1418 cm³, p=0.033).

Dose to infield bone was similar between VMAT and IMRT plans. Minimum dose (8.3 Gy for both, p=0.296), maximum dose (53.0 vs 52.3 Gy, p=0.048) and V50 (115.9 vs 114.9 cm³, p=0.601) were slightly higher with VMAT plans, while mean dose (39.1 vs 39.5 Gy, p=0.778) was lower.

Regarding soft tissue structures, VMAT plans had a lower maximum dose (38.9 vs 40.7 Gy, p=0.066), with slightly lower minimum dose (2.4 vs 2.5 Gy, p=0.327) and higher mean dose (17.6 vs 17.3 Gy, p=0.767), although not statistically significant.

VMAT plans had significantly lower average MU (480 vs 862 MU, p<0.001) and overall treatment time (300 vs 153 seconds, p<0.001).

Conclusion: In extremity soft tissue sarcoma, VMAT plans demonstrated a favourable trend toward tumour coverage and dose conformity compared to IMRT along with significantly lower monitor units and half the overall treatment time.

Table 1. Summary of dosimetric results for PTV

Parameter	IMRT	VMAT	P value
Average Minimum Dose (Gy)	38.26	42.282	0.008
Average Maximum (Gy)	52.69	53.728	0.062
Mean Dose (Gy)	49.79	50.518	0.856
D5% (Gy)	51.12	51.7175	0.896
D95% (Gy)	48.17	49.0985	0.108
V95% (cm ³)	1418.04	1422.413	0.027
Conformity Index	0.99	1.00	0.03
Homogeneity Index	5.92	5.18	0.042
Monitor Units	881.48	484.85	<0.001

Table 2. Summary of dosimetric results for In Field Bone

Parameter	IMRT	VMAT	P value
Minimum Dose (Gy)	8.81	8.55	0.878
Maximum Dose (Gy)	51.30	52.28	0.124
Mean Dose (Gy)	27.58	27.79	0.723
V50% (cm ³)	166.30	160.90	0.281



Poster #201 #1819064

A PHASE II STUDY ON THE NEO-ADJUVANT COMBINATION OF PAZOPANIB AND RADIOTHERAPY IN PATIENTS WITH HIGH-RISK, LOCALIZED SOFT TISSUE SARCOMA

Milan Van Meekeren, PhD¹; Judith V.M.G. Bovée, MD PhD¹; Frits van Coevorden, MD, PhD²; Winan J. van Houdt, MD PhD MSc³; Anne Miek Koenen⁴; Aisha Miah⁵; Shane Zaidi⁵; Andrew J. Hayes, PhD⁶; Khin Thway, MD, PhD⁷; Augustinus Krol, MD PhD⁸; Marta Fiocco, PhD⁸; Hans Gelderblom, MD, PhD¹; Neeltje Steeghs, MD, PhD⁹; Rick L. Haas, MD PhD³

¹Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ²The Netherlands Cancer Institute, Amsterdam, Zuid-Holland, NETHERLANDS, ³The Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS, ⁴Netherlands Cancer Institute, Amsterdam, Zuid-Holland, NETHERLANDS, ⁵The Royal Marsden NHS Foundation Trust, London, England, UNITED KINGDOM, ⁶The Royal Marsden Hospital NHS Foundation Trust, London, England, UNITED KINGDOM, ⁷Royal Marsden Hospital, London, England, UNITED KINGDOM, ⁸The Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ⁹Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS

Objective: Peri-operative radiotherapy for localized soft tissue sarcoma results in high local control rates, but has a limited effect on distant metastases and survival, hence the importance of examining other (combinations of) treatment modalities. Angiogenesis plays an important role in soft tissue sarcoma and inhibitors of angiogenesis have a potential synergistic effect when used together with radiotherapy. Our phase I PASART-1 study investigated neo-adjuvant pazopanib (small molecule inhibitor of the VEGF-axis) and radiotherapy. The combination treatment was well tolerated, and induced promising pathological responses in soft-tissue sarcoma patients. Results of the subsequent prospective, multicenter phase II, PASART-2 trial are presented here, further investigating efficacy and safety of this combination.

Methods: Patients with high-risk, localized soft-tissue sarcoma received neo-adjuvant radiotherapy, 50 Gy in 25 fractions (PASART-2A) or 36 Gy in 18 fractions (PASART-2B). This was combined with 800 mg once daily pazopanib, which started one week prior to radiotherapy and finished simultaneously. After an interval of 4-8 weeks, surgical resection was performed. Primary endpoint was the rate of pathological complete responses (pCR), defined as $\leq 5\%$ viable cells on central pathology review. A pCR rate of 30% or higher should be observed for the treatment regimen to be declared effective.

Results: 25 patients were registered in the study, 21 in PASART-2A and 4 in PASART-2B. The combination treatment led to a pCR in 5 patients (20%). 17 patients (68%) experienced grade 3+ toxicities during neo-adjuvant treatment. The majority of these were asymptomatic liver enzyme elevations or hypertension. Grade 3+ acute post-operative toxicities occurred in 5 patients (20%), of which the most common was wound infection. Pazopanib was discontinued prior to completion in 9 patients (36%), due to elevated ALT and/or AST, and shortly interrupted in 2 patients (8%), due to hypertension. After a median follow-up of 39 months (range 19-57 months), 6 patients have deceased, 8 distant metastases and 2 local recurrences were observed.

Conclusion: Apart from asymptomatic hepatotoxicity, the study regimen was well tolerated. This trial showed that neo-adjuvant pazopanib and RT for STS is tolerable and is able to induce a pathological complete response in 20% of the patients. Although the primary endpoint was not met, this pCR rate is still twice as high as observed after 50 Gy external beam radiotherapy alone. As currently there are no drugs available for the neo-adjuvant treatment of STS with the aim to increase the pCR rate, this would justify further investigation in patients being marginally resectable, while the long term results of PASART-2 are eagerly awaited.

Characteristic	
Total no. of patients	25
Sex	
Male	15 (60%)
Female	10 (40%)
Median age (range)	57 (24-79)
Histological subtype	
UPS	9 (36%)
Myxofibrosarcoma	8 (32%)
Spindle cell sarcoma, NOS	2 (8%)
Liposarcoma	2 (8%)
MPNST	1 (4%)
Synovial sarcoma	1 (4%)
Clear cell sarcoma	1 (4%)
Rhabdomyosarcoma, spindle cell	1 (4%)
Location	
Lower extremity	16 (64%)
Trunk	6 (24%)
Upper extremity	2 (8%)
Chest wall	1 (4%)
Grade	
I	3 (12%)
II	11 (44%)
III	11 (44%)
Depth	
Superficial	4 (16%)
Deep	21 (84%)
Median size in mm (range)	79 (28-211)

Table 1: Baseline characteristics of the PASART-2 study

Abbreviations: UPS=undifferentiated pleiomorphic sarcoma; NOS=not otherwise specified; MPNST=malignant peripheral nerve sheath tumor; mm=millimetre

RT dose	Subtype	Central pathology review					Local pathology	RECIST reponse
		pCR	%VC	%N	%H/F	SA	%VC	
50 Gy	Myxoid liposarcoma*	Yes	5	0	50	All (11)	15	PR
50 Gy	UPS	Yes	5	90	5	5**	2	SD
50 Gy	Spindle cell sarcoma, NOS	Yes	5	70	25	All (16)	1	SD
50 Gy	UPS	Yes	5	95	0	All (12)	1	PD
50 Gy	Clear cell sarcoma	Yes	5	85	10	5**	0	SD
50 Gy	UPS	No	10	60	30	All (20)	5	SD
50 Gy	UPS	No	15	80	5	All (20)	5	SD
50 Gy	Myxofibrosarcoma	No	15	50	35	All (9)	5	SD
50 Gy	UPS	No	15	70	15	All (12)	2	SD
50 Gy	Myxofibrosarcoma	No	15	10	75	5**	20	SD
50 Gy	UPS	No	20	20	60	All (23)	60	SD
50 Gy	UPS	No	25	65	10	5**	1	SD
50 Gy	Synovial sarcoma	No	30	60	10	All (12)	10	SD
50 Gy	Myxofibrosarcoma	No	30	30	40	5**	5	PR
50 Gy	UPS	No	35	60	5	All (19)	30	SD
50 Gy	UPS	No	35	45	20	All (13)	45	SD
36 Gy	Myxofibrosarcoma	No	45	20	35	All (8)	45	SD
50 Gy	Spindle cell sarcoma, NOS	No	50	25	25	All (12)	50	SD
36 Gy	Myxofibrosarcoma	No	50	25	25	All (14)	60	SD
50 Gy	Spindle cell rhabdomyosarcoma	No	50	50	0	5**	35	SD
50 Gy	Myxofibrosarcoma	No	60	35	5	All (8)	51	SD
36 Gy	Myxofibrosarcoma	No	85	10	5	All (6)	90	SD
50 Gy	Myxofibrosarcoma	No	90	5	5	5**	55	SD
50 Gy	Pleomorphic liposarcoma	No	90	10	0	All (8)	95	SD
36 Gy	MPNST	No	100	0	0	All (13)	80	SD

Table 2: Pathological and radiological response of patients with soft-tissue sarcoma treated with neo-adjuvant radiotherapy and pazopanib

Sorted on percentage of viable cells on central pathology review

*The resection specimen of this myxoid liposarcoma also showed 45% fatty maturation

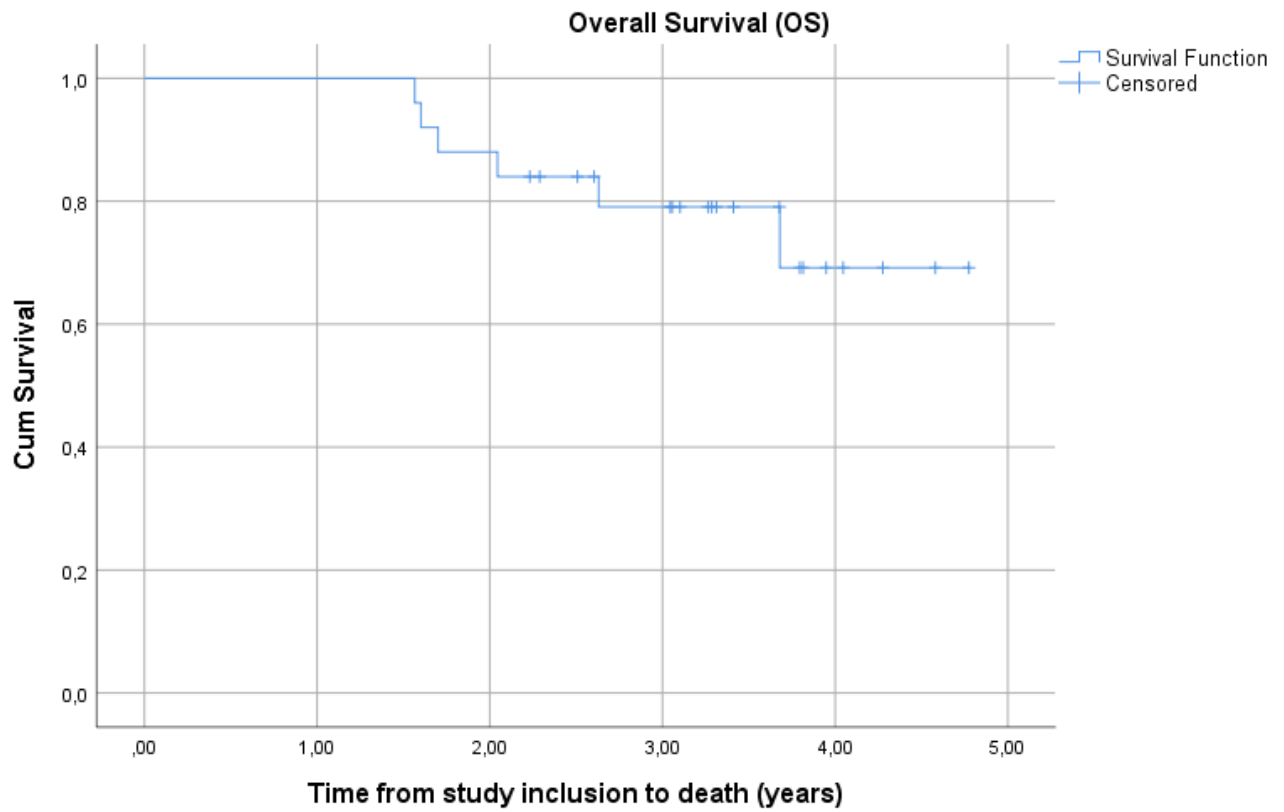
** For these London patients, 5 blocks representative of the whole tumour were selected by the local pathology team

Abbreviations: RT=radiotherapy; Gy=Gray; UPS=undifferentiated pleiomorphic sarcoma; NOS=not otherwise specified; MPNST=malignant peripheral nerve sheath tumor; %VC=percentage viable tumor cells; pCR=pathological complete response; %N=percentage necrosis; %H/F=percentage hyalinization/fibrosis; SA=amount of slides analysed; PR=partial response; SD=stable disease; PD=progressive disease

	Patient N=25			
	All grades		Grade 3+	
	N	%	N	%
Toxicities during neo-adjuvant treatment				
ALT increased	13	52	9	36
AST increased	13	52	8	32
Hypertension	13	52	8	32
Tumor pain	9	36	1	4
Lymphocytopenia	4	16	1	4
Proteinuria	4	16	1	4
Fatigue	14	56	-	-
Nausea	7	28	-	-
AP increased	4	16	-	-
Diarrhea	4	16	-	-
Hypocalcemia	4	16	-	-
Anorexia	3	12	-	-
Dermatitis radiation	3	12	-	-
Dysgeusia	3	12	-	-
Erythema	3	12	-	-
Myalgia	3	12	-	-
Thrombocytopenia	3	12	-	-
Weight loss	3	12	-	-
Bilirubin increased	2	8	-	-
Dizziness	2	8	-	-
Dyspepsia	2	8	-	-
Dry mouth	2	8	-	-
Fever	2	8	-	-
Flu-like symptoms	2	8	-	-
Hair depigmentation	2	8	-	-
Headache	2	8	-	-
Hypoalbuminemia	2	8	-	-
Leukopenia	2	8	-	-
Localized edema	2	8	-	-
Nightly sweating	2	8	-	-
Oral pain	2	8	-	-
Palmar-plantar erythrodysesthesia syndrome	2	8	-	-
Pruritus	2	8	-	-
Acute post-operative toxicities				
Wound-infection	9	36	5	20
Wound dehiscence	3	12	1	4
Deep vein thrombosis	2	8	1	4
Seroma	5	20	-	-
Late toxicities				
Fibrosis	5	20	1	4
Joint range of motion decreased	2	8	-	-
Localized edema	2	8	-	-

Table 3: Toxicities of patients with soft-tissue sarcoma treated with neo-adjuvant radiotherapy and pazopanib

Sorted on frequency of grade 3+ toxicities first and on frequency of all grades subsequently. Only toxicities that occurred in two patients or more are presented.



No. at risk 25 25 22 16 4 0

Figure 2: Overall survival of patients with soft-tissue sarcoma treated with neo-adjuvant radiotherapy and pazopanib

Abbreviations: cum.=cumulative; no.=number



Poster #202 #1818854

LACK OF RADIOSENSITIVITY PREDICTS POOR ONCOLOGIC OUTCOME IN EXTREMITY MYXOID LIPOSARCOMA

Matthew T. Houdek, MD; Katerine Mallett, MD; Steven I. Robinson, MD; Brittany L. Siontis, MD; Safia Ahmed, MD; Ivy A. Petersen, MD; Peter S. Rose, MD
Mayo Clinic, Rochester, Minnesota, UNITED STATES

Objective: Myxoid liposarcoma is a common variant of soft-tissue sarcoma which is known to be radiosensitive, with improved oncologic outcomes compared to other soft-tissue sarcomas. Like other types of soft-tissue sarcomas, clinical factors such as tumor depth, presence of a round cell component and depth are known to be associated with oncologic outcome. Although these tumors are known to “shrink” following radiotherapy, there is a paucity of data examining the degree of radiosensitivity in terms of oncologic outcome. The purpose of the current series was to evaluate pre- and post-radiotherapy tumor volume to determine if size reduction impacts oncologic outcome.

Methods: We retrospectively reviewed 65 patients with non-retroperitoneal myxoid liposarcoma undergoing surgical resection combined with preoperative radiotherapy, with pre- and post-radiotherapy MRI. This included 36 (55%) males, with a mean age of 48±14 years at the time of surgery. All tumors were located deep to the fascia, with 14 (22%) patients having tumors with a round-cell component on the resected specimen. Volumes were calculated based on the cross sectional measurements by musculoskeletal trained radiologists prior to the start of radiotherapy and following radiotherapy prior to surgical resection.

Results: There was a significant reduction in the mean maximum tumor size (15 ± 6 vs 12 ± 5 cm, p<0.01) and volume (1,176 ± 1,181 cm³ vs. 647 ± 836 cm³, p<0.01) between the pre- and post-radiotherapy MRI, which translated into a tumor volume reduction of 50±30%. The 10-year disease specific survival was 76%. To compare patients based on the change in volume, patients were grouped into either no change or tumor growth (Group 1; n=7, 11%), 0-25% volume reduction (Group 2; n=7, 11%), >25% to 50% volume reduction (Group 3; n=12, 18%), >50 to <75% volume reduction (Group 4; n=26, 40%) or ≥75% volume reduction (Group 5; n=13, 20%). There was a 10-year survival difference (Figure 1, p=0.03) of the groups (Group1, 0%; Group 2, 42%; Group 3, 100%; Group 4 79%; and Group 5, 83%). For further analysis Groups 1 and 2 were combined to categorized patients into those who had tumors which were not radiosensitive and Groups 3, 4, and 5 were combined into those who had tumors that were radiosensitive. With this break down, a significant difference (Figure 2) in 10-year disease specific survival was observed between patients with radiosensitive tumors and non-radiosensitive tumors (84% vs. 29%, p<0.01). The lack of radiosensitivity translated into a higher risk of death due to disease (HR4.54, p<0.01), while those with radiosensitive tumors had a lower risk of death due to disease (HR 0.21, p<0.01). Local recurrence occurred in 5 patients (8%) at a mean 3 years (range 1-5 years) postoperative. The 10-year local recurrence

Figure 1:

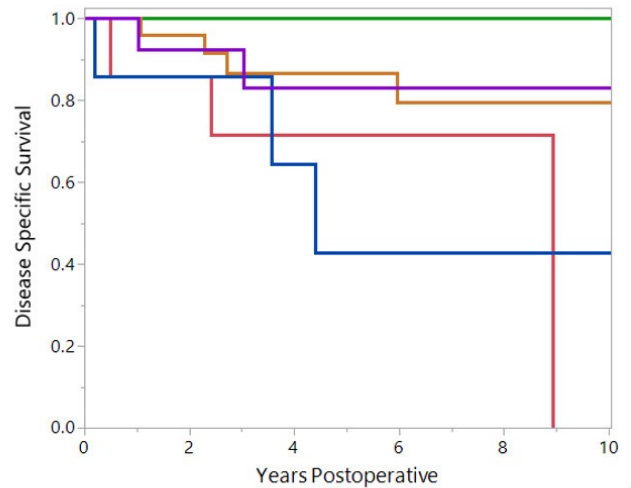


Figure 1: Following preoperative radiotherapy there was a significant difference between the 10-year patient survival based on radiosensitivity in patients with myxoid liposarcomas. Group 1 (Red, tumor growth or no change, 0%); Group 2 (Blue, 0-25% volume reduction, 42%); Group 3 (Green, >25-50% volume reduction, 100%); Group 4 (Orange, >50-75% volume reduction, 79%); and Group 5 (Purple, >75% volume reduction, 83%).

Figure 2:

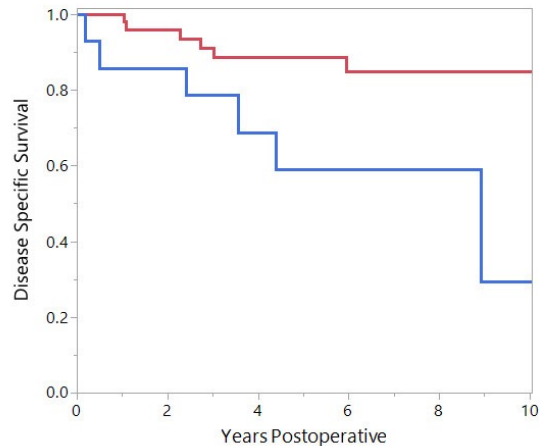


Figure 2: With stratification of patients based on radiosensitivity (≤25% volume reduction – blue, non-radiosensitive and >25% volume reduction – red, radiosensitive), there was a significant difference in the 10-year disease specific survival (84% vs. 29%) in patients undergoing preoperative radiotherapy and surgical resection of a extremity myxoid liposarcoma.

free survival was 89%. No analyzed factor was found to be associated with local recurrence. Metastatic disease occurred in 21 (32%) patients at a mean 2 years (range 3 months – 6 years postoperative. The 10- year metastatic disease-free survival rate was 62%. Patients with non-radiosensitive tumors were at increased risk of metastatic disease (HR 3.47, p<0.01), while those with radiosensitive tumors were at reduced risk (HR 0.28, p<0.01).

Conclusion: Myxoid liposarcoma is a common variant of liposarcoma that is known to be radiosensitive when compared to other types of soft-tissue sarcoma. The radiosensitivity of this tumor has translated into improved patient outcome, however the results of the current series highlights that not all myxoid liposarcomas are radiosensitive and those that do not respond to radiotherapy are higher risk for metastatic disease and subsequent death due to disease.

Table 1: Oncologic Outcome Following Combined Radiotherapy and Surgical Resection of Myxoid Liposarcoma

Factor	Hazard Ratio (95% CI)	P Value
Male Gender	1.46 (0.47-4.55)	0.50
Female Gender	0.68 (0.21-2.10)	0.50
Age > 50 Years	1.87 (0.63-5.59)	0.25
Round Cell Component	2.63 (0.85-8.11)	0.09
Intraoperative Radiotherapy or Brachytherapy	0.46 (0.10-2.09)	0.31
Non-Radiosensitive Tumor	4.54 (1.52-13.55)	<0.01
Radiosensitive Tumor	0.21 (0.07-0.65)	<0.01
Tumor Size ≥10 cm on Resected Specimen	1.75 (0.48-6.38)	0.39

Table 2: Hazard Ratios for Factors Associated with Local and Distant Recurrence

Factor	Local Recurrence (95% CI)	P Value	Distant Recurrence (95% CI)	P Value
Male Gender	∞		1.34 (0.55-3.24)	0.51
Female Gender	∞		0.74 (0.30-1.80)	0.51
Age > 50 Years	0.39 (0.04-3.52)	0.40	0.57 (0.24-1.35)	0.20
Round Cell Component	1.09 (0.12-9.82)	0.93	1.54 (0.59-3.99)	0.37
Intraoperative Radiotherapy or Brachytherapy	0.63 (0.07-5.71)	0.68	0.79 (0.29-2.17)	0.65
Non-Radiosensitive Tumor	0.95 (0.10-8.56)	0.96	3.47 (1.46-8.28)	<0.01
Radiosensitive Tumor	1.04 (0.11-9.37)	0.96	0.28 (0.12-0.68)	<0.01
Positive Margin	4.99 (0.83-29.97)	0.07	0.37 (0.04-2.77)	0.33
Tumor Size ≥10 cm on Resected Specimen	0.13 (0.80-65.26)	0.07	2.67 (0.89-7.94)	0.07



Poster #203 #1818881

PREOPERATIVE CHEMORADIATION THERAPY IN THE MANAGEMENT OF LOCALIZED SOFT TISSUE SARCOMAS

Brittany L. Siontis, MD; Judith Jebastin Thangaiah, MD; Thanh P. Ho, MD; Safia Ahmed, MD; Travis Grotz, MD; Matthew T. Houdek, MD; Andrew Folpe, MD; Scott Okuno, MD; Steven Robinson, MBBS
Mayo Clinic, Rochester, Minnesota, UNITED STATES

Objective: Soft tissue sarcoma (STS) is a heterogenous group of rare mesenchymal neoplasms. Localized STS is often treated with complete surgical resection with or without radiotherapy (RT). The utility of concurrent chemotherapy (CT) as a radiosensitizer has not been extensively studied. We report on our single institution experience of concurrent chemoradiotherapy in localized STS management.

Methods: We queried the Mayo Clinic Cancer Center (MCCC) treatment records for patients who received CT consisting of mitomycin, cisplatin and doxorubicin (MitoAP) concurrently with RT for treatment of localized STS from 1/1/85-12/12/19. Patient (pt) and tumor demographics, treatment details and outcomes were extracted from the medical record. Treatment response was defined as "% viable tumor". When treatment response was not available in the record, archival tissue sections were reviewed by two experienced bone and soft tissue (BST) pathologists.

Results: We identified 179 pts. The median age at diagnosis was 58 yrs (range) and 107 (59.8%) were male. Table 1 outlines baseline pt and tumor demographics. One hundred thirty-one pts (73.2%) received neoadjuvant (NA) CT in addition to concurrent chemoradiation therapy (CCRT). Doxorubicin/ifosfamide was the most common NA regimen (n=102, 77.9%). Interim scans revealed stable disease (SD) in 101 pts (84.9%) while 6 (5.0%) experienced progressive disease (PD) per RECIST. All patients received concurrent MitoAP with radiation and 160 (89.4%) completed 2 planned cycles. Cytopenias were the primary reason for early discontinuation (n=8). Median RT dose was 50 Gy (44-62.5 Gy). Median viable tumor for all pts was 30% (0-100). Median viable tumor for pts who received NA CT vs those who did not was 30% (0-100) vs 45% (0-95, p=0.39) respectively. Median viable tumor varied significantly by histology (Figure 1, p < 0.001). Median relapse-free survival (RFS) for all pts was 150 months (mo, 95% CI 77, not reached (NR); Figure 2A). Median RFS for pts who received peri-operative CT in addition to CCRT was NR (95% CI 63,NR) while median RFS for pts who received CCRT alone was 150 mo (95% CI 51,NR; p=0.932, Figure 2B). Median RFS varied by histologic subtype and was NR in the UPS, LPS and synovial sarcoma cohorts (Figure 2C). RFS was lowest in the other cohort at 22 mo. Overall survival (OS) for all pts was 146 mo (95% CI 105,193; Figure 3A). Five pts (2.8%) experienced local relapse (LR), of whom 4 received peri-operative CT plus CCRT. Those who received concurrent chemoradiation alone had a median OS of 157 mo (95% CI 96,NR) vs to 146 mo (95% CI 105,216) for those who additionally received perioperative CT (p=0.678, Figure 3B). OS varied by histology, with UPS cohort having the longest median OS (203 mo, Figure 3C) while myxofibrosarcoma had the shortest median OS (81 mo, p=0.12).

Conclusion: The role of CT as a radiosensitizer in management of localized STS has not been well studied. Our institutional protocol utilizing 2 cycles of MitoAP with radiation was well tolerated with minimal toxicity. LR in our cohort was similar to historical data using perioperative radiation alone, suggesting no added benefit to CCRT. Our data showed significant variability in treatment response between STS histologic subtypes suggesting potential benefit for CCRT in certain subtypes such as UPS, LPS, and SS. The addition of perioperative CT to CCRT did not improve RFS or OS.

Table 1. Patient Demographics and Disease Characteristics

	N (%)
Male	107 (59.8)
Female	72 (40.2)
Age, (years) median (range)	58 (18-83)
Tumor size (cm), median (range)	9.5 (2.7-30)
Primary Tumor Location	
Extremity/Trunk	150 (83.8)
Retroperitoneum	28 (15.6)
Intra-thoracic	1 (0.6)
Histology ¹	
UPS	61 (34.1)
LMS	29 (16.2)
LPS	25 (14.0)
SS	19 (10.6)
Myxofibrosarcoma	14 (7.8)
Malignant Peripheral Nerve Sheath Tumor	7 (3.9)
Other	24 (13.4)

¹ UPS = undifferentiated pleomorphic sarcoma LMS = leiomyosarcoma, LPS = liposarcoma, SS = synovial sarcoma

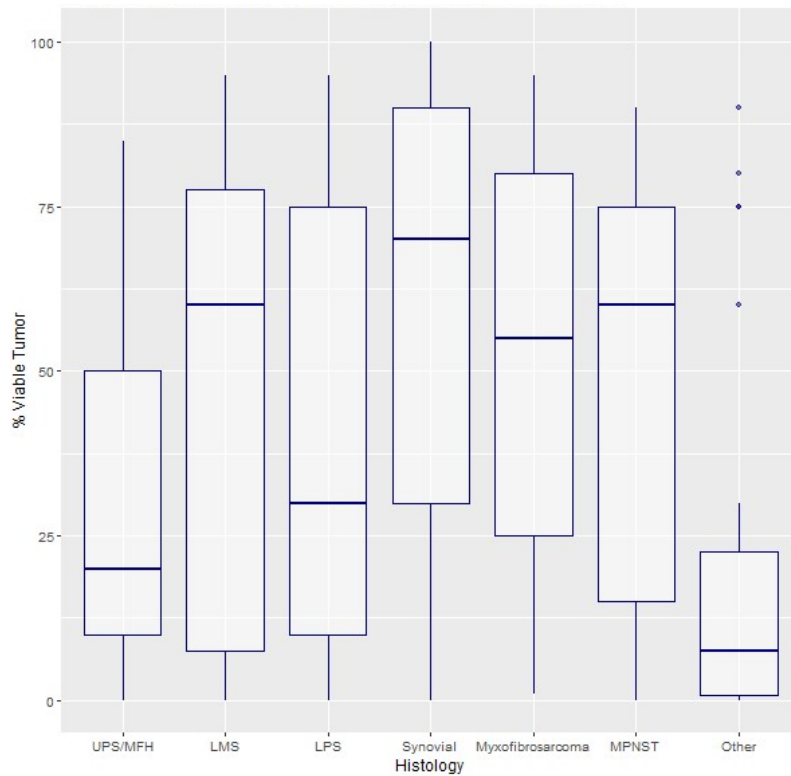


Figure 1: Percent viable tumor by histology. Median % viable tumor was 20% (0-85) for UPS, LMS 60% (0-95), LPS 30% (0-95), synovial sarcoma 70% (0-100), Myxofibrosarcoma 55% (1-95), MPNST 60% (0-90) and other 7.5% (0-90, $p < 0.001$).

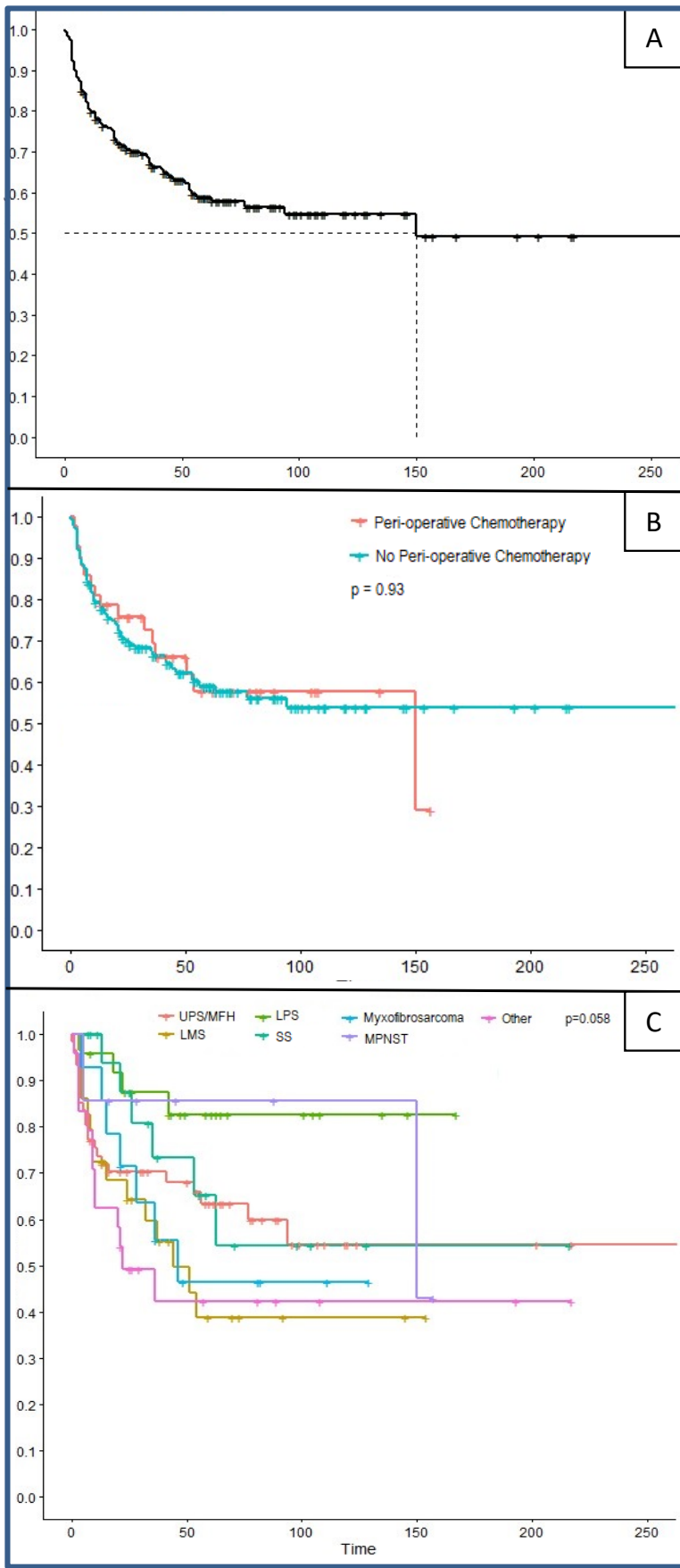


Figure 2. Relapse free survival. (A) All patients. (B) RFS for those who received peri-operative CT in addition to concurrent therapy vs those who did not. (C) RFS by histology.

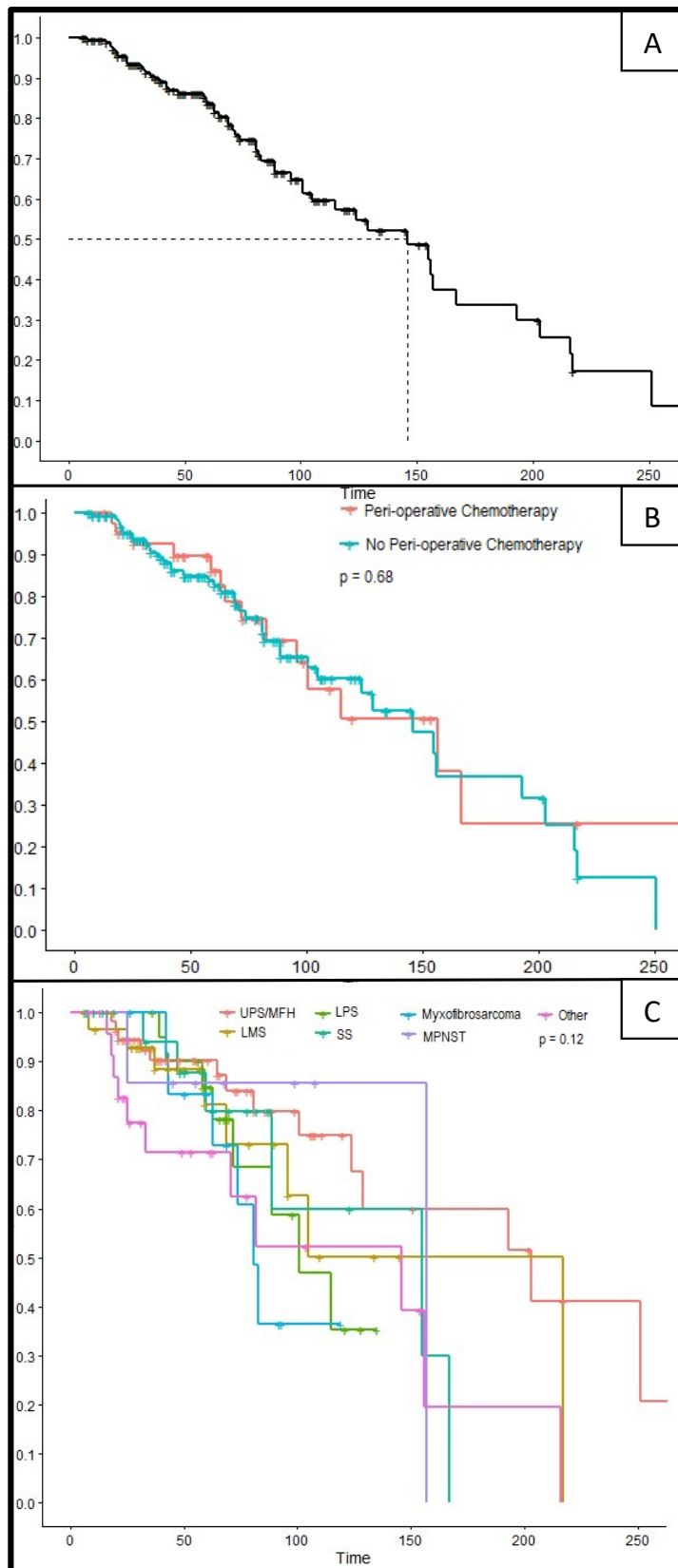


Figure 3. Overall survival. (A) All patients. (B) Pts who received peri-operative CT in addition to concurrent therapy vs those who did not. (C) By histology.



Poster #204 #1818852

NEOADJUVANT DENOSUMAB IN GCT. LONG TERM INJECTION CAN DECREASE THE RISK OF LOCAL RECURRENCE

Anastasia Tararykova¹; Alexander Fedenko, PhD²; Elmar Musaev, PhD³; Valerii Burliaev, PhD⁴, ¹Federal State Budgetary Institution «N.N. Blokhin National Medical Research Center of Oncology» of the Ministry of Health of the Russian Federation (N.N. Blokhin NMRCO), Moscow, Russia, Odintcovo, Moskva, RUSSIA, ²National Medical Research Radiological Center of the Ministry of Health of the Russian Federation, Moscow, Russia, Moscow, Moskva, RUSSIA, ³Federal State Budgetary Institution «N.N. Blokhin National Medical Research Center of Oncology» of the Ministry of Health of the Russian Federation (N.N. Blokhin NMRCO), Moscow, Moskva, RUSSIA, ⁴Federal State Budgetary Institution «N.N. Blokhin National Medical Research Center of Oncology» of the Ministry of Health of the Russian Federation (N.N. Blokhin NMRCO), Moscow, Russia, Moscow, Moskva, RUSSIA

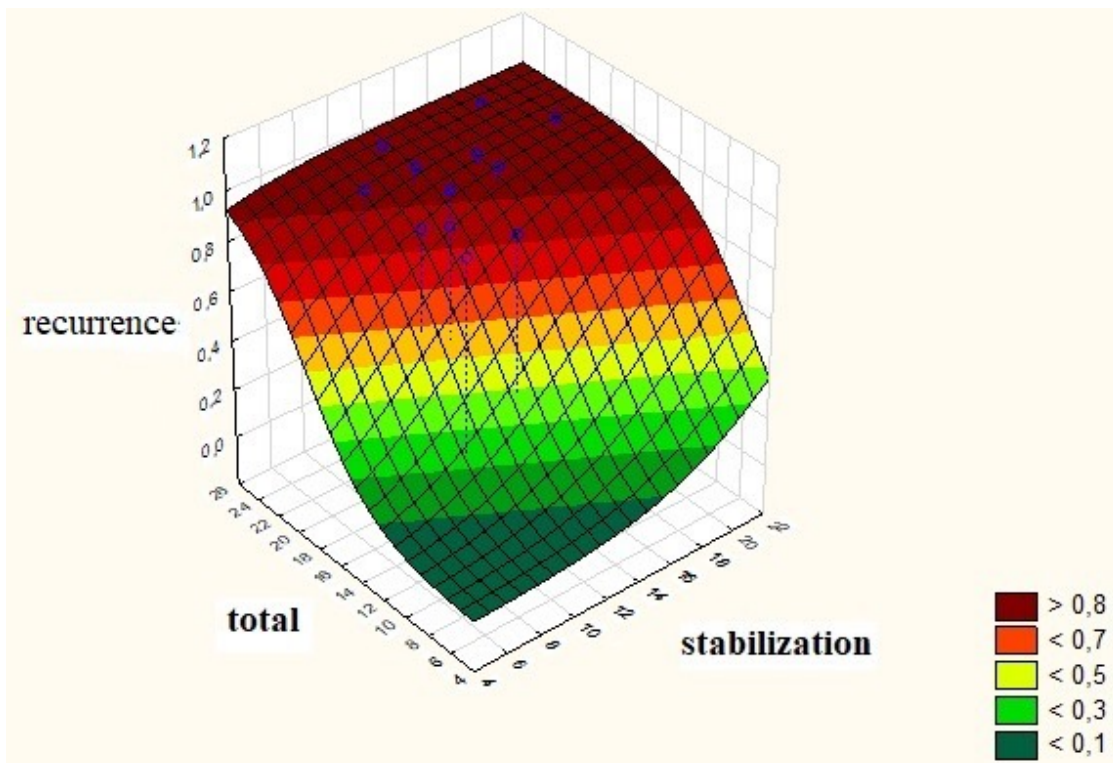
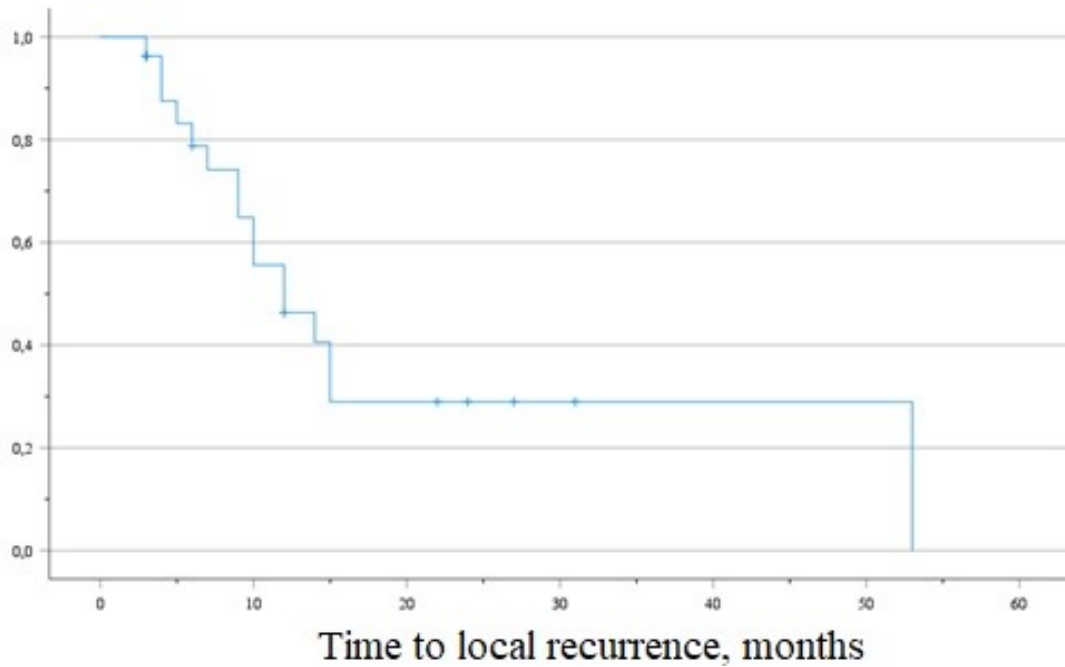
Objective: Giant cell tumor of bone (GCT) is a relatively rare, benign but locally aggressive osteolytic skeletal neoplasm of young adults, most frequently occurs at the epiphysis of long bones [1]. Surgery is the treatment of choice for GCT involving the long bones [2]. Disease involving the pelvis and spine is more difficult to control surgically. Such patients should be referred for a multidisciplinary evaluation that incorporates the input of a surgical (orthopedic) oncologist, medical oncologist, and radiation oncologist with experience in the treatment of GCT. For patients with potentially resectable GCT for whom initial surgery would result in unacceptable functional compromise or significant morbidity, most centers offer treatment with denosumab rather than initial resection [3]. Denosumab is approved by the US Food and Drug Administration (FDA) for this indication [4]. There were typically administering denosumab at 120 mg subcutaneously every 28 days, with two additional loading doses on days 8 and 15 during the first month of therapy. Although the optimal duration of preoperative denosumab is not established, most centers limit the neoadjuvant duration to the minimum needed to convert the patient to operability, especially given the risks of longer term treatment, in order to achieve this goal, most patients are typically treated for approximately six months [5]. The aim of this study is to analyze the efficiency of long term neoadjuvant denosumab for potential operable GCT in N.N. Blokhin National Medical Research Center of Oncology, Moscow (Russia).

Methods: We observed 65 GCT cases from 2016 till 2020 in N.N. Blokhin National Medical Research Center of Oncology. Disease was histologically confirmed by a sarcoma pathologist. Patients underwent CT/MRI every 3 months of neoadjuvant treatment and every 3, 6 or 12 months of follow up period. Options for surgical treatment include intralesional curettage or marginal excision (alone or followed by filling of the defect), and a wide excision or en bloc resection (with or without reconstructive surgery). All patients received daily calcium and vitamin D supplement. The duration of neoadjuvant treatment was determined as follows. The minimum number of injections was 6 injections, which represents 3 months of therapy and the first control examination. In all cases, with a continuing positive clinical and radiological picture, treatment continued until two control studies confirmed stabilization disease (SD). The extent of operation, which was planned before the initial treatment, was also taken into account. With anatomically complex localizations, the patient performed at least 15 injections, i.e. a year of neoadjuvate treatment. Again, in cases of continued radiological or clinical effect, treatment could be continued. Using binary logistic regression, the total number of denosumab injections was calculated to exclude disease recurrence. With its help, it is possible to investigate the dependence of a binary variable (in this case, the variable "recurrence" - the presence or absence of recurrence) on independent interval variables (in this case there are three of them: stabilization, additional injection, and all).

Results: The average follow-up period was 23.5±18.3 months (from 2 to 86 months). The average age of patients was 33,4±10,9 years (from 18 to 64 years), and the women and men ratio was about 1,2:1. The most commonly affected sites were lower long bones (44,6%), upper long bones (32,3%), sacrum (7,7%), vertebra (6,2%), upper short bones (3,1%), pelvis (3,1%), lower short bones (1,5%) and thorax (1,5%). According Campanacci classification G3 was the most commonly grade (53,9%). 58,5% cases were anatomically compounded due to tumor localization and 69,2% cases were primary disease. The average denosumab injections was 14.7 ± 7.8 (from 6 to 50 injections). SD according to X-ray and clinical data occurred on average at 10.7 ± 5.3 injections (from 6 to 39 injections). Local recurrence (LR) rate for wide excision or en bloc resection was 0% (p < 0,05) and 57,6% for intralesional curettage or marginal excision (p > 0,05). Median time to local recurrence was 12 months (95% CI: 7.5-16.5). By using logistic regression model we could suggest that for anatomically complex localization minimum 18 neoadjuvant denosumab injections could decrease risk of LR (overall uncertainty 82,14%). Based on

the data, it is possible to build a graph that visually represents the probability of LR at the selected amounts of denosumab injections, taking into account the SD and the total number of injections. Type of surgery was significant for LR ($p < 0,01$).

Conclusion: In this study we represented statistically confirmation the effectiveness of long-term neoadjuvant denosumab therapy. The minimum number of neoadjuvant denosumab is determined, which reduces the risk of LR in a case of attenuated surgery. Despite an increase of LR rate (statistically insignificant, $p > 0.05$) combined treatment with neoadjuvant denosumab for patients with anatomically complex localization of GCT is the preferred method, especially with high risks of postoperative complications after mutilating surgery. However, taking into account the rarity of cases with axial localizations, further study for this group of patients is required, taking into account the developing additive technologies in reconstructive surgery.





Poster #205 #1818867

NEOADJUVANT RADIATION INFLUENCES THE PSEUDOCAPSULE IN SOFT TISSUE SARCOMA: A HISTOPATHOLOGIC AND RADIOGRAPHIC EVALUATION

Nicholas J. Waldvogel, BA¹; Sarah C. Tepper, MD²; Charles A. Gusho, BS³; Ira Miller, MD, PhD²; Gregory M. White, MD²; Michael Ralls, MD²; Dian Wang, MD, PhD²; Steven Gitelis, MD²; Alan T. Blank, MD, MS²; Linus Lee, BE²

¹Rush University Medical College, Chicago, Illinois, UNITED STATES, ²Rush University Medical Center, Chicago, Illinois, UNITED STATES, ³Rush University Medical Center, Milwaukee, Wisconsin, UNITED STATES

Objective: Achieving negative margins during soft tissue sarcoma (STS) resections is critical in minimizing local recurrence and maximizing all disease related outcomes. Margins are defined relative to an acquired pseudocapsule that is noted clinically, but its pathologic composition, radiographic appearance, and response to neoadjuvant radiation is poorly understood. We asked: ¹What is the pathologic composition and radiologic appearance of the pseudocapsule in soft tissue sarcoma? ²What is the effect of neoadjuvant radiation on the thickness and composition of the pseudocapsule?

Methods: We created two retrospective cohorts and studied 17 patients with biopsy-proven high-grade soft tissue sarcoma who were treated at our tertiary academic medical center. Patients were divided into a cohort who underwent neoadjuvant radiation and a cohort who did not receive neoadjuvant radiation. As 50% of the irradiated cohort was additionally treated with chemotherapy, additional subgroup analysis was conducted to evaluate the effect modification of chemotherapy. Slides of resected specimens were re-reviewed at the time of the study qualitatively by a blinded board-certified pathologist specialized in musculoskeletal pathology. Specimen thickness was reviewed by a blinded study member by measuring pseudocapsule thickness at the periphery of pathology specimen slides, measured by determining a representative site of the pseudocapsule at which it was demarcated at the tumor periphery. This measurement process was repeated three times at different sites of each tumor to acquire the mean pseudocapsule thickness. Qualitative and quantitative radiographic measurements were conducted by two board-certified, musculoskeletal fellowship-trained subspecialty radiologists by reviewing patient magnetic resonance images (MRI) by qualitatively determining radiographic appearance and quantitatively by measuring the pseudocapsule point of maximal thickness in an axial T2-weighted MRI or a comparable fluid-sensitive series.

Results: Pathologic evaluation observed a yellow-brown pseudocapsule composed of fibroblastic stroma oriented orthogonally to the tumor with tumor cells infiltrating the tumor, the pseudocapsule, and the reactive zone surrounding the pseudocapsule. MRI review demonstrated a non-enhancing, smooth pseudocapsule best observed on axial T2-weighted MRI. In patients treated with neoadjuvant radiation, the pseudocapsule was well-demarcated with fewer viable tumor cells in the pseudocapsule and surrounding tissues when compared to untreated samples. The pseudocapsules of the irradiated cohort were thicker using pathology mean pseudocapsule thickness measurements (0.76 mm, standard deviation (SD) = 0.37 mm) versus non-irradiated pseudocapsules (0.37 mm, SD = 0.16 mm) ($p < 0.001$). The irradiated cohort was also thicker when measured using MRI point of maximal thickness (2.36 mm, SD = 1.22 mm) versus the non-irradiated cohort (1.42 mm, SD = 0.65 mm) ($p = 0.015$). Pathology mean pseudocapsule thickness was positively correlated with tumor necrosis percentage ($p = 0.044$), and negatively correlated with mitotic rate ($p = 0.043$). When the irradiated cohort was separated into pseudocapsules exposed to radiation only and those exposed to radiation and chemotherapy, those exposed to radiation only were thickest using pathology mean pseudocapsule thickness measurements, followed by radiation and chemotherapy, while no neoadjuvant treatment was the thinnest (radiation only = 0.95 mm, SD = 0.32 mm; chemotherapy and radiation = 0.57 mm, SD = 0.31 mm; no neoadjuvant therapy = 0.37 mm, SD = 0.16 mm) ($p < 0.001$).

Conclusion: This study is the first to describe the STS pseudocapsule both on histopathology as well as MRI. The pathologic and radiologic features of the pseudocapsule are influenced by neoadjuvant radiation, and pseudocapsule thickness may correlate with measurements used to monitor tumor response to radiation. We believe a thicker pseudocapsule, as is demonstrated in the irradiated cohort, may assist the surgeon during negative margin resection and potentially decreases the chance of inadvertent positive margins compared to non-irradiated STS. Studies are required to identify if the pseudocapsule may be used as a pre-operative assessment tool to evaluate tumor response to radiation, a predictive measure of disease-related outcomes, or a tool to assess indication for post-resection adjuvant therapy.

Table 1. T-tests of differences in thickness in irradiated and non-irradiated pseudocapsules

Measurement Method	Non-irradiated (Mean ± SD)	Irradiated (Mean ± SD)	p value
Pathology Mean Thickness (mm)	0.37 ± 0.16	0.76 ± 0.37	< 0.001
MRI Point of Max. Thickness (mm)	1.42 ± 0.65	2.36 ± 1.22	0.015

SD = standard deviation. P values represent the outcome of the Welch's T-Test and Independent Samples T-Test of Pathology and MRI data, respectively.

Table 2. Pseudocapsule measured thicknesses after different neoadjuvant treatment regimens

Measurement Method	No Treatment (Mean ± SD)	Neoadjuvant Radiation + Chemotherapy (Mean ± SD)	Neoadjuvant Radiation (Mean ± SD)	p value
Pathology Mean Thickness (mm)	0.37 ± 0.16	0.57 ± 0.31	0.95 ± 0.32	<0.001
MRI Point of Maximal Thickness (mm)	1.43 ± 1.64	2.34 ± 0.76	2.40 ± 1.64	0.14

	Post-Hoc Differences of Pathology Mean Thickness	p value
No Treatment vs Neoadjuvant Radiation only	0.59	<0.001
Neoadjuvant Radiation only vs Neoadjuvant Radiation + Chemotherapy	0.38	0.007

P values represent the outcome of One-way ANOVA and Games-Howell post-hoc analysis, respectively

Table 3. Pearson's correlation matrix of tumor radiation response measures with measured thicknesses

	Pathology Mean Thickness (Pearson's r)	MRI Point of Maximal Thickness (Pearson's r)	Tumor Necrosis Percentage (Pearson's r)
MRI Point of Maximal Thickness	0.40	—	—
Tumor Necrosis Percentage	0.49*	0.22	—
Mitotic Rate	-0.49*	-0.29	-0.80****

* p < .05, ** p < .01, **** p < 0.001

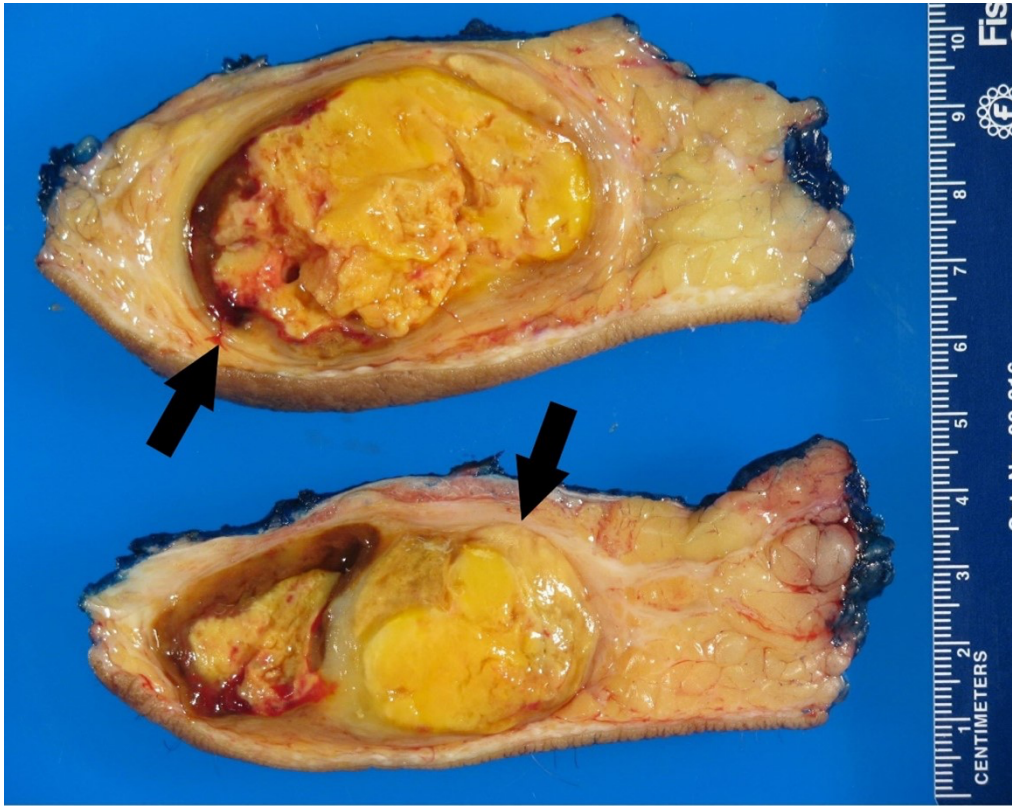


Fig. 2. Gross photograph of undifferentiated pleomorphic soft tissue sarcoma exposed to neoadjuvant radiation with a thick yellow pseudocapsule (arrows).



Poster #206 #1818974

UNEXPECTED BENEFIT OF CHEMOTHERAPY IN PATIENTS TREATED WITH PULMONARY METASTECTOMY FOR SOFT TISSUE SARCOMA

Samantha Armstrong, MD; Daniel Rushing, MD; Kenneth Kesler, MD; Hao Liu, Ph. D.; Daniel Wurtz, MD; Karen Rieger, MD

Indiana University, Indianapolis, Indiana, UNITED STATES

Objective: Pulmonary metastatectomy (PM) in patients (pts) with soft tissue sarcoma (STS) has demonstrated an improvement in overall survival (OS) but adding chemotherapy (CT) to surgery has not shown improvement in OS. In view of the increase number of (#) effective CT regimens over time we analyzed whether there may now be benefit of using CT for pts with STS undergoing PM.

Methods: We retrospectively studied the survival of 122 patients undergoing PM for STS between 01/01/1992 and 12/31/2011. The 10-year time 01/01/1992 through 12/31/2001 (Cohort 1) was compared to 10-year time 01/01/2002 to 12/31/2011(Cohort 2). Univariate cox regression model of survival from 1st PM to death were compared for Age, race, sex, disease free interval, low vs. high grade histology, largest metastasis resected and number of metastases resected. The survival statistics are based on a minimum follow up of 9 years and truncated at 10 years to avoid bias in cohort 1.

Results: Of the 122 patients, there were a total of 211 surgical procedures death occurred in 4 and 8 patients within 30 to 90 days respectively from the last procedure. The median OS was 1.52 years for Cohort 1 and 2.81 years for Cohort 2 P= 0.146. Pts aged ≥50 had a 42% lower hazard of death than those <50 P= 0.042. Those with a DFI ≥ 13 months had a 42% lower hazard of death than those with a DFI <13 months P = 0.069. No other variables affected OS. There were 5 effective CT used in Cohort 1 and 11 in Cohort 2. The # pts undergoing one, two and ≥3 PM increased from 24 to 97, from 7 to 45 and 1 to 15 in Cohort 1 to Cohort 2 respectively. The survival from the last thoracotomy to death in Cohort 1 was 1.27 yrs and cohort 2 was 1.28 yrs P=0.808.

The median time for repeat PM on the right lung was 1.42 years and 1.23 years on the left.

Conclusion: The increase in # effective CT regimens over time was associated the increasing # pts eligible for 1st, 2nd subsequent PM. The use of effective CT also invalidated the previous prognostic variables except for DFI.

Table1. Clinical and Demographic Characteristics

Variable	Label	Frequency		Total #	Percent (%)
		Time #1 01/1/1992 12/31/2001	Time #2 01/01/2002 12/31/2011		
Age	≥50	21	77	98	80.3
	Less than 50	3	21	24	19.7
Sex	male	11	36	47	38.5
	female	13	62	75	61.5
Race	Asian	1	0	1	0.8
	Black /Afr Amer	2	8	10	8.2
	White	21	89	110	90.2
Disease-free interval	Prefer no response	0	1	1	0.8
	<=13 months	17	43	60	49.2
	>13months	7	55	62	50.8
Sarcoma Grade	High-grade type	21	76	97	79.5
	Low-grade type	3	22	25	20.5
Largest metastasis 1st surgery	≤2cm	17	61	78	63.9
	> 2cm	7	37	44	36.1
Largest metastasis 2nd surgery	≤2cm	7	27	35	66.7
	≥2cm	0	17	17	33.3
Number metastases resected 1st surgery	0-3	18	70	88	72.1
	≥4	6	28	34	27.9
Number metastases resected 2nd surgery	0-3	5	33	38	73.1
	or ≥4	2	12	14	26.9

TABLE 2 presents the univariate Cox regression of survival from the first thoracotomy to death.

Predictor	p-value
Age >= to 50 vs. < 50 years	0.042
Disease free interval <= 13mo vs. > 13mo	0.069
Histologic subtype high grade vs. low	0.708
Largest metastases first surgery <= 2cm vs. > 2cm	0.617
Number of pulmonary metastases resected in first surgery 0-3 vs. >=4	0.166

Figure 1. Kaplan-Meier estimates of the survival from the first thoracotomy to death for sarcoma patients who did their first surgeries for pulmonary metastatectomy between Jan 1, 1992 through Dec 31, 2001 as opposed to those who did their first surgeries for pulmonary metastatectomy between Jan 1, 2002 and Dec 31, 2011.

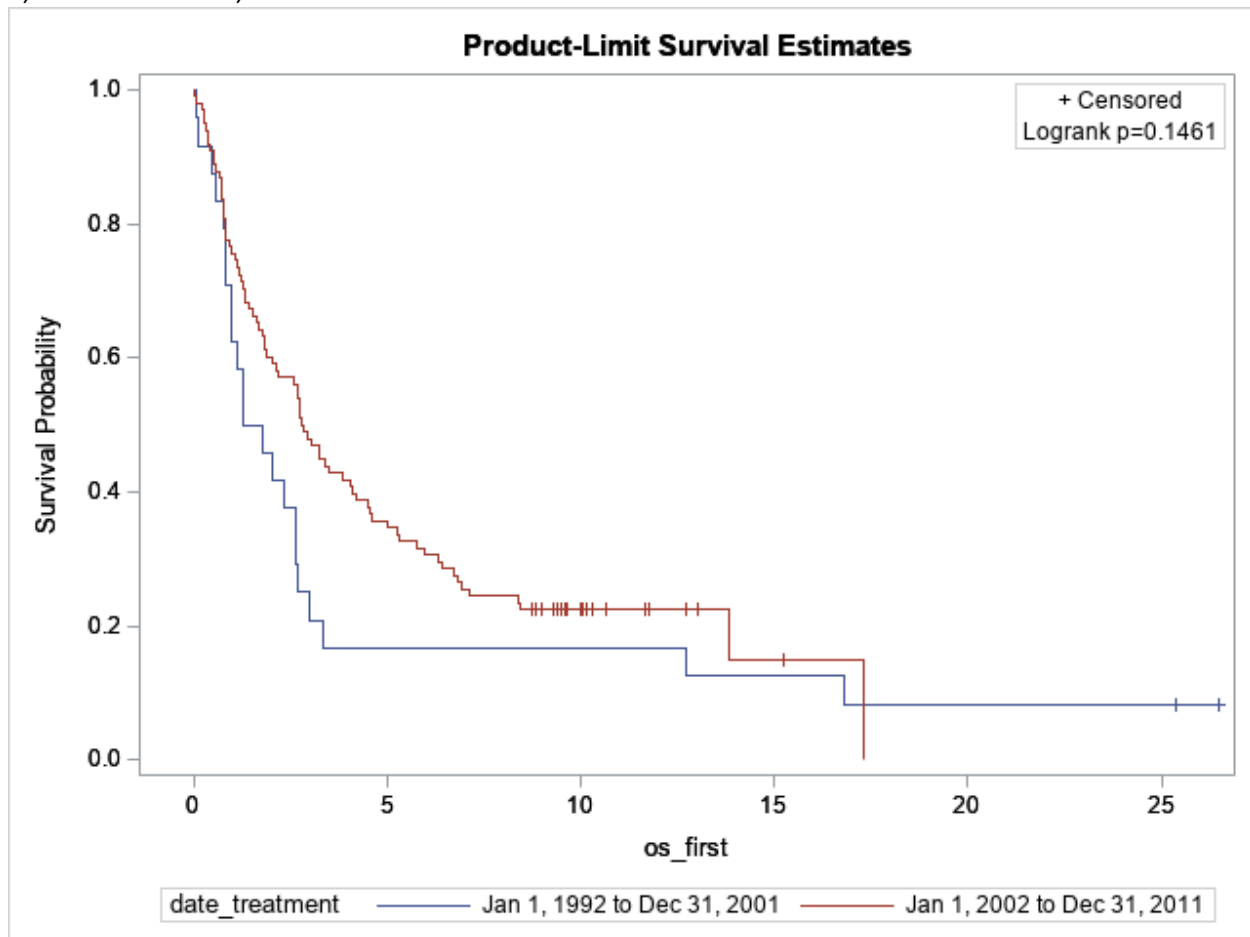
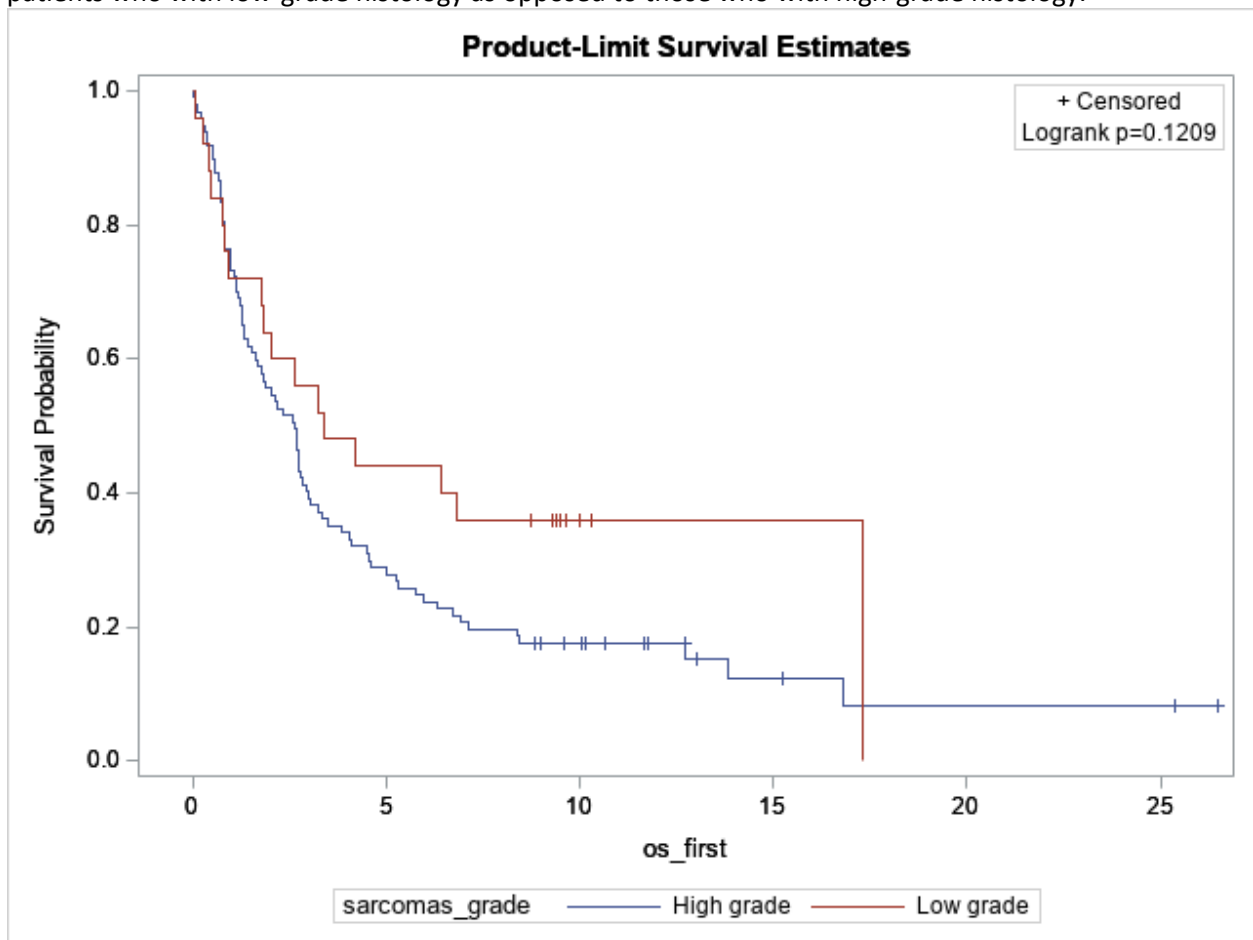


Figure 2. Kaplan-Meier estimates of the survival from the first thoracotomy to death for sarcoma patients who with low-grade histology as opposed to those who with high-grade histology.





Poster #207 #1819073

NEOADJUVANT PACLITAXEL IN BREAST ANGIOSARCOMA

Luke V. Selby, MD, MS¹; Emma Clark, MD¹; James L. Chen, MD²; Gabriel Tinoco, MD, FACP¹; Joal Beane, MD³; Raphael Pollock, MD³; David Liebner, MD¹; Valerie Grignol, MD³

¹The Ohio State University, Columbus, Ohio, UNITED STATES, ²Ohio State University, Columbus, Ohio, UNITED STATES,

³James Cancer Hospital, The Ohio State University, Columbus, Ohio, UNITED STATES

Objective: Breast angiosarcoma either arises primarily in the breast or is associated with prior radiation therapy. Adjuvant chemotherapy in resected sarcoma has shown limited benefit in large studies, but angiosarcoma is uniquely sensitive to paclitaxel. This study seeks to evaluate the impact of neoadjuvant paclitaxel therapy on surgical outcomes, tumor recurrence, and survival.

Methods: Patients with angiosarcoma of the breast, either primary or radiation-associated, were identified from a prospectively maintained database. Patients who received neoadjuvant Paclitaxel were compared to those treated with a surgery-first approach. Clinical and pathological variables were compared using Student’s t-test or Fisher’s exact test, differences in survival were calculated using Kaplan-Meyer methods.

Results: Ten patients with angiosarcoma of the breast were identified, five with primary angiosarcoma and five with radiation-associated angiosarcoma. Of the five patients treated with neoadjuvant paclitaxel, three had a diagnosis of primary angiosarcoma, while two had radiation-associated angiosarcoma. Four of these five patients had a complete pathological response to paclitaxel. All patients who received neoadjuvant paclitaxel had a margin negative resection, while two patients (n=2/5, 40%) who had a surgery-first approach had positive surgical margins and required reoperation (p = 0.4). With a median follow-up of 21 months, one neoadjuvant paclitaxel patient had recurrence (20%) compared to three patients in the surgery-first group (60%) (p = 0.5).

Conclusion: High rates of complete pathological response and margin-negative resection were seen in patients who received neoadjuvant paclitaxel for breast angiosarcoma. Longer follow-up is needed to understand the impact on recurrence and survival.

Table 1: Clinical and pathological characteristics of patients with breast angiosarcoma.

	Surgery First (n = 5)	Neoadjuvant Taxol (n = 5)	p-value
Age	58.9 (11.4)	44.1 (16.5)	NS
Radiation-induced	3 (60%)	2 (40%)	NS
Complete Pathological Response to NAC	N/A	4 (80%)	N/A
Primary Closure	3 (60%)	2 (40%)	NS
Margin Negative Resection	3 (60%)	5 (100%)	NS
Reoperation for Positive Margin	2 (40%)	0	NS
Recurrence	3 (60%)	1 (20%)	NS
Median follow-up period [Months, (range)]	33.4 (7.6-98.3)	8.5 (0.68-54.2)	NS



Poster #208 #1818928

ANALYSING THE EFFECT OF METASTASECTOMY ON POST-METASTASIS SURVIVAL IN BONE SARCOMA PATIENTS WITH SECONDARY LUNG METASTASES

Maria Anna Smolle, MD¹; Angelika Kogler¹; Joerg Friesenbichler, MD¹; Susanne Scheipl, MD²; Marko Bergovec, MD²; Christoph Castellani, Assoc.-Prof. MD³; Holger Till, Prof. MD³; Freyja-Maria Smolle-Juettner, Prof. MD⁴; Andreas Leithner, Prof. Dr.⁵

¹Department of Orthopaedics and Trauma, Medical University Graz, Graz, Steiermark, AUSTRIA, ²Medical University Graz, Graz, Steiermark, AUSTRIA, ³Department of Paediatric and Adolescent Surgery, Medical University of Graz, Graz, Steiermark, AUSTRIA, ⁴Division of Thoracic and Hyperbaric Surgery, Department of Surgery, Medical University of Graz, Graz, Steiermark, AUSTRIA, ⁵Department of Orthopedics and Trauma, Medical University of Graz, Graz, Steiermark, AUSTRIA

Objective: The prognosis of primary bone sarcoma patients with secondary pulmonary metastases is poor, with systemic treatment options available being of limited efficacy. Therefore, locally acting treatments as radiotherapy or surgery may be likewise considered in this patient population. The aim of this study was to assess the independent effect of metastasectomy on post-metastasis-survival (PMS) in bone sarcoma patients with secondary pulmonary metastases.

Methods: Forty-six bone sarcoma patients (71.7% with osteosarcomas; 50.0% females; mean age: 30.9±20.7 at time of metastasis), treated at a single tertiary sarcoma centre for primary localised disease and later on developed lung metastases were retrospectively included. Median follow-up of the entire cohort amounted to 37.0 months (IQR: 25.0-89.0 months). A propensity score of the likelihood of a patient to undergo metastasectomy was calculated, on which an inverse probability of treatment weight (IPTW) was based on, allowing assessment of the independent effect of metastasectomy on PMS. After weighting the data for the IPTW, uni- and multivariate Cox-regression models for PMS, with death as end-point, were performed.

Results: Nineteen patients (41.3%) had at least two lung metastases, and 11 patients (23.9%) bilateral lesions at diagnosis of metastasis. Thirty-seven patients of the entire cohort underwent metastasectomy (80.4%). Patients undergoing metastasectomy rather had an unilateral involvement ($p=0.013$), only one pulmonary nodule ($p=0.001$), low CRP ($p=0.014$), and low LDH levels ($p < 0.001$). According to the naïve univariate Cox-regression model, patients undergoing metastasectomy had a significantly better PMS (HR: 0.136; 95%CI: 0.047-0.393; $P<0.001$) in comparison to patients treated by other measures (e.g. chemotherapy or radiotherapy). This positive association prevailed after weighting the data for the IPTW (which included CRP- and LDH-levels, as well as bilateral disease; HR: 0.138; 95%CI: 0.054-0.353; $p<0.001$). In the multivariate model, metastasectomy remained a significant positive prognostic factor for PMS (HR: 0.146; 95%CI 0.055-0.386; $p<0.001$), independent from gender (female HR: 2.770; $p=0.025$), or patient age (HR: 1.038; $p=0.001$).

Conclusion: Metastasectomy of secondary pulmonary metastases seems to be beneficial with regards to PMS in bone sarcoma patients, even after adjusting for confounding factors. Thus, metastasectomy may be considered as a valid treatment option in these patients.



Poster #209 #1818845

WHAT IS THE CLINICAL IMPACT OF SENDING TISSUE FOR HISTOPATHOLOGY DURING SURGERY FOR KNOWN, DIFFUSE METASTATIC DISEASE TO BONE?

Charles A. Gusho, BS¹; Linus Lee, BE²; Alan T. Blank, MD, MS²

¹Rush University Medical Center, Milwaukee, Wisconsin, UNITED STATES, ²Rush University Medical Center, Chicago, Illinois, UNITED STATES

Objective: During surgery for patients with known, diffuse metastatic bone disease (MBD), lesional tissue is routinely sent for pathology evaluation. However, there are limited data to assess whether additional tissue yields a positive sample despite time and cost for interpretation, or whether a positive sample changes the subsequent treatment course.

Methods: Sixty-six cases from 2017 to 2020 were reviewed retrospectively. The median age at surgery was 63.5 years (range, 23 to 84 years), and the primary tumor was most frequently breast (24.2%, n = 16), renal (21.2%, n = 14), or lung (15.2%, n = 10). The most common location of MBD was the femur (60.6%, n = 40).

Results: The overall yield of a positive tissue sample of MBD was 77.3% (n = 51). The positive rate from sending intramedullary reamings was 65.4% (n = 17 of 26). Among the 66 cases (63 patients), a change in the subsequent clinical management was recorded in 9.1% (n = 6). The most common change was with respect to the medication regimen (n = 5), and the remaining change was recognition of the origin of a carcinoma via histology which was previously unknown.

Conclusion: Despite the routine practice of sending tissue for histology during surgery for known and diffuse MBD, a change in the subsequent clinical management is uncommon. Prior to sending tissue, surgeons should discuss this practice with the multidisciplinary care team on a per-patient basis.

Table I. Demographics of the included patients (n = 63) along with tumor and treatment characteristics of the lesional sites (n = 66).

Variable	n (%)
Age (years) ^a	63.5 (23-84)
Female	38 (57.6)
Male	28 (42.4)
Primary tumor	
Breast	16 (24.2)
Renal	14 (21.2)
Lung	10 (15.2)
Prostate	6 (9.1)
Thyroid	2 (3.0)
Lymphoma	2 (3.0)
Myeloma	3 (4.5)
Other	13 (9.7)
Location	
Femur	40 (60.6)
Acetabulum	10 (15.2)
Humerus	9 (13.6)
Tibia	2 (3.0)
Other	5 (7.6)
Pathological fracture	40 (60.6)
Surgery performed	
IF	26 (39.4)
THA	16 (24.2)
EPR	14 (21.2)
Modified Harrington	5 (7.6)
Other	5 (7.6)
MBD confirmed	51 (77.3)
Tissue received (cm³) ^b	166 (359.6)
Crushing or necrosis on sample	9 (13.6)

^a median (range).

^b mean (standard deviation).

IF = internal fixation; THA = total hip arthroplasty; EPR = endoprosthetic reconstruction; MBD = metastatic bone disease.

Table II. Changes in clinical management as a result of a positive tissue sample based off lesional specimens sent during surgery for known, widespread metastatic bone disease.

Case	Age (years)	Primary	Procedure	Description of change
1	61	Breast	IF	Patients switched from cytotoxic regimen to targeted therapy with Capecitabine.
2	76	Lung	IF	Medication switch from targeted therapy to cytotoxic agents plus targeted therapy based off tissue immunohistochemistry.
3	72	Unknown	THA	Histology from tissue received suspected sinonasal cavity origin, prompted directed management.
4	71	Prostate	THA	Patient was switched to abiraterone acetate following tissue confirmation.
5	41	Colon	THA	Patient was switched from systemic therapy to targeted Panitumumab regimen after tissue diagnosis.
6	23	Lymphoma	IF	Hematologic metastasis confirmed on histopathology, after which patient was started on cytotoxic agents.

IF = internal fixation; THA = total hip arthroplasty.



Poster #210 #1819080

THE MANAGEMENT OF HEPATIC METASTASIS FROM SOFT TISSUE SARCOMA: A SYSTEMATIC REVIEW

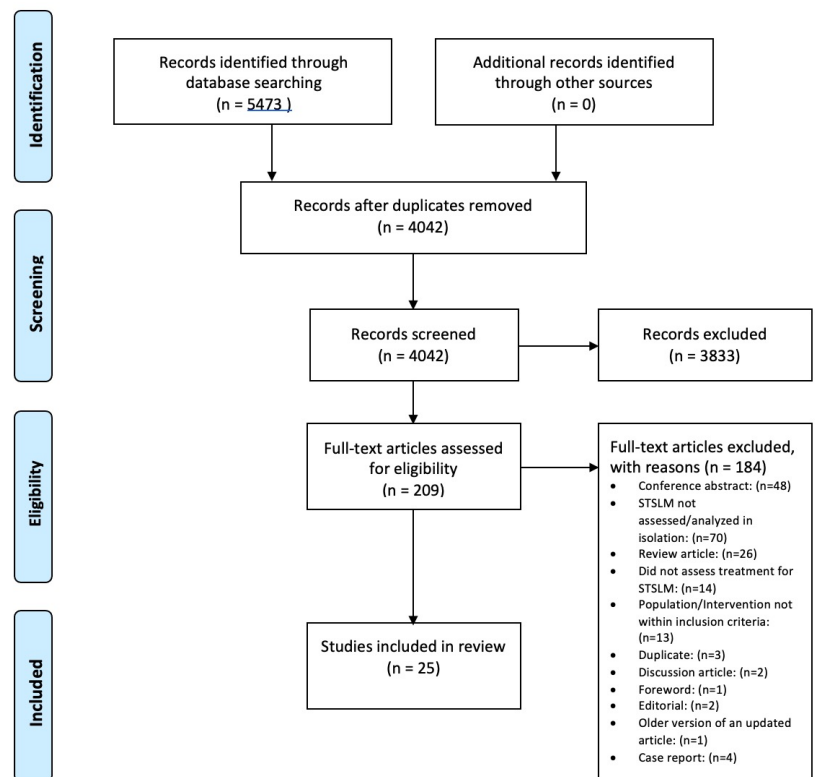
Aqeel Ashraf, B.Med.Sc., BMBCh; Abdulaziz Al-Mubarak, MD; Simon Gauvin, MD; Neil Kopek, MD; Jeffrey Barkun, MD, MSc, FRCS(C), FACS; Sinziana Dumitra, MD, MSc (Epi), FRCS(C)
 McGill University, Montreal, Province du Québec, CANADA

Objective: While for lung metastases from soft tissue sarcoma (STS) surgical resection is the preferred treatment modality, the management strategy of liver metastases from STS continues to remain unclear. Indeed, the role of treating liver metastasis from STS is quite controversial when compared to other pathologies, such as colorectal and neuroendocrine tumors, with limited retrospective data. We propose using a multimodal approach, which includes surgical resection, ablative therapies, radiotherapy and hepatic intra-arterial embolization. In order to assess optimal strategies and establish a treating algorithm we performed a systematic review to assess optimal treatment strategies.

Methods: Following PRISMA guidelines, an extensive search using major databases was conducted to identify studies that assessed the treatment modalities for hepatic metastasis from soft tissue sarcoma. Articles that included management with surgical resection, ablative techniques (radiofrequency and microwave ablation), stereotactic body radiotherapy (SBRT) and hepatic intra-arterial embolization were included. Data regarding gastrointestinal stromal tumors (GIST), pediatric and skeletal sarcomas were excluded. Given data heterogeneity, a descriptive analysis was performed. A meta-analysis could not be performed given extensive heterogeneity and quality of data. End points included oncological and survival outcomes.

Results: A total of 25 articles were included in the review where 17 studies discussed surgical resection and 8 assessed hepatic intra-arterial embolization. No articles regarding ablative techniques or SBRT were eligible for inclusion. Leiomyosarcoma was the most frequent pathology assessed across most studies. Most patients underwent adjuvant systemic therapy after hepatic resection. Patients who underwent hepatic intra-arterial embolization, in addition, had no immediate progression of hepatic lesions in most studies. Overall survival after surgical resection and arterial embolization for unresectable metastatic lesions ranged from 13-72 months and 9-24 months, respectively. Post-operative mortality was low across all surgical articles and none was encountered in the embolization studies.

Conclusion: Liver resection for soft tissue metastasis followed by systemic therapy is a reasonable method of intervention in those who are surgical candidates with acceptable survival rates and safety profile. Hepatic arterial embolization is another option for those who are not surgical candidates as it limits initial progression of disease in the vast majority of patients. No solid conclusions can be drawn with regards to ablative techniques or SBRT given the non-eligibility of studies in this review. Large-scale, multi-center trials are necessary to further assess the beneficial effects of the different targeted treatment modalities for the management of soft tissue sarcoma liver metastasis.





Poster #211 #1819005

ROLE OF MULTIDISCIPLINARY APPROACH IN A CASE OF SPINE OSTEOSARCOMA WITH OLIGOMETASTATIC HEART DISEASE

Anastasia Tararykova¹; Aslan Valiev, PhD²; Pavel Kononets, PhD²; Ruslan Kabardaev³; Antonio Chekini, PhD³; Nikolay Koslov, PhD³, ¹Federal State Budgetary Institution «N.N. Blokhin National Medical Research Center of Oncology» of the Ministry of Health of the Russian Federation (N.N. Blokhin NMRCO), Moscow, Russia, Odintcovo, Moskva, RUSSIA, ²Federal State Budgetary Institution «N.N. Blokhin National Medical Research Center of Oncology» of the Ministry of Health of the Russian Federation (N.N. Blokhin NMRCO), Moscow, Moskva, RUSSIA, ³Federal State Budgetary Institution «N.N. Blokhin National Medical Research Center of Oncology» of the Ministry of Health, Moscow, Moskva, RUSSIA

Objective: Osteosarcoma of the spine represents 3.6%–14.5% of primary spinal tumors and 0.85%–3% of all osteosarcomas. Age of onset follows a bimodal distribution, being more common in adolescents and young adults, with a second peak in the elderly population. The low incidence of spinal osteosarcoma, its anatomic location, and its proximity to vital structures make the treatment of osteosarcoma challenging; this applies particularly to neo-adjuvant chemotherapy with subsequent en bloc excision and postoperative chemotherapy. According to literature the local recurrence is 20% after en block excision and 60% after intraregional excision. Survival rates of patients with osteosarcoma are much lower in the spinal affliction in comparison to limb-non-metastatic patients, with 5 year overall survival reaching 30%–40%. The frequency of occurrence of metastases at the initial treatment is up to 16%. According to EURAMOS1, the incidence of extrapulmonary localization of osteosarcoma metastases is 4.5%. The exact incidence of venous extension of osteosarcoma and its prognostic significance are not known. Vascular invasion confirmed by histological examination has been reported in 2% of patients with resected extremity soft-tissue or bone sarcoma, including osteosarcoma, and has been associated with very poor prognosis. Cardiac involvement is a strong predictor of disease elsewhere and mandates careful surveillance, with surgical management likely providing the best outcome. The aim of this study is to demonstrate the efficiency of multidisciplinary approach, high-dose chemotherapy and active surgery tactic in cases with oligometastatic spine osteosarcoma disease in N.N. Blokhin National Medical Research Center of Oncology, Moscow (Russia).

Methods: We observed patient with Th8 spine osteosarcoma and solitary metastatic lesion of the right atrium from 2019 till now in N.N. Blokhin National Medical Research Center of Oncology. Disease of the primary site was histologically confirmed by a sarcoma pathologist. Patient underwent PET-CT, MRI and CTA every 2 months of treatment and every 3 months of follow up period. For primary site we preferred MRI and CT and for metastatic lesion - heart MRI and CTA with contrast. After each examination during treatment multidisciplinary sarcoma round table made decision about next step of treatment.

Results: For the first time, complaints appeared in May 2019: back pain and weakness in the legs. In August 2019, a pathological fracture of the Th8 vertebra with stenosis of the spinal canal was revealed. In September 2019 due to the deteriorating conditions and the need to verify the diagnosis, decompression laminectomy with a tumor biopsy was performed. Chest CT showed a soft tissue formation in the right atrium. There are no other signs of the disease according to PET-CT. The diagnosis was verified: osteosarcoma of the thoracic vertebra. The first line of high-dose chemotherapy for osteosarcomas, including high doses of platinum and doxorubicin (75/100), was prescribed. From October 2019 to February 2020 patient received 4 cycles of treatment. According to PET-CT there was a positive dynamic within stable disease: significant decrease in the metabolic activity of the primary site, as well as a size reduction metastatic lesion in the atrium. Taking into account the positive effect and the presence of a solitary lesion, it was decided to conduct radical surgery in two steps separated for the primary site and for the metastatic lesion. On March 2020 spondylectomy of the Th8 vertebra with combined stabilization was performed. PostOp histological examination confirmed diagnosis and therapeutic pathomorphosis was consisted 99%. According to CT examinations there was a volume decrease of the metastatic heart lesion. From May 2020 to July 2020 patient received additional 4 cycles of same treatment. Examination revealed a positive trend in a further reduction in the size of the solitary heart lesion. Next step at September 2020 was subtotal resection of the right atrium with xenopericardium plasty, tricuspid valve plasty with Batista's autopericardium, right coronary artery replacement with autovenous prosthesis. PostOp histological examination confirmed osteosarcoma heart metastatic disease and therapeutic pathomorphosis was consisted 48-81%. The follow-up period was 9 months.

Conclusion: In this study we represented successful case of treatment patient with spine osteosarcoma and oligometastatic heart lesion. Similar multidisciplinary approaches including high-dose chemotherapy and most importantly en-block resection or at least marginal surgery are justified in a case of oligometastatic disease. Thorough examination for this case needs in each steps of treatment.

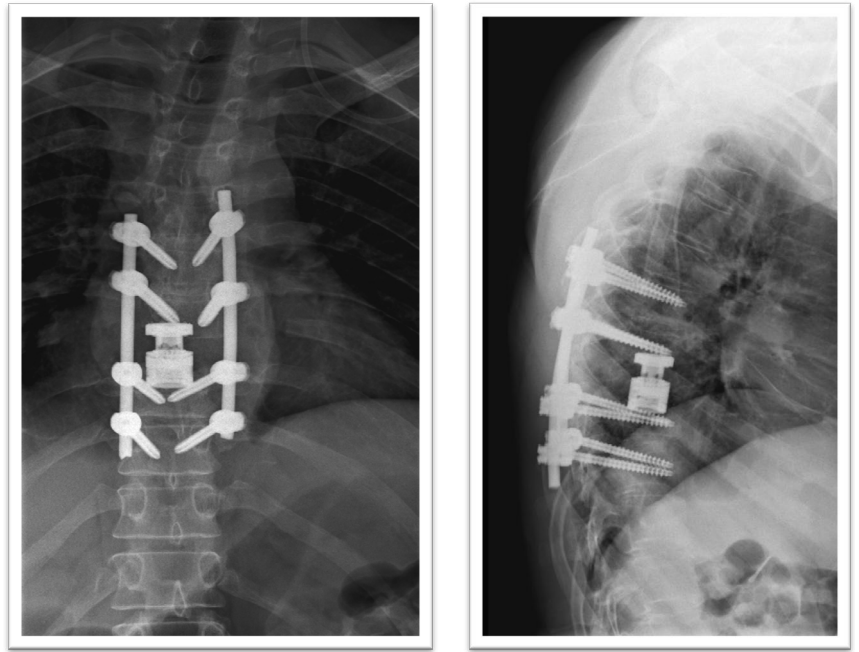


Fig.1. PostOp imaging of the spine

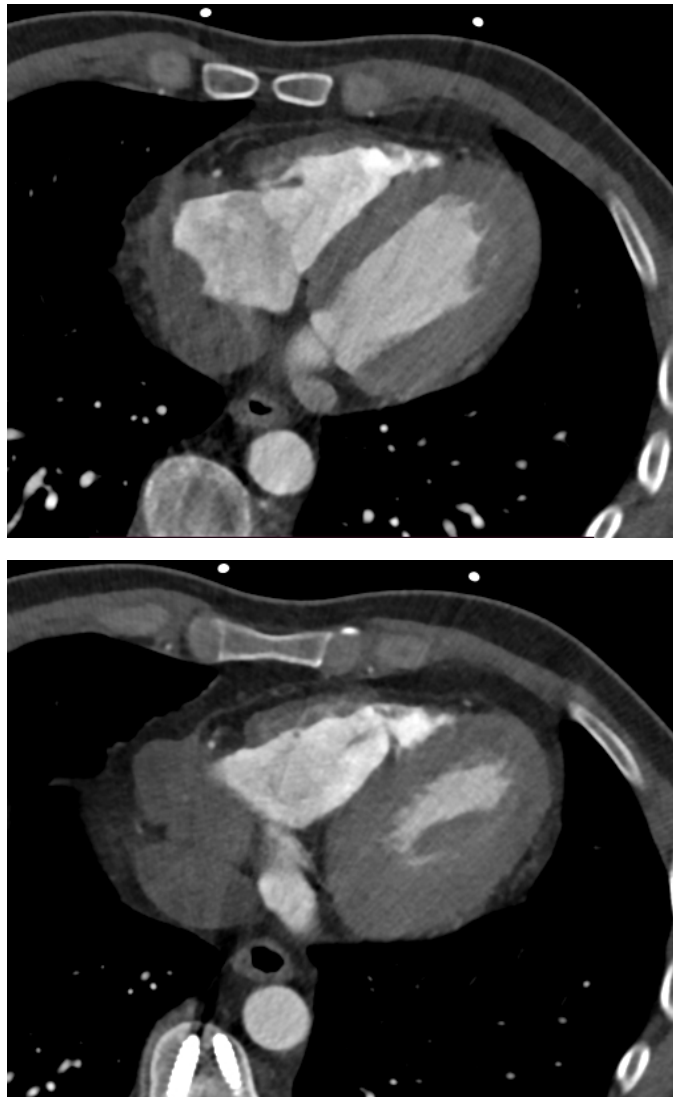


Fig.2. PredOp imaging of the heart

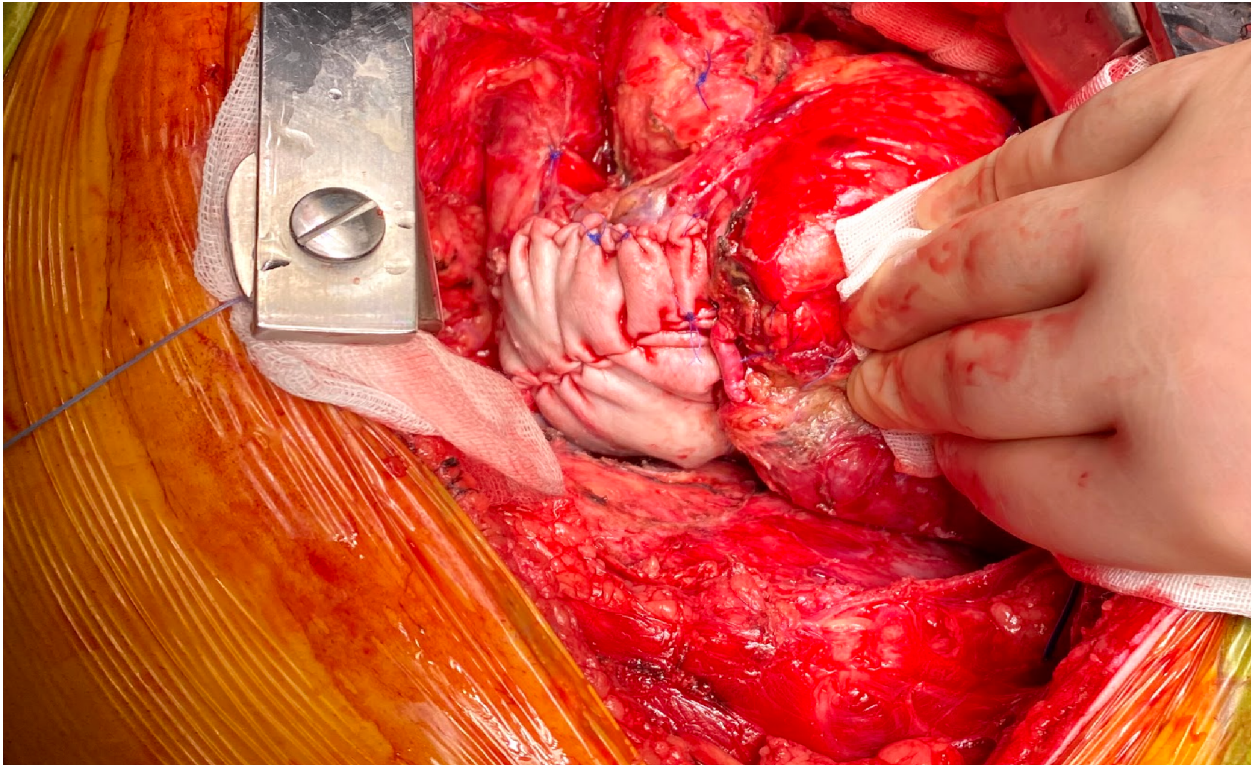


Fig.3. FINAL HEART VIEW AFTER PLASTIC WITH XENOPERICARDIUM

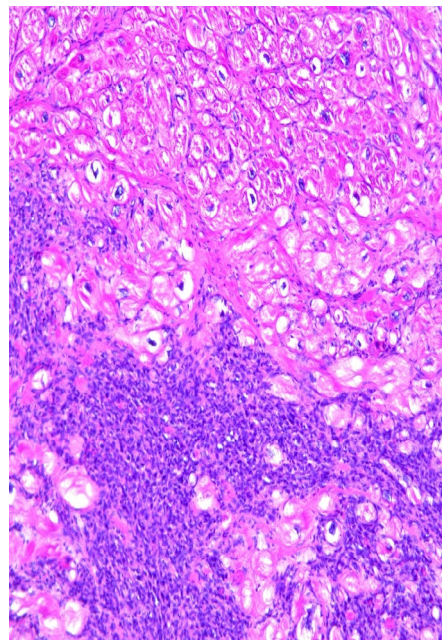


Fig.4. Fragment of the atrial wall, osteosarcoma node with signs of therapeutic pathomorphosis.



Poster #212 #1819031

OUTCOMES FOLLOWING MULTI-DISCIPLINARY MANAGEMENT OF METASTATIC MALIGNANT PHYLLODES TUMOURS

Ru Xin Wong, MBBS¹; Jian Bang Chiang, MBBS¹; Fuh Yong Wong, MBBS¹; Wenshen Looi, MBBS¹; Jason Chan, MBBS¹; Mohamad Farid, MBBS¹; Xuan Rong Thong²

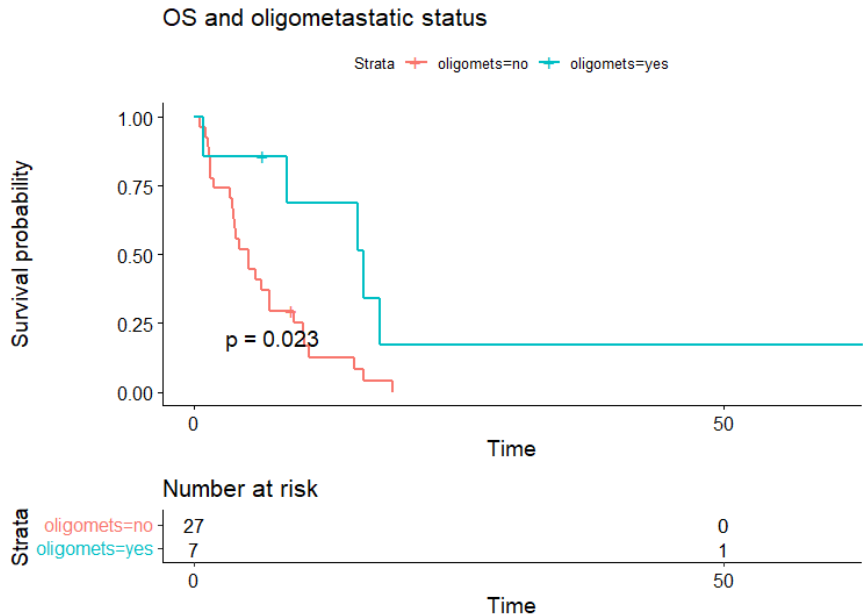
¹National Cancer Centre Singapore, SINGAPORE, ²Lee Kong Chian School of Medicine, Singapore, SINGAPORE

Objective: Metastatic disease is an important source of morbidity and mortality in patients with malignant phyllodes tumours (MPT). This report describes our experience with metastatic MPT in terms of tumour characteristics, behaviour, outcomes, and response to various treatment modalities.

Methods: We queried an IRB-approved (CIRB number 2019/2419) institutional database for patients with malignant MPT diagnosed between 2001 and 2020. All patients had histologically confirmed evidence of MPT either at diagnosis or follow-up. Patients who were lost to follow-up were excluded. Death data was corroborated with the National Death Registry.

Results: Thirty-four patients were eligible. All were female from varied ethnic groups with a median age of 55.0 (range 31 to 85) years at diagnosis. All except 1 were non-metastatic at diagnosis and had curative surgeries (26 mastectomy, 7 wide excision). Four patients (12%) had initial benign/borderline PT that subsequently underwent malignant transformation. The median size at diagnosis was 80.0 mm (IQR 60.0-141.2). Of patients whose initial surgical pathological reports were available, 24 had negative margins, 3 with diffuse involvement, 5 with focal involvement. Eleven patients had heterologous elements. None had adjuvant chemotherapy, 1 had neoadjuvant chemotherapy as initially thought to be triple negative breast cancer/metaplastic. Nine had adjuvant radiotherapy. The median interval from first diagnosis to metastasis was 13.8 months (IQR 3.0 – 24.7). Upon relapse, 24 patients had tissue-confirmation of metastases. Twenty (59%) patients had local chest wall, breast, adjacent anterior pleura relapse simultaneously with distant metastases. Four out of 9 patients (44.4%) who had adjuvant radiotherapy relapsed locally. Most common sites of disease were lungs/pleura (n=31), bones (4), liver (4), intra-abdominal (3), cutaneous (3). Fourteen patients received palliative RT. Six received local radiotherapy for fungating tumours with doses ranging from 25 Gy – 50 Gy in 5- 25#. Most experienced good palliation. Sixteen patients received palliative systemic therapy. Four patients had documented response (partial response: doxorubicin, doxo/ifosphamide, mixed response: gemcitabine/docetaxel, doxorubicin). Six patients received 2nd line chemotherapy; 2 demonstrated response (both single agent ifos). Other treatment included pazopanib (n=3), pembrolizumab (n=1), taxanes and erbulin. Median survival was 6.1 months (IQR 3.5-10.4). Six patients with oligometastatic disease had metastasectomy. Oligometastatic patients had better OS (log rank p=0.023).

Conclusion: Although metastatic disease generally portends a poor prognosis, our results suggest that a small subset of patients with oligometastatic MPT may have longer disease-free intervals. Radiotherapy plays palliation of local disease. There is some documented response to systemics. Further studies are needed for this deadly disease.





Poster #213 #1819021

**MULTIDISCIPLINARY MANAGEMENT OF PLEOMORPHIC DERMAL SARCOMA OF THE SCALP:
A SINGLE INSTITUTION EXPERIENCE**

Megan L. Sulciner, MD¹; Jiping Wang, MD, PhD¹; Miranda B. Lam, MD, MBA¹; Jason L. Hornick, MD, PhD¹; Dennis Orgill, MD, PhD¹; Elizabeth H. Baldini, MD, MPH¹; Chandrajit P. Raut, MD, MSc²; Mark Fairweather, MD¹
¹Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES, ²Dana-Farber Cancer Institute, Harvard University, Boston, Massachusetts, UNITED STATES

Objective: Undifferentiated pleomorphic mesenchymal neoplasms of sun-damaged skin include atypical fibroxanthoma and pleomorphic dermal sarcoma (PDS); the latter diagnosis is made when there is infiltration of subcutaneous tissue. PDS can present a local and distant therapeutic challenge. The scalp creates technical and cosmetic challenges that require a multidisciplinary approach to balance local control and wound healing. The optimal management strategy has yet to be defined. The aim of this study was to review our institution's multidisciplinary approach and outcomes in the management of PDS of the scalp.

Methods: We identified all patients with PDS of the scalp treated at our multidisciplinary sarcoma center. Patient characteristics, treatment approach, and outcomes were analyzed.

Results: Between 2000-2020, 15 patients with PDS of the scalp were evaluated at our sarcoma center. Thirteen patients (87%) presented with primary disease, one patient (7%) presented with recurrent disease after initial resection at another institution, and one patient (7%) presented with both primary and metastatic disease. Median tumor size was 1.5 cm (range, 0.2 – 6.2 cm). Only 1 patient had multifocal disease on presentation. All 15 patients underwent tumor resection with microscopically negative margins. Radiation therapy (RT) was recommended in 10 patients (67%) and 8 (53%) underwent RT. Three patients (20%) received preoperative RT and 5 patients (33%) received postoperative RT. One patient refused RT and one did not complete RT for an undocumented reason. RT was not offered to 5 patients due to wound healing complications (n=1), no residual tumor or small tumor size (n=3), and undocumented reasons (n=1). The median time to postoperative RT was 67 days. Eight patients (53%) underwent a second stage plastic surgery complex wound closure. In these patients, a dermal regeneration template was used for initial coverage followed by either split-thickness skin graft or rotational/advancement flap closure. The median time to definitive closure was 28.5 days. Two patients (13%) developed postoperative complications, one of whom underwent preoperative RT and required additional surgery for wound debridement and closure. With a median follow-up of 19 months from the time of surgery, local recurrence occurred in 2 patients (13%). One patient with primary and metastatic disease at presentation who underwent resection of scalp tumor and lung metastases developed both local and distant recurrence. The second patient's primary resection was complicated by wound infection requiring return to the operating room for debridement. Both of these patients received preoperative RT. Thirteen patients were alive without disease and one patient was alive with disease at time of last follow-up.

Conclusion: Limited data are available to help guide management of PDS of the scalp. Due to the possible need for a two-staged complex plastic surgery closure to optimize wound healing, the initiation of postoperative RT may be delayed and thus better timed preoperatively. Future multi-institutional study of these tumors is required to better understand the inherent biology of these tumors and further define the role and timing of RT.

TABLE. Patient and tumor characteristics for patients undergoing management of scalp pleomorphic dermal sarcoma (n = 15)

Characteristic	n	%/range
Age at presentation (years)		47-82
Sex		
Male	13	87
Female	2	13
Prior skin cancer history		
Yes	10	67
No	5	33
Disease type		
Primary	13	87
Recurrent	1	7
Primary/Metastatic	1	7
Biopsy type		
Excisional biopsy	7	47
Shave biopsy	8	53
Radiation therapy		
Preoperative	3	20
Postoperative	5	33
None	7	47
Median time to postoperative radiation (days)	67	62-84
Staged plastic surgery closure		
Yes	8	53
No	7	47
Median time to definitive closure (days)	28.5	8-123
Postoperative complications		
Yes	2	13
No	13	87
Margin status		
Negative microscopic margins	15	100
Positive microscopic margins	0	0
Recurrent disease		
Local	2	13
None	13	87
Median follow up (mos)	19	4-79



Poster #214 #1819035

UNDIFFERENTIATED PLEOMORPHIC SARCOMA OF THE EXTREMITIES, FACTORS ASSOCIATED WITH POOR OVERALL SURVIVAL

Dorian Y. Garcia-Ortega, MD, MSc, FACS¹; Alethia Alvarez-Cano, MD, MSc²; Miguel Angel Clara-Altamirano, MD, MSc³; Claudia HS Caro-Sanchez, MD, MSc³; Kuauhyama Luna-Ortiz, MD⁴

¹Instituto Nacional de Cancerología, Mexico, Distrito Federal, MEXICO, ²Christus Muguerza, Monterrey, Nuevo Leon, MEXICO, ³Instituto Nacional de Cancerologia, Tlalpan, Distrito Federal, MEXICO, ⁴Instituto Nacional de Cancerología, Tlalpan, Distrito Federal, MEXICO

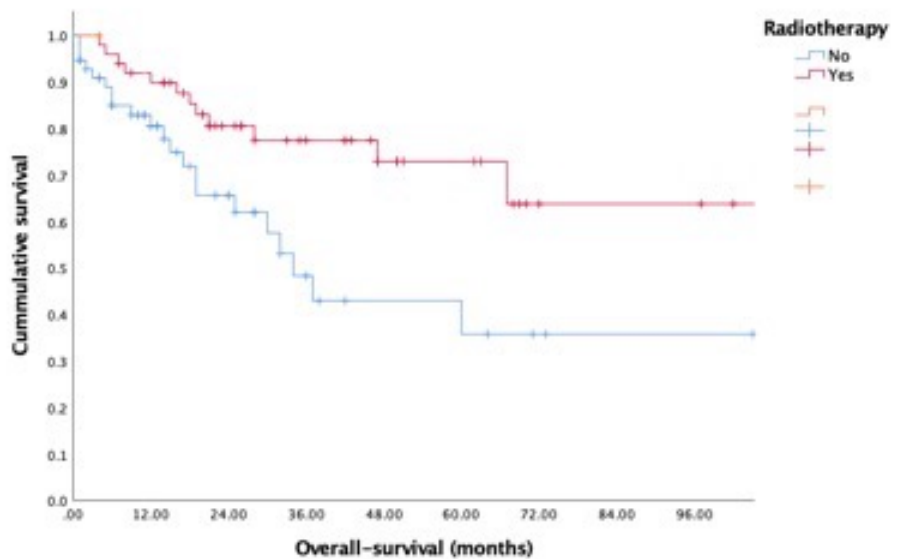
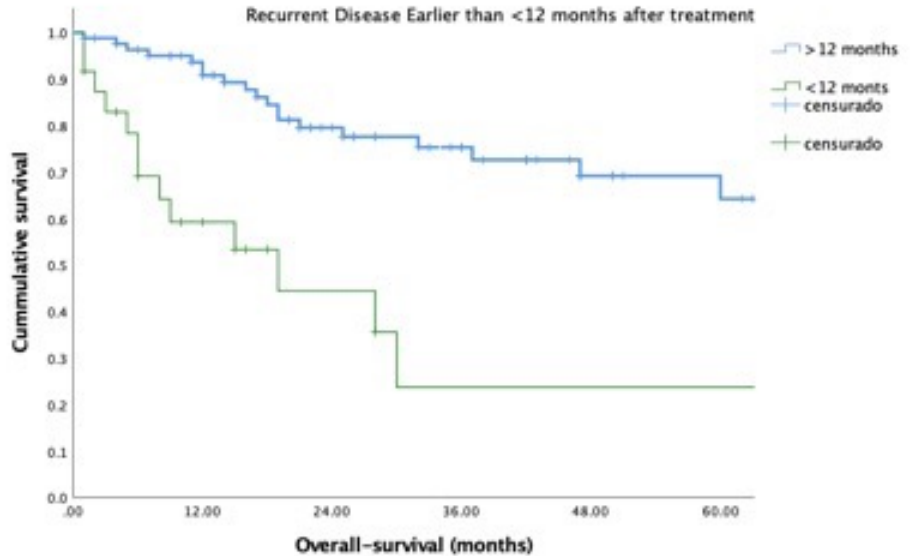
Objective: Undifferentiated pleomorphic sarcoma (UPS) is a rare neoplasm that can arise in any anatomical site, mainly in the lower extremities. UPS clinical behavior tends to be aggressive, but data regarding specific prognostic factors for this entity are limited.

Objective: To identify prognostic factors in a cohort of UPS cases in a sarcoma center.

Methods: A retrospective cohort study with prospective follow-up was carried out in a sarcoma reference center in Latin America. Patients with a diagnosis of extremity UPS were analyzed. The demographic variables associated with poor overall survival (OS) were analyzed using the long-Rank test and Kaplan-Meier curves.

Results: We analyzed 113 patients with a median age of 59.8 years (IQR 49-71), median tumor size was 11.5 cm (IQR 6-17), the most frequent location was the thigh 44.2%, male:female ratio was 1.1 :1 (MF), clinical stage was IIIA (32.7%), IIIB (31%), IV (23%). Factors associated with low overall survival were the presence of lymph node disease at diagnosis ($p=0.028$), metastatic disease at diagnosis ($p0.001$), resection status (R0 / 1 vs R2 $p=0.001$), use of radiotherapy ($p 0.035$), and recurrent disease (RFS) earlier than <12 months after treatment ($p=0.001$).

Conclusion: Our study confirmed classical prognostic factors associated with poor OS such as presence of lymph node disease, metastatic disease at presentation and resection status. We also found use of RT and a RFS of less than 12months were also adverse. Perhaps the use of RT is in relation to tumor size. From the first year of follow-up, we found no difference between the patients who received CT in our series.





Poster #215 #1818870

TENOSYNOVIAL GIANT CELL TUMOR OBSERVATIONAL PLATFORM PROJECT (TOPP): 2-YEAR OBSERVATIONAL ANALYSIS OF PATIENT-REPORTED OUTCOMES BASED ON TREATMENT STRATEGIES FROM AN EU/US PROSPECTIVE REGISTRY

Emanuela Palmerini, MD¹; Silvia Stacchiotti, MD²; John H. Healey, MD, FACS³; Sebastian Bauer, MD⁴; Nicholas M. Bernthal, MD⁵; Bart Schreuder, MD, PhD⁶; Andreas Leithner, MD, PhD⁷; Javier Martin-Broto, MD, PhD⁸; Francois Gouin, MD, PhD⁹; Hans Gelderblom, MD, PhD¹⁰; Eric L. Staals, MD¹; Julio Lopez-Bastida, MSc, PhD¹¹; Petra Laeis, PhD¹²; Florence Mercier, MSc¹²; Xin Ye, PhD¹³; Michiel van de Sande, MD PhD¹⁰

¹IRCCS Istituto Ortopedico Rizzoli, Bologna, Emilia-Romagna, ITALY, ²Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY, ³Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES, ⁴West German Cancer Center, University of Duisburg-Essen, Essen, Nordrhein-Westfalen, GERMANY, ⁵David Geffen School of Medicine at UCLA, Santa Monica, California, UNITED STATES, ⁶Radboud University, Nijmegen, Gelderland, NETHERLANDS, ⁷Medical University of Graz, Graz, Steiermark, AUSTRIA, ⁸Fundacion Jimenez Diaz University Hospital, Madrid, Madrid, SPAIN, ⁹Center Leon Berard, Lyon, Rhone-Alpes, FRANCE, ¹⁰Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ¹¹University Castilla-La Mancha, Talavera de la Reina, Castilla-La Mancha, SPAIN, ¹²Daiichi Sankyo Europe GmbH, Munich, Bayern, GERMANY, ¹³Daiichi Sankyo, Inc., Basking Ridge, New Jersey, UNITED STATES

Objective: Diffuse-type tenosynovial giant cell tumor (D-TGCT) is a rare, locally aggressive neoplasm. Previously, the prospective international TOPP registry described the impact of TGCT on patient reported outcomes (PRO) from a baseline (BL) snapshot. This analysis is the first to describe the impact of the disease on PRO as a 2-year follow-up (f/u) based on treatment strategies.

Methods: TOPP is an observational prospective study conducted at 12 sites (7 European countries and at 2 US sites). For patients (pts) with histologically confirmed D-TGCT, captured PRO measurements were assessed starting at BL (at the time of enrollment in the registry), and at 1 year (Y1) and 2 years (Y2). Pts with no post baseline data were excluded from the analysis. PRO endpoints (Brief Pain Inventory [BPI] Pain Interference, BPI Pain Severity, Worst Pain, EuroQol-5 Dimension visual analog scale [EQ-5D VAS], EQ-5D, Worst Stiffness, Patient-Reported Outcomes Measurement Information System [PROMIS]) were calculated as medians in pts where scores were collected at each time point. Pts who did not complete the questionnaire were excluded from PRO analysis at that time point. Treatment interventions were classified as follows: no current/planned treatment (off-treatment), systemic treatment only, surgery only and other (not reported in this abstract due to small population size). Pts who received systemic treatment or surgery at BL, followed by treatment course or wait-and-see at Y1 and/or Y2 were documented as remaining on the same treatment.

Results: Of the 183 pts (BL analysis set) who entered the study, 176 (108 female, 61.4%) were included in the Full Analysis Set (FAS) (mean age: 43.5 years; range 18-77), while pts with no post-baseline data were excluded. Of the FAS, 165/176 (93.8%) had a f/u visit at Y1 and 168/176 (95.5%) had a f/u visit at Y2. At BL, most tumors were in the knee (120/176, 68.2%), and most common number of prior surgeries received was 1 (71/176, 40.3%). At BL, 79/176 pts (44.9%) were off-treatment (Table 1), while 97/176 pts (55.1%) were being treated or had a planned treatment (45 systemic treatment only [Table 2], 39 surgery only [Table 3], and other [n=13; 5 radiotherapy, 4 future surgery, 2 surgery + systemic, 1 surgery + 90Yttrium and 1 systemic treatment + future surgery]).

For pts off-treatment at BL (Table 1), median BPI Pain Interference and BPI Pain Severity scores were numerically lower in pts who remained off-treatment at Y1 (1 and 1.5, respectively) as compared to those who changed treatment at Y1 (2.86 and 3.0, respectively). At Y2, median BPI Pain Interference Worst Pain scores were numerically lower in pts who remained off-treatment (0.57 and 2.0, respectively) compared to those who changed treatment (2.57 and 4.5, respectively); EQ-5D VAS was numerically higher in the pts who remained off-treatment (80) as compared with those who changed to a treatment (65). For pts under systemic treatment at BL (Table 2), median BPI Pain Interference, BPI Pain Severity, Worst Pain, and Worst Stiffness scores were numerically lower in pts who remained on systemic therapy at Y1 (2.79, 3.63, 4.5, and 4.0, respectively) compared to those who changed course at Y1 (5.93, 6.38, 7.5, and 7.5, respectively). At Y2, EQ-5D VAS was numerically higher in pts who changed from systemic treatment (77.5) compared to those who remained on systemic treatment (65). Within 2 years after surgery, no pt changed treatment course (Table 3), and median Worst Pain ranged from 4 at Y2 to 6 at Y1.

Conclusion: The present study underscores how D-TGCT has a major impact on QoL and is responsible for pain and various degrees of limitations sustained over time impacting the selection of treatment strategy. Even though selection biases cannot be ruled out, pts who remained on systemic treatment showed better PRO measurements compared to those who stopped their treatment. These findings should be considered in future studies.

Table 1. PROs for patients completing questionnaires at each time point: No Current/ planned treatment patients (off-treatment)

Baseline							
Off-treatment (n = 79)							
	BPI Pain INT	BPI Pain Sev	Worst Pain	EQ-5D VAS	EQ-5D	W-Stiff	PROMIS
Completed PROs	n = 73	n = 74	n = 74	n = 75	n = 74	n = 72	n = 75
Mean	2.27	2.56	3.43	71.81	0.78	3.61	44.29
SD	2.50	2.13	2.64	22.21	0.17	2.55	7.73
Median	1.29	2.25	3.00	78.00	0.81	3.00	45.40
Min	0.00	0.00	0.00	5.00	0.24	0.00	27.50
Max	9.29	8.50	9.00	100.00	1.00	9.00	60.90
1-Year							
Treatment course remained off-treatment (n = 60)							
	BPI Pain INT	BPI Pain Sev	Worst Pain	EQ-5D VAS	EQ-5D	W-Stiff	PROMIS
Completed PROs	n = 47	n = 46	n = 46	n = 48	n = 48	n = 48	n = 47
Mean	1.77	2.20	3.26	79.38	0.82	3.29	46.20
SD	2.04	1.95	2.57	14.24	0.15	2.65	8.05
Median	1.00	1.50	3.00	80.00	0.83	3.00	44.50
Min	0.00	0.00	0.00	30.00	0.20	0.00	30.60
Max	7.14	8.00	10.00	100.00	1.00	9.00	61.70
Treatment course changed from off-treatment (n = 11)							
	BPI Pain INT	BPI Pain Sev	Worst Pain	EQ-5D VAS	EQ-5D	W-Stiff	PROMIS
Completed PROs	n = 9	n = 9	n = 9	n = 10	n = 10	n = 10	n = 10
Mean	3.98	2.94	4.33	70.00	0.71	4.40	42.08
SD	2.82	1.47	2.35	17.80	0.22	2.84	10.06
Median	2.86	3.00	4.00	67.50	0.74	4.50	39.85
Min	0.00	0.00	0.00	30.00	0.20	0.00	30.00
Max	9.00	5.50	8.00	95.00	1.00	9.00	61.70
Unknown treatment (n = 8)							
2-Year							
Treatment course remained off-treatment (n=54)*							
	BPI Pain INT	BPI Pain Sev	Worst Pain	EQ-5D VAS	EQ-5D	W-Stiff	PROMIS
Completed PROs	n = 43	n = 44	n = 44	n = 46	n = 45	n = 45	n = 46
Mean	1.38	1.79	2.45	78.02	0.82	2.71	47.31
SD	1.99	1.78	2.39	19.10	0.17	2.02	8.94
Median	0.57	1.13	2.00	80.00	0.85	2.00	48.40
Min	0.00	0.00	0.00	30.00	0.28	0.00	28.70
Max	8.43	6.25	8.00	100.00	1.00	8.00	61.70
Treatment course changed from off-treatment (n = 5)*							
	BPI Pain INT	BPI Pain Sev	Worst Pain	EQ-5D VAS	EQ-5D	W-Stiff	PROMIS
Completed PROs	n = 4	n = 4	n = 4	n = 3	n = 3	n = 4	n = 4
Mean	2.89	3.00	4.00	55.00	0.84	3.25	45.08
SD	3.38	3.18	3.56	50.74	0.19	3.77	6.71
Median	2.57	2.63	4.50	65.00	0.88	3.00	46.25
Min	0.00	0.00	0.00	0.00	0.63	0.00	36.20
Max	6.43	6.75	7.00	100.00	1.00	7.00	51.60
Unknown treatment (n=1)*							

BPI = brief pain inventory; EQ-5D VAS = EuroQol-5 Dimension visual analog scale; INT = interference; Max = maximum; Min = minimum; NRS = numerical rating scale; PRO = patient reported outcomes; PROMIS = Patient-Reported Outcomes Measurement Information System; SD = standard deviation; Sev = severity; W-Stiff = worst stiffness.

*Patient population at Year-2 comes from sub-group of patients who remained No current/ planned treatment at Year-1.

Scale:

Pain: NRS from 0 to 10, 0 = no pain, 10 = pain as bad as you can imagine.

Interference: NRS from 0 to 10, 0 = does not interfere, 10 = completely interferes.

Stiffness: NRS from 0 to 10, 0 = no stiffness, 10 = stiffness as bad as you can imagine.

EQ-5D VAS: NRS from 0 to 100, 0 = worst health you can imagine, 100 = best health you can imagine.

EQ-5D: NRS from 0 to 10, 0 = worst imaginable health state, 10 = best imaginable health state.

Table 2. PROs for patients completing questionnaires at each time point: Systemic treatment only patients

Baseline							
Systemic Treatment only (n = 45)							
	BPI Pain INT	BPI Pain Sev	Worst Pain	EQ-5D VAS	EQ-5D	W-Stiff	PROMIS
Completed PROs	n = 42	n = 42	n = 42	n = 43	n = 42	n = 43	n = 43
Mean	3.44	3.91	5.02	65.60	0.66	5.14	40.19
SD	2.61	2.12	2.38	20.83	0.22	2.70	8.35
Median	2.86	3.88	5.50	70.00	0.70	6.00	39.80
Min	0.00	0.50	1.00	0.00	0.01	0.00	25.20
Max	8.57	7.75	9.00	98.00	1.00	10.00	61.70
1-Year							
Treatment course remained on systemic (n = 38)							
	BPI Pain INT	BPI Pain Sev	Worst Pain	EQ-5D VAS	EQ-5D	W-Stiff	PROMIS
Completed PROs	n = 28	n = 30	n = 30	n = 30	n = 29	n = 29	n = 30
Mean	3.17	3.43	4.30	66.80	0.70	4.24	41.02
SD	2.39	2.14	2.68	19.48	0.17	2.61	8.76
Median	2.79	3.63	4.50	67.50	0.72	4.00	41.55
Min	0.00	0.00	0.00	20.00	0.18	0.00	24.20
Max	7.00	6.50	9.00	98.00	1.00	10.00	61.70
Treatment course changed from systemic (n = 6)							
	BPI Pain INT	BPI Pain Sev	Worst Pain	EQ-5D VAS	EQ-5D	W-Stiff	PROMIS
Completed PROs	n = 6	n = 6	n = 6	n = 6	n = 6	n = 6	n = 6
Mean	5.71	5.92	7.33	49.17	0.41	6.83	32.98
SD	2.18	1.77	1.63	23.96	0.42	2.64	8.09
Median	5.93	6.38	7.50	52.50	0.54	7.50	33.15
Min	3.14	2.75	5.00	20.00	-0.31	2.00	20.80
Max	9.14	7.75	9.00	75.00	0.80	9.00	42.80
Unknown treatment (n = 1)							
2-Year							
Treatment course remained on systemic (n = 30)*							
	BPI Pain INT	BPI Pain Sev	Worst Pain	EQ-5D VAS	EQ-5D	W-Stiff	PROMIS
Completed PROs	n = 22	n = 22	n = 22	n = 21	n = 21	n = 21	n = 21
Mean	3.19	3.26	4.77	66.57	0.62	5.00	39.13
SD	2.78	2.40	3.09	20.36	0.29	2.86	9.19
Median	3.15	3.00	6.50	65.00	0.65	6.00	38.40
Min	0.00	0.00	0.00	20.00	-0.18	0.00	18.40
Max	10.00	7.50	9.00	98.00	1.00	10.00	61.70
Treatment course changed from systemic (n = 6)*							
	BPI Pain INT	BPI Pain Sev	Worst Pain	EQ-5D VAS	EQ-5D	W-Stiff	PROMIS
Completed PROs	n = 6	n = 6	n = 6	n = 6	n = 6	n = 6	n = 6
Mean	3.88	3.79	4.83	75.00	0.74	4.50	38.35
SD	3.07	2.50	2.79	18.97	0.16	3.02	3.88
Median	4.07	4.13	6.00	77.50	0.72	5.50	39.90
Min	0.00	0.00	0.00	50.00	0.57	0.00	32.10
Max	7.14	6.75	7.00	95.00	1.00	7.00	41.60
Unknown treatment (n = 2)*							

BPI = brief pain inventory; EQ-5D VAS = EuroQol-5 Dimension visual analog scale; INT = interference; Max = maximum; Min = minimum; NRS = numerical rating scale; PRO = patient reported outcomes; PROMIS = Patient-Reported Outcomes Measurement Information System; SD = standard deviation; Sev = severity; W-Stiff = worst stiffness.

*Patient population at Year-2 comes from sub-group of patients who remained No current/ planned treatment at Year-1.

Scale:

Pain: NRS from 0 to 10, 0 = no pain, 10 = pain as bad as you can imagine.

Interference: NRS from 0 to 10, 0 = does not interfere, 10 = completely interferes.

Stiffness: NRS from 0 to 10, 0 = no stiffness, 10 = stiffness as bad as you can imagine.

EQ-5D VAS: NRS from 0 to 100, 0 = worst health you can imagine, 100 = best health you can imagine.

EQ-5D: NRS from 0 to 10, 0 = worst imaginable health state, 10 = best imaginable health state.

PROMIS: NRS from 0 to 100, 0 = worst health you can imagine, 100 = best health you can imagine.

Table 3. PROs for patients completing questionnaires at each time point: Surgery only patients

Baseline							
Surgery only (n = 39)							
	BPI Pain INT	BPI Pain Sev	Worst Pain	EQ-5D VAS	EQ-5D	W-Stiff	PROMIS
Completed PROs	n =38	n =38	n =38	n =38	n =38	n =37	n =38
Mean	3.47	3.91	4.71	71.50	0.67	5.19	40.99
SD	2.84	2.75	2.99	18.90	0.21	3.13	7.33
Median	2.72	4.38	4.50	75.00	0.74	6.00	40.40
Min	0.00	0.00	0.00	20.00	0.21	0.00	26.30
Max	9.14	8.50	9.00	100.00	1.00	10.00	56.00
1-Year							
Treatment course remained on surgery (n = 32)							
	BPI Pain INT	BPI Pain Sev	Worst Pain	EQ-5D VAS	EQ-5D	W-Stiff	PROMIS
Completed PROs	n = 19	n = 20	n = 20	n = 21	n = 20	n = 22	n = 22
Mean	3.23	4.09	5.60	74.43	0.72	5.59	43.48
SD	2.45	2.10	2.52	17.69	0.16	2.52	9.49
Median	3.29	3.75	6.00	80.00	0.72	7.00	44.05
Min	0.00	0.25	0.00	40.00	0.38	0.00	30.10
Max	8.43	8.00	9.00	95.00	1.00	9.00	61.70
Changed from surgery (n = 0)							
Unknown treatment (n = 7)							
2-Year							
Treatment course remained on surgery (n = 30)*							
	BPI Pain INT	BPI Pain Sev	Worst Pain	EQ-5D VAS	EQ-5D	W-Stiff	PROMIS
Completed PROs	n = 21	n = 21	n = 21	n = 22	n = 21	n = 20	n = 22
Mean	2.35	2.52	3.71	78.32	0.76	3.80	43.65
SD	2.11	1.76	2.43	15.25	0.17	2.67	6.81
Median	2.43	2.50	4.00	82.50	0.81	4.50	43.50
Min	0.00	0.00	0.00	40.00	0.22	0.00	30.50
Max	8.00	5.00	8.00	100.00	1.00	9.00	61.70
Changed from surgery (n = 0)*							
Unknown treatment (n = 2)*							

BPI = brief pain inventory; EQ-5D VAS = EuroQol-5 Dimension visual analog scale; INT = interference; Max = maximum; Min = minimum; NRS = numerical rating scale; PRO = patient reported outcomes; PROMIS = Patient-Reported Outcomes Measurement Information System; SD = standard deviation; Sev = severity; W-Stiff = worst stiffness.

*Patient population at Year-2 comes from sub-group of patients who remained No current/ planned treatment at Year-1. Scale:

Pain: NRS from 0 to 10, 0 = no pain, 10 = pain as bad as you can imagine.

Interference: NRS from 0 to 10, 0 = does not interfere, 10 = completely interferes.

Stiffness: NRS from 0 to 10, 0 = no stiffness, 10 = stiffness as bad as you can imagine.

EQ-5D VAS: NRS from 0 to 100, 0 = worst health you can imagine, 100 = best health you can imagine.

EQ-5D: NRS from 0 to 10, 0 = worst imaginable health state, 10 = best imaginable health state.

PROMIS: NRS from 0 to 100, 0 = worst health you can imagine, 100 = best health you can imagine.



Poster #216 #1836519

OUTPATIENT OPIOID UTILIZATION AMONG PEDIATRIC PATIENTS WITH PRIMARY BONE SARCOMAS AFTER TUMOR RESECTION

Lee M. Zuckerman, MD¹; Omar Ramos, MD²; Alex Mierke, MD²; Ryan Filler, MD²; Nadine Williams, MD²

¹City of Hope National Medical Center, Duarte, California, UNITED STATES, ²Loma Linda University Medical Center, Loma Linda, California, UNITED STATES

Objective: The majority of children with bone sarcomas experience pain. This pain can be severe and significantly decrease their quality of life. Opioids remain the mainstay of treatment for malignancy associated pain in children. The patterns of outpatient opioid prescription after tumor resection surgery for malignant bone neoplasms remains unknown. The purpose of this study is to evaluate the patterns of outpatient opioid prescription in patients with malignant bone sarcomas after tumor resection surgery, and to assess for factors that may lead to increased opioid dosing in these patients.

Methods: All patients 18 years and younger who were diagnosed with a primary malignant neoplasm of bone (ICD-10-CM codes C40-C41) and underwent surgery for tumor resection during the period of January 2010 to January 2018 were considered eligible. Patients were excluded if they did not have postoperative follow up for at least 120 days. The following data was collected from all patients: age at diagnosis, sex, body mass index (BMI), sex, ethnicity, insurer, diagnosis, location of neoplasm, presence of metastases at time of diagnosis, preoperative opioid use, length of stay, surgery performed (salvage versus amputation, prosthetic versus allograft reconstruction) and narcotic prescriptions after discharge. Patients filling no opioid prescriptions within the 30 days prior to surgery were considered opioid naïve. Patients with one or more opioid prescription in the 30 days prior to surgery were considered preoperative opioid users. The primary outcome of interest was opioid use in the first 120 days after discharge in patients undergoing resection of a primary sarcoma of bone. Oral morphine, hydrocodone, oxycodone, meperidine, codeine, hydromorphone, tramadol, and fentanyl were all classified as opioids. Opioid utilization rates were reported in Morphine Milligram Equivalents (MMEs). The number of pills and total MMEs was calculated for each patient both preoperatively and on the initial discharge prescription after tumor resection surgery. Additionally, the cumulative MMEs were also categorized in 30-day intervals for a total of 120 days after discharge. Secondary analysis compared cohorts again after stratification by tumor location, presence of metastasis at diagnosis, and preoperative opioid use. A Student's t-test or Mann-Whitney U test were used as appropriate for comparison of continuous variables. Chi-squared analysis was used for comparison of categorical variables. Backwards stepwise linear and logistic regression modeling with robust standard error was performed to determine factors independently associated with increased 30-day postoperative opioid use, total 120-day postoperative opioid use, and predictors of chronic opioid utilization after adjusting for confounding variables.

Results: Twenty-eight patients with bone sarcomas who underwent primary tumor resection were identified. The mean age was 13 (SD 3.4, range 6-18), the mean BMI was 22.4 kg/m² (SD 6.3, range 12.0-32.9) and 40% were female. The groups were similar in terms of age, gender, BMI, race, diagnosis, length of stay, and insurance ($p > 0.05$). Patients with preoperative opioid use were prescribed significantly more opioids in every 30-day postoperative interval and for the 120-day total. When stratified by tumor location, patients with malignant bone neoplasms of the pelvis had significantly greater postoperative opioid utilization during the third and fourth postoperative intervals when compared to patients with tumors located in the lower and upper extremities during postoperative days 61-90 (5,970 vs. 1060.4 and 0 MMEs, respectively, $p = 0.048$) and during post-operative days 91-120 (6,450 vs. 829.6 and 0 MMEs respectively, $p = 0.015$). Patients with metastatic disease at time of surgery also received more opioids than patients without metastasis at time of surgery (3261.7 vs. 1580.5 MMEs, $p = .015$). Older age, diagnosis of osteosarcoma, presence of metastases, and longer length of stay were associated with higher 30-day postoperative opioid utilization. Preoperative opioid use and increased length of stay were associated with increased total 120-day opioid utilization.

Conclusion: Patients with preoperative opioid use, metastatic disease, and primary sarcomas in the pelvis require more postoperative opioids. The results of this study can be used to stratify the average opioid requirement of pediatric patients undergoing primary bone sarcoma resection.



Poster #217 #1836512

OUTCOMES INCLUDING LATE AMPUTATION AFTER TREATMENT FOR LOWER EXTREMITY SARCOMA: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY

Erik J. Geiger, MD¹; Wei Liu, PhD²; Kumar Srivastava, PhD²; Nicholas M. Bernthal, MD³; Yutaka Yasui, PhD²; Kirsten Ness, PT, PhD²; Kevin Krull, PhD²; Wendy Leisenring, Sc.D.⁴; Gregory Armstrong, MD, MSCE²; Rosanna Wustrack, MD⁵

¹UCLA, Santa Monica, California, UNITED STATES, ²St. Jude Children's Research Hospital, Memphis, Tennessee, UNITED STATES, ³David Geffen School of Medicine at UCLA, Santa Monica, California, UNITED STATES, ⁴Fred Hutchinson Cancer Research Center, Seattle, Washington, UNITED STATES, ⁵UCSF, San Francisco, California, UNITED STATES

Objective: Though limb salvage surgery (LSS) is the standard of care for pediatric lower extremity sarcomas, a fraction of patients today are treated with primary amputation when necessary. Improved pediatric sarcoma survivorship with modern chemotherapy protocols creates a need for ongoing clinical surveillance of treatment sequelae and challenges the longevity of oncologic reconstructions. A devastating outcome of failure after LSS is late amputation occurring years after the index surgery. The purposes of this study were 1) to investigate the incidence of late amputation after lower extremity LSS in pediatric sarcoma survivors at 20 years of follow up, 2) to determine clinical and treatment-related risk factors for late amputation, and 3) to compare psychosocial and physical outcomes among survivors treated with primary amputation, successful LSS (never experiencing late limb loss), and LSS complicated by late amputation.

Methods: The Childhood Cancer Survivor Study (CCSS) is a retrospectively-ascertained cohort of 5-year survivors of cancer diagnosed when < 21 years of age treated at one of 31 collaborating North American institutions between 1970-1999. Patients with lower extremity bone sarcoma or rhabdomyosarcoma treated with primary amputation (n=547; mean age at diagnosis 13.0 years, range 0.27-20.88) or primary LSS (n=510; 14.0 years, 0.42-20.98) were included. Demographic, clinical, and treatment details were abstracted from the medical record. Cumulative incidence (CIN) of late amputation among LSS survivors, with death as competing risk, was calculated from the date of CCSS cohort entry to last follow-up, amputation, or death. Poisson regression analyses estimated the impact of demographic, clinical, and treatment variables on the risk of late amputation after LSS. Outcomes including ability to work or attend school were taken from survivors' answers to CCSS follow up surveys, as were assessments of impaired physical performance and ability to manage needs of daily living. Health related quality-of-life (HRQOL) was evaluated using the 36-Item Short-Form Health Survey (SF-36). Emotional distress and global mental health were measured with the Brief Symptom Inventory-18 (BSI-18). A modified Poisson approach was utilized to estimate the relative risk of HRQOL, physical/functional, and psychosocial impairments (impairment yes/no) among treatment groups.

Results: The CIN of late amputation at 20 years after LSS was 17.9% (95% CI 14.4-21.3%) (Figure 1), and there was no difference in long term survival between LSS and primary amputation cohorts [88.1 % (95% CI: 85.0%-91.2%) vs 86.6% (95% CI: 82.1-91.1%), respectively]. Multivariable analyses identified male sex (RR=2.06, CI:1.16-3.64, p=0.013), vinca alkaloid exposure (RR=1.95, CI:1.05-3.60, p=0.033) joint replacement (RR=2.64, CI:1.47-4.72, p=0.001), and developing a grade 3-4 chronic health condition (RR=1.86, CI:1.04-3.33, p=0.038) to be independently associated with late amputation (Table 1). Survivors treated with a primary amputation (RR=2.04, CI:1.15-3.64) and LSS complicated by late amputation (RR=3.85, CI:1.66-8.92) were more likely to be unemployed or unable to attend school compared to the successful LSS cohort. A significant increase in risk for needing help with routine activities of daily living was associated with having a primary amputation (RR=2.76, 95% CI: 1.29-5.89) or late amputation (RR=4.45, 95% CI: 1.44-13.7) (Table 2). Outcomes from the SF-36 and BSI-18 showed that survivors reported equivalent mental and emotional health outcomes regardless of treatment group. However, survivors treated with primary amputation and those with LSS complicated by late amputation reported worse physical health scores compared to successful LSS survivors (Table 3).

Conclusion: This is the first study to utilize a large, geographically-diverse survivor population to identify factors associated with failed LSS over long-term follow up, and the first CCSS report to compare outcomes of LSS and primary amputation after treatment of pediatric lower extremity sarcoma. There is substantial risk for late amputation after LSS, so developing ways to mitigate risks imparted by the clinical and treatment variables identified in this study will be critical to enhance sarcoma survivorship. All survivors of pediatric sarcoma require lifelong surveillance and support for personal and social

challenges faced as a byproduct of their oncology treatments, but survivors treated initially with primary amputation and those who undergo late amputation represent groups at higher risk of poor outcomes, particularly in physical domains.

Figure 1: Cumulative incidence of amputation among LSS survivors.

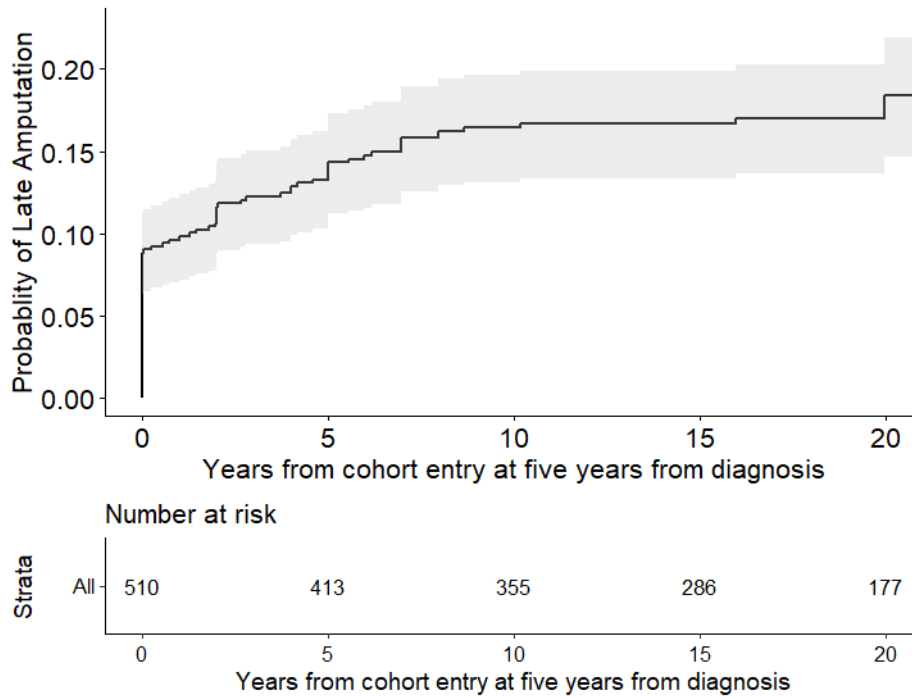


Table 1. Multivariable analysis of risk factors (including treatment modalities chemo and XRT) for late amputation after initial limb salvage surgery.

	RR	CI	p-value
Sex			
Male	2.06	1.16- 3.64	0.013
Female	1	1.00- 1.00	.
Alkylating agent			
Yes	1.89	0.76- 4.68	0.17
No	1	1.00- 1.00	.
Vinca alkaloid			
Yes	1.95	1.05- 3.60	0.033
No	1	1.00- 1.00	.
Joint replacement procedure			
Yes	2.64	1.47- 4.72	0.001
No	1	1.00- 1.00	.
Cancer recurrence			
Yes	1.9	0.94- 3.83	0.075
No	1		
Grade 3-4 CHC			
Yes	1.86	1.04- 3.33	0.038
No	1		

Table 2: Physical and social outcomes as captured by Children’s Cancer Survivor Study follow up surveys

	Modified Poisson Regression adjusted for age at physical function			
Outcome	Yes n(%)	RR	CI	p-value
Limited physical performance				
LSS with late Amp	14(73.68)	1.81	1.29-2.52	0.0005
Primary Amp	189(46.78)	1.1	0.89-1.37	0.37
Successful LSS	59(42.14)	1		.
Help needed for routine needs				
LSS with late Amp	4(23.53)	4.45	1.44-13.7	0.009
Primary Amp	57(15.28)	2.76	1.29-5.89	0.009
Successful LSS	7(5.51)	1		.
Cannot work or attend school				
LSS with late Amp	6(35.29)	3.85	1.66-8.92	0.002
Primary Amp	73(19.57)	2.04	1.15-3.64	0.015
Successful LSS	12(9.52)	1		.
Driver's license (over 16 years old)				
LSS with late Amp	3(18.75)	2.59	0.82-8.21	0.11
Primary Amp	32(8.65)	1.55	0.70-3.43	0.28
Successful LSS	7(5.51)	1		

Table 3: Physical and psychosocial outcomes as measured by the Short Form Health Survey (SF-36) and Brief Symptom Inventory (BSI-18) for survivors treated with primary amputation, successful LSS, and LSS complicated by late amputation

	Impairment n(%)	RR(95%CI)	p-value
HR-QOL			
Physical health			
Physical functioning			
LSS with late Amp	12(70.59)	2.46(1.66-3.63)	<.0001
Primary Amp	132(38.15)	1.34(1.04-1.72)	0.024
Successful LSS	61(27.23)	1	
Physical role			
LSS with late Amp	8(47.06)	1.87(1.06-3.30)	0.030
Primary Amp	75(21.68)	0.87(0.64-1.19)	0.38
Successful LSS	53(23.77)	1	
Bodily pain			
LSS with late Amp	8(47.06)	2.33(1.27-4.26)	0.006
Primary Amp	104(30.14)	1.50(1.10-2.06)	0.011
Successful LSS	42(18.67)	1	
General health			
LSS with late Amp	8(47.06)	1.98(1.10-3.56)	0.022
Primary Amp	71(23.43)	1.00(0.72-1.38)	0.99
Successful LSS	48(22.22)	1	
Mental health			
Vitality			
LSS with late Amp	6(35.29)	1.59(0.78-3.24)	0.20
Primary Amp	76(25.08)	1.15(0.83-1.59)	0.41
Successful LSS	45(20.74)	1	
Social functioning			
LSS with late Amp	4(23.53)	1.39(0.56-3.47)	0.48
Primary Amp	60(17.29)	1.03(0.71-1.49)	0.89
Successful LSS	37(16.44)	1	
Role-emotional			
LSS with late Amp	2(11.76)	0.68(0.18-2.62)	0.58
Primary Amp	76(22.03)	1.28(0.90-1.82)	0.17
Successful LSS	38(17.12)	1	
Mental Health			
LSS with late Amp	6(35.29)	2.20(1.07-4.52)	0.032
Primary Amp	67(22.11)	1.39(0.95-2.01)	0.087
Successful LSS	34(15.67)	1	
BSI-18			
Depression			
LSS with late Amp	3(18.75)	0.95(0.86-1.06)	0.39
Primary Amp	45(14.95)	0.97(0.94-1.00)	0.079
Successful LSS	21(9.68)	1	
Anxiety			
LSS with late Amp	0(0)	NA	NA
Primary Amp	28(9.30)	0.99(0.96-1.01)	0.37
Successful LSS	16(7.37)	1	
Somatic			
LSS with late Amp	3(18.75)	0.96(0.86-1.07)	0.43
Primary Amp	42(13.95)	0.98(0.95-1.01)	0.20
Successful LSS	21(9.63)	1	



Poster #218 #1836522

THE IMPACT OF DISTANCE FROM TREATMENT CENTER: A PRELIMINARY ANALYSIS SUGGESTING A ROLE FOR TELEMEDICINE IN SARCOMA CARE

Matthew J. Thompson, MD¹; Elizabeth Heath²; Emily Robinson³; Shamele Battan³; Nirnaya Miljadic, MS, PhD⁴; Nayak Polissar, PhD⁴; Jesse Roberts, MD¹; Edward Kim, MD⁵; Stephanie Schaub, MD⁶; Elizabeth T. Loggers, MD, PhD⁷; Michael J. Wagner, MD⁸; Lee D. Cranmer, MD, PhD⁹

¹Seattle Cancer Care Alliance Sarcoma Clinic, Department of Orthopaedics and Sports Medicine, University of Washington School of Medicine, Seattle, Washington, UNITED STATES, ²University of Washington, Seattle, Washington, UNITED STATES, ³University of Washington School of Medicine, Seattle, Washington, UNITED STATES, ⁴The Mountain-Whisper-Light Statistics, Seattle, Washington, UNITED STATES, ⁵Seattle Cancer Care Alliance Sarcoma Clinic, Department of Radiation Oncology, University of Washington School of Medicine, Seattle, Washington, UNITED STATES, ⁶Seattle Cancer Care Alliance Sarcoma Clinic, Department of Radiation Oncology, University of Washington School of Medicine, Seattle, Washington, UNITED STATES, ⁷University of Washington/Fred Hutch/Seattle Cancer Care, Seattle, Washington, UNITED STATES, ⁸University of Washington/Fred Hutch/Seattle Cancer Care Alliance, Seattle, Washington, UNITED STATES, ⁹Univ Washington/Fred Hutchinson Cancer Res Ctr, Seattle, Washington, UNITED STATES

Objective: It is established that the care of patients with sarcoma is best administered at a tertiary sarcoma treatment center. Our group previously observed that treatment at a high-volume center may even mitigate the importance of socio-economic factors on overall survival. However, little is known about how the distance between a patient's home and the treatment center may impact timeliness of care or financial strain on the patient. In addition to potentially preventing inappropriate care of patients with sarcoma through earlier and more convenient access to specialists, telemedicine may be useful in moderating these potential disparities for patients traveling from remote or underserved areas.

Telehealth consumes resources while potentially adversely impacting iterative financial outcomes for institutions in the form of facility fees and/or fees for diagnostic tests that may be performed in remote locations when the patient is not traveling to the center. The utility of telemedicine was, by necessity, demonstrated during the COVID-19 pandemic, especially at centers caring for patients across state lines. Yet, as interstate waivers for licensure expire, institutional investment in telehealth will require ongoing justification. As a virtual bridge to geographic distance, we aimed to assess patient and institutional factors most likely impacted by the routine use of telemedicine in sarcoma care.

Methods: Following institutional IRB approval and utilizing funding from an institutional pilot grant, a retrospective review of our sarcoma database identified 506 eligible adult patients treated between January 2017 and December 2020 for a newly diagnosed sarcoma. Distance to the treatment center for each subject was determined using widely available online mapping software. Cost of travel was derived in a standardized fashion for each subject utilizing standardized indices by year of travel (e.g. IRS Standard Mileage Rates, United States Department of Transportation Bureau of Transportation Statistics Average Domestic Airline Itinerary Fares) and accounted for relevant tolls. State and national Area Deprivation Indices (sADI and nADI) and Rural-Urban Continuum (RUC) Codes were recorded for each subject based on zip code. All professional, procedural, and facility fees, in the form of relative value units, were tabulated for the initial patient visit (RVU1) and for the entire care episode (RVU2) during the study period. Stage was coded at four levels from Stage 1 to Stage 4 according to the AJCC Staging System for Soft Tissue Sarcoma.

Linear regression was used to analyze the relationship between outcome (dependent) variables and (a) the primary independent variable (distance from SCCA) and (b) known control variables. The results are presented as regression coefficients and their standard error (SE) and the p-value for the null hypothesis that the true coefficient is zero. A univariate, unadjusted analysis is presented and an adjusted analysis is also presented (including one or more control variables in the analysis, aside from the test variable). A few observations were removed prior to analysis: impossible values or outliers (based on extreme separation from other values of the variable). $P < 0.05$ was considered statistically significant.

Results: Expectedly, in-state patients who lived a further distance from our treatment center experienced a higher cost of travel ($p < 0.001$), and cost of out-of-state travel was greater than in-state ($p < 0.001$). Cost of travel correlated positively with sADI ($p < 0.001$), nADI ($p < 0.001$), and RUC ($p < 0.001$) in univariate and multivariate analyses.

Time to first visit was not associated in a statistically significant way with distance to our center, in- vs. out-of-state status, ADI, or RUC. Patients with a higher disease stage were more likely to experience a longer time to first visit in univariate ($p=0.0064$) and multivariate analysis controlled for distance and sADI ($p=0.0025$). See Table 1 for regression coefficients and standard errors.

Time to diagnosis did not have a statistically significant association with distance from the treatment center, in- vs. out-of-state status, RUC, or disease stage. A longer time to diagnosis was associated with a higher sADI (univariate, $p=0.041$) and nADI (univariate $p=0.0085$, multivariate $p=0.017$).

Total RVUs generated at the first visit did not have a statistically significant association with any individual variable in univariate or multivariate analyses. Total RVUs generated during an entire patient care episode had a negative association with distance from the treatment center that was close to statistical significance ($p=0.077$) when controlled for disease stage. Total RVU generation displayed a statistically significant negative association with sADI ($p=0.072$), nADI ($p=0.009$), and RUC ($p=0.047$) in univariate analysis and when controlled for disease stage (sADI $p=0.007$, nADI $p=0.007$, and RUC $p=0.027$). Disease stage positively associated with total RVU generation in univariate analysis ($p=0.0064$) and when controlled for distance and sADI ($p=0.0025$). Figure 1.

Conclusion: Patients traveling a longer distance, from out-of-state, from more rural areas or with a higher deprivation index are strained by greater costs of travel. Patients residing in areas with a higher deprivation index experience a longer time to diagnosis and may benefit most from earlier access to tertiary care through telemedicine, which might also help moderate the cost of repeated travel to the center. Total RVU generation controlled for disease stage was less for patients in more rural and deprived areas. The thoughtful and routine adoption of telemedicine in sarcoma care might benefit patients and institutions by improving the center's ability to remotely coordinate care, allowing for concentration of necessary diagnostics and interventions at the time of rationed travel to the center.

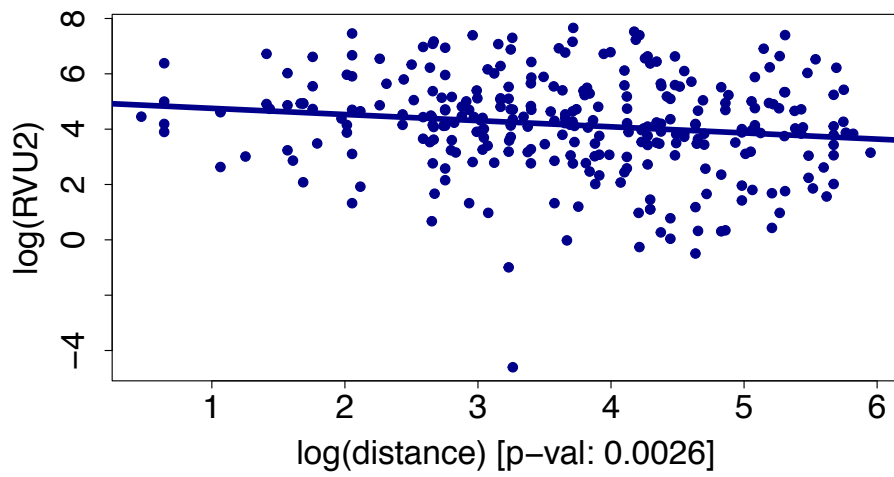
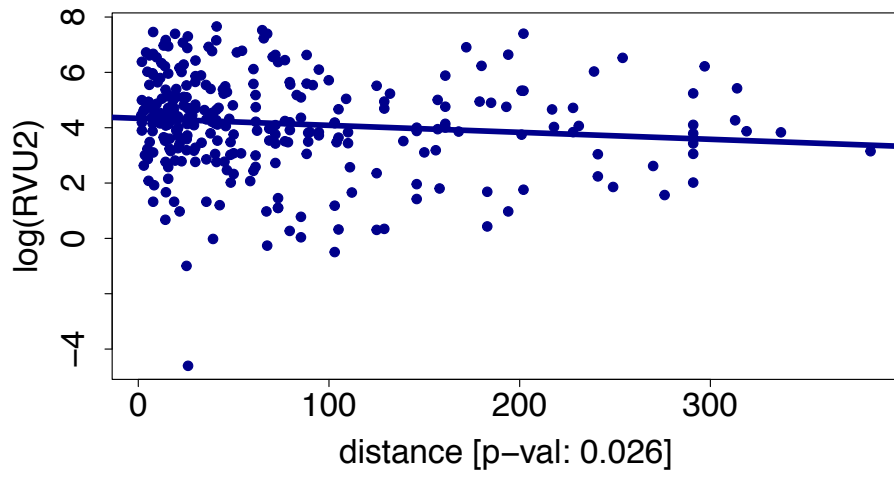
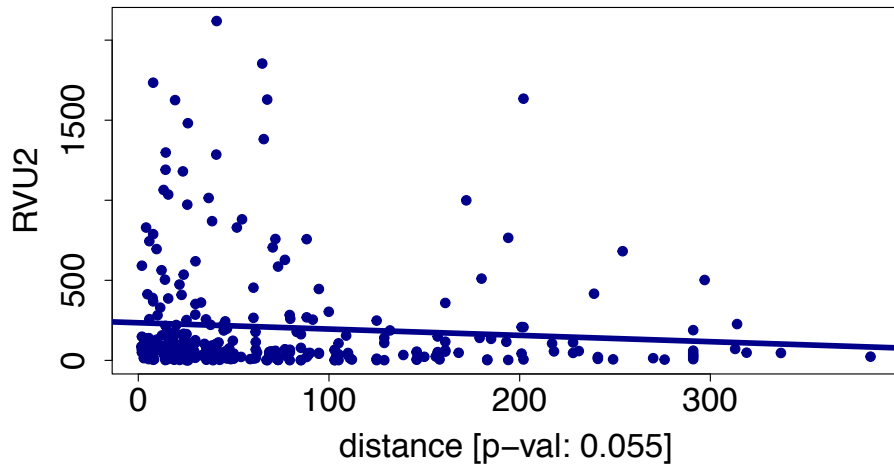
Table 1 – Table of Regressions

	Distance to Center				In/Out of State (0/1)				ADI State				ADI National				Rural Urban Code Status				Disease Stage			
	controlled for	coefficient	st.err	p-value	controlled for	coefficient	st.err	p-value	controlled for	coefficient	st.err	p-value	controlled for	coefficient	st.err	p-value	controlled for	coefficient	st.err	p-value	controlled for	coefficient	st.err	p-value
Cost to travel to SCCA	univariate	1.053	0.00987	< 0.001	univariate	435.3	12.3	< 0.001	univariate	16.41	1.27	< 0.001	univariate	2.381	0.182	< 0.001	univariate	38.06	2.71	< 0.001	univariate	8.158	4.1	0.047
	D.Stage	1.042	0.0115	< 0.001	D.Stage	430.2	13.1	< 0.001	D.Stage	16.32	1.37	< 0.001	D.Stage	2.327	0.195	< 0.001	D.Stage	36.03	2.89	< 0.001	Distance	-0.8954	0.855	0.3
	D.Stage, ADI St.	1.01	0.0187	< 0.001																	Distance, ADI St.	-0.5708	1.11	0.61
Total RVU first encounter	univariate	-	0.002691	0.93	univariate	-0.08579	0.6	0.89	univariate	0.002542	0.101	0.98	univariate	0.00811	0.0148	0.59	univariate	-0.1006	0.189	0.6	univariate	-0.009518	0.266	0.97
	D.Stage	-0.001077	0.0035	0.76	D.Stage	-0.07442	0.672	0.91	D.Stage	0.05325	0.113	0.64	D.Stage	0.015	0.0164	0.36	D.Stage	-0.1554	0.217	0.47	Distance	-0.001458	0.268	1
	D.Stage, ADI St.	-0.001148	0.00533	0.83																	Distance, ADI St.	-0.03605	0.312	0.91
Total RVU subsequent encounters	univariate	-0.3941	0.259	0.13	univariate	-24.75	54.9	0.65	univariate	-21.73	8.01	0.0072	univariate	-3.048	1.15	0.0087	univariate	-32.2	16.2	0.047	univariate	56.74	20.6	0.0064
	D.Stage	-0.4969	0.28	0.077	D.Stage	-34.48	60.9	0.57	D.Stage	-23.46	8.55	0.0066	D.Stage	-3.287	1.22	0.0074	D.Stage	-39.57	17.8	0.027	Distance	60.37	20.6	0.0038
	D.Stage, ADI St.	-0.3005	0.419	0.47																	Distance, ADI St.	69.79	22.8	0.0025
Time to first visit at SCCA	univariate	0.1526	0.103	0.14	univariate	-42.75	26	0.1	univariate	4.708	3.81	0.22	univariate	0.8608	0.558	0.12	univariate	-7.348	7.05	0.3	univariate	17.51	9.07	0.055
	D.Stage	0.1717	0.12	0.15	D.Stage	-48.15	29	0.098	D.Stage	4.528	4.22	0.28	D.Stage	0.8277	0.61	0.18	D.Stage	-7.698	7.8	0.32	Distance	17.58	9.16	0.056
	D.Stage, ADI St.	0.1473	0.198	0.46																	Distance, ADI St.	24.04	11.5	0.037
Time to diagnosis	univariate	0.01379	0.0661	0.83	univariate	-16.32	16.8	0.33	univariate	5.058	2.46	0.041	univariate	0.9501	0.358	0.0085	univariate	-5.188	4.48	0.25	univariate	0.7676	5.71	0.89
	D.Stage	0.04478	0.0764	0.56	D.Stage	-18.52	18.6	0.32	D.Stage	4.69	2.71	0.085	D.Stage	0.9413	0.39	0.017	D.Stage	-4.556	4.93	0.36	Distance	0.976	5.8	0.87
	D.Stage, ADI St.	0.02733	0.127	0.83																	Distance, ADI St.	2.338	7.38	0.75

Table 2 – Pearson Correlations

	distance	area_state	area_nation	rural	stage
distance	1	0.58	0.58	0.57	0.12
area_state	0.58	1	0.97	0.44	0.1
area_nation	0.58	0.97	1	0.45	0.1
rural	0.57	0.44	0.45	1	0.11
stage	0.12	0.10	0.10	0.11	1

Notes. (1) All correlations between two different variables have $p < 0.001$ (2-sided test) except correlations with stage. (2) P-values for stage, bottom row, left to right: 0.021, 0.089, 0.084, 0.025, N/A.





Poster #219 #1836523

THE IMPACT OF DISTANCE ON SARCOMA ONCOLOGIC OUTCOMES: A RETROSPECTIVE COHORT STUDY

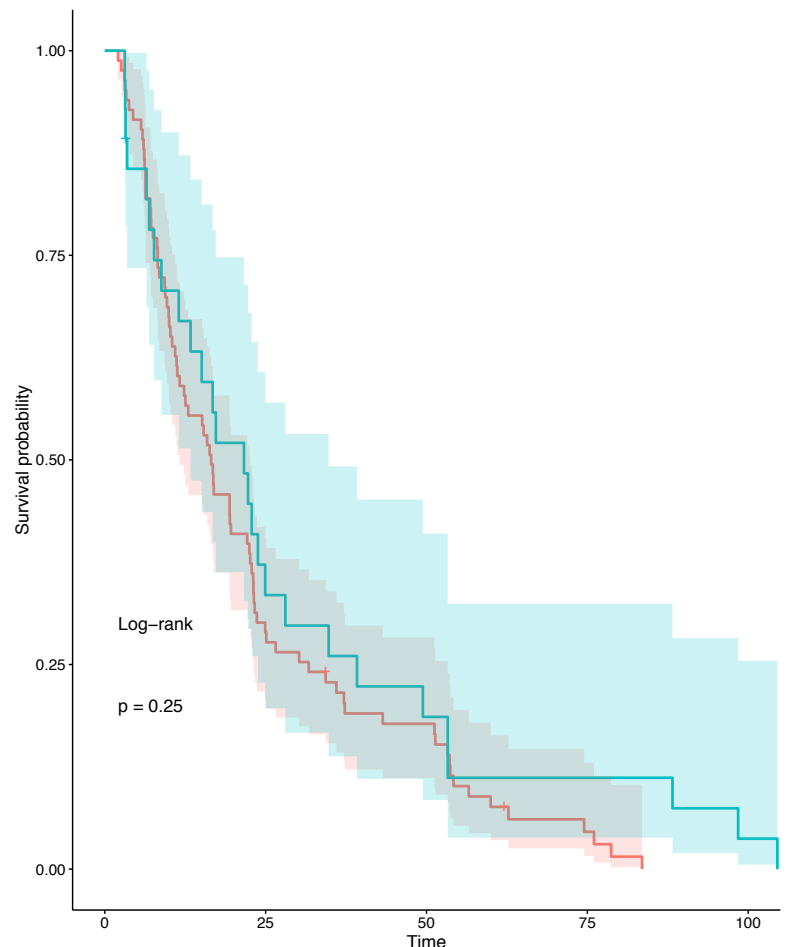
Abdulaziz Al-Mubarak, MD¹; Giuseppe Frenda, MD¹; Mireille Dessureault, MSc¹; Ahmed Aoude, .²; Robert Turcotte, MD¹; Sinziana Dumitra, MD, MSc (Epi), FRCSC(C)¹, ¹McGill University, Montreal, Province du Québec, CANADA, ²McGill, Montreal, Province du Québec, CANADA

Objective: Management of soft tissue sarcomas (STS) varies depending on site, location, subtype and due to the complexity of the disease a dedicated multidisciplinary team is needed for optimal management. Previous investigations have shown that treatment of STS at high volume centers is associated with superior outcomes, which has led to the centralization of care for STS patients. This may subject these patients to difficulty in obtaining care. We thus aimed to assess the impact of distance decay on oncologic outcomes in sarcoma patients.

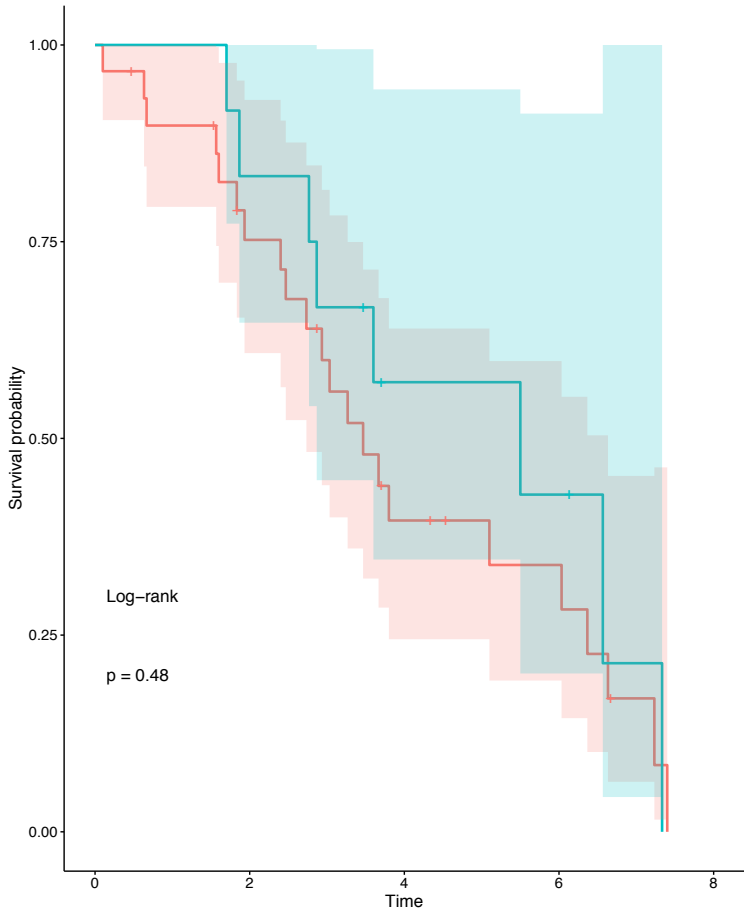
Methods: A single-center prospective database was queried for extremity sarcoma patients managed at a tertiary referral center from 2008 to 2018. The data obtained included patient and sarcoma characteristics and outcomes. Geographic information software (ArcGIS) was used to calculate the straight-line distance from patient's home address to the treating center. The data-points were divided into quartile categories and skewed line distances were taken into consideration. The cohort were stratified according to home addresses being in the Greater Metropolitan Area (GMA), or Outer Metropolitan Area (OMA). Data was used to compare several endpoints between quartile categories including time to surgery, time to assessment of all specialists, disease free survival (DFS) and overall survival (OS). A univariate and multivariate Cox regression model was used to assess association with survival.

Results: A total of 492 patients were identified of which median age was 60 (range 16-90). 40.2% of the GMA group and 42.6% of the OMA group were female and the most encountered histology was myxofibrosarcoma in both groups (15.7% and 13.4% respectively). There was no overall difference in time to initiation of treatment (44.68 vs 42.71; days, p=0.748) as well as time to initiation of neo-adjuvant radiation (39.84 vs 34.39; days, p=0.308), time to adjuvant radiation (54 vs 51.03; days, p=0.537) and time to neo-adjuvant systemic therapy (58.27 vs 32.09; days, p=0.107). Disease-free survival and progression free survival were worse for those in the GMA compared to OMA, 23.27 vs 27.3 (p=0.411) and 3.36 vs 4.1 (p=0.293) months respectively. The overall survival was worse for the population in the GMA 57.36 vs 75.43 months (p=0.054). After correcting for patient and tumor characteristics, DFS was significantly better in the OMA group (HR=1.98 95%CI 1.15-3.41) as was PFS in the multivariate analysis.

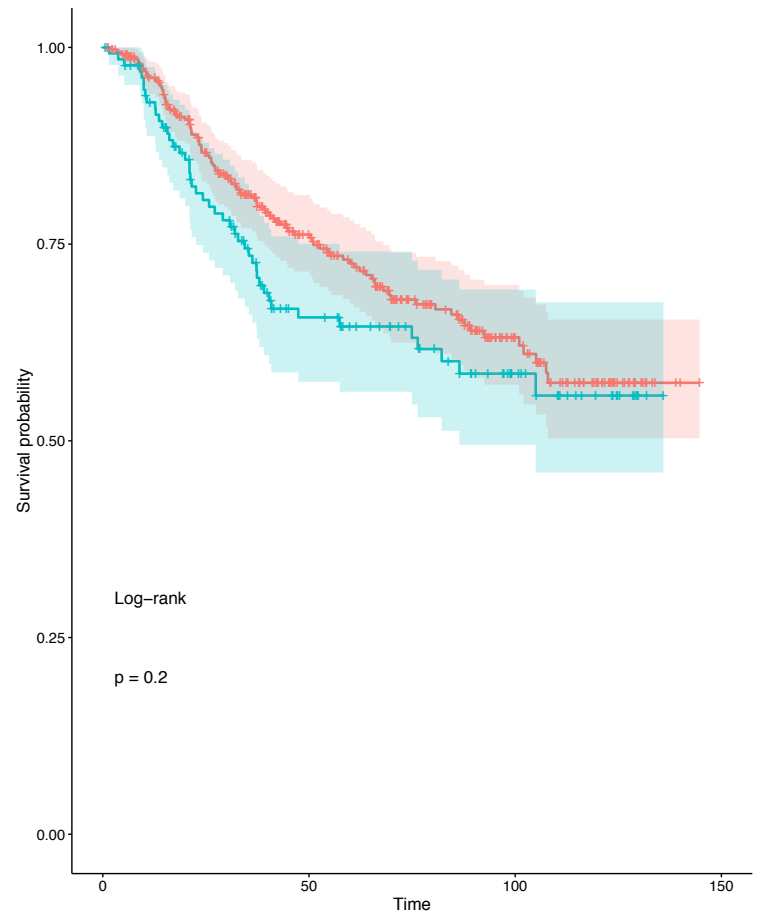
Conclusion: This study confirms health inequalities related to differences in distance in sarcoma patients. There was no delay in initiation of treatment but improved DFS and PFS. Further, multi-institutional observational studies are needed to investigate the impact of distance on outcomes of sarcoma patients.



A. DFS in patients in MA vs OMA group MA OMA



MA OMA



MA OMA



Poster #220 #1836514

THE COSTS OF COVERAGE: EFFECTS OF INSURANCE PROVIDER ON SOFT TISSUE SARCOMA FINANCIAL AND HEALTH OUTCOMES

Hayley Hansen, BSBA; Qiang An, MBBS, MPH; Benjamin J. Miller, MD MS
University of Iowa, Iowa City, Iowa, UNITED STATES

Objective: Our primary goals were to report the costs of soft tissue sarcoma care and impacts of insurance provider type on the total charges of treatment billed by a tertiary institution, the reimbursement paid by insurance, and the out-of-pocket costs paid by patients. In addition, we evaluated whether patients treated for soft tissue sarcoma at a sarcoma center demonstrated differences in delay of initial medical contact or delay in initiating treatment when covered by public insurance versus private insurance.

Methods: Patients 18 years and older, diagnosed with soft tissue sarcoma between 2011 and 2020, were retrospectively identified from a prospective sarcoma patient database. We included patients with a primary, non-recurrent, non-metastatic soft tissue sarcoma >5 cm in greatest dimension, deep to the fascia, and whose surgical resection and adjuvant treatment was performed at our institution. Financial data was obtained from the Billing, Insurance, and Medical Records department. Charges were recorded from the initial date of evaluation at our institution to three months post-operative from tumor excision. Patients were grouped by insurance type at the time of treatment. The private insurance group included Blue Cross Blue Shield (BCBS) and unspecified commercial insurance. The public insurance group included Medicaid, Medicare, and Veterans Administration. Statistical analyses were conducted via SAS. Continuous variables were analyzed with Wilcoxon rank sum test. Categorical variables were analyzed using chi-square test, Fisher's exact test, and logistic regression.

Results: Seventy-four patients met inclusion criteria: 31 Medicare, 26 BCBS, 11 unspecified commercial insurance, 3 Veterans Administration, and 3 Medicaid (41 males, 33 females). The average age of patients was 74 years old in the public insurance group and 48 years old in the private insurance group. The median charges for sarcoma care billed by the institution were \$203,245 and \$189,701 for patients covered by public insurance and private insurance, respectively. The median reimbursement by public insurers was \$31,741 compared to \$54,537 for private insurers (p < .0001). On average, out-of-pocket costs (in addition to premiums and deductibles) for sarcoma care were \$247 for patients with public insurance and \$667 for private insurance (p < .0001). These findings remained statistically significant after adjustment for patient enrollment in a clinical trial. The median institutional charges were \$61,119 for patients treated with surgical excision alone, \$206,503 for patients treated with surgical excision and radiation therapy, and \$290,735 for patients treated with surgical excision, radiation therapy, and chemotherapy. The average time from first medical contact with any provider which led to the diagnosis of sarcoma to receipt of treatment (surgery, radiation, chemotherapy) was 46 days for those with public insurance and 57 days with private insurance (p = .322). Fifty-six percent (21/37) of privately insured patients presented in the first half of the calendar year (January – June) while 59% (22/37) of publicly insured patients presented in the second half (July – December) (p = .162).

Conclusion: At the institutional level, charges for soft tissue sarcoma care were greater in the public insurance group. However, public insurers reimbursed less of these costs compared to private insurers. About 84% of the charges incurred in the public insurance group and 71% in the private insurance group were absorbed by the institution. Out-of-pocket costs for patients insured by public or private insurance were reasonable and unlikely to be financially damaging, not accounting for monthly premiums, deductibles, and other financial liabilities related to sarcoma diagnosis and treatment. There was a shorter time duration between initial medical point of contact and receipt of treatment for those with public insurance, but no association between this benefit and insurance type.

Table 1. Demographics of study participants

Variables		n = 74	Percent (%)
Sex	Male	41	55.4%
	Female	33	44.6%
Age range	18 - 19	2	2.7%
	20 - 39	10	13.5%
	40 - 59	19	25.7%
	60 - 79	33	44.6%
	>= 80	10	13.5%
Race	White	71	96.0%
	Black	3	4.0%
Insurance Provider	Blue Cross Blue Shield	26	35.1%
	Commercial Insurance	11	14.9%
	Medicaid	3	4.1%
	Medicare	31	41.9%
	Veterans Administration	3	4.1%



Poster #221 #1836515

VALIDATING THE HEALTH-RELATED QUALITY OF LIFE DATA OF THE PROSA-STUDY BY COMPARISON PATIENT AND TUMOR CHARACTERISTICS OF RPS PATIENTS WITH THE TARPS-WG COHORT

Jens Jakob, MD¹; Leopold Hentschel, Dipl. Psych²; Stephan Richter, MD, PhD²; Peter Hohenberger, MD, PhD³; Bernd Kasper, MD, PhD⁴; Dimosthenis Andreou, MD, PhD⁵; Daniel Pink, MD, PhD⁶; Jochen Schmitt, MD, PhD⁷; Markus K. Schuler, MD, PhD⁸; Martin Eichler, PhD⁹

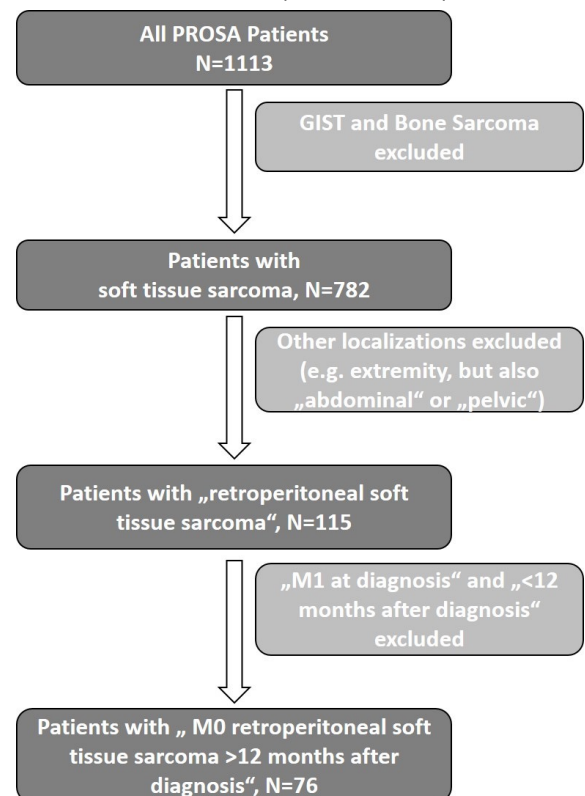
¹University Medical Center Göttingen, Göttingen, Niedersachsen, GERMANY, ²University Hospital Carl Gustav Carus, University Cancer Center/Medical Department I, Dresden, Dresden, Sachsen, GERMANY, ³Mannheim University Medical Center, University of Heidelberg, Mannheim, Baden-Württemberg, GERMANY, ⁴University of Heidelberg, Mannheim University Medical Center, Mannheim Cancer Center, Sarcoma Unit, Mannheim, Germany, Mannheim, Baden-Württemberg, Germany, ⁵Helios Klinikum Bad Saarow, Bad Saarow, Brandenburg, GERMANY, ⁶Helios Klinikum Bad Saarow, Universitätsmedizin Greifswald, Bad Saarow, Brandenburg, GERMANY, ⁷National Center for Tumor Diseases (NCT/UCC), Dresden, Germany, Dresden, Sachsen, GERMANY, ⁸University Hospital Carl Gustav Carus/ Medical Department I, Dresden, Berlin, Berlin, GERMANY, ⁹University Hospital Carl Gustav Carus/ National Center for Tumor Diseases (NCT/UCC), Dresden, Germany, Dresden, Sachsen, GERMANY

Objective: Few randomized trials are available to guide multimodal treatment in distinct sarcoma subtypes. The consideration of Quality of life (QoL) data is therefore crucial for shared decision-making in sarcoma treatment. The “Patient-Reported Outcome measures in Sarcoma” (PROSA) study prospectively evaluated the quality of life of sarcoma patients in general. It is questionable whether the published data are meaningful for distinct sarcoma subtypes. Therefore, we compared the patient and tumor characteristic of PROSA with the prospective multicenter retroperitoneal sarcoma (RPS) cohort of the Transatlantic Australasian Retroperitoneal Sarcoma Working Group (TARPS-WG).

Methods: PROSA was a multicenter study that assessed 1113 adult sarcoma patients and survivors assessed in Germany using standardized, validated questionnaires (European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30)). The initial TARPS-WG study evaluated 1007 consecutive patients with primary RPS treated at 6 European and 2 North American institutions between 2002 and 2011. Data of the PROSA study were filtered (e.g. inclusion of retroperitoneal site, exclusion of bone tumors, compare figure 1) to identify RPS survivors. Patient, tumor and treatment characteristics of the selected patients were compared to those of the TARPS-WG cohort. QoL data of the validated PROSA cohort were extracted.

Results: Patient and tumor characteristics of the defined PROSA-cohort and the TARPS-WG cohort are displayed in table 1. Confidence intervals for patient sex, tumor histological subtype (LPS vs. non-LPS), grading (G1 vs. G2/3), quality of surgery (R2 vs. no R2) and application of perioperative Chemo and RT (yes vs. no) were overlapping. The Evaluation of the the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) demonstrated clinically important limitations is displayed in table 2 with comparison to the complete STS cohort of PROSA demonstrating distinct HRQoL challenges of the specified RPS survivor cohort (table 2).

Conclusion: Patient, tumor and therapy related factors of the selected RPS-PROSA and the TARPS-WG cohort were similar. The QoL data of the selected PROSA RPS cohort may be used as a benchmark for future prospective trials (e.g. STRASS II). Differences between the complete STS cohort and the complete PROSA cohort (not presented here) underline the need of multidimensional stratification and validation of cross sectional QoL studies. Otherwise the joint evaluation of sarcoma subtype with divergent treatment strategies (e.g. extremity STS vs. GIST vs. RPS) may reveal inaccurate results.



	PROSA	TARPSWG
n	76 (100%)	1007 (100%)
Sex		
Female	40 (53%)	483 (48%)
male	36 (47%)	524 (52%)
age (years)		
Median	54	58
Range	31-80	unknown
quartile	49-61	48-67
Size (7th AJCC-Staging)		
T1	1	N/A
T2	59	
Unknown	6	
Size (cm)		
Median	N/A	20
quartile		3-30
Histotype		
LPS	57 (75%)	633 (63%)
LMS	14 (18%)	194 (19%)
other	5 (7%)	180 (18%)
Grading (FNCLCC)		
G1	21 (28%)	329 (33%)
G2/3	52 (68%)	637 (63%)
unknown	3 (4%)	0
R-Status		
R0/1	57 (75%)	960 (95%)
R2	2 (3%)	47 (5%)
unknown	17 (22%)	0
Perioperative Chemotherapy		
Yes	16 (21%)	183 (18%)
No	60 (79%)	824 (82%)
Perioperative Radiation therapy		
Yes	25 (33%)	322 (32%)
no	51 (67%)	685 (68%)

	PROSa – complete STS cohort (n=780)		PROSa – RPS survivors (n=76)	
	mean	standard deviation	mean	standard deviation
C30 global health t0	59.5	22.4	62.9	19.2
C30 physical functioning t0	72.9	23.8	71.4	20.7
C30 role functioning t0	54.8	33.2	56.3	29.2
C30 emotional functioning t0	59.8	26.2	58.8	25.2
C30 cognitive functioning t0	77.6	24.9	76.8	21.1
C30 social functioning t0	58.2	32.7	62.9	30.2
C30 fatigue t0	43.0	27.9	45.9	29.6
C30 nausea and vomiting t0	7.4	15.8	5.3	11.8
C30 pain t0	32.8	31.0	30.8	30.7
C30 dyspnoea t0	26.6	30.5	36.4	31.0
C30 insomnia t0	39.2	33.9	36.4	29.7
C30 appetite loss t0	17.3	27.4	19.7	28.0
C30 constipation t0	15.8	27.7	19.7	30.9
C30 diarrhea t0	11.4	23.0	11.6	22.3
C30 financial difficulties t0	25.0	32.0	23.2	30.4
t0_C30_sum	71.5	18.3	70.5	17.1
EORTC Item Library COUGH	21.9	27.1	17.2	23.6
EORTC Item Library LACK OF ENERGY	45.4	31.7	48.2	32.3
EORTC Item Library BLOATED STOMACH	23.1	31.2	33.8	33.3
EORTC Item Library HAIR LOSS	16.6	29.6	12.0	21.7
EORTC Item Library pain in the mouth	6.5	17.4	6.6	16.8
EORTC Item Library HEAD BURN	16.6	26.0	17.2	27.6
EORTC Item Library BURNING EYES	14.5	25.0	12.3	25.4
EORTC Item Library decreased sexual interest	46.9	38.1	51.4	36.8
EORTC Item Library tickling hands or feet	23.7	31.7	23.1	31.1
EORTC Item Library RUSH	9.9	22.6	6.1	14.2
EORTC Item Library HEADACHE	16.9	25.4	17.2	27.6

Table 3: Univariate Comparison. HRQoL of soft tissue sarcoma patients and patients with retroperitoneal sarcoma. Bold: p<0.05.



Poster #222 #1836517

PREDICTION OF EARLY POSTOPERATIVE WALKING FUNCTION OF SO-CALLED HIP TRANSPOSITION ARTHROPLASTY AFTER RESECTION OF MALIGNANT PERIACETABULAR TUMORS: A MULTICENTER COHORT ANALYSIS

 Liuzhe Zhang, MD¹; Saito Masanori, MD²; Toru Akiyama, MD³; Makoto Nakagawa, MD⁴; Satoshi Tsukushi, MD⁵; Shinichiro Yoshida, MD⁶; Tabu Gokita, MD⁷; Keisuke Ae, MD²; Seiya Nakashima⁸; Munenori Watanuki, MD⁶; Shintaro Iwata, MD⁹

¹The University of Tokyo Hospital, Bunkyo-ku, Tokyo, JAPAN, ²The Cancer Institute Hospital, Tokyo, Tokyo, JAPAN, ³Jichi Medical University Saitama Medical Center, Omiya, Saitama, JAPAN, ⁴National Cancer Center, Chuo-ku, Tokyo, JAPAN, ⁵Aichi Cancer Center, Aichi, Aichi, JAPAN, ⁶Tohoku University Hospital, Miyagi, Miyagi, JAPAN, ⁷Saitama Prefecture Cancer Center, Saitama, Saitama, JAPAN, ⁸Aichi Cancer Center, Tokyo, Tokyo, JAPAN, ⁹National Cancer Center Hospital, Chuo-ku, Tokyo, JAPAN

Objective: Hip joint reconstruction after resection of periacetabular tumors is challenging. Reconstruction methods using metal acetabular implants offer decent ambulatory function; however, those methods usually require a large bone graft or bulky prosthesis, can be technically demanding and may have a high complication rate. On the other hand, the reconstruction methods without acetabular implant—including so-called hip transposition—requires minimal bone graft or prosthesis, are more technically simple and may have lower complication rates. However, the postoperative structural stability of the hip joint can be lower, especially for the short term, and early postoperative walking functions are more difficult to anticipate. Since the oncological prognosis of patients with malignant pelvic tumors is generally poor, the data on short-term postoperative function can be critical for both patient selection and patient counseling. In the current study, we tried to examine the time course of walking function recovery after so-called hip transposition arthroplasty and investigated the associated risk factors.

Methods: Forty-two patients who received the index surgery and followed for more than six months were included. The medical records were reviewed to identify each ambulatory function milestone (wheelchair, standing (with parallel bars), walker, double crutches, single cane, and walking with no support). The demographic factors and surgical factors were also reviewed, and the association between those factors and the functional recovery was analyzed (Fisher exact test).

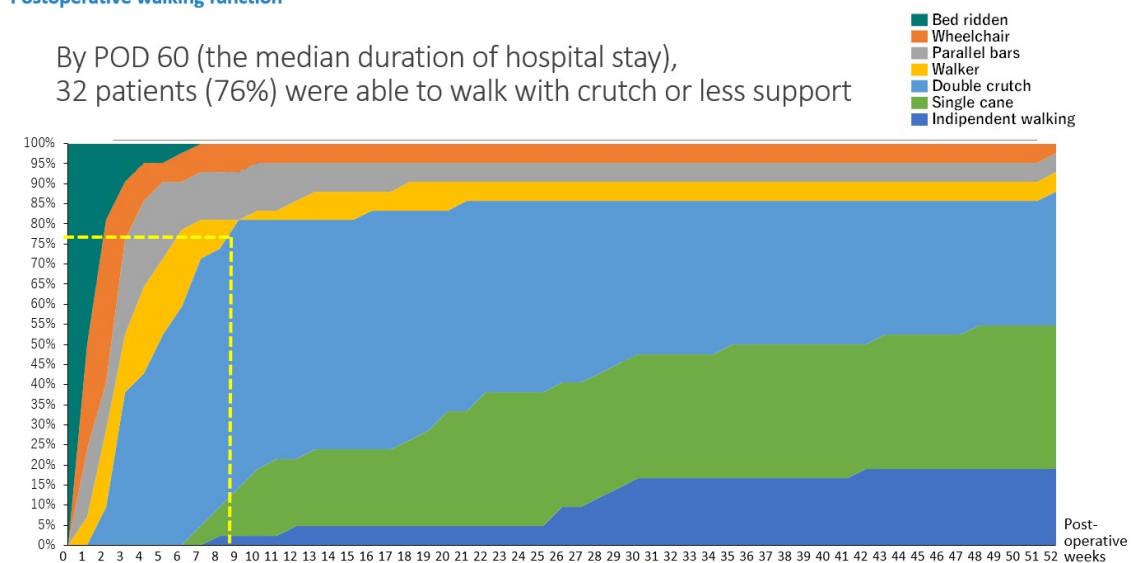
Results: Median age of the patients was 47 (range: 9-76), median follow-up was 16 months (range: 6-110). By the postoperative day (POD) 60, which was the median duration of hospital stay, 32 patients (76%) were able to walk with a double crutch or less support (Early recovery group); in comparison, ten patients (24%) required a walker or more support (Delayed recovery group). One year postoperatively, most of the patients (72%) of the Early recovery group walked with a single cane or no support; however, all the patients of the Delayed recovery group required a double crutch or more support.

No significant difference in background factors was identified between the two groups, including the age and leg length discrepancy. Nevertheless, resection of the iliac bone (OR=4.5, $p=0.07$) and femoral nerve (OR=6.4, $p=0.08$) may have been associated with delayed recovery.

Conclusion: Reconstruction without acetabular implant offered fair early ambulatory function, and the walking ability as of POD 60 can be a predictor of future recovery. The resection of the iliac bone and femoral nerve may be associated with delayed recovery.

Postoperative walking function

By POD 60 (the median duration of hospital stay), 32 patients (76%) were able to walk with crutch or less support





Poster #223 #1836513

PATIENT REPORTED DATA OF DESMOID TUMORS DURING AND AFTER PREGNANCY FROM AN INTERNATIONAL NATURAL HISTORY STUDY

Amanda L. Lucas¹; Maneesh Kumar, MD, PhD²; Danielle Braggio, PhD, BCMAS³; Lynne Hernandez⁴; Kelly Mercier, PhD⁵
¹Desmoid Tumor Research Foundation, Jacksonville Beach, Florida, UNITED STATES, ²Desmoid Tumor Research Foundation, Cedar Rapids, Iowa, UNITED STATES, ³Desmoid Tumor Research Foundation, Houston, Texas, UNITED STATES, ⁴Desmoid Tumor Research Foundation, Philadelphia, Pennsylvania, UNITED STATES, ⁵Desmoid Tumor Research Foundation, Cary, North Carolina, UNITED STATES

Objective: Desmoid tumors (DTs), a subtype of sarcoma, are a rare disease with variable and unpredictable clinical course. It has an incidence of 5-6 per million/year with a median age of 30-40, affecting females more than males. To date, there are very few studies that provide data on the impact of pregnancy to DT behavior. Patient reported outcomes of pregnancy with a DT are described here.

Methods: The web-based natural history study launched September 2017 in collaboration with the National Organization of Rare Disorders. It contains 15 surveys covering diagnostics, disease, treatment, care management, and quality of life. The pregnancy survey was conditionally provided to participants who reported their sex as female and age > 18 years old. The questionnaire poses questions about the status of the participant's DT(s) before, during, and following pregnancy.

Results: Of the 696 participants that have consented and started all surveys, 182 have completed the pregnancy survey. Eighteen of the 182 (9.9%) reported that they had a DT at the time of becoming pregnant. Thirteen are from the United States, and one from each of Australia, United Kingdom, Jersey, China, and Belgium. Of these 18 pregnancies, five (27.7%) were premature (less than 37 weeks) and 3 of those did not result in live birth (16.7%). Comparatively, in the United States, 10.3% of all pregnancies end in premature deliveries and 10-20% of miscarriages are reported. During pregnancy, the participants reported that their DT grew (n=7, 41%), shrank (n=2, 12%), and was stable (n=4, 24%). For most women, the DT behaved the same after pregnancy as it did during pregnancy. For one participant, the DT was stable during pregnancy and grew postpartum, while another participant had DT growth during pregnancy and stable DT postpartum. Treatment and surveillance data is not currently collected during pregnancy. The distribution of the location of the DT for the pregnancy survey was similar to that of the entire dataset ($p = 0.48$). There were lower numbers of head and neck DTs (0% vs. 10%) and chest wall (5% vs. 18%) in the pregnancy dataset (0% vs. 10%), but higher rates of abdominal wall DTs (25% vs. 18%). Six participants reported having FAP mutations, and two reported CTNNB1 mutations. There did not appear to be a correlation between mutations and preterm or live births.

Conclusion: DTs are most common in females with a median age of 30-40 years. However, few studies have investigated the effects of pregnancy on DTs. The pregnancy dataset from the Natural History Study indicates that DTs do not change behavior due to pregnancy and presumably exposure to hormone fluxuations. In addition, DT location and mutation status do not seem to be correlated with preterm or live births. In the future, the study will capture the use of active surveillance during pregnancy.

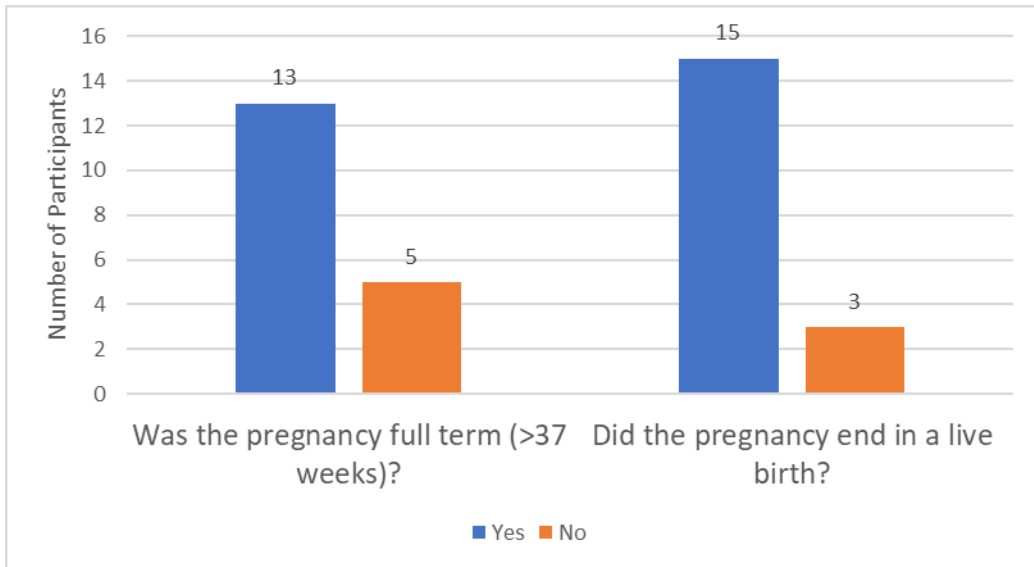


Figure 1. The participants who reported if their pregnancy was full term (yes, no) and if their pregnancy resulted in a live birth (yes, no). While there is a slightly higher rate of a pre-term delivery with a DT, the rate of pregnancy loss does not appear to be dissimilar to rates found in a general population.

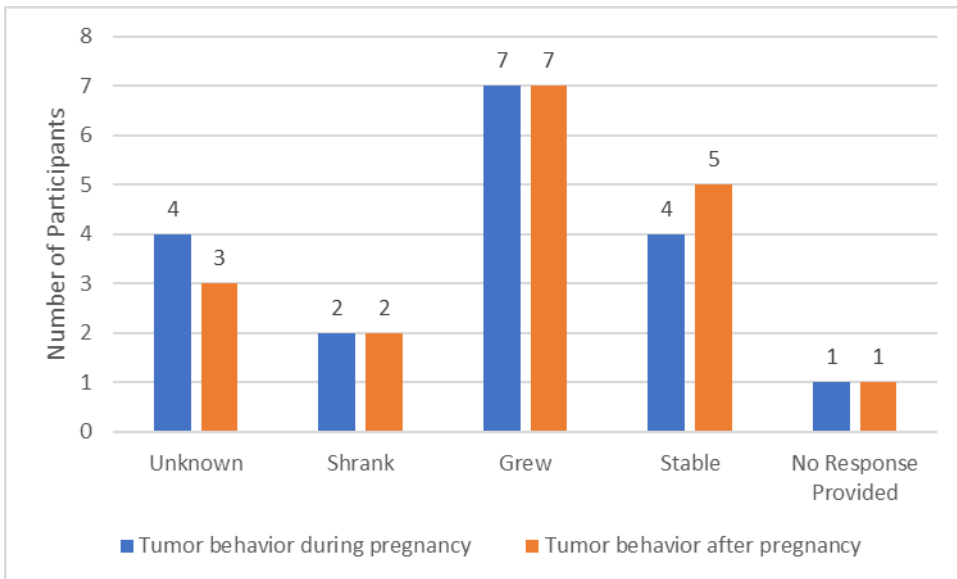


Figure 2. Characteristics of how the DT behaved during the pregnancy and after delivery. With the small number of respondents thus far, no trends are apparent with the impact of pregnancy hormones on the growth of the DTs during or after pregnancy. No response reflects that the participants did not answer that question.



Poster #224 #1836511

A PILOT STUDY OF THE FEASIBILITY AND UTILITY OF A FITNESS TRACKER TO CORRELATE ACTIVITY LEVEL WITH PATIENT REPORTED OUTCOMES IN SARCOMA PATIENTS UNDERGOING SYSTEMIC THERAPY

Elizabeth J. Davis, MD; Gregory D. Ayers, B.S.; Elizabeth Ryan, APRN; Deborah Wallace, APRN; Vicki L. Keedy, MD, MSCL; Rajiv Agarwal, MD

Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES

Objective: Commercially available fitness trackers have been shown to provide objective and quantifiable measures of physical activity in cancer patients. Lack of physical activity has been shown to negatively impact the quality of life in patients. To date, there have been no studies of wearable devices in sarcoma patients. Here, we test the ability of a wearable device to aid in the assessment of objective activity level, body composition, and PROs to facilitate understanding of the tolerability and toxicity of cancer treatment.

Methods: Between 6/11-10/12/2020, we enrolled people with sarcoma who were receiving systemic therapy to a prospective study evaluating activity levels and sleep via a Fitbit Charge 3, body composition with the Inbody 570, and PROs using NIH PROMIS short forms (fatigue, pain, physical function, and sleep disturbance), the Generalized Anxiety Disorder Scale, and the Patient Health Questionnaire Depression Scale. Time on study was 12-16 weeks depending upon treatment. The Fitbit was worn continuously. Body composition and PROs were assessed every 3-4 weeks. Feasibility was defined as successful device wearing and data syncing. Data was collected through a cloud-based application, Fitabase.

Results: 22 pts were approached, and all enrolled. Two pts did not complete the first study assessment due to disease progression and were excluded from analysis. Participant characteristics are included in Table 1. 50% of pts were female. 90% of pts were white. Median age was 47 years (range 20-81). The most common histologies were ewing sarcoma and leiomyosarcoma. Feasibility of incorporation of the Fitbit is described in Table 2. 85% (17/20) of pts wore the Fibit for >3 weeks, median time was 65 days (5-112) (Figure 1). All pts were able to sync data. Median step count was 2614 steps (376-19806) (Figure 2). High step counts, defined as greater than the median, were associated with improved sleep ($p=0.14$) and physical function ($p=0.22$), and decreased pain ($p=0.15$), but these associations were not statistically significant. Low step counts, defined as lower than the median, were associated with skeletal muscle mass loss ($p=0.22$), but this was not statistically significant.

Table 1. Participant and tumor characteristics

Characteristic	N=20
Female	10 (50)
Male	10 (50)
Median age in years (range)	47 (20-81)
Race	
White	18 (90)
Black	1 (5)
Other	1 (5)
ECOG (baseline/end of study)	
0	16 (80)/ 12 (60)
1	4 (20)/ 8 (40)
Histology	
Ewing sarcoma	7 (35)
Leiomyosarcoma	4 (20)
Undifferentiated pleomorphic sarcoma	3 (15)
Other*	6 (30)
Treatment goal	
Curative	11 (55)
Palliative	9 (45)

*Angiosarcoma, malignant peripheral nerve sheath tumor, myxofibrosarcoma, osteosarcoma, solitary fibrous tumor, and synovial sarcoma

Conclusion: Incorporating a fitness tracker is feasible and useful in sarcoma pts receiving systemic therapy. It provides a longitudinal and objective evaluation of activity levels and sleep patterns. Correlation of activity level with sleep, body composition, and PROs was limited due to small numbers; however, a larger prospective pilot study is ongoing.

Outcome	N=20 (%)
Median days Fitbit worn (range)	65 (5-112)
Success wearing Fitbit	
<20 days	3 (15)
>20 days	17 (85)
Success of syncing Fitbit	20 (100)
Median steps per day (range)	2614 (463-19806)
Median sleep in minutes (range), n=18	463 (87-617)

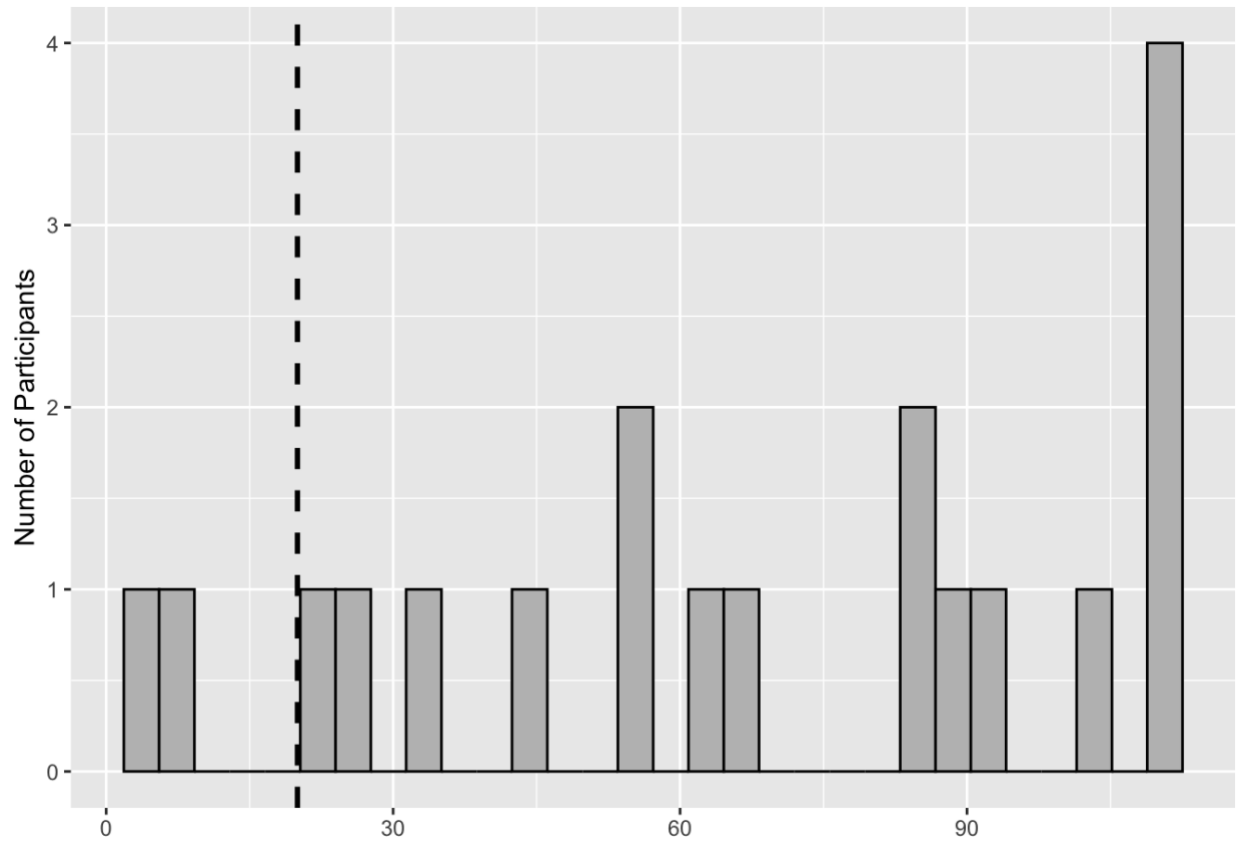


Figure 1. Number of days Fitbit worn

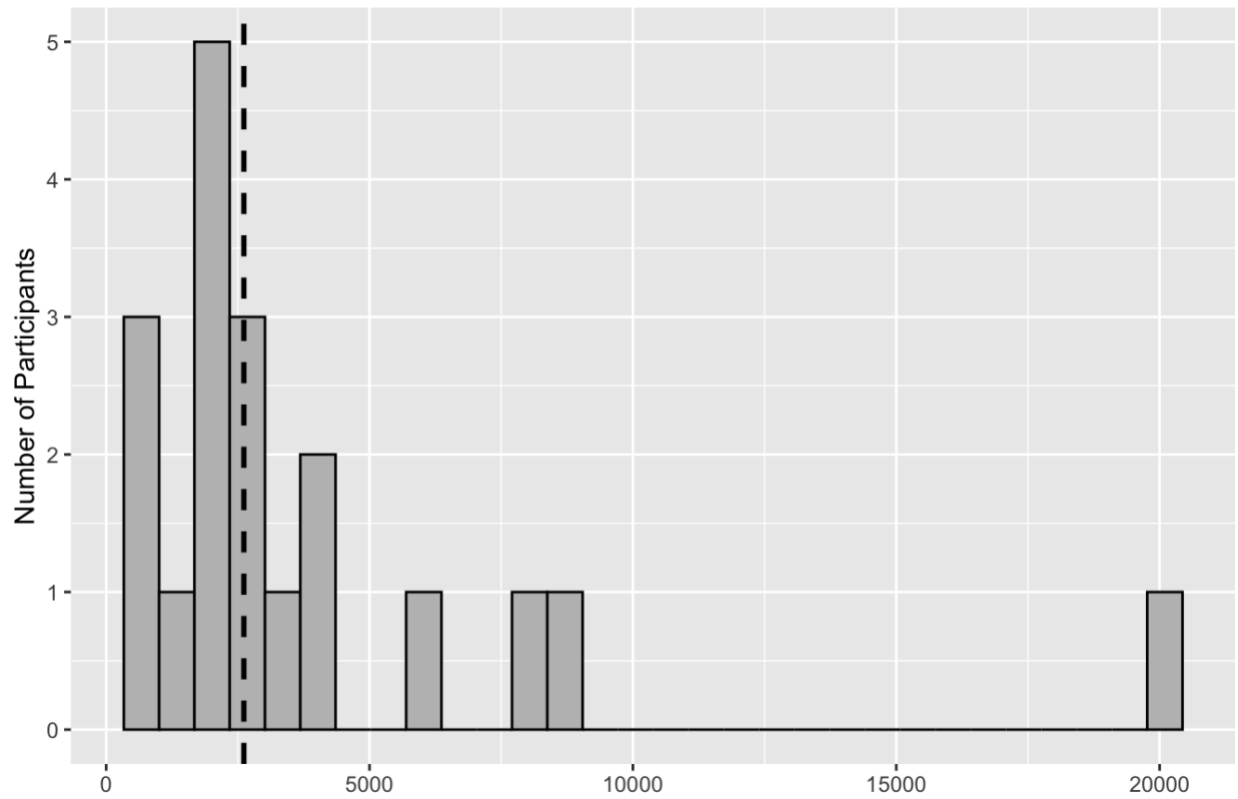


Figure 2. Average daily step count



Poster #225 #1836518

HEALTH-RELATED QUALITY OF LIFE IN YOUNG BONE SARCOMA SURVIVORS

Carolina C. Pereira, MD¹; Diana Pessoa, MD¹; Susana Esteves, MSc Biostatistics¹; Ana Catarina Freitas, MD²; Teresa Alexandre, MD¹; Margarida Ferreira, MD¹

¹Instituto Português de Oncologia de Lisboa Francisco Gentil, E.P.E., Lisbon, Lisboa, PORTUGAL,

²Fundação Champalimaud, Lisbon, Lisboa, PORTUGAL

Objective: Bone sarcomas are rare and aggressive tumours that occur more frequently in children and young adults. Advances in multimodal treatment have extended survival, however, evidence regarding its impact on long-term quality of life is lacking. We aim to evaluate the health-related quality of life (HRQoL) in young bone sarcoma survivors and whether there are groups of patients more at risk for developing limitations.

Methods: Cross-sectional and observational study of bone sarcoma survivors (osteosarcoma and Ewing sarcoma), who were diagnosed between the age of 14 and 40 and treated in a Portuguese cancer center, between May 2002 and June 2020. Patients were assessed using the SF-36 standard questionnaire for HRQoL and compared to published normative data for the general population. Clinical data were collected from retrospective chart review.

Results: Of 35 eligible patients, 23 agreed to enroll on the study: 13 female, median age at diagnosis 21.3 years (range 14.1-39.1), 12 patients had osteosarcoma and 11 had Ewing sarcoma. Primary location was lower limbs in 14 patients, trunk and mandible in 4 patients each, and only one patient with upper limb sarcoma. Most patients were treated with surgery (n=19) – conservative surgery in 12, limb amputation in 3, and mandibulectomy in 4 patients. Neoadjuvant/adjuvant chemotherapy was used in 22 patients, while 11 also had radiotherapy. Two patients had recurrent disease treated with curative intent and were also included. Median follow-up time was 7.2 years (range 0.9-18.8). Results of SF-36 questionnaire are shown and compared to normative data in table 1. Women scored lower in physical functioning, energy, emotional well-being and social functioning variables (p < 0.05). We also observed an association between mandible primary tumours and lower scores on role limitations due to physical health, energy and social functioning (p < 0.05). No other associations were found between SF-36 variables and patient or tumour characteristics.

Conclusion: In our study, young bone sarcoma survivors had a similar HRQoL compared to the general population. However, most studies have reported lower scores, suggesting that our young population could better adapt to their limitations. Special attention should be paid to groups at higher risk for low HRQoL, particularly women and those with mandible primary tumours. HRQoL assessment in sarcoma patients is challenging due to the heterogeneity of the disease, so specific measures to evaluate this population are necessary.

	Bone sarcoma survivors, mean (SD)	General population, mean (SD)
Physical functioning	71.45 (25.07)	70.61 (27.42)
Role limitations due to physical health	64.13 (41.85)	52.97 (40.78)
Role limitations due to emotional problems	65.22 (40.80)	65.78 (40.71)
Energy/ fatigue	56.09 (24.31)	52.15 (22.39)
Emotional well-being	70.39 (20.69)	70.38 (21.97)
Social functioning	73.91 (27.16)	78.77 (25.43)
Pain	78.48 (19.94)	70.77 (25.46)
General health	65.77 (19.23)	56.99 (21.11)

Table 1. Comparison of health-related quality of life measured by SF-36 in young bone sarcoma survivors and published normative data for the general population.



Poster #226 #1836521

HEALTH-RELATED QUALITY OF LIFE AFTER ISOLATED LIMB PERFUSION COMPARED TO EXTENDED RESECTION, OR AMPUTATION FOR LOCALLY ADVANCED EXTREMITY SARCOMA: IS A LIMB SALVAGE STRATEGY WORTH THE EFFORT?

Sophie JM Reijers, MD¹; Olga Husson, PhD¹; Vicky Soomers, MD, PhD²; Lukas Been, MD, PhD³; Han Bonekamp, MD, PhD²; Michiel van de Sande, MD, PhD⁴; Cornelis Verhoef, MD, PhD⁵; Winette T. A. van der Graaf, MD, PhD¹; Winan J. van Houdt, MD, PhD, MSc⁶

¹Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS, ²Radboud University Medical Center, Nijmegen, Gelderland, NETHERLANDS, ³University Medical Center Groningen, Groningen, Groningen, NETHERLANDS, ⁴Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ⁵Erasmus MC Cancer Institute, Rotterdam, Zuid-Holland, NETHERLANDS, ⁶The Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS

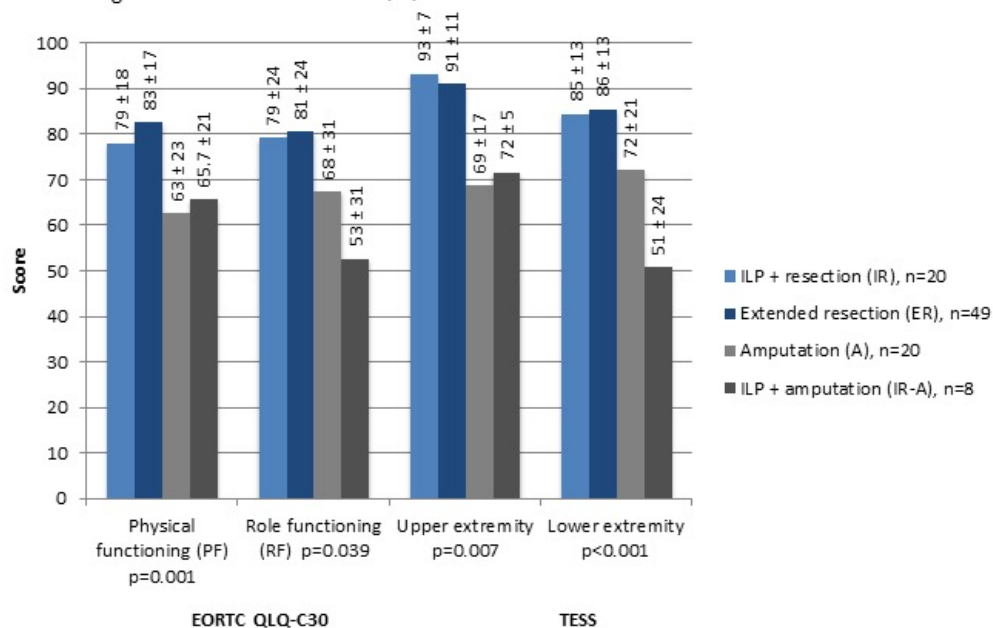
Objective: The aim of this study was to compare long-term patient reported outcomes (PROs) in patients with locally advanced extremity soft tissue sarcoma (eSTS) after isolated limb perfusion followed by resection (IR), compared to extended resection (ER), primary amputation (A) or secondary amputation after IR (IR-A).

Methods: Patients were selected from the respondents of a multi-institutional cross-sectional cohort survivorship study (SURVSARC) conducted among sarcoma survivors registered in the Netherlands Cancer Registry (NCR), 2-10 years after diagnosis. Used PROs were the EORTC QLQ-C30, the Cancer worry scale (CWS), the Hospital Anxiety and Depression Scale (HADS), and the Toronto Extremity Salvage Score (TESS).

Results: We identified 97 eSTS survivors: IR=20, ER=49, A=20, IR-A=8. While there were no differences in PROs between IR and ER, results showed better functioning and functionality in both groups versus the amputation groups. The amputation groups scored significantly lower on physical functioning (A=62.7, IR-A=65.7 versus IR=78.0, ER=82.7, $p=0.001$) and role functioning (A=67.5, IR-A=52.8 versus IR=79.2, ER=80.6, $p=0.039$), both EORTC QLQ-C30 scales. Also for the TESS, the scores were significantly lower for the amputation groups compared to the limb sparing groups (upper extremity $p=0.007$ with A=68.9, IR-A=71.6 versus IR=93.3, ER=91.1; lower extremity $p<0.001$ with A=72.2, IR-A=50.9 versus IR=84.5 and ER=85.5). There were no significant differences between the groups on cancer worry, anxiety and depression.

Conclusion: HRQoL in eSTS survivors treated with IR or ER is equal; for maintenance of physical functioning and functionality IR and ER outperform an amputation.

Statistical significant differences: EORTC QLQ-C30 and TESS





Poster #227 #1836520

THE EVALUATION OF HEALTH-RELATED QUALITY OF LIFE ISSUES EXPERIENCED BY PATIENTS WITH DESMOID-TYPE FIBROMATOSIS (THE QUALIFIED STUDY) - A PROTOCOL FOR AN INTERNATIONAL COHORT STUDY

Anne-Rose W. Schut, MD¹; Milea Timbergen, MD, PhD¹; Emma Lidington, MSc²; Dirk J. Grünhagen, MD PhD³; Winette T. A. van der Graaf, MD PhD⁴; Stefan Sleijfer, MD, PhD¹; Winan J. van Houdt, MD PhD MSc⁵; Han Bonekamp, MD PhD⁶; Eugenie Younger, MbChB Hons; MRCP²; Alison Dunlop²; Robin L. Jones, BSc, MBBS, MD⁷; Spyridon Gennatas, BSc, MBChB, PhD, MRCP²; Cornelis Verhoef, MD PhD⁸; Olga Husson, PhD²

¹Erasmus Medical Center, Rotterdam, Zuid-Holland, NETHERLANDS, ²Royal Marsden NHS Foundation Trust, London, England, UNITED KINGDOM, ³Erasmus MC Cancer Institute, Rotterdam, Zuid-Holland, NETHERLANDS, ⁴Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS, ⁵The Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS, ⁶Radboud University Medical Center, Nijmegen, Gelderland, NETHERLANDS, ⁷The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, England, UNITED KINGDOM, ⁸Erasmus MC Cancer Institute, Rotterdam, Zuid-Holland, NETHERLANDS

Objective: Sporadic desmoid-type fibromatosis (DTF) is a rare soft tissue tumour with an unpredictable clinical course. Although histologically benign and incapable of metastasizing, the morbidity can be significant, resulting in a substantial symptom burden. Measuring the impact of DTF on the health-related quality of life (HRQoL) can be challenging due to the heterogeneous character of the disease. Therefore, HRQoL instruments assessing DTF-specific issues are needed. Previously, a DTF-specific questionnaire, the DTF-QoL, was designed based on the results of focus groups, patient interviews and ranking of issues by patients and health care professionals from the Netherlands and the United Kingdom. This paper describes the design of the QUALIFIED study (The evaluation of health-related quality of life issues experienced by patients with desmoid-type fibromatosis). The QUALIFIED study aims to ¹gain insight into DTF-specific HRQoL problems; ²validate the DTF-specific HRQoL tool (the DTF-QoL); ³identify subgroups at risk for impaired HRQoL.

Methods: The QUALIFIED study is an international, multicentre, cross-sectional, observational cohort study. Patients ≥ 18 years with pathologically proven, sporadic DTF from the Netherlands and United Kingdom (three centres in the Netherlands; one centre in the United Kingdom) will be invited to complete a set of questionnaires specifically composed for this patient group. Questionnaires will be completed using PROFILES (Patient Reported Outcomes Following Initial treatment and Long term Evaluation of Survivorship), a system to electronically capture questionnaire responses. Analyses will include content validation of the DTF-QoL and evaluating frequencies of HRQoL-problems using the DTF-QoL, EORTC QOL-C30 and EQ-5D-5L, among other questionnaires.

Results: Preliminary results are expected after June 2021 and will be presented at conferences.

Conclusion: The QUALIFIED study will provide insight into HRQoL-problems experienced by patients with DTF. Awareness of these problems and the implementation of the DTF-QoL could help to improve overall patient experience, clinical care and HRQoL. Trial registration: This study is registered on clinicaltrials.gov, number NCT04289077.



Poster #228 #1818936

RHABDOMYOBLASTIC DEDIFFERENTIATION IN RETROPERITONEAL LIPOSARCOMAS IS ASSOCIATED WITH REDUCED IMMUNE INFILTRATION

Beatrice Valenti, MSc¹; Sandro Pasquali, MD, PhD²; Monica Brenca, PhD¹; Silvia Brich, PhD³; Davide Baldazzi, MSc¹; Dominga Racanelli, PhD¹; Ilaria De Benedictis, MSc¹; Chiara Colombo, MD⁴; Marta Sbaraglia, MD⁵; Viviana Vallacchi, PhD⁶; Chiara Castelli, PhD⁶; Silvia Stacchiotti, MD⁷; Angelo Paolo Dei Tos, MD⁸; Paola Collini, MD⁹; Alessandro Gronchi, MD¹⁰; Roberta Maestro, PhD¹

¹CRO Aviano IRCCS National Cancer Institute, Aviano, Friuli-Venezia Giulia, ITALY, ²Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ³Fondazione IRCCS Istituto Nazionale dei Tumori (INT), Milano, Lombardia, ITALY, ⁴Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ⁵Azienda Ospedaliera Università di Padova (UniPD), Padova, Veneto, ITALY, ⁶Immunotherapy of Human Tumors, Department of Research, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ⁷Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY, ⁸Università di Padova (UniPD), Padova, Veneto, ITALY, ⁹Department of Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Lombardia, ITALY, ¹⁰Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, Milan, Lombardia, ITALY

Objective: In dedifferentiated liposarcomas (DDLPS) the dedifferentiation toward a myogenic lineage, namely the rhabdomyoblastic dedifferentiation marked by the activation of myogenin (MYOG), has been shown to correlate with poor outcome. To gain insights into the molecular bases of this phenotype, a series of 41 retroperitoneal DDLPS (13 MYOG+ and 28 MYOG-) were analyzed by RNA-seq transcriptional profiling and immunohistochemistry.

Methods: A series of 41 DDLPS, including 13 cases classified as DDLPS with rhabdomyoblastic differentiation as according to myogenin (MYOG) positive staining, were retrieved from the pathological files of INT and UniPD. To determine the extent of immune infiltration, slides were immunostained for CD20, CD3, CD4, CD14, CD163, CD209 and the percentage of immune cells (marker positive/total cells) was calculated by counting 4 random low-magnification fields (>500 cells). RNA was extracted from FFPE sections with a tumor cellularity >70%. RNA sequencing was performed as previously described (Gasparotto et al., JCI Insight 2020). Functional annotation of the genes differentially expressed was performed by using different tools (Metascape, IPA, GSEA, GeneTrail). The extent of immune infiltrate and the abundances of immune cell types was extrapolated from gene expression data by using different deconvolution algorithms (xCell, ssGSEA, CIBERSORT, TIP).

Results: Transcriptome analysis corroborated the subtype classification of DDLPS, with MYOG mRNA expression being detected exclusively in rhabdomyoblastic DDLPS. PCA (Principal Component Analysis) indicated a trend of separation for MYOG+ and MYOG- DDLPS, with MYOG- cases forming a more compact group. Intriguingly, the gradient of separation between the two clusters seems to follow the extent of myogenic dedifferentiation, as assessed by the activation of a whole set of transcription factors involved in skeletal muscle differentiation (MYOG, MYF5, MYOD1, PAX7 and MYF6). Functional annotation of the transcriptome corroborated a net activation of a myogenic dedifferentiation program in MYOG+ tumors. Enrichment of the MYC signature (hallmark MYC target) was also observed. Conversely, MYOG- DDLPS featured a maintenance of pre-adipogenic transcriptional traits and enrichment for immune related signatures, particularly marked in the two cases of inflammatory DDLPS. The greater immunogenic degree of MYOG- DDLPS was confirmed by both in situ by immunohistochemical analyses, with a good correlation between the fraction of tumor cells labeled for immune-specific cell markers and the expression levels of the cognate mRNAs, and by the interrogation of different in silico immune predictors. IHC and deconvolution analyses indicated that monocytes/macrophages were the species more represented in inflamed tumors.

Conclusion: Our data suggest that DDLPS dedifferentiation toward the rhabdomyoblastic lineage is sustained by a profound transcriptional reprogramming with activation of a whole set of genes involved in skeletal muscle differentiation. Moreover, the gain of a rhabdomyoblastic phenotype is associated with a reduced immune infiltration. Intriguingly, MYOG+ DDLPS featured enrichment for the MYC signature, which was associated with an elevated expression of MYC genes, particularly MYCL. Since MYC is known to induce phenomena of immune exclusion, the activation of the MYC pathway could contribute, at least in part, to the immune-cold phenotype of DDLPS with rhabdomyoblastic dedifferentiation.



Poster #229 #1818950

RETROSPECTIVE EVALUATION OF THE ROLE OF GEMCITABINE- DOCETAXEL IN WELL-DIFFERENTIATED AND DEDIFFERENTIATED LIPOSARCOMA

Prapassorn Thirasastr, MD, MSc.¹; Behrang Amini, MD, PhD²; Heather Lin, PhD²; Christina L. Roland, MD¹; Elise F. Nassif, MD³; Alejandra Zarzour²; Anthony P. Conley, MD³; Dejka M. Araujo, MD¹; Emily Z. Keung, MD¹; J Andrew Livingston, MD³; Ravin Ratan, MD⁴; Joseph A. Ludwig, IV, MD⁴; Robert S S. Benjamin, MD⁵; Xiao Zhou, MD, PhD⁵; Shreyaskumar Patel, MD²; Vinod Ravi, MD¹; Barry W. Feig, MD¹; Neeta Somaiah, MD¹

¹The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ²MDACC, Houston, Texas, UNITED STATES, ³MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁴Sarcoma Medical Oncology, University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁵University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES

Objective: Well-differentiated (WDLPS) and dedifferentiated liposarcoma (DDLPS) are most common types of liposarcoma which share common genetic alteration in chromosome 12q13-15. Response rate of doxorubicin-based combination chemotherapy in first line setting for DDLPS ranged from 12%-21% and median PFS 4-4.6 months from retrospective studies[1, 2]. Gemcitabine-docetaxel is the established standard second line treatment for soft tissue sarcoma[3, 4]. However, with the limited number of liposarcoma patients included (16.4% and 3.9% in the above referenced trials), the efficacy of this regimen in WDLPS/DDLPS is not established. This retrospective analysis looks at the efficacy of gemcitabine-based regimens in WDLPS/DDLPS over the past 20 years at the University of Texas MD Anderson Cancer Center.

Ref.

1. Italiano A, Toulmonde M, Cioffi A, et al. Advanced well-differentiated/dedifferentiated liposarcomas: role of chemotherapy and survival. *Ann Oncol* 2012; 23: 1601-1607. 2011/11/01.
2. Livingston JA, Bugano D, Barbo A, et al. Role of chemotherapy in dedifferentiated liposarcoma of the retroperitoneum: defining the benefit and challenges of the standard. *Sci Rep* 2017; 7: 11836-11836.
3. Maki RG, Wathen Jk Fau - Patel SR, Patel Sr Fau - Priebe DA, et al. Randomized phase II study of gemcitabine and docetaxel compared with gemcitabine alone in patients with metastatic soft tissue sarcomas: results of sarcoma alliance for research through collaboration study 002.
4. Seddon B, Strauss SJ, Whelan J, et al. Gemcitabine and docetaxel versus doxorubicin as first-line treatment in previously untreated advanced unresectable or metastatic soft-tissue sarcomas (GeDDiS): a randomised controlled phase 3 trial. *The Lancet Oncology* 2017; 18: 1397-1410.

Methods: Patients (pts) with pathologically confirmed WDLPS or DDLPS treated with gemcitabine-based regimens were identified using electronic medical records (Epic SlicerDicer search: January 2014 to January 2021 and tumor registry: September 2002 to March 2014). All instances of gemcitabine-based therapy were included for efficacy analysis as long as the patient completed at least 1 cycle of treatment and had follow up imaging available in our system. Descriptive statistics were used to summarize patient's characteristics. Response evaluation was done by RECIST1.1 criterion with assessment from an independent radiologist. The Kaplan-Meier method was used to estimate distributions of time-to progression (TTP) and overall survival (OS). Log-rank test was performed to test the difference in survival between groups.

Results: Sixty-six WDLPS/DDLPS pts received gemcitabine-based therapy. Median age at diagnosis was 63 years (R: 30-79 years); majority of the pts (40 patients, 62%) had retroperitoneum as the primary site (Table 1). Forty-nine pts (74%) were diagnosed with DDLPS at baseline and 62 pts (94%) had DDLPS at some point during the course of their disease. Majority of the pts had localized disease at initial diagnosis (41 pts, 62%). Sixty two patients (93.9%) underwent surgery in the primary setting, out of which 21 pts (33.9%) also received systemic treatment. Eighty-one instances of gemcitabine-based therapy were included as 13 pts (19.7%) received gemcitabine-based therapy more than once for different recurrences. Of those, 72 (88.9%) were gemcitabine-docetaxel based therapy and 9 (11.1%) were gemcitabine alone (Table 2). Gemcitabine-based therapy was most often used in the second line. Median cycles received were 4 (R: 1-25) with median duration of treatment 2.71 months (R: 0.36-19.45). The major reason for discontinuation was treatment progression as determined by the treating physician (47.5%), with 17 (21.25%) stopping for local therapy. Overall response rate (RR) by RECIST was 9.88% (8/81 records), SD 81.48% (66/81) and PD 8.6% (7/81). All responses were seen in DDLPS subtype (Figure 1). RR of

gemcitabine-docetaxel was 8.22% while gemcitabine single agent was 22.2% (n=9). Median TTP was 9.13 months (95% CI 6.77-12.32) as evaluated by RECIST1.1. Median OS from diagnosis was 50.96 (95% CI 34.14-123.86) months. Median OS from diagnosis for those with DDLPS at initial diagnosis was 48.59 (95% CI: 30.39, 123.86) months and for those with WDLPS at diagnosis (n=17) was 82.6 (95% CI: 30.36, NR) months. Median OS from start gemcitabine-based therapy was 18.73 (95% CI: 13.14, 24.71) months.

Conclusion: Gemcitabine-docetaxel is an efficacious second line treatment for patients with DDLPS. The activity of gemcitabine-docetaxel compares favorably to trabectedin and eribulin in this subset of patients, though cross study comparisons might not be accurate. This combination is a valid comparator arm for future trials of novel agents in DDLPS.

Table 1 | Baseline Characteristics

Characteristics		Frequency N= 66	Percent (%)
Sex	Female	29	43.94
	Male	37	56.06
Race	Caucasian	41	62.12
	Asian	9	13.64
	African American	3	4.55
	Other	9	13.64
	Missing or unknown	4	6.06
Ethnicity	Hispanic or Latino	15	22.73
	Not Hispanic or Latino	47	71.21
	Missing or unknown	4	6.06
Present of secondary malignancy	*Yes	17	25.76
	No	49	74.24
Histologic subtype at diagnosis	WDLPS	17	25.76
	**DDLPS	49	74.24
Histologic subtype in overall clinical course	WDLPS	4	6.06
	**DDLPS	62	93.94
Primary tumor location	Retroperitoneum	40	60.61
	Inguinal Canal	5	7.58
	Extremities	5	7.58
	***Others	16	24.25
Stage at diagnosis	Localized	41	62.12
	Localized with multifocal	16	24.24
	Metastatic	9	13.64
Primary Treatment	Surgery	62	93.93
	Systemic treatment	25	37.88
	Radiation	11	16.67

*Secondary malignancy include; prostate cancer 5 patients (29.41%), malignant melanoma 2 patients (11.76%), bladder cancer 2 patients (11.76%), leukemia 2 patients (11.76%), renal cell carcinoma 1 patient (5.88%), breast cancer 1 patient (5.88%), DCIS of breast 1 patient (5.88%), colon cancer 1 patient (5.88%), thyroid cancer 1 patient (5.88%), and skin cancer 1 patient (5.88%).

**Classified with DDLPS if any dedifferentiated component was present.

***Others include; intraabdominal 7 patients (10.60%), superficial trunk 1 patient (1.51%), chest 1 patient (1.51%), bladder 1 patient (1.51%), small bowel 1 patient (1.51%), colon 1 patient (1.51%), mesentery 1 patient (1.51%), pancreatic tail 1 patient (1.51%), pelvic cavity 1 patient (1.51%), presacral space 1 patient (1.51%).

Table 2| Details on Gemcitabine-based therapy

Parameter		Frequency N= 81	Percent (%)
Gemcitabine-based regimen	Gemcitabine-docetaxel	70	86.42
	Gemcitabine-docetaxel with/without olaratumab (clinical trial)	1	1.23
	Gemcitabine single agent	10	12.35
Line of systemic therapy for gemcitabine-based regimen	1 st line	14	17.28
	2 nd line	43	53.09
	3 rd line or later	24	29.63
Number of cycles received	Less than 4	36	44.44
	≥ 4 cycles	44	54.32
	Missing data	1	1.23
Reasons for discontinuation	Disease progression determined by treating physician - Confirmed by RECIST --15 (42.86%)	36	44.45
	Toxicity	18	22.22
	Planned stop for local therapy	18	22.22
	*Other	7	8.64
Surgery after gemcitabine-based therapy	Yes	35	41.03
	- Right after	23	65.71
	- Following other intervening therapy (radiation/other chemotherapy)	12	34.29
	No		
Missing	44	54.32	
		2	2.47
Pathologic response per report for patients undergoing surgery (N=16)**	Necrosis more than 50%	4	25.00
	Necrosis more than 30%	8	50.00
	No treatment effect	3	18.75

*Other reason of treatment discontinuation include; 3 treatment breaks (3.70%), 1 rupture brain aneurysm (1.23%), 1 to evaluate possible secondary malignancy (1.23%), 1 complete treatment (1.23%), and 1 dead (1.23%).

**From 23 instances of surgery after gemcitabine-based treatment, only 16 report included detail on response.

Figure 1 | Waterfall plot of percent change of tumor size from baseline to best response evaluated by RECIST1.1 criteria

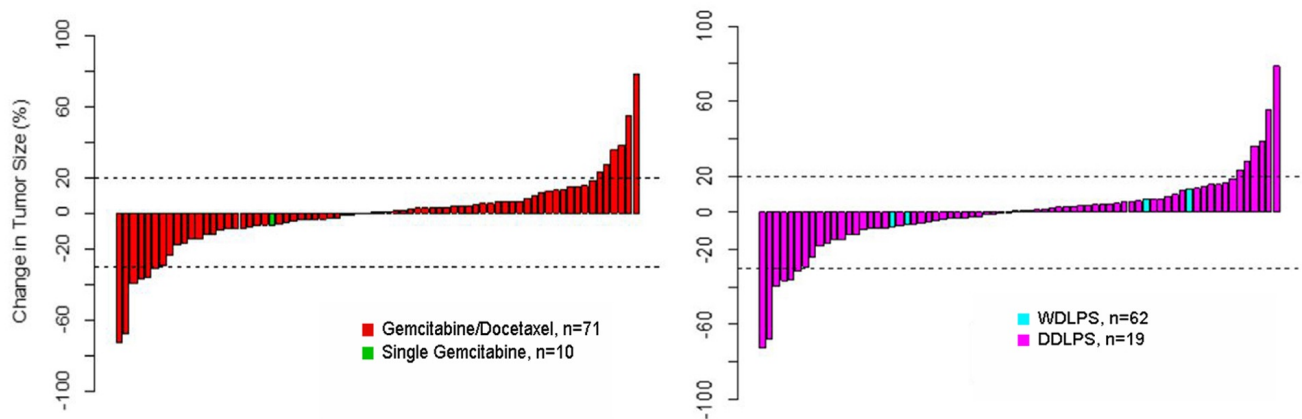
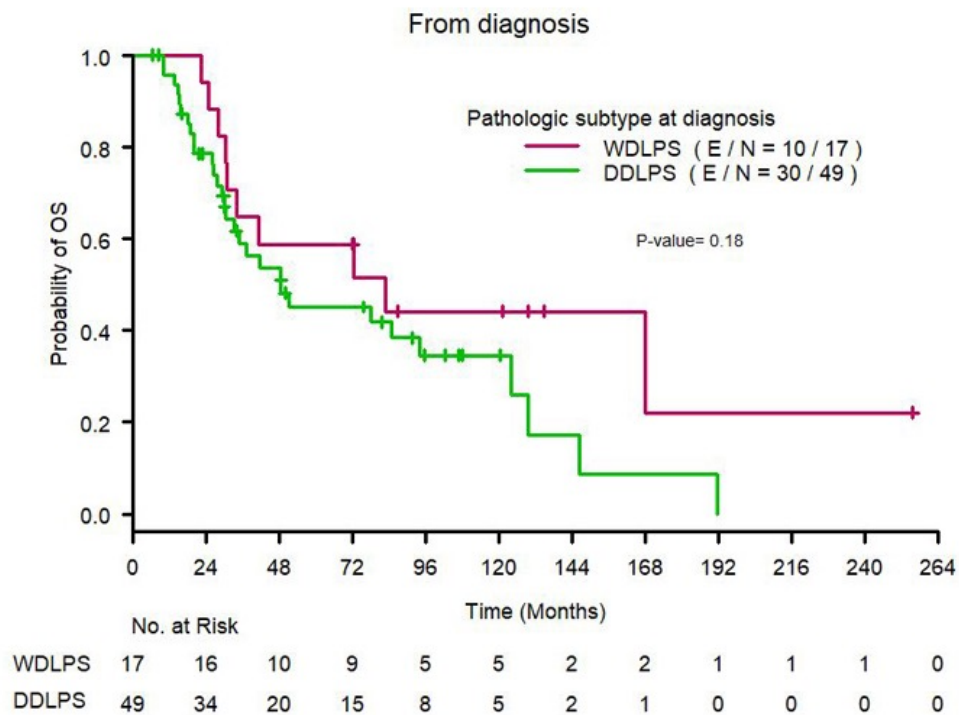


Figure 2 | Kaplan-Meier curve of overall survival by subtypes at diagnosis





Poster #230 #1818957

A PHASE I/II TRIAL COMBINING AVELUMAB AND TRABECTEDIN FOR ADVANCED LIPOSARCOMA AND LEIOMYOSARCOMA

Michael J. Wagner, MD¹; Graeme Black, B.S.²; Yuzheng Zhang, M.S.²; Lee D. Cranmer, MD, PhD³; Elizabeth T. Loggers, MD, PhD²; Sabrina McDonnell, B.S.²; Shannon Maxwell, B.S.³; Rylee Johnson, B.S.³; Roxanne Moore, M.S.³; Qianchuan He, PhD²; Robin L Jones, MD, PhD⁴; Seth M. Pollack, MD⁵

¹University of Washington/Fred Hutch/Seattle Cancer Care Alliance, Seattle, Washington, UNITED STATES,

²Fred Hutchinson Cancer Research Center, Seattle, Washington, UNITED STATES, ³University of Washington, Seattle, Washington, UNITED STATES, ⁴Royal Marsden NHS Foundation Trust, London, England, UNITED KINGDOM,

⁵Northwestern University, Chicago, Illinois, UNITED STATES

Objective: Leiomyosarcoma (LMS) and liposarcoma (LPS) are soft tissue sarcoma subtypes that frequently express PD-L1 and are infiltrated with T-cells. They are generally resistant to PD-1/PD-L1 inhibition, possibly due to infiltration with high levels of immunosuppressive, tumor-associated macrophages (TAMs). Trabectedin is FDA-approved for refractory LMS and LPS. Prior studies demonstrated trabectedin activity against TAMs. We hypothesized that PD-L1 inhibition by avelumab would be enhanced by trabectedin through its inhibition of immunosuppressive TAMs.

Methods: This was a single-arm, open-label, Phase I/II study of avelumab combined with trabectedin for patients with advanced LMS and LPS. In the phase I portion, we evaluated safety and feasibility at three trabectedin doses (1, 1.2 and 1.5 mg/m²) with avelumab at standard dosing (10 mg/kg every two weeks) in a 3+3 design. The primary endpoint of the phase II portion was the objective response rate (ORR) by RECIST 1.1. Twenty-four patients were included in the phase II component. Secondary objectives were duration of response, progression-free survival (PFS), clinical benefit rate (CBR; defined as partial response (PR)+ stable disease (SD) at 12 weeks), and overall survival. Exploratory correlative studies included TCR sequencing and multiplex immunohistochemistry.

Results: 35 patients enrolled; 33 were evaluable. 24 had LMS. 11 had LPS. In Phase 1, there were DLTs in 2 of 6 patients at both higher doses of trabectedin, including grade 3 GGT elevation, bilirubin and alanine aminotransferase (ALT) elevation, small bowel obstruction, and reduced ejection fraction. The recommended Phase 2 dose (RP2D) was 1.0 mg/m² trabectedin and 10 mg/kg avelumab. At the Phase 2 dose, the most common adverse events (AEs) attributed to study drug were fatigue, ALT increase, diarrhea, anorexia, nausea, and infusion reaction. There were 8 instances of implanted catheter inflammation or infection. The most common Grade 3 AEs attributed to study drug were neutropenia and ALT increase. There were no grade 4/5 AEs at the Phase 2 dose. Twenty-three patients were evaluable for response. Three (13%) had partial response, ten (43%) had stable disease as best response. CBR at 12 weeks was 56%. 6-month PFS was 52%; median PFS was 8.3 months. In a secondary analysis of all patients, the ORR was 11.4% (4/35 with PR) and median PFS was 8.1 months. In correlative analysis, patients with a partial response had higher Productive Simpson Clonality versus those with SD (0.182 vs 0.067, $p = 0.02$) or PD (0.182 vs 0.064, $p = 0.01$).

Conclusion: Administration of this combination was feasible with acceptable toxicity. RP2D was 1.0 mg/m² trabectedin and 10 mg/kg avelumab. The combination failed to meet the primary endpoint of ORR. However, PFS appears favorable compared to prior studies of trabectedin in this population and warrants further investigation.



Poster #231 #1818954

SURGICAL OUTCOMES FOLLOWING TREATMENT WITH PALBOCICLIB IN OF PATIENTS WITH WELL-DIFFERENTIATED AND DEDIFFERENTIATED RETROPERITONEAL LIPOSARCOMAS

Elise F. Nassif, MD¹; Christina L. Roland, MD²; Prapassorn Thirasastr, MD, MSc.²; Christopher P. Scally, MD²; Alejandra Zarzour³; Raul F. Valenzuela, MD³; Keila E. Torres, MD, PhD²; Kelly K. Hunt, MD²; Barry W. Feig, MD²; Wei-Lien Wang, MD²; Alexander Lazar, MD, PhD²; Neeta Somaiah, MD²; Emily Z. Keung, MD²

¹MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ²The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ³MDACC, Houston, Texas, UNITED STATES

Objective: Well-differentiated liposarcoma (WDLPS) and dedifferentiated liposarcoma (DDLPS) are characterized by MDM2 amplification with CDK4 co-amplification found in 85% of cases. Palbociclib, a CDK4/6 inhibitor, has been evaluated in two phase 2 trials of WDLPS/DDLPS reporting a median progression-free survival (PFS) of 18 weeks in 30 and 60 patients, respectively. Herein, we report our real-world use and surgical outcomes associated with palbociclib treatment of retroperitoneal WDLPS or DDLPS.

Methods: We retrospectively reviewed all patients with retroperitoneal WDLPS or DDLPS treated with single agent palbociclib from 03/01/2016 to 02/28/2021 at The University of Texas MD Anderson Cancer Center (IRB approval 04/23/2021). Data was extracted from eElectronic hHealth rRecords. For survival analyses, Kaplan-Meier curves were drawn, and cox models were used to identify potential prognostic factors. PFS and overall survival (OS) were calculated from the date of palbociclib initiation.

Results: At palbociclib initiation, median age was 64 (interquartile range [IQR] 56-72) and ECOG performance status was 0/1 in 86% of patients (Table 1). In WDLPS (N=14) and DDLPS (N=47) cohorts, the median number of prior systemic treatments was 0 (IQR 0-0) and 2 (IQR 0-4), respectively. Median number of prior surgeries was 2 (WDLPS IQR 1-2.75) and 2 (DDLPS IQR 1-3). At palbociclib initiation, 79% (WDLPS) and 96% (DDLPS) of patients had documented progressive disease. Median duration of palbociclib treatment was 7.1 (WDLPS IQR 3.5-12.9) and 2.7 months (DDLPS IQR 2.0-5.7). Median PFS was 9.2 (WDLPS IQR 3.9-21.9) and 2.6 months (DDLPS IQR 2.0-6.1). Median follow-up after palbociclib initiation was 17.3 months (WDLPS IQR 10.4-29.0) and 13.6 months (DDLPS IQR 10.2-34.1). A surgical opinion was obtained at palbociclib initiation for 86% of WDLPS and 47% of DDLPS patients with tumors considered unresectable in 50% (WDLPS N=6/12) and 36% (DDLPS N=8/22) of patients. Twelve patients ultimately underwent surgical resection at median of 6.1 months (IQR 4.2-9.5) after palbociclib initiation: WDLPS 9.5 months (IQR 7.5-20.4) and DDLPS 4.2 months (IQR 2.1-6.1). All patients who underwent surgery after palbociclib had undergone at least one prior resection, with 8 (67%) having undergone at least two previous resections (Table 2). Eleven surgeries were performed after progression on palbociclib treatment. Half of the resections were macroscopically complete. No patient has recurred following macroscopically complete resection, although median post-operative follow-up is only 6 months (IQR 2.0-NA) to date. Among patients who underwent macroscopically incomplete resection, all had progression following surgery with median time to progression of 3.3 months (IQR 2.3-4.4). Median OS from palbociclib initiation was not reached (WDLPS) and 14.8 months (DDLPS IQR 5.2-NR). Surgical resection after palbociclib treatment was not associated with improved OS for either WDLPS (Fig 1) or DDLPS (Fig 2).

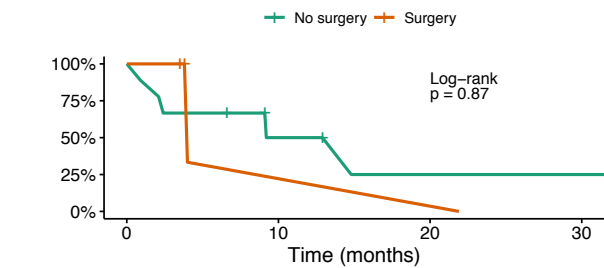
Conclusion: In our experience to date, palbociclib has primarily been used in an older, heavily pretreated cohort of patients with WDLPS/DDLPS whose systemic treatment options are limited. While palbociclib may have been used to delay surgery in this cohort, there were no responses to treatment and few patients achieved prolonged disease stabilization. Whether palbociclib offers any benefit as a neoadjuvant strategy in this population is unclear.

Characteristic median (IQR), N (column %)	Well-Differentiated		Dedifferentiated	
	All patients, N = 14	Patients with surgical resection following Palbociclib, N = 5	All patients, N = 47	Patients with surgical resection following Palbociclib, N = 7
Age, median (IQR)	61 (52 - 78)	64 (51 - 77)	65 (60 - 72)	62 (57 - 63)
Gender, N (%)				
Female	10 (71%)	1 (20%)	18 (38%)	5 (71%)
Male	4 (29%)	4 (80%)	29 (62%)	2 (29%)
Stage at baseline, N (%)				
Unifocal abdominal	4 (29%)	2 (40%)	2 (4%)	1 (14%)
Multifocal abdominal disease	9 (64%)	3 (60%)	27 (57%)	4 (57%)
Lung metastasis	1 (7%)	0	15 (32%)	1 (14%)
Other metastatic sites	0	0	3 (6%)	1 (14%)
Performance Status at baseline, N (%)				
0	7 (50%)	3 (60%)	24 (51%)	4 (57%)
1	4 (29%)	2 (40%)	11 (23%)	2 (29%)
2	2 (14%)	0	5 (11%)	1 (14%)
Unknown	1 (7%)	0	7 (15%)	0
Number of surgeries prior to Palbociclib, N (%)				
0	2 (14%)	0	3 (6%)	0
1	3 (21%)	3 (60%)	14 (30%)	1 (14%)
2	5 (36%)	1 (20%)	11 (23%)	3 (43%)
3	2 (14%)	0	10 (21%)	3 (43%)
4	1 (7%)	1 (20%)	6 (13%)	0
5	0	0	2 (4%)	0
6	1 (7%)	0	0	0
7	0	0	1 (2%)	0
Number of radiation therapies prior to Palbociclib, N (%)				
0	14 (100%)	5 (100%)	33 (70%)	4 (57%)
1	0 (0%)	0 (0%)	11 (23%)	2 (29%)
2	0 (0%)	0 (0%)	3 (6%)	1 (14%)
Number of systemic treatment lines prior to Palbociclib, N (%)				
0	11 (79%)	4 (80%)	13 (28%)	1 (14%)
1	3 (21%)	1 (20%)	6 (13%)	0
2	0	0	7 (15%)	2 (29%)
3	0	0	5 (11%)	0
4	0	0	6 (13%)	3 (43%)
5	0	0	3 (6%)	0
6	0	0	2 (4%)	0
7	0	0	5 (11%)	1 (14%)
Progressive disease at baseline, N (%)	11 (79%)	4 (80%)	45 (96%)	6 (86%)
Unknown	1 (7%)	0	1 (2%)	0
Routine surveillance by surgical team before Palbociclib initiation, N (%)				
Yes	3 (21%)	3 (60%)	25 (53%)	4 (57%)
No	11 (79%)	2 (40%)	22 (47%)	3 (43%)
Surgical opinion obtained at time of Palbociclib initiation, N (%)				
Not resectable	6 (43%)	2 (40%)	8 (17%)	0
Likely not resectable, to be re-evaluated	0	0	2 (4%)	1 (14%)
Only for palliation of symptoms	1 (7%)	0	2 (4%)	1 (14%)
Tumor response needed	0	0	2 (4%)	0
Surgery possible if stabilization	0	0	2 (4%)	0
Potentially resectable	1 (7%)	0	3 (6%)	1 (14%)
Resectable	3 (21%)	2 (40%)	2 (4%)	1 (14%)
Palbociclib started post-operatively	1 (7%)	0	1 (2%)	0
No surgical opinion	2 (14%)	1 (20%)	25 (53%)	3 (42%)
Best response as assessed by treating physician, N (%)				
Partial response	0	0	1 (2%)	1 (14%)
Stable disease	9 (64%)	3 (60%)	19 (40%)	3 (43%)
Progressive disease	4 (29%)	2 (40%)	23 (49%)	2 (28%)
Unknown	1 (7%)	0	4 (9%)	1 (14%)
Number of surgeries after Palbociclib, N (%)				
0	7 (50%)	–	36 (77%)	–
1	5 (36%)	4 (80%)	10 (21%)	7 (100%)
2	1 (7%)	1 (20%)	0	0
Unknown	1 (7%)	0	1 (2%)	0
Number of radiation therapies after Palbociclib, N (%)				
0	12 (86%)	4 (80%)	42 (89%)	6 (86%)
1	1 (7%)	1 (20%)	3 (6%)	1 (14%)
Unknown	1 (7%)	0	2 (4%)	0
Number of systemic treatment lines after Palbociclib, N (%)				
0	9 (64%)	3 (60%)	24 (51%)	4 (57%)
1	3 (21%)	1 (20%)	15 (32%)	2 (29%)
2-3	0	0	6 (13%)	1 (14%)
4-6	1 (7%)	1 (20%)	1 (2%)	0
Unknown	1 (7%)	0	1 (2%)	0

Interquartile range, IQR

Histotype	Disease stage at Palbociclib initiation	N prior lines of systemic therapy	N prior surgeries	Surgical resectability documented at Palbociclib initiation	Palbociclib treatment duration (months)	Disease status at surgery	Resection margins at surgery	Progression post-surgery	Progression-free survival post-surgery (months)	Alive	Overall survival following post-Palbociclib surgery
WD	Unifocal	0	1	Not resectable	3.9	Progression	R2	Yes	5.1	Yes	8.5
WD	Unifocal	0	4	Not resectable	3.5	Progression	R0/1	No	2.2	Yes	2.2
WD	Multifocal	1	1	No surgical opinion	7.1	Progression	R2	Yes	2.3	Yes	25.9
WD	Multifocal	0	2	Resectable	21.9	Stable	R0/1	No	1.7	Yes	1.7
WD	Multifocal	0	1	Resectable	3.8	Progression	R0/1	No	6	Yes	6
DD	Multifocal	7	3	No surgical opinion	<1	Progression	R2	Yes	2.5	No	3.7
DD	Multifocal	4	3		5.7	Progression	R2	Yes	1.3	No	3.1
DD	Unifocal	2	1	Potentially for debulking	1	Progression	R0/1	No	2.5	No	2.5
DD	Multifocal: abdominal and extra-abdominal disease	4	2	No surgical opinion	3.9	Progression	R2	Yes	4.4	Yes	6.6
DD	Multifocal	2	2	Potentially resectable	6.1	Progression	R0/1	No	25.5	Yes	25.5
DD	Multifocal: abdominal and extra-abdominal disease	4	3	Potentially resectable	3.7	Progression	R2	Yes	3.3	Yes	7.6
DD	Multifocal	0	2	Resectable	4.2	Progression	R0/1	No	2	Yes	2

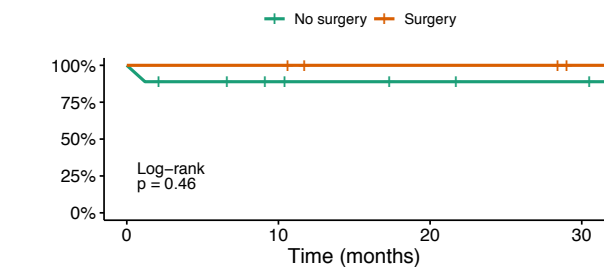
Progression-free Survival WDLPS



Number at risk

No surgery	9	3	1	1
Surgery	5	1	1	0

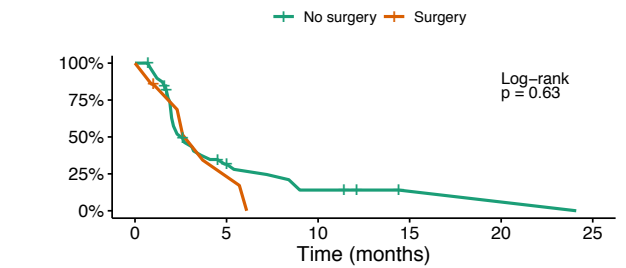
Overall Survival WDLPS



Number at risk

No surgery	9	5	3	2
Surgery	5	5	3	1

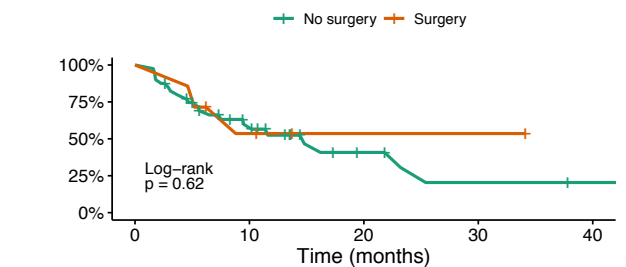
Progression-free Survival DDLPS



Number at risk

No surgery	40	10	4	1	1	0
Surgery	7	2	0	0	0	0

Overall Survival DDLPS



Number at risk

No surgery	40	18	5	2	1
Surgery	7	3	1	1	0



Poster #232 #1818935

PREDICTIVE VALUE OF NEUTROPHIL TO LYMPHOCYTE RATIO IN SOFT TISSUE SARCOMA: A NORTH AMERICAN PERSPECTIVE

Chloé Thériault, BSc; Dan Moldoveanu, BSc, MDCM, PhD Candidate; Abdulaziz Al-Mubarak, MD; Giuseppe Frenda, MD; Ian Watson, PhD; Sarkis Meterissian, MD; Sinziana Dumitra, MD, MSc (Epi), FRCS(C)
 McGill University, Montreal, Province du Québec, CANADA

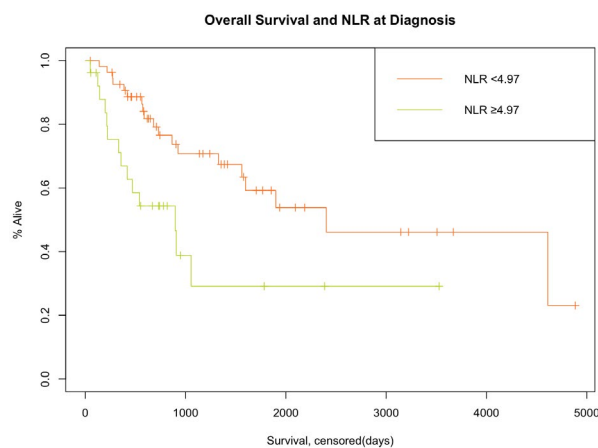
Objective: The neutrophil-to-lymphocyte ratio (NLR) is a metric that captures the balance between the innate and adaptive immune system, and has been described as a prognostic factor for multiple solid tumors, including soft tissue sarcomas (STS). Our study aims to confirm the prognostic value of the NLR in STS in the North American population, while further exploring the relationship between NLR fluctuations and mortality.

Methods: In this retrospective study, we reviewed our institution's experience with STS patients treated between 2006 and 2018. The main study outcome was overall survival, while secondary outcomes included disease progression and disease recurrence. Statistical analysis was performed using the "R" statistical software, as well as Kaplan Meier curves, Cox proportional-hazards survival analysis models, and simple descriptive statistics of the studied population.

Results: A total of 81 patients met our inclusion criteria, comprising both metastatic and resectable retroperitoneal sarcomas, with a median age of 58. The most common diagnosis was liposarcoma, present in 40 patients (49.3%), followed by leiomyosarcoma, present in 20 patients (24.7%). An NLR greater than 4.97 at diagnosis was associated with decreased overall survival (hazard ratio [HR], 2.34; 95% confidence interval [CI], 1.23-4.46) and increased rates of disease recurrence (hazard ratio [HR], 2.10; 95% confidence interval [CI], 1.01-4.35). A maximal NLR at any time during the patient's clinical trajectory in excess of 42.22 was associated with a worse survival (hazard ratio [HR], 2.07; 95% confidence interval [CI], 1.10-3.88). The median NLR also showed a significant rise during the last 6 months of life ($p < 0.001$).

Conclusion: The NLR is an important prognostic marker in STS, and dynamic changes in its value throughout the trajectory of care correlate significantly with oncologic outcomes.

Figure 1: Overall survival ($p = 0.007$) for patients with retroperitoneal sarcoma according to their neutrophil-to-lymphocyte ratio (NLR) at diagnosis.


Table 1: Patient Demographics.

	Overall (N=81)
Sex	
Male	43 (53.1%)
Female	38 (46.9%)
Age (years)	
Mean (SD)	60.4 (12.8)
Median [Min, Max]	58.0 [26.0, 89.0]
Histology	
Dedifferentiated liposarcoma	27 (33.3%)
Leiomyosarcoma	20 (24.7%)
Other	21 (25.9%)
Well differentiated liposarcoma	13 (16.0%)
Surgery	
Resected	61 (75.3%)
Not Resected	20 (24.7%)
Tumor Size (mm)	
Mean (SD)	176 (113)
Median [Min, Max]	150 [30.0, 600]
Missing	22 (27.2%)
Nodes	
Involved	2 (2.5%)
Not Involved	55 (67.9%)
Missing	24 (29.6%)

Figure 2: Overall survival ($p = 0.02$) for patients with retroperitoneal sarcoma according to their maximal neutrophil-to-lymphocyte ratio (NLR) throughout their clinical follow-up.

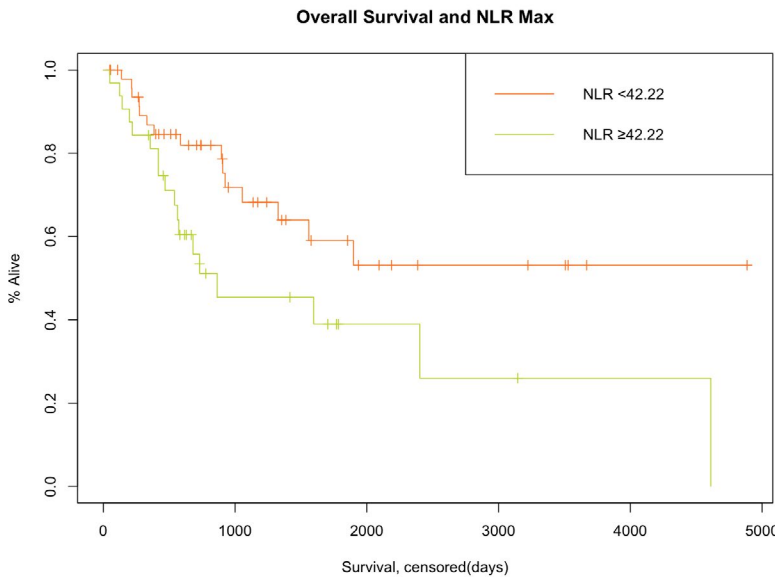
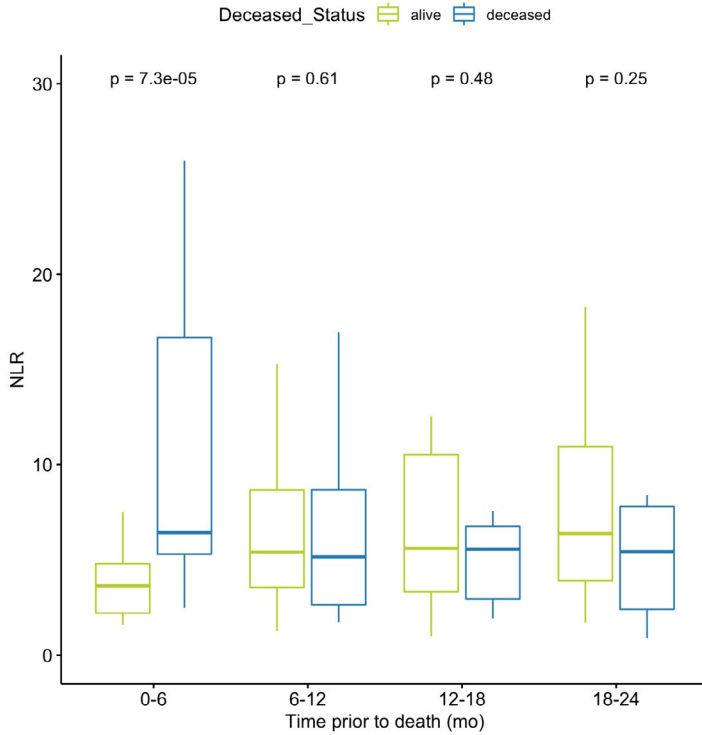


Figure 3: The difference in the neutrophil-to-lymphocyte ratio (NLR) between deceased patients and alive patients becomes more pronounced during the 6 months preceding the time of censorship.





Poster #233 #1819016

THE COMPREHENSIVE COMPLICATION INDEX REFLECTS THE REAL IMPACT OF POSTOPERATIVE MORBIDITY AND IT IS A NOVEL COST ASSESSMENT TOOL FOR RETROPERITONEAL SOFT TISSUE SARCOMA SURGERY

Laura Ruspi, MD¹; Laura Samà, MD²; Fulvia Aymerito, MD³; Federica Barzaghi, MD³; Sonia Kumar, MD³; Federico Sicoli, MD⁴; Ferdinando Cananzi, MD⁵; Vittorio Lorenzo Quagliuolo, MD⁴

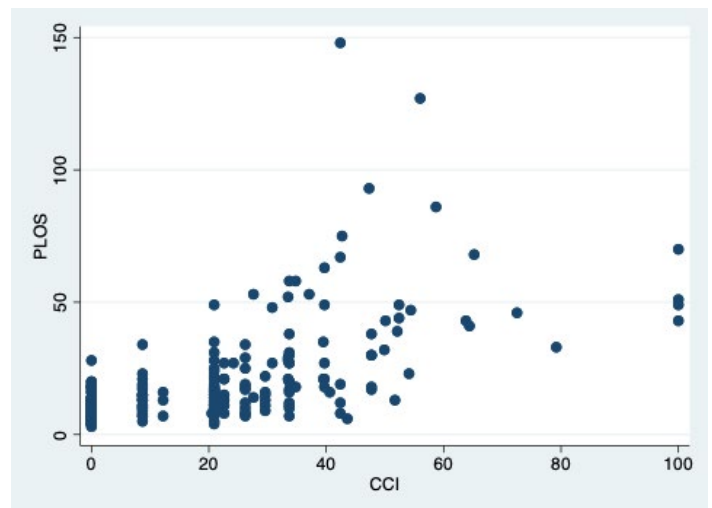
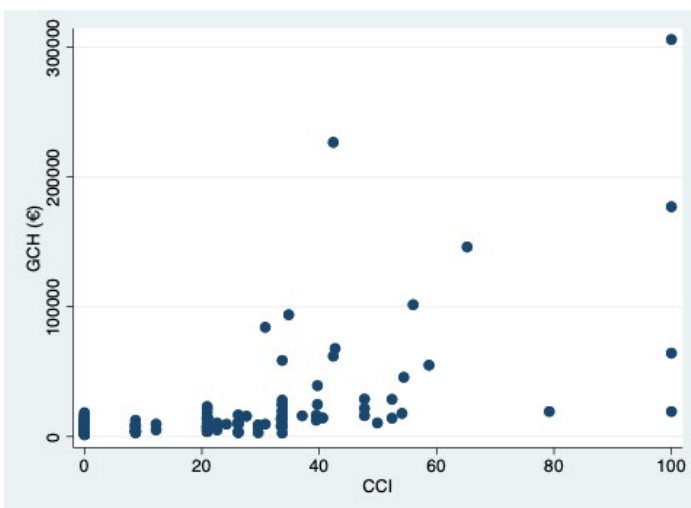
¹Humanitas Clinical and Research Center, Rozzano (MI), Lombardia, ITALY, ²Humanitas Clinical and Research Hospital/ Humanitas University, Milan, Lombardia, ITALY, ³Humanitas University, Milan, Lombardia, ITALY, ⁴Humanitas Clinical and Research Hospital, Milan, Lombardia, ITALY, ⁵Humanitas Clinical and Research Center, Humanitas University, Milan, Lombardia, ITALY

Objective: Surgery is the mainstay of treatment for localized retroperitoneal sarcoma (RPS) and it often requires a technically demanding en bloc multivisceral resection to optimize outcomes, with the subsequent risk of multiple complications. Postoperative morbidity significantly impacts on cost in surgical patients. The aim of our study was to demonstrate that the Comprehensive complication Index (CCI) is a readily available, reproducible, and applicable cost assessment tool for RPS.

Methods: Data on 417 surgical procedures performed on 322 patients underwent surgery for both primary and recurrent retroperitoneal sarcoma in a referral center between January 2000 and December 2017 were retrieved. Patients' demographics, operative reports, complications and their treatments, and postoperative length of stay (PLOS) were reviewed. In addition, data on costs of hospitalization were analyzed. Comorbidities were measured by means of the Charlson comorbidity index and also CCI was instead calculated.

Results: The costs of hospitalization ranged from 135000 to 305900 € (mean 13379.2€); postoperative complications occurred in 170/417 procedures and CDC>3 complications occurred in 76/417 surgeries. Considering all procedures, mean CCI was 12.2 (range 0-100) while in complicated cases mean CCI was 30 (range 8.7 - 100). Median PLOS was 10 days (range 3-148). One-hundred and six patients experienced just one complications, while 64 patients had more than one complication. Spearman's rank coefficient was 0.693 when correlation between CCI and PLOS was tested, and 0.686 between CDC and PLOS; rho was 0.5819 between CCI and costs, and 0.5812 between CDC and costs. Two different multivariable linear regressions showed that both CDC and CCI were independent prognostic factor for both costs and PLOS and the AIC and BIC for the CCI models were smaller for both costs and PLOS.

Conclusion: Overall postoperative morbidity correlates highly with cost. The CCI is strongly correlated with PLOS and costs, and it is able to take into account the impact of multiple complications, which often occur after surgery for RPS. This finding may enable objective cost comparisons among centers, or over time obviating the need to look at complex country-specific cost calculations.





Poster #234 #1818961

POSTOPERATIVE OUTCOMES OF DISTAL PANCREATECTOMY FOR RETROPERITONEAL SARCOMA ABUTTING THE PANCREAS IN THE LEFT UPPER QUADRANT

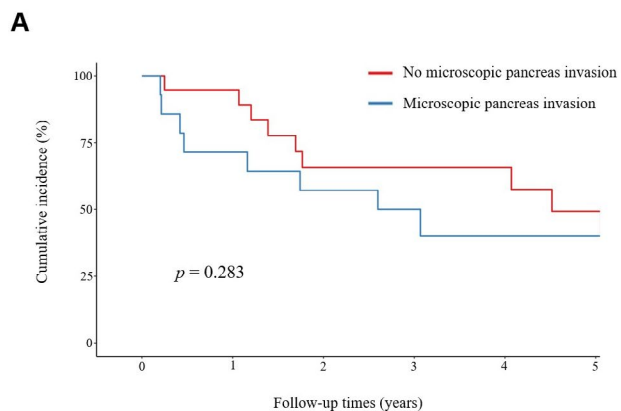
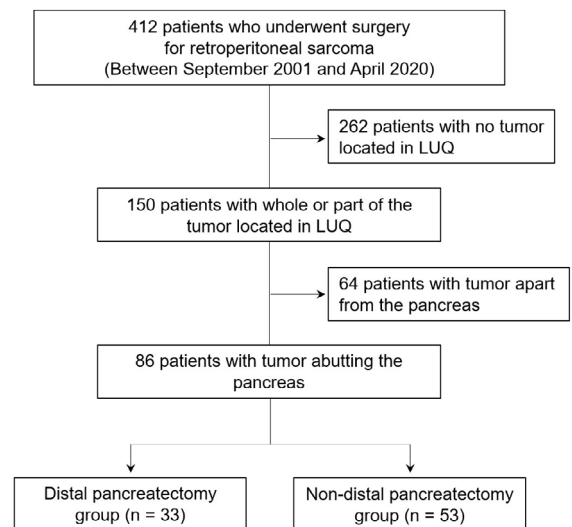
Kyeong Deok Kim, MD; Kyo Won Lee, MD/Ph.D.; Manuel Lim, MD; Ji Eun Kwon, MD; Eun Sung Jeong, MD; Jaehun Yang, MD; Young Ju Oh, MD; Sunghae Park, MD; Sang Oh Yun, MD; Jae Berm Park, MD/PhD
 Samsung Medical Center, Seoul, Seoul-t'ukpyolsi, Republic of Korea

Objective: Surgical en bloc resection of the tumor with adjacent organs is recommended for localized retroperitoneal sarcoma (RPS). However, when the tumor is adjacent to the pancreas, resection of the pancreas is controversial because it may cause serious complications such as pancreatic fistula or bleeding. Thus, we evaluated the outcome of distal pancreatectomy (DP) in the pancreas abutting mass in the left upper quadrant (LUQ).

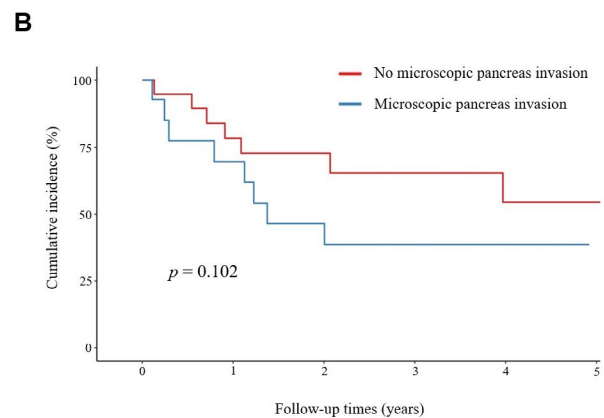
Methods: We retrospectively reviewed all consecutive patients who underwent surgery for RPS between September 2001 and April 2020. We selected 150 patients with whole or part of the tumor located in LUQ on preoperative CT images. 86 patients who had the tumor abutting the pancreas were finally enrolled in our study.

Results: Fifty-three patients (61.6%, 53/86) were included in the non-DP group, and 33 patients (38.4%, 33/86) were included in the DP group. The postoperative complication and Clavien-Dindo 3 or higher complication rates were similar between the non-DP group and DP group ($p = 0.290$ and $=0.550$). In the DP group, grade B pancreatic fistula occurred in 21.2% (7/33), but grade C was absent, and microscopic pancreas invasion was noted in 42.4% (14/33). In multivariate analysis, microscopic pancreas invasion was a risk factor for the local recurrence ($p = 0.029$). However, there were no significant differences in the pre-operative CT findings between the pancreas invasion group and the pancreas non-invasion group.

Conclusion: It may be better to perform a distal pancreatectomy for RPS in the LUQ area abutting the pancreas.



Number at risk	0	1	2	3	4	5
No microscopic pancreas invasion	19	17	11	10	8	6
Microscopic pancreas invasion	14	10	8	6	4	2



Number at risk	0	1	2	3	4	5
No microscopic pancreas invasion	19	14	10	8	5	4
Microscopic pancreas invasion	14	9	6	4	2	0

Overall survival and disease-free survival between the No microscopic pancreas invasion and microscopic pancreas invasion groups. (A) Overall survival between the No microscopic pancreas invasion and microscopic pancreas invasion groups. (B) Disease-free survival between the No microscopic pancreas invasion and microscopic pancreas invasion groups. Group comparisons were performed using the Kaplan-Meier and log-rank tests.



Poster #235 #1818963

COMPARISON OF SURGICAL OUTCOMES BETWEEN LEIOMYOSARCOMA OF INFERIOR VENA CAVA AND OTHER LOCATIONS

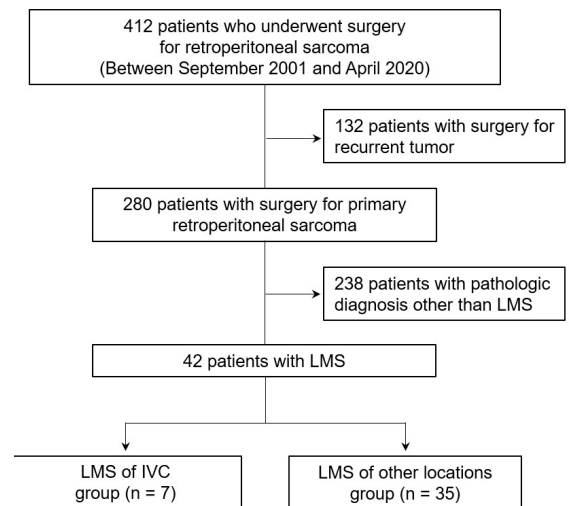
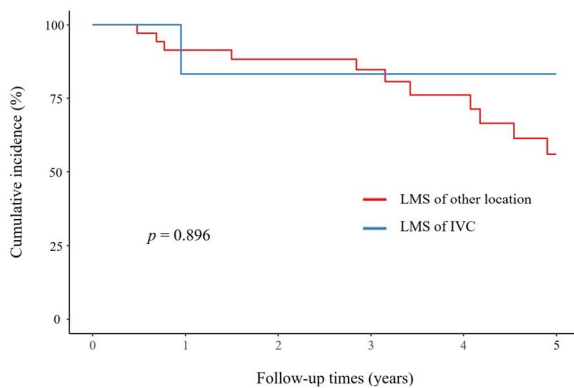
Kyeong Deok Kim, MD; Kyo Won Lee, MD/PhD; Manuel Lim, MD; Eun Sung Jeong, MD; Jaehun Yang, MD; Ji Eun Kwon, MD; Young Ju Oh, MD; Sunghae Park, MD; Sang Oh Yun, MD; Jae Berm Park, MD, PhD
 Samsung Medical Center, Seoul, Seoul-t'ukpyolsi, REPUBLIC OF KOREA

Objective: Primary leiomyosarcoma (LMS) of inferior vena cava (IVC) is rare, but the prognosis is poor due to frequent invasion of adjacent structures. Surgery is the only potential treatment for LMS of IVC, but surgical resection remains a challenge. In this study, we compared the outcomes after resection of LMS of IVC with LMS of other locations. Also, we evaluated the patency of the graft used for IVC reconstruction.

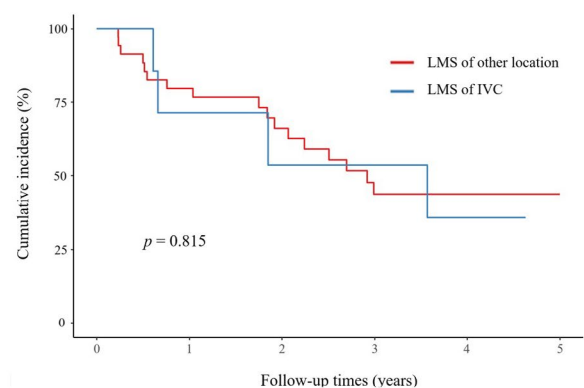
Methods: All patients who underwent surgery for LMS from September 2001 and April 2020 were retrospectively reviewed. In the LMS of the IVC group, all patients underwent complete gross resection of the tumor with the involved IVC for curative intention. Reconstruction of the IVC was performed in all patients by patch or interposition using autograft, allograft, or polytetrafluoroethylene (PTFE) graft.

Results: Seven patients (16.7%, 7/42) were included in the LMS of the IVC group, and 35 patients (83.3%, 35/42) were included in the LMS of other locations group. The operation time was significantly longer in the LMS of the IVC group than the LMS of other locations group ($p = 0.029$). However, the postoperative complication and Clavien-Dindo 3 or higher complication rates were similar between the LMS of IVC group and LMS of other locations group ($p = 0.063$ and 0.309 , respectively). Also, the 5-year overall survival and disease-free survival were similar between the two groups ($p = 0.896$ and 0.815 , respectively). Only one case that used allograft for interposition was occluded 4 months after the operation.

Conclusion: The resection of LMS of IVC may achieve outcomes equivalent to resection of LMS of other locations.


A

Number at risk

LMS of other locations	35	32	27	21	16	10
LMS of IVC	7	5	5	4	2	1

B

Number at risk

LMS of other locations	35	27	19	11	8	4
LMS of IVC	7	4	3	3	1	0

Overall survival and disease-free survival between the LMS of other location and LMS of IVC groups. (A) Overall survival between the LMS of other location and LMS of IVC groups. (B) Disease-free survival between the LMS of other location and LMS of IVC groups. Group comparisons were performed using the Kaplan-Meier and log-rank tests.



Poster #236 #1819028

DEDIFFERENTIATED LIPOSARCOMA OF THE RETROPERITONEUM: A TRANSCRIPTOMIC ANALYSIS OF PAIRED WELL DIFFERENTIATED AND DEDIFFERENTIATED TUMOUR COMPONENTS

Sandro Pasquali, MD, PhD¹; Stefano Percio, MSc, PhD²; Silvia Brich, PhD³; Alessia Bertolotti, MSc, PhD²; Marta Barisella, MD⁴; Paola Collini, MD⁵; Andrea Careno, Dr⁶; Edoardo Marchesi, MSc²; Arianna Micali, MSc²; Anna Maria Frezza, MD⁷; Dario Callegaro, MD⁸; Loris De Cecco, PhD⁶; Nadia Zaffaroni, PhD²; Alessandro Gronchi, MD⁹
¹Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ²Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Lombardia, ITALY, ³Fondazione IRCCS Istituto Nazionale dei Tumori (INT), Milano, Lombardia, ITALY, ⁴Department of Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ⁵Department of Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Lombardia, ITALY, ⁶Platform of Integrated Biology, Department of Applied Research and Technology Development, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Lombardia, ITALY, ⁷Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY, ⁸Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ⁹Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, Milan, Lombardia, ITALY

Objective: Retroperitoneal dedifferentiated liposarcoma (DDLPS) are characterised by a high risk of local recurrence and distant metastasis. Patients are treated with multivisceral surgery and there is an unmet need for histology- and molecularly-tailored treatment strategies. Here we report on a transcriptomic analysis conducted in a retrospective series of patients with primary retroperitoneal DDLPS aimed at characterising these tumours and identifying new therapeutic targets.

Methods: We retrospectively analysed clinic-pathological data and tumours from patients with a primary retroperitoneal sarcoma who underwent surgery at our sarcoma reference institute (Jan2011-Dec2015). These data are part of the SARCOMICS, an observational study that aims at investigating the integration of radiomic, genomic and immunological markers to improve the performance of clinical-based prognostic and predictive models. SARCOMICS has been conducted at Istituto Nazionale Tumori, Milan, Italy, since 2018 and includes both retrospective and prospective cohorts of patients with retroperitoneal and extremity soft tissue sarcoma. Each tumour surgical specimen was reviewed by a pathologist and a representative sample from tumour and homologous normal tissue was taken. Paired samples from WD, DD and normal adipose (A) components were selected for each DDLPS. RNA was extracted from formalin fixed paraffin embedded (FFPE) blocks and RNA-seq analysis conducted. A haematoxylin and eosin control slide was performed in order to assess the quality of the material.

Results: Some 135 retroperitoneal sarcomas underwent transcriptomic analysis, including 41 well-differentiated liposarcoma (WDLPS), 68 DDLPS, 17 leiomyosarcoma (LMS), 4 solitary fibrous tumour (SFT), 3 malignant peripheral nerve sheath tumours (MPNST), and 2 undifferentiated pleomorphic sarcoma (UPS). After data normalization, principal component analysis (PCA) showed that tumours clustered according to their sarcoma histology. Interestingly, WDLPS span the space between DDLPS and normal phenotypes, while LMS grouped together. In DDLPS, a segregation of WD and DD components was observed. In keeping with the non-lipogenic phenotype of DDLPS, genes involved in adipogenesis and lipid metabolism were down-regulated in the DD component. Conversely, pathways related to cell cycle, DNA repair, epithelial to mesenchymal transition, and MYC signalling emerged as up-regulated in the DD component of DDLPS. Differences in transcription of potential therapeutic targets across paired WD, DD, and A components of DDLPS were investigated. In addition to MDM2 and CDK4, other cell cycle-related genes such as PLK1 and AURKA were upregulated in the DD compared to WD and A components. Other therapeutic targets such as CHEK1, XPO1 and WNT5A also showed an higher expression in the DD component. Interestingly, epigenetic regulators such as EZH2 and the DNA methyltransferase DNMT1, were also found to be over-expressed in the DD component. The differential expression of these therapeutic targets was independently validated in a prospectively collected series of 15 DDLPS (years 2017-2018) from our Institution, where the transcriptomic profiles of paired DD, WD and A components were assessed.

Conclusion: Transcriptomic profile of DDLPS revealed significant differences between the WD and the DD tumour components. The identification of several therapeutic targets has implications for generating hypothesis to design new treatment approaches for these patients. Further analyses are in progress to better characterise DDLPS tumour components with a view of stratifying patient prognosis and will be presented.



Poster #237 #1819052

CINSARC IS PROGNOSTIC IN PATIENTS WITH RETROPERITONEAL SARCOMA (RPS) BUT DOES NOT ADD TO CLINICAL-BASED NOMOGRAMS

Dario Callegaro, MD¹; Andrea Careno, Dr²; Silvia Brich, PhD³; Alessia Bertolotti, PhD⁴; Gabriele Callegaro, MSc⁴; Marta Barisella, MD⁵; Paola Collini, MD⁶; Arianna Micali, MSc⁷; Edoardo Marchesi, MSc⁷; Anna Maria Frezza, MD⁴; Loris De Cecco, PhD²; Rosalba Miceli, PhD¹; Sandro Pasquali, MD, PhD⁸; Alessandro Gronchi, MD⁹

¹Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ²Platform of Integrated Biology, Department of Applied Research and Technology Development, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Lombardia, ITALY, ³Fondazione IRCCS Istituto Nazionale dei Tumori (INT), Milano, Lombardia, ITALY, ⁴Fondazione IRCCS Istituto Nazionale Tumori Milan, Milan, Lombardia, ITALY, ⁵Department of Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ⁶Department of Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Lombardia, ITALY, ⁷Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Lombardia, ITALY, ⁸Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ⁹Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, Milan, Lombardia, ITALY

Objective: The Complexity INdex in SARComas (CINSARC) transcriptional signature has been proven to be prognostic when applied to patients with soft tissue sarcoma by discriminating low-risk (C1) vs high-risk (C2) patients. No specific validation of the signature has been carried out in patients with RPS. SARCOMICS is an observational study that aims at investigating whether the integration of radiomic, genomic and immunological markers could improve the performance of clinical-based prognostic and predictive models. SARCOMICS is being carried out at Istituto Nazionale Tumori, Milan, Italy, since 2018. It includes both retrospective and prospective cohorts. The aims of the present study were ¹to provide the first independent validation of CINSARC on a series of patients with primary RPS and ²to investigate whether the addition of CINSARC to the Sarculator RPS nomogram would improve the nomogram performance.

Methods: This retrospective study included patients with primary localized RPS resected between 2011 and 2015 and included in the retrospective cohort of SARCOMICS. Each tumor surgical specimen was reviewed by a pathologist and a representative sample from tumor and normal tissue was taken. In dedifferentiated liposarcoma, the dedifferentiated component was considered. RNA was extracted from FFPE blocks and RNA-seq analysis conducted. A H&E control slide was performed in order to assess the quality of the material. Patients were classified in the two CINSARC categories C1 and C2 following CINSARC definition (PMID 33023949). The Sarculator RPS overall survival (OS) and disease free-survival (DFS) nomograms were applied to all patients. The nomograms predict 7-yr OS and DFS based upon patient age, tumor size, grade, histology, multifocality and completeness of resection. Primary study endpoints were OS and DFS. Survival curves were estimated with the Kaplan-Meier method and compared with the log rank test. Multivariable analyses for OS and DFS were carried out using Cox regression models. Nomogram performance was assessed in terms of discrimination (Harrell C index) before and after including CINSARC in the Cox model.

Results: The cohort consisted of 117 patients. After applying CINSARC, 63 (53.8%) were classified as low-risk (C1) and 54 (45.8%) as high-risk (C2). Clinicopathological characteristics are summarized in Table 1. The median follow-up was 79.3 months (IQR 69.7-100.7). Five- and 8-yr OS were 87.2% (95%CI 79.3,95.9) and 73.1% (95%CI 60.8,87.8) in C1 patients, 64.1% (95%CI 52.3,78.5) and 51.9% (95%CI 39.3,68.5) in C2 patients (Figure 1, p=0.004). In the OS multivariable analysis including the nomogram score and the CINSARC risk category, only the nomogram score was significantly associated with survival (Table 2) with a HR of 2.84 (95% CI, 1.51,5.32, p < 0.001). By applying the Sarculator OS nomogram to this cohort, the Harrell C index was 0.70 without CINSARC and 0.70 after adding CINSARC to the nomogram model. Five- and 8-yr DFS were 69.7% (95%CI 59.1,82.04) and 45.1% (95%CI 33.0,61.6) in C1 patients, 44.4% (95%CI 32.9,59.8) and 35.2% (95%CI 24.1,51.3) in C2 patients (Figure 2, p=0.055). In the DFS multivariable analysis (Table 2) only the nomogram score was associated with DFS. Harrell C index was 0.63 in the nomogram model without CINSARC and 0.62 with CINSARC.

Conclusion: In this series of patients with primary RPS treated with surgery, CINSARC risk category, which was analysed on a tumor sample representative of tumor histopathologic characteristics, was significantly associated with OS and DFS at univariable analysis but not at multivariable analysis including the Sarculator nomogram score. This likely reflects the collinearity between CINSARC and clinical characteristics in these tumors, in particular grading and histology (p < 0.001, Table

1). For this reason, adding the CINSARC risk category to the OS and DFS RPS Sarculator nomograms did not improve the nomograms performance. New biomarkers are needed to improve the performance of Sarculator.

Table 1: clinicopathological characteristics of the study cohort by CINSARC risk category

	C1 (n=63)	C2 (n=54)	<i>p</i>
Sex			0.331
Male	40 (63.5)	39 (72.2)	
Female	23 (36.5)	15 (27.8)	
Age			0.202
Median (IQR)	63 (56-68)	64 (56-74)	
Histology			<0.001
WDLPS	29 (46.0)	11 (20.4)	
DDLPS	28 (44.4)	27 (50.0)	
LMS	2 (3.2)	12 (22.2)	
SFT	3 (4.8)	0	
MPNST	1 (1.6)	2 (3.7)	
UPS	0	2 (3.7)	
Grade (FNCLCC)			<0.001
I	31 (49.2)	11 (20.4)	
II	26 (41.3)	20 (37.0)	
III	6 (9.5)	23 (42.6)	
Tumor size (cm)			0.239
Median (IQR)	23 (18-30)	22 (13-30)	
Chemotherapy			0.035
yes	3 (4.8)	10 (18.5)	
no	60 (95.2)	44 (81.5)	
Radiotherapy			0.407
yes	10 (15.9)	5 (9.3)	
no	53 (84.1)	49 (90.7)	
Status at last FU			
NED	39 (61.9)	23 (42.6)	
AWD	10 (15.9)	7 (13.0)	
DOD	8 (12.7)	20 (37.0)	
DOC	6 (9.5)	4 (7.4)	

Table legend: IQR, interquartile range; WDLPS, well differentiated liposarcoma; DDLPS, dedifferentiated liposarcoma; LMS, leiomyosarcoma; SFT, solitary fibrous tumor; MPNST, malignant peripheral nerve sheath tumor; UPS, undifferentiated pleomorphic sarcoma; FNCLCC, Federation Nationale des Centres de Lutte Contre le Cancer; FU, follow-up; NED, no evidence of disease; AWD, alive with disease; DOD, dead of disease; DOC, dead of other causes.

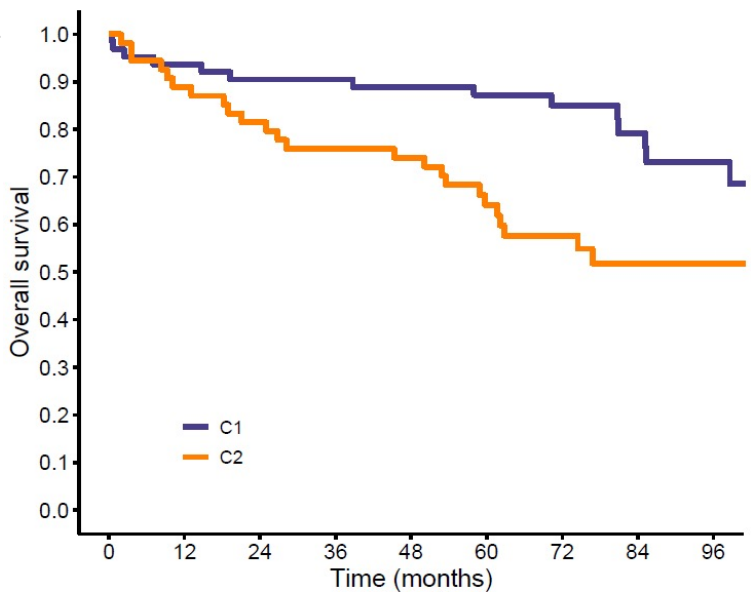
Table 2: results from the multivariable Cox model on OS and DFS

	OS			DFS		
	HR	95%CI	<i>p</i>	HR	95%CI	<i>p</i>
Nomogram score 152 vs 103*	2.84	(1.51, 5.32)	0.001	1.79	(1.26, 2.55)	0.001
CINSARC risk category C2 vs C1	1.66	(0.81, 3.42)	0.81	1.20	(0.71, 2.03)	0.503

Table legend: OS, overall survival; DFS, disease free-survival; HR, hazard ratio; CI, confidence interval.

* The two values are, respectively, the 3rd and 1st quartile of the nomogram score distribution, corresponding to approximate values of OS=44% and 84%, and DFS=27% and 63%.

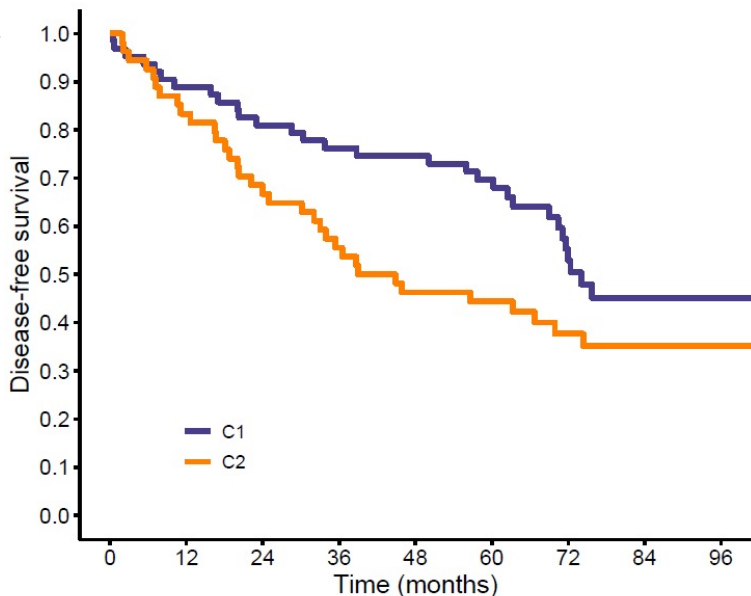
Figure 1



Number at risk (number censored)

■ C1	63 (0)	59 (0)	57 (0)	57 (0)	56 (0)	51 (4)	37 (17)	26 (26)	17 (33)
■ C2	54 (0)	48 (0)	44 (0)	40 (1)	39 (1)	30 (5)	22 (10)	11 (19)	6 (24)

Figure 2



Number at risk (number censored)

■ C1	63 (0)	56 (0)	51 (0)	48 (0)	47 (0)	41 (3)	22 (14)	14 (19)	8 (25)
■ C2	54 (0)	45 (0)	36 (0)	30 (0)	25 (0)	21 (3)	16 (5)	8 (12)	4 (16)



Poster #238 #1818879

DISCOVERY OF A POTENT AND SELECTIVE BRD9 DEGRADER FHD-609 FOR THE TREATMENT OF SYNOVIAL SARCOMA AND OTHER CANCERS WITH DYSREGULATION OF CHROMATIN REMODELER COMPLEXES

Qianhe Zhou, PhD; Huawei (Ray) Chen, PhD; Mengni (Christina) Xu, MS; Ammar Adam, PhD; Marissa, Martinez, PhD; Sarah Reilly, MD; Sean Brennan, BS; Salonee Parikh, MS; Ketaki Adhikari, MS; Michael Bocker, PhD; Kimberly Barnash, PhD; Luis Soares, PhD; Jordana Muwanguzi, MS; Zhaoxia (Joyce) Yang, PhD; Jason Lowe, PhD; David Lahr, PhD; Laura Zawadzke, PhD; Johannes Voigt, PhD; Liyue Huang, PhD; Sabine Ruppel, PhD; Murph Hentemann, PhD; Scott Innis, MS; Homan Chan, PhD; Ryan Kruger, PhD; David Millan, PhD; Steve Bellon, PhD; Sam Agresta, MD; Carl Decicco, PhD; Salih Topal, PhD; Hsin-Jung Wu, PhD
Foghorn Therapeutics, Cambridge, Massachusetts, UNITED STATES

Objective: Synovial sarcoma (SS) is a malignant soft tissue sarcoma with a poor prognosis due to high rates of local recurrence and metastasis. Standard treatment of primary SS involves surgical resection ± radiotherapy ± (neo-)adjuvant chemotherapy. Despite achieving excellent local control with these interventions, more than half of patients go on to develop metastatic disease, typically more than 5 years after initial diagnosis. Once SS metastasizes (~80% to the lungs), prognosis is poor, with median overall survival ranging from 7 to 37 months and 5-year overall survival rate estimated at just 50-60%. Options are limited once disease escapes from standard treatment regimens. The poor prognosis, inadequate impact of current systemic treatments on survival outcomes, and the young age of the patient population clearly render SS an area of significant unmet medical need. Thus, we set out to discover and develop a novel targeted therapy, FHD-609, to improve the treatment outcome of synovial sarcoma. A phase 1 study to evaluate FHD-609 in individuals with advanced synovial sarcoma is now underway. Emerging data from this Phase 1 trial will be used for further development of FHD-609 in SS as well as in other cancers with dysregulation of chromatin remodeling complexes (CRCs).

Methods: Synovial sarcoma is characterized by the hallmark genetic chromosomal translocation t(X;18)(p11;q11) resulting in production of the fusion oncoprotein SS18-SSX that is incorporated into BAF (BRG1/BRM-associated factors) chromatin remodeler complexes leading to dysregulated function and oncogenesis. Direct targeting of SS18-SSX has not been fruitful due to the lack of druggable small molecule binding pockets. Fortunately, functional genomic and mechanistic studies suggest a unique dependency of synovial sarcoma cells on the chromatin remodeler complex, non-canonical BAF (ncBAF), and specifically, its BRD9 subunit. While small molecule ligands are able to target the bromodomain of BRD9, these inhibitors are not sufficient to abolish ncBAF function. We chose to leverage a targeted protein degradation (TPD) modality by hijacking the ubiquitin-proteasome system to remove the BRD9 protein altogether. TPD molecules typically contain an anchor moiety that binds to the targeted protein (in this case the BRD9 bromodomain), a linker, and a recruiter motif that binds the cereblon E3 ubiquitin ligase complex. BRD9 TPD compounds induce BRD9-TPD-CRBN ternary complex ubiquitination and subject BRD9 to proteasome-dependent protein degradation. A dedicated medicinal chemistry campaign led to the discovery of FHD-609, a BRD9 degrader clinical candidate, which was characterized mechanistically and pharmacologically.

Results: FHD-609 potently and efficiently degrades BRD9 in synovial sarcoma cell lines with degradation potency (DC50) in the range of 0.025-0.10 nM and near complete degradation achieved within 0.5-2 h of degrader treatment. BRD9 degradation induced by FHD-609 is UPS-dependent, as including the proteasome inhibitor, Bortezomib, largely abrogated the BRD9 degradation activity. FHD-609 is highly selective and does not degrade other bromodomain-containing proteins such as BRD7 or BRD4 at concentrations up to 1000-fold over DC50 in SYO-1 synovial sarcoma cells. In a quantitative global proteomic analysis, BRD9 was the only protein whose degradation reached statistical significance ($p=1.05e-05$) with a ~16-fold reduction in protein levels following treatment with FHD-609 at the concentrations of 200- or 1000-fold over the DC50 in SYO-1 cells. Potent BRD9 degradation activity translated into strong anti-tumor effect in SYO-1, ASKA, and HS-SY-II synovial cell lines in colony formation assays (IC50 ~0.3-0.6 nM). FHD-609 showed a dose- and time-dependent profile of modulation of BRD9 protein levels in a SYO-1 xenograft model. This pharmacodynamic (PD) effect was durable, allowing for optimal anti-tumor efficacy without the need for daily drug administration. Tumor growth inhibition (TGI) of 91.9% and 92.4% was observed with twice weekly (BIW) dosing of 1 mg/kg FHD-609 in SYO-1 and ASKA synovial sarcoma xenograft models, respectively.

Conclusion: We have discovered and advanced to the clinic a potent, selective, and efficient BRD9 degrader, FHD-609. This drug candidate possesses suitable drug like properties and potently degrades BRD9, which translates into strong anti-tumor

activity in synovial sarcoma cell lines. FHD-609 has a durable PD profile and shows strong efficacy as mono-agent therapy in synovial sarcoma xenograft models with an intermittent (BIW) administration and compares favorably to standard-of-cares, such as ifosfamide or pazopanib, that were tested in the same models. Taken together, our data demonstrates that FHD-609 is a promising drug candidate and supports its progression into Phase I clinical trials for advanced synovial sarcoma patients and other cancers with dysregulated CRCs.



ctos®

2021 *Virtual* Annual Meeting

Poster Presentations

Poster Session 2



Poster #239 #1819049

EXTRASKELETAL MYXOID CHONDROSARCOMA: A RETROSPECTIVE CLINICOPATHOLOGIC STUDY OF 15 CASES

Linus Lee, BE¹; Pavan Kottamasu, MS¹; Michael P. Fice, MD¹; Matthew Cohn, MD¹; Charles A. Gusho, BS²; Steven Gitelis, MD¹; Alan T. Blank, MD, MS¹

¹Rush University Medical Center, Chicago, Illinois, UNITED STATES, ²Rush University Medical Center, Milwaukee, Wisconsin, UNITED STATES

Objective: Extraskeletal myxoid chondrosarcoma (EMC) is a rare malignant soft tissue sarcoma (STS) that accounts for less than 30% of all soft tissue tumors. The conventional treatment for primary EMC is wide local excision with or without radiation therapy, but the available literature guiding treatment management is limited due to tumor rarity. Here we describe our treatment outcomes for 15 patients evaluated at our institution and provide a review of the current literature.

Methods: This study was a retrospective review of all EMC cases treated within a single institution between 1992 and 2019. Histologic review of resected specimens was conducted by a trained musculoskeletal pathologist and fluorescence in situ hybridization (FISH) was used to identify gene rearrangement. Continuous and categorical data were analyzed using descriptive statistics and overall survival (OS) and disease specific survival (DSS) were defined using Kaplan-Meier analysis.

Results: Fifteen patients were evaluated, including 11 males and 4 females. The average age at time of presentation was 51.7 ± 20.4 years and the mean follow-up time was 61.5 months (range, 5-286 months). Fourteen patients (93.3%) presented with disease of the extremity and one patient (6.7%) presented with axial disease. The average resected tumor size at largest dimension was 7.14cm (range, 2.4-18.7). Twelve of fifteen (80%) patients underwent wide local excision, and nine of these twelve (75%) patients underwent local radiation therapy. The 1-, 5-, and 10-year OS in our cohort was 80% (95% CI, 59.8-100), 72% (95% CI, 48.5-95.5), and 72% (95% CI, 48.5-95.5). The 1-, 5-, and 10-year DSS for this cohort was 92.3% (95% CI, 77.8-100), 83.1% (95% CI, 61.5-100), and 83.1% (95% CI, 61.5-100). At time of last follow-up eleven patients were alive and ten (90.9%) were disease free.

Conclusion: EMC is a very rare soft tissue sarcoma most often seen in males and in the extremities. Our cohort was too small to provide meaningful statistical analysis however, we observed lower rates of local recurrence in patients treated with radiation.

Table 1 – Patients with EMC who received surgical resection

Patient #	Primary Site	Size of Tissue Resected (cm), largest dimension	Stage (based on surgical pathology)	Location of Metastasis (if any)	Chemotherapy	Radiation Cumulative Dose (adjuvant)	Outcome After Resection	Time (months)
1	Buttocks	N/A	1	Colon	5-FU	None	Alive	3
2	Thigh	14.8	N/A	N/A	None	None	Alive	42
3	Finger	0.3	N/A	Lung, lymph nodes	None	None		2
4	Thigh	23.1	3	N/A	Doxorubicin, ifosfamide, mesna	None	Alive	90
5	Arm	6.5	3	N/A	Vincristine, doxorubicin, cyclophosphamide	None	Alive	5
6	Thigh	4.9	N/A	N/A	None	None	Alive	4
7	Forearm	2.4	4	N/A	None	None	Alive	72
8	Shoulder	N/A	3	Lung, brain, pancreas	None	75 gy	Alive	9
9	Thigh	18.7	2	Breast	None	60 gy	Alive	5
10	Chest wall	4.6	N/A	Chest wall	None	None	Alive	84
11	Knee	4.0	2	N/A	None	50 gy	Alive	72
12	Thigh	10.4	2	N/A	None	50 gy	Alive	4
13	Thigh	5.0	2	N/A	None	50 gy	Alive	16
14	Arm	6.5	N/A	N/A	None	None	Alive	14
15	Foot	N/A	N/A	N/A	None	None	Alive	5

Table 2 – Pathological Analyses of EMC Patients

Patient #	Primary Site	+Stains	FISH Analysis	Mitoses	Necrosis
1	Buttocks	N/A	N/A	N/A	N/A
2	Thigh	S100	No EWSR1 gene rearrangement	N/A	N/A
3	Finger	N/A	Break in EWSR1 locus	rare	N/A
4	Thigh	CD99	No EWSR1 gene rearrangement	N/A	N/A
5	Arm	CD99	Negative for FKHR, SYT, and EWSR1 breaks	N/A	N/A
6	Thigh	N/A	EWSR1 gene rearrangement	none	N/A
7	Forearm	Vimentin, CD68	EWSR1 gene rearrangement	40 per 10 hpf	N/A
8	Shoulder	N/A	Negative for EWSR1, 22q12 breaks	10 per 10 hpf	Present
9	Thigh	CD117	NR4A3 gene fusions with EWSR1	N/A	Present
10	Chest wall	S100	N/A	N/A	N/A
11	Knee	S100, CD117	EWSR1 gene rearrangement	none	Absent
12	Thigh	CD117	EWSR1 gene rearrangement	1 per 10 hpf	Present
13	Thigh	N/A	NR4A3 rearrangement	none	Present
14	Arm	Desmin, S100, EMA	breaks in EWSR1 and NR4A3	<1 per 10 hpf	Absent
15	Foot	EMA	breaks in EWSR1 and NR4A3	none	Absent



Poster #240 #1818861

THE POTENTIAL LONG-TERM COMPARATIVE EFFECTIVENESS OF LAROTRECTINIB VS. DOXORUBICIN IN COMBINATION WITH IFOSFAMIDE FOR TREATMENT OF METASTATIC TRK FUSION SOFT TISSUE SARCOMA

Kangho Suh, PharmD, PhD¹; Josh J. Carlson, MPH, PhD²; Fang Xia, PhD³; Todd Williamson, PhD³; Sean D. Sullivan, PhD²,
¹University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES, ²Comparative Health Outcomes, Policy, and Economics (CHOICE) Institute, University of Washington, Seattle, Washington, UNITED STATES, ³Bayer U.S. LLC, Whippany, New Jersey, UNITED STATES

Objective: Soft tissue sarcomas (STS) are challenging to treat as nearly 50% of patients with high-grade STS develop metastases and die from their disease. The standard of care for first-line therapy in metastatic STS is an anthracycline (e.g. doxorubicin) in combination with an alkylating agent (e.g. ifosfamide). Larotrectinib is approved for patients with TRK fusion advanced solid tumors including STS. Our objective was to compare expected life-years (LYs) and quality-adjusted life-years (QALYs) for metastatic TRK fusion STS patients eligible to receive larotrectinib against unknown NTRK gene fusion status patients on doxorubicin in combination with ifosfamide.

Methods: We developed a partitioned survival model to project long-term comparative effectiveness of larotrectinib vs. doxorubicin in combination with ifosfamide. Larotrectinib survival data, assessed by independent review committee, were derived from an updated July 2020 analysis of 23 adult (≥ 18 years of age) metastatic TRK fusion STS patients from the larotrectinib clinical trials program (ClinicalTrials.gov NCT02122913, NCT02637687, and NCT02576431). Gastrointestinal stromal tumor patients were excluded. Survival inputs for doxorubicin in combination with ifosfamide were derived from EORTC 62012, a randomized controlled Phase III clinical trial with patients of unknown NTRK gene fusion status (ClinicalTrials.gov NCT00061984).¹ Progression free (PFS) and overall survival (OS) for both larotrectinib and doxorubicin in combination with ifosfamide were estimated using survival distributions (Exponential, Weibull, Log-logistic, and Log-normal) fit to the available data. Exponential fits were used based on goodness-of-fit and clinical plausibility. QALYs were estimated by adjusting the time spent in the pre progression and post progression health states by health state utilities derived from publicly available literature. In accordance with standard practice in health economics and outcomes research on future health benefits, a constant discount rate of 3% was applied to the LYs and QALYs. Model uncertainty was evaluated using one-way sensitivity analysis and probabilistic sensitivity analysis with 10,000 simulations.

Results: Estimated pre-progression survival for patients treated with larotrectinib was 2.08 LYs (1.03 QALYs) compared to 0.65 LYs (0.30 QALYs) for doxorubicin in combination with ifosfamide (Table 1). In total, larotrectinib resulted in 7.00 LYs and 2.51 QALYs compared to 1.51 LYs and 0.56 QALYs for doxorubicin in combination with ifosfamide. These estimates yielded additional gains of 5.49 LYs and 1.95 QALYs for larotrectinib versus doxorubicin in combination with ifosfamide.

Conclusion: In metastatic STS, larotrectinib may produce substantial life expectancy and quality-adjusted life-year gains compared to doxorubicin in combination with ifosfamide. Additional data with longer follow-up times will further inform this comparison.

References

1. Judson I, Verweij J, Gelderblom H, et al. Doxorubicin alone versus intensified doxorubicin plus ifosfamide for first-line treatment of advanced or metastatic soft-tissue sarcoma: a randomised controlled phase 3 trial. *Lancet Oncol.* 2014;15(4):415-423.

Table 1. Base case comparative effectiveness estimates

	Larotrectinib	Doxorubicin + Ifosfamide
Pre-progression LYs, mean (95% CI)	2.08 (1.23, 3.42)	0.65 (0.57, 0.74)
Post-progression LYs, mean (95% CI)	4.92 (1.05, 9.56)	0.86 (0.64, 1.09)
Total life-years, mean (95% CI)	7.00 (3.33, 11.62)	1.51 (1.30, 1.73)
Pre-progression QALYs, mean (95% CI)	1.03 (0.61, 1.70)	0.30 (0.25, 0.35)
Post-progression QALYs, mean (95% CI)	1.48 (0.32, 2.89)	0.26 (0.19, 0.34)
Total QALYs, mean (95% CI)	2.51 (1.39, 3.95)	0.56 (0.48, 0.64)

CI: credible interval, LY: life-year, QALY: quality-adjusted life-year

Figure 1. Extrapolated progression-free survival

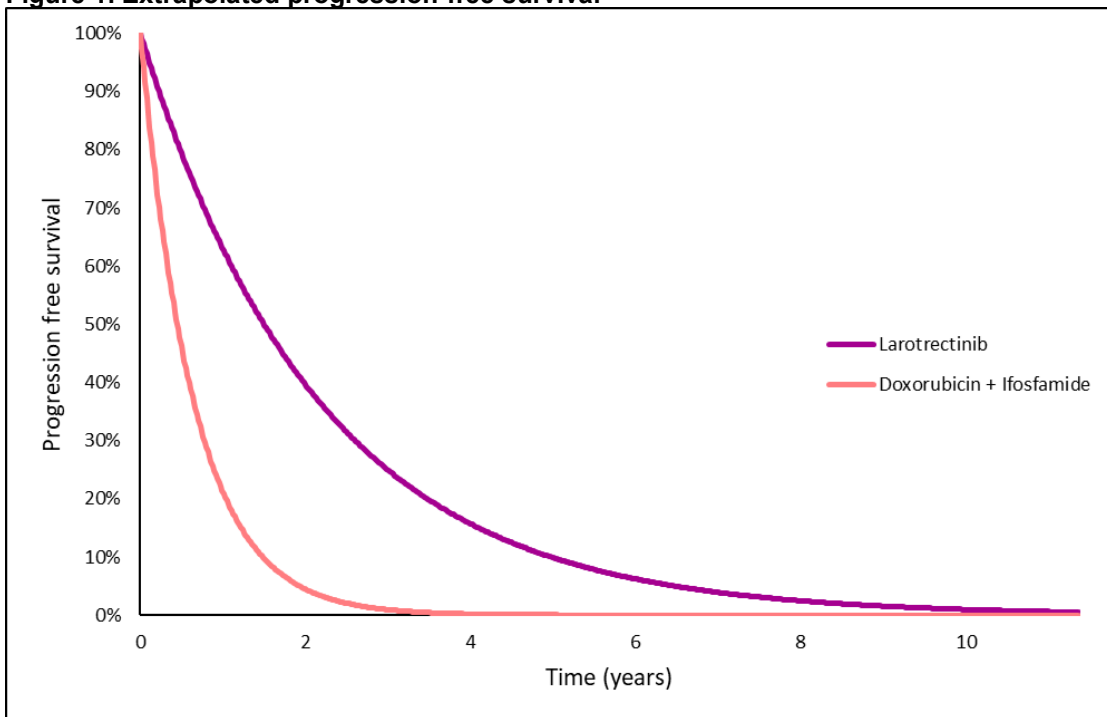
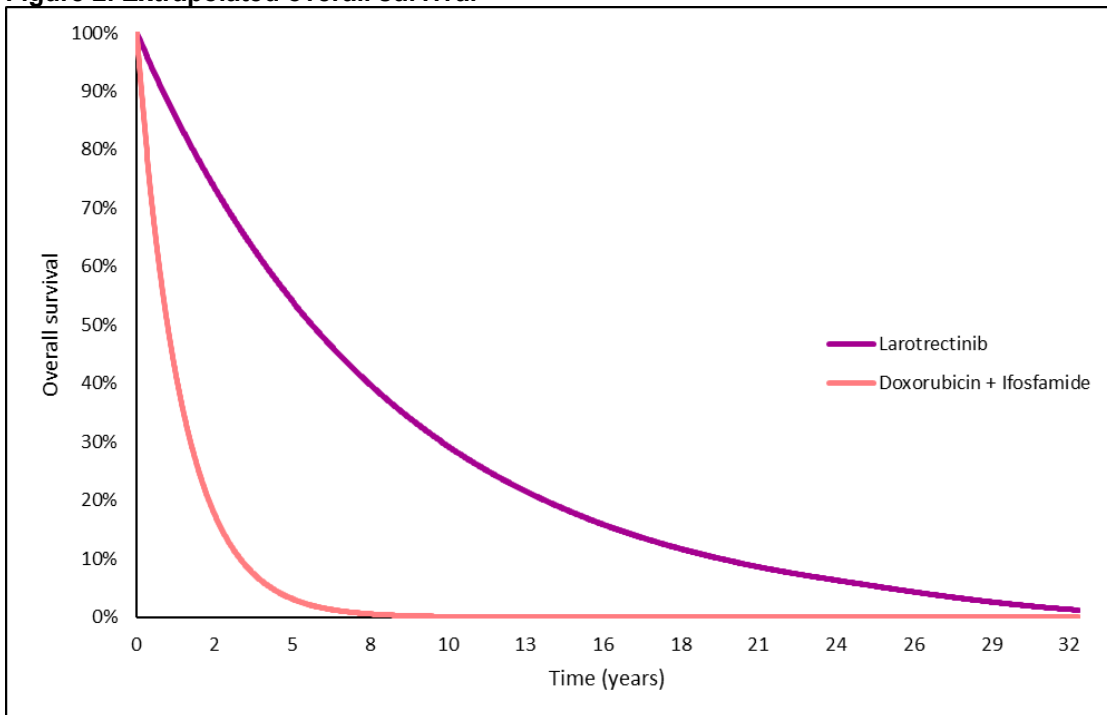


Figure 2. Extrapolated overall survival





Poster #241 #1818904

LAROTRECTINIB IN PEDIATRIC PATIENTS WITH TRK FUSION SARCOMAS: UPDATED EFFICACY AND SAFETY

Catherine M. Albert, MD¹; Stefan Bielack, MD²; Daniel Orbach, MD³; Steven G. DuBois, MD⁴; Noah C. Federman, MD⁵; Birgit Georger, MD, PhD⁶; Leo Mascarenhas, M.D, M.S.⁷; Ramamoorthy Nagasubramanian, MD⁸; Ruihua Xu, MD, PhD⁹; Julia Chisholm, BMBCh, PhD, FRCPC¹⁰; Soledad Gallego Melcon, MD, PhD¹¹; Hiroaki Goto, MD, PhD¹²; Daniel A. Morgenstern, MB BChir, PhD¹³; Cormac Owens, MD¹⁴; Alberto Pappo, MD¹⁵; Sébastien Perreault, MD, FRCPC¹⁶; Johannes Schulte, MD¹⁷; Neerav Shukla, MD¹⁸; Christian Michel Zwaan, MD, PhD¹⁹; Ricarda Norenberg, MS²⁰; Pierre Avis, MD²¹; Esther De La Cuesta, MD, MBA²²; Theodore W. W. Laetsch, MD²³; Cornelis M. van Tilburg, MD, PhD²⁴

¹Seattle Children's Hospital, University of Washington, Fred Hutchinson Cancer Research Center, Seattle, Washington, UNITED STATES, ²Klinikum Stuttgart-Olgahospital, Stuttgart, Baden-Wurtemberg, GERMANY, ³Institut Curie and University of Paris, Paris, Ile-de-France, FRANCE, ⁴Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, Massachusetts, UNITED STATES, ⁵UCLA Medical Center, Los Angeles, California, UNITED STATES, ⁶Gustave Roussy Cancer Center, Université Paris-Saclay, INSERM U1015, Villejuif, Ile-de-France, FRANCE, ⁷Children's Hospital Los Angeles, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES, ⁸Nemours Children's Hospital, Orlando, FL, ⁹Sun Yat-sen University Cancer Center, Guangzhou, Guangdong, CHINA (PEOPLE'S REPUBLIC), ¹⁰Children and Young Peoples Unit, Royal Marsden Hospital, Surrey, England, UNITED KINGDOM, ¹¹Pediatric Oncology and Hematology, Vall d'Hebron Children's Hospital, Barcelona, Catalonia, SPAIN, ¹²Kanagawa Children's Medical Center, Yokohama, Kanagawa, JAPAN, ¹³Hospital for Sick Children, Toronto, Ontario, CANADA, ¹⁴The National Children's Cancer Centre, Children's Health Ireland, Dublin, Dublin, IRELAND, ¹⁵St. Jude Children's Research Hospital, Memphis, TN, ¹⁶Department of Neurosciences, CHU Sainte Justine, Montreal, Province du Québec, CANADA, ¹⁷Charité-Universitätsmedizin Berlin, Berlin, Berlin, GERMANY, ¹⁸Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES, ¹⁹Prinses Maxima Centrum, Utrecht, Utrecht, NETHERLANDS, ²⁰Chrestos Concept GmbH & Co. KG, Essen, Nordrhein-Westfalen, GERMANY, ²¹Bayer Pharmaceuticals, Lille, Nord-Pas-de-Calais, FRANCE, ²²Bayer HealthCare Pharmaceuticals, Inc., Whippany, New Jersey, UNITED STATES, ²³University of Texas Southwestern Medical Center/Children's Health, Dallas, Texas, UNITED STATES, ²⁴Hopp Children's Cancer Center Heidelberg (KITZ), Heidelberg University Hospital and German Cancer Research Center (DKFZ), Heidelberg, Baden-Wurtemberg, GERMANY

Objective: Neurotrophic tyrosine receptor kinase (NTRK) gene fusions are oncogenic drivers in a diverse range of tumor types, including infantile fibrosarcomas (IFS) and other pediatric sarcomas. Larotrectinib is a first-in-class, highly selective, central nervous system (CNS)-active tropomyosin receptor kinase (TRK) inhibitor approved for the treatment of adult and pediatric patients with TRK fusion cancer, with an objective response rate (ORR) of 75% in 206 evaluable adult and pediatric patients with various non-primary CNS solid tumors (Hong et al, ASCO 2021). Here, we report the updated efficacy and safety of larotrectinib in pediatric patients with TRK fusion sarcomas from an expanded dataset with longer follow-up.

Methods: Pediatric patients (<18 years old) with sarcomas harboring NTRK gene fusions and treated with larotrectinib were identified from two clinical trials (NCT02576431, NCT02637687). Patients received larotrectinib 100 mg/m² (maximum dose of 100 mg) twice daily. Response was investigator assessed per Response Evaluation Criteria In Solid Tumors (RECIST) version 1.1. Data cut-off date was July 20, 2020.

Results: At the data cut-off date, 73 pediatric patients with TRK fusion sarcomas had initiated larotrectinib therapy (Table 1): 44 (60%) had IFS and 29 (40%) had other soft tissue sarcomas (12 spindle cell sarcoma, five not otherwise specified, four inflammatory myofibroblastic tumor, four malignant peripheral nerve sheath tumor, and one each lipofibromatosis, myofibromatosis, myopericytoma, and small round cell sarcoma). Median age at enrollment was 1.6 years (range 0.1–17.8), with 30 (41%) patients <1 year old. Overall, 48 (66%) and 25 (34%) patients had locally advanced and metastatic disease, respectively. Twenty-one (29%) patients were treatment-naïve, 26 (36%) had received 1 prior systemic therapy, and 26 (36%) had received ≥2 prior systemic therapies. ORR for the 71 patients evaluable for efficacy was 89% (95% confidence interval [CI] 79–95), 93% (95% CI 81–99) in patients with IFS, and 81% (95% CI 62–94) in patients with other soft tissue sarcomas (Table 2). Median time to response was 1.8 months (range 0.9–9.1). Median duration of response (DoR), progression-free survival (PFS), and overall survival (OS) were not reached after a median follow-up of 18.6, 19.3, and 19.9 months, respectively. The 24-month rates for DoR, PFS, and OS were 60% (95% CI 43–77), 62% (95% CI 47–77), and 97% (95% CI 92–100), respectively. The 24-month rates for the sarcoma subsets are listed in Table 2. Treatment duration ranged from 0.3+ to

50.6+ months. At data cut-off, 41 (56%) of patients were still on treatment. Eighteen (25%) patients had tumor progression while on therapy, with seven patients continuing larotrectinib post-progression for >28 days. Treatment-related adverse events (TRAEs) occurred in 59 (81%) patients. The most common TRAEs were increased AST, increased ALT, and decreased neutrophil count. Grade 3–4 TRAEs occurred in 21 (29%) patients. Three (4%) patients discontinued treatment due to a TRAE, of which two were Grade 3 (hypoventilation and decreased neutrophil count).

Conclusion: Larotrectinib demonstrated robust and durable responses, extended survival benefit, and a favorable safety profile in pediatric patients with TRK fusion sarcomas, including IFS and other soft tissue sarcomas. These data strongly support testing for NTRK gene fusions in pediatric patients with sarcomas to identify those more likely to benefit from TRK inhibitors.

Table 1: NTRK gene fusions

	IFS (n=44)	Other soft tissue sarcomas (n=29)	All pediatric sarcomas (N=73)
<i>NTRK1</i>	7	21	28
<i>NTRK2</i>	0	3	3
<i>NTRK3</i>	37	5	42
<i>ETV6-NTRK3</i>	35*	5	40
<i>Other</i>	2	0	2

*10 fusions were inferred.
 NGS (n=47), PCR (n=14), FISH (n=10), NanoString (n=1), and Chromosome Microarray (n=1)
 FISH, fluorescence in situ hybridization; IFS, infantile fibrosarcoma; NGS, next generation sequencing; *NTRK*, neurotrophic tyrosine receptor kinase; PCR, polymerase chain reaction.

Table 2: Response to treatment

	IFS (n=44)	Other soft tissue sarcomas (n=29)	All pediatric sarcomas (N=73)
Evaluable patients, n	44	27	71
ORR, % (95% CI)	93 (81–99)	81 (62–94)	89 (79–95)
Best overall response, n (%)			
Complete response	13 (30)*	5 (19)	18 (25)*
Pathological complete response[‡]	6 (14)	3 (11)	9 (13)
Partial response[§]	22 (50)	14 (52)	36 (51)
Stable disease	3 (7)	3 (11)	6 (8)
Progressive disease	0	1 (4)	1 (1)
Not determined	0	1 (4)	1 (1)
24-month DoR rate, % (95% CI)	62 (40–85)	58 (31–84)	60 (43–77)
24-month PFS rate, % (95% CI)	69 (50–88)	51 (27–75)	62 (47–77)
24-month OS rate, % (95% CI)	100 (100–100)	91 (79–100)	97 (92–100)

*Includes 3 patients in the IFS group with complete responses pending confirmation. [‡]Pathological complete response is defined as no pathologic evidence of tumor, negative surgical margins, and no other evidence of disease. [§]Includes 2 patients each in the IFS and soft tissue sarcomas groups with a partial response pending confirmation.
 CI, confidence interval; DoR, duration of response; IFS, infantile fibrosarcoma; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.



Poster #242 #1818947

SARCOMA AS AN EXTRACOLONIC MALIGNANCY OF LYNCH SYNDROME

Steven Bialick, DO, MS¹; Brianna Valdes²; Philippos Costa, MD³; Priscila Barreto Coelho, MD³; Andrea Espejo-Freire, MD³; Gina D'Amato, MD⁴; Emily Jonczak, MD⁵; Aditi Dhir, MD³; Andrew Rosenberg, MD³; Irman Forghani, MD³; Jonathan C. Trent, MD, PhD⁵

¹University of Miami/Sylvester Comprehensive Cancer Center, Miami, Florida, UNITED STATES, ²University of Miami, Miller School of Medicine, Miami, Florida, UNITED STATES, ³University of Miami, Miami, Florida, UNITED STATES,

⁴Medical Oncology, Sylvester Comprehensive Cancer Center/University of Miami, Miami, Florida, UNITED STATES,

⁵Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES

Objective: Lynch syndrome (LS) is an autosomal dominant inherited disorder associated with an increased risk of multiple cancer types – most commonly adenocarcinoma of the colon and endometrium, with an estimated incidence of 1 in 2000 per year. The diagnosis of LS is established when a germline heterozygous pathogenic variant in one of the mismatch repair (MMR) genes (MLH1, MSH2, MSH6, or PMS2) or a deletion of the EPCAM gene is identified. Other cancers associated with LS are all carcinoma including stomach, ovary, liver, kidney, breast, and prostate; however, literature is limited regarding the risk of sarcoma in patients with underlying LS. Sarcomas are rare malignancies of mesenchymal origin with an estimated incidence of 5 per million people annually. Several histological sarcoma subtypes have been shown to arise in the background of well-defined hereditary predisposition syndromes (Li-Fraumeni, Neurofibromatosis Type 1, Hereditary Retinoblastoma, Carney's Triad), but the rarity and vast biological heterogeneity of sarcomas – and that of cancer genetic syndromes – leaves the possible association of sarcoma with a predisposition syndrome overlooked. Our aim is to investigate the prevalence of sarcoma in patients with LS.

Methods: A retrospective chart review identified 57 patients with both a genetic susceptibility to malignant neoplasm and a concomitant soft/connective tissue malignancy between April 2011 and March 2021. Inclusion criteria included a biopsy proven diagnosis of sarcoma and a clinical or molecular diagnosis of LS. Those with non-LS cancer genetic susceptibilities (ie: Li-Fraumeni syndrome, BRCA mutations), non-sarcoma malignancies, or sarcoma diagnoses without institutional pathologic review were excluded from the study. We analyzed patient demographics, tumor characteristics, and clinical outcomes to identify any common factors associating sarcoma with LS. We used a standardized incidence ratio (SIR) with 95% confidence intervals (CI) to interpret whether the association between LS and sarcoma was due to chance alone.

Results: We identified 10 LS patients who developed sarcoma – 9 arising in soft tissue (pleomorphic sarcoma, spindle cell sarcoma, gastrointestinal stromal tumor, angiosarcoma, desmoid fibromatosis) and 1 within bone (osteosarcoma). MLH1 and PMS2 were the most common MMR genes affected, and one patient had deletion (the 3' end) of EPCAM. The median age at diagnosis of this 60% female population was 48 years, ranging 17-72. All patients had at least one first-degree relative with cancer and 50% had a personal history of ≥ 1 additional primary malignancy. Metastatic disease was present at the time of diagnosis in 20% of the patients. Among the 80% with locoregional disease treated with surgical resection, the mean post-operative sarcoma-specific relapse free survival was 20.7 months, ranging 1 month to 9 years. One patient was lost to follow-up, one died (3 years from diagnosis), one remains on immunotherapy and radiation, and 7 are undergoing active surveillance. Given the catchment area of our institution (6.5 million people) and assuming independence, the expected number of patients with both LS and sarcoma is 0.163 between 2011-2021. Our $n=10$, indicating a SIR of 61.5 [95% CI: 29-107]. Thus, the estimated risk of having sarcoma and LS was 61.5 times higher than expected if these events were independent.

Conclusion: Lynch syndrome is a hereditary condition that conveys an increased risk of developing certain cancers; however, sarcomas have not historically been included within the LS phenotype. We identified 10 patients with both sarcoma and LS of varying subtypes. Soft-tissue sarcomas were more common than bone sarcomas and most of these patients presented with sarcoma as their first cancer. Additional research will help highlight any correlations between the two diagnoses. Cancer screening, adequate review of family history, and larger studies to elucidate the potential biologic relationship between LS and sarcoma are warranted.



Poster #243 #1819076

ERCC2 PATHOGENIC VARIANT IDENTIFIED IN EPITHELIOID SARCOMA

Steven Bialick, DO, MS¹; Kurt Statz-Geary²; Emily Jonczak, MD³; Gina D'Amato, MD⁴; Jonathan C. Trent, MD, PhD³; Andrew Rosenberg, MD PhD⁵; Elizabeth Montgomery, MD⁶; Aditi Dhir, MD⁶, ¹University of Miami/Sylvester Comprehensive Cancer Center, Miami, Florida, UNITED STATES, ²University of Miami, Miller School of Medicine, Miami, Florida, UNITED STATES, ³Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES, ⁴Medical Oncology, Sylvester Comprehensive Cancer Center/University of Miami, Miami, Florida, UNITED STATES, ⁵University of Miami, University of Miami, Florida, UNITED STATES, ⁶University of Miami, Miami, Florida, UNITED STATES

Objective: Sarcomas are rare malignancies of mesenchymal origin that develop in bone and soft tissue, comprising roughly 20% of pediatric and 1% of adult cancers. ERCC2 is a gene encoding the Xeroderma Pigmentosum Complementation group D (XPD) protein, which is part of the transcription factor IIH complex involved in the nucleotide excision repair of damaged DNA. Mutations in ERCC2 are classically associated with the UV sensitivity conditions XP and trichothiodystrophy, but have also been reported in approximately 11% of urothelial carcinomas and 2% of solid tumors overall. Pathogenic variant mutations of ERCC2 are extremely rare in sarcomas, detected in less than 0.85% of all soft tissue sarcomas. In a recent large study of monogenic and polygenic determinants of sarcoma risk that included 1162 patients, rare variant burden analysis identified ERCC2 variants in 23 patients with various sarcoma types, suggesting that ERCC2 may be a newly recognized sarcoma susceptibility gene. Of the genes in the analysis, only TP53 had a higher pathogenic variant to total variant burden than ERCC2. There have been studies exploring the effect of ERCC2 mutations on response to cisplatin-based therapy in osteosarcoma, however literature is scant regarding ERCC2 mutations' significance in soft tissue sarcomas. Additionally, the clinical impact of ERCC2 mutations on sarcoma outcomes is not yet known. The primary aim of this report is to describe a pediatric patient with multiply relapsed epithelioid sarcoma, noted to have a pathogenic variant of ERCC2 on molecular profiling of his lung metastasis. This has prompted the authors to further explore the impact of ERCC2 mutations on outcome in patients with soft tissue sarcoma.

Methods: Case description, as below.

Results: A 17-year-old African American male was initially diagnosed in 2018 at an outside institution with an undifferentiated sarcoma, not otherwise specified (NOS) of his left lower extremity. Metastatic bilateral pulmonary and left inguinal lymph node disease was documented at presentation and treatment consisted of ifosfamide/doxorubicin and radiation. The patient then received gemcitabine/docetaxel for disease recurrence for fifteen cycles complicated by bilateral pleural and pericardial effusions. He developed bilateral pulmonary relapse after six-months off therapy, requiring lung metastasectomy at our institution. A diagnosis of metastatic epithelioid sarcoma was made based on hematoxylin and eosin review of the slides, confirmed by keratin expression and loss of SMARCB1/INI1 on immunostaining. Biomarker analysis (Caris Life Sciences®) revealed a pathogenic or likely pathogenic alteration of the ERCC2 gene at Exon 10 (p.Q279, c.835C>T) with a 29% variant frequency. The SMARCB1 gene was not mutated, thereby suggesting an epigenetic silencing of the gene. The patient is currently being treated with Tazemetostat with no notable adverse events. A collaboration with Caris Life Sciences® is underway to identify additional patients with ERCC2-mutated sarcoma to further understand this association as well the role of the DNA damage response pathway in soft tissue sarcomas.

Conclusion: Although the association of ERCC2 mutations with carcinoma is well established, there are few data on the incidence and significance of ERCC2 mutations in soft tissue sarcomas. This case demonstrates the presence of an ERCC2 mutation in a pediatric patient with metastatic epithelioid sarcoma, warranting further study of the role of this gene in sarcoma biology and treatment.



Poster #244 #1818905

TRK FUSION SARCOMAS IN LAROTRECTINIB TRIALS: CONCORDANCE OF INDEPENDENT AND LOCAL DIAGNOSIS

Jessica L. Davis, MD¹; Alexander Lazar, MD, PhD²; Ricarda Norenberg, MS³; Marc Fellous, MD⁴; David S. Hong, MD²; Theodore W. W. Laetsch, MD⁵; Alexander Drilon, MD⁶; Angelo Paolo Dei Tos, MD⁷

¹Oregon Health & Science University, Portland, Oregon, UNITED STATES, ²The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ³Chrestos Concept GmbH & Co. KG, Essen, Nordrhein-Westfalen, GERMANY, ⁴Bayer HealthCare Pharmaceuticals, Basel, Basel-Stadt, SWITZERLAND, ⁵University of Texas Southwestern Medical Center/Children's Health, Dallas, Texas, UNITED STATES, ⁶Memorial Sloan Kettering Cancer Center, New York, New York, UNITED STATES, USA and Weill Cornell Medical College, New York, New York, UNITED STATES, ⁷Università di Padova (UniPD), Padova, Veneto, ITALY

Objective: Neurotrophic tyrosine receptor kinase (NTRK) gene fusions are oncogenic drivers in a diverse range of tumor types. NTRK gene fusions are present in 70–90% of infantile fibrosarcomas (IFS) and have also been detected in other sarcomas at lower frequencies. Larotrectinib is a first-in-class, highly selective, central nervous system-active tropomyosin receptor kinase (TRK) inhibitor approved in over 40 countries for patients with TRK fusion cancer, with an objective response rate (ORR) of 75% in 206 evaluable patients (Hong et al, ASCO 2021). Here we report an ad hoc analysis comparing independently reviewed histological diagnosis versus local assessment for the subset of patients with sarcoma from larotrectinib trials.

Methods: Patients with locally assessed TRK fusion sarcoma with available digitized hematoxylin and eosin (H&E) slides were identified from three larotrectinib clinical trials (NCT02122913, NCT02576431, NCT02637687). Images of H&E stained slides of formalin-fixed paraffin-embedded tissue were evaluated by a panel of three expert soft tissue pathologists. The independent histological classification resulted from a consensus diagnosis by the panel. The expert panel was provided patient age, location of tumor, and H&E slides only; all other information was blinded including immunohistochemistry (IHC) staining profiles. Concordance in histological diagnosis of sarcoma between local and independent pathology review was then evaluated using two ratings. The first analysis was scored 'Yes' vs 'Plausible or No'. The second analysis was scored 'Yes + Plausible' vs 'No'. Plausible indicates that without the benefit of specific IHC stained images, the independent review result could be concordant with the local pathology report. Responses assessed by investigators per Response Evaluation Criteria In Solid Tumors Version 1.1 (RECIST v1.1) were reported by independent histological grouping. Data cut-off: July 20, 2020.

Results: At the data cut-off, 64 patients (age range 0.1–61 years old) with TRK fusion sarcomas treated with larotrectinib were included. Independent assessment could not be performed in five patient samples due to technical issues. The concordance analysis was based on the remaining 59 patients. The concordance between local and independent histological diagnosis, by the two different ratings, was 95.8% for IFS, 45.2–51.6% for other soft tissue sarcomas and 0–75.0% for gastrointestinal stromal tumor (Table 1). The overall concordance rate was 62.7% ('Yes' vs 'Plausible or No') and 71.2% ('Yes + Plausible' vs 'No'). Per independent pathology review, 34 patients had IFS, 14 had unclassified spindle cell sarcoma (USC), four had low-grade NTRK sarcoma, four had unclassified epithelioid sarcoma, and three had inflammatory myofibroblastic tumors. Based on the independent pathology assessment, the ORR was 94% (95% confidence interval [CI] 80–99) in patients with IFS (n=24) and 100% (95% CI 77–100) in patients with USC (n=14). PFS rate at 24 months was 77% (95% CI 60–94) for IFS and 61% (95% CI 34–88) for USC (Table 2).

Conclusion: For patients with TRK fusion sarcoma, agreement between the independent and local pathologists was high for IFS and approximately 50% for other soft tissue sarcomas, although only H&E digitalized slides were provided for independent assessment. Nonetheless, response rates to larotrectinib were high across all independent histologic subsets of soft tissue sarcoma. Further studies are warranted to better identify the sarcoma subsets which are more likely to harbor NTRK gene fusions.

Table 1: Concordance rate by tumor type

	GIST (N=4)	IFS (N=24)	Other soft tissue sarcoma (N=31)	Overall (N=59)
'Yes' vs 'Plausible + No', n (%)	0	23 (95.8)	14 (45.2)	37 (62.7)
'Yes + Plausible' vs 'No', n (%)	3 (75.0)	23 (95.8)	16 (51.6)	42 (71.2)
Five patients with centrally undefined sarcoma were excluded from the analysis. GIST, gastrointestinal stromal tumor; IFS, infantile fibrosarcoma.				

Table 2: Response to treatment#

	IFS N=34	IMT N=3	LG <i>NTRK</i> N=4	USC N=14	UE N=4	UC N=5	Total N=64
ORR, % (95% CI)	94 (80–99)	67 (9–99)	50 (7–93)	100 (77–100)	75 (19–99)	100 (48–100)	91 (81–96)
Best overall response, n (%)							
Complete response	10 (29)*	0	2 (50)	4 (29)	1 (25)	0	17 (27)
Surgical complete response	6 (18)	0	0	0	0	0	6 (9)
Partial response	16 (47)	2 (67)	0	10 (71)	2 (50)	5 (100)	35 (55)
Stable disease	1 (3)	1 (33)	1 (25)	0	1 (25)	0	4 (6)
Progressive disease	1 (3)	0	1 (25)	0	0	0	2 (3)
12-month PFS, % (95% CI)	87 (74–99)	0	50 (1–99)	86 (67–100)	50 (1–99)	75 (33–100)	77 (67–88)
24-month PFS, % (95% CI)	77 (60–94)	0	50 (1–99)	61 (34–88)	50 (1–99)	NE	67 (54–79)

#Histology based on independent review. *Includes two patients in the IFS group with a complete response pending confirmation. CI, confidence interval; IFS, infantile fibrosarcoma; IMT, inflammatory myofibroblastic tumor; LG, low-grade; NE, not estimable; *NTRK*, neurotrophic tyrosine receptor kinase; ORR, objective response rate; PFS, progression-free survival; UC, undefined centrally; UE, unclassified epithelioid; USC, unspecified spindle cell.



Poster #245 #1818958

ROLE OF PREOPERATIVE RADIOTHERAPY IN THE CURATIVE MANAGEMENT OF ABDOMINAL SOLITARY FIBROUS TUMOUR

Karineh Kazazian, MD, PhD, FRCSC¹; Harini Suraweera, MSc²; Deanna Ng, MD³; Peter Chung, MD⁴; Charles Catton, MD, FRCPC⁴; David Shultz, MD, PhD⁵; Philip Wong, MD, MSc, MDCM, FRCPC⁴; Rebecca A. Gladdy, MD, PhD, FRCSC, FACS²; Savtaj Brar, MD, MSc, FRCSC⁶; Elizabeth G. Demicco, MD, PhD⁷; Carol J. Swallow, MD, PhD, FRCSC, FACS²

¹Department of Surgical Oncology, Princess Margaret Hospital, University Health Network and Mount Sinai Hospital; Lunenfeld Tanenbaum Research Institute, Sinai Health System, Toronto, Toronto, Ontario, CANADA, ²Department of Surgical Oncology, Princess Margaret Hospital, University Health Network and Mount Sinai Hospital, Toronto; Lunenfeld Tanenbaum Research Institute, Sinai Health System, Toronto, Toronto, Ontario, CANADA, ³University of Toronto, Toronto, Ontario, CANADA, ⁴Department of Radiation Oncology, Princess Margaret Hospital, University Health Network, Toronto, Toronto, Ontario, CANADA, ⁵Department of Radiation Oncology, Princess Margaret Hospital, University Health Network, University of Toronto, Toronto, Ontario, CANADA, ⁶Department of Surgical Oncology, Princess Margaret Hospital, University Health Network and Mount Sinai Hospital, Toronto, Toronto, Ontario, CANADA, ⁷Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, Toronto, Ontario, CANADA

Objective: The second most common site of extrameningeal solitary fibrous tumour (SFT) is the abdomen/pelvis, where SFT can grow to a large size while remaining largely asymptomatic. Margins of resection that lie in close proximity to important viscera and neurovascular structures may be compromised. For these reasons, preoperative external beam radiotherapy (XRT) can be considered, but its value is unknown. Here we retrospectively investigated the use and impact of preoperative XRT for abdominal SFT.

Methods: Patients managed at our centre between 07/97 and 03/21 for primary SFT of the retroperitoneum, abdominal/pelvic cavity or abdominal wall were identified from a prospectively maintained database. Patients with unresectable disease and/or distant metastases at presentation were excluded. Preoperative XRT was delivered as 50-50.4 Gy in 25-28 fractions. Data were compared using Student's t (continuous variables) and Chi-squared/Fisher's exact (categorical variables) tests using Prism software (GraphPad Software, La Jolla, CA). Progression free survival (PFS) curves were created using the Kaplan–Meier method and compared by Cox proportional hazards analysis.

Results: Of 41 patients with primary abdominal SFT identified in the abdominal sarcoma database, 4 were excluded from further analysis due to metastatic (n=3) or unresectable (n=1) disease at presentation. For the study cohort of 37 patients (18F, 19M), median age was 55 (23-84). The most common anatomical site was intra-abdominal/pelvic (n=23). 12 of 37 patients (32%) had preoperative XRT, with no significant association between this choice of treatment strategy and patient age, sex, tumour site or size (Table). In the group who received preoperative XRT, there were no grossly incomplete (R2) resections, vs. 4/25 (16%) R2 without preoperative XRT. On pathologic evaluation of the resected specimens, preoperative XRT was strongly associated with a lower mitotic index (p=0.0001), as well as a trend towards lower cellularity, compared to the no preop XRT group. Furthermore, the proportion of patients in whom microscopic margins of resection were recorded as clear (R0) was higher (92% vs. 60%, p=0.03, χ^2) with preoperative XRT. In a subset of preoperative XRT patients for whom pretreatment core biopsies were sufficient for analysis, there were trends to lower mitotic index, more necrosis, and decreased cellularity in the resected specimens compared to matched core biopsies. When baseline pre-treatment imaging was compared to preoperative imaging in the patients who received preoperative XRT, a decrease of 3cm in greatest dimension was observed (median 12cm, range 5-17 vs. 9cm, range 4-14; p<0.05, Wilcoxon Signed Rank). No patient received adjuvant XRT. Median follow-up time was 55mos (1-283). Two of 4 patients with R2 resection have died of disease at a median of 11mos post-operatively. Of those who had grossly complete resection of their primary SFT, 3 developed a local recurrence at a median of 28mos after resection: 3/21 in the no XRT group and 0/12 in the preoperative XRT group. PFS at 5yrs was 100% in the preoperative XRT group and 74% in the no XRT group (Figure, p=0.06).

Conclusion: Preoperative XRT has activity in abdominal SFT, as judged by a reduction in radiographic size vs. baseline and lower mitotic index in the resected specimens. Our data further indicate that preoperative XRT may reduce R2 and facilitate R0 resection, potentially improving local control.

Table 1. Clinical and histopathologic characteristics

	Preoperative Radiotherapy			P value
	All (n=37)	NO (n=25)	YES (n=12)	
Median Age, y (range)	55 (23 – 84)	55 (30 – 80)	59 (23 – 84)	0.41
Sex, N(%)				0.08
Male	19 (51)	10 (40)	9 (75)	
Female	18 (49)	15 (60)	3 (25)	
Anatomical site				0.22
Abdomino-Pelvic cavity	23 (62)	16 (64)	7 (59)	
Retroperitoneal	7 (19)	3 (12)	4 (33)	
Abdominal Wall	7 (19)	6 (24)	1 (8)	
Tumour size*, cm median (range)	8.4 (1.2 – 41)	7.9 (0.6 – 41)	8.4 (3.6 – 18.5)	0.86
Mitotic figures/10 HPF*, median (range)	2 (0 – 21)	2 (0 – 21)	0 (0 – 3)	0.0001
Necrosis*				0.23
Present	15 (40)	8 (32)	7 (59)	
Absent	14 (38)	10 (40)	4 (33)	
Unknown	8 (22)	7 (28)	1 (8)	
Cellularity*				0.25
Low	5 (14)	3 (12)	2 (17)	
Moderate	2 (4)	2 (8)	0 (0)	
High	5 (14)	5 (20)	0 (0)	
Unknown/not reported	25 (68)	15 (60)	10 (83)	
Margin status				0.12
R0	26 (70)	15 (60)	11 (92)	
R1	4 (11)	4 (16)	0 (0)	
R2	4 (11)	4 (16)	0 (0)	
Unknown	3 (8)	2 (8)	1 (8)	

*measured on resected specimen

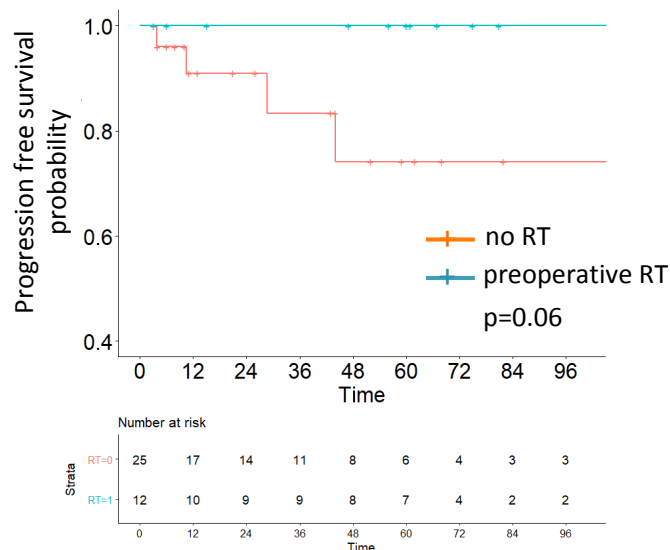


Figure 1. Progression free survival



Poster #246 #1819048

SURGICAL RESECTION OF BORDERLINE AND MALIGNANT PHYLLODES TUMOURS OF THE BREAST: EXPERIENCE AT A TERTIARY CENTRE

Gausihi Sivarajah, MBBS FRACS¹; Charlotte Benson, BMed Sci, FRCR, MD¹; Robin L Jones, MD, PhD²; Shane Zaidi¹; Gerald Gui¹; Nicola Roche¹; Peter Barry¹; Fiona MacNeill¹; Dirk Strauss, MD³; Andrew J. Hayes, PhD³; Myles Smith, PhD³; Aisha Miah¹

¹The Royal Marsden NHS Foundation Trust, London, England, UNITED KINGDOM, ²Royal Marsden NHS Foundation Trust, London, England, UNITED KINGDOM, ³The Royal Marsden Hospital NHS Foundation Trust, London, England, UNITED KINGDOM

Objective: Phyllodes tumours (PT) are a rare fibroepithelial breast neoplasm, characterised by a proliferation of epithelial and stromal elements. Borderline and malignant are considered more aggressive in nature, with local recurrence (LR) and distant metastases (DM) reported as high as 25%. Current NCCN Guidelines recommend local surgical resection with at least a 1cm tumour-free margin as the mainstay of treatment, however this may not be achievable in large tumours. The use of adjuvant radiotherapy is suggested following the same indications as of other soft tissue sarcomas. We present a large series of PT referred to a sarcoma tertiary centre to assess patterns of practice and oncological outcomes.

Methods: 207 patients were retrospectively identified with a borderline and malignant PT diagnosis at a sarcoma institution between 1999 and 2020. Demographics; histopathological details: malignant/borderline, clearance margins; and surgical and radiotherapy treatment were collected. Survival data, including LR and DM, were assessed using the Kaplan-Meier method and Cox regression. Patients referred for a second opinion only were excluded from survival analysis.

Results: Patients presented with a median age of 50 years (17-86). The median tumour size was 5.5 cm (0.9-42), with 15.9% of patients having a tumour >10cm (T3 stage), reflecting late representation. 3 patients had metastatic disease on presentation. 71.0% of patient underwent breast conserving surgery with more than half (53.1%) of these requiring further re-excision for involved or close margins (<5mm). Re-excision (n = 78) either involved further local excision of cavity margins/therapeutic mammoplasty (61.5%), or a mastectomy (34.6%). It should be noted that 71.5% of patients underwent their primary excision (WLE or mastectomy) at a non-sarcoma specialist unit. 19.3% had axillary staging all of which was found to be negative for disease. 18.7% of patients received adjuvant radiotherapy with a median dose 60Gy at 30# and one patient received chemotherapy. The median follow-up was 58 months (3-250) for the 134 patients managed at the tertiary centre, who underwent survival analysis. 20.1% had LR, occurring at a median time of 12 months (2-80). On univariate analysis adjuvant radiotherapy was associated with reduced risk of LR, HR 0.15 (95% CI 0.02-1.13) p<0.05, with older age (>65 years, p<0.05) and positive margins (p < 0.005) associated with higher LR. Margin clearance was not found to be associated with reduced local relapse. All patients who developed LR, with the exception of one who died prior to further treatment, underwent surgical excision with 37.0% receiving radiotherapy. DM was reported in 20.1% of patients; those with lung metastases receiving chemotherapy treated as per the soft tissue sarcoma pathway. 5- and 10-year disease-specific survival (DSS) and overall (OS) was 83.8% vs 82.4% and 74.9% vs 73.6%.

Conclusion: Surgery (breast resection with no axillary staging) remains the standard of care for primary breast borderline and malignant phyllodes tumour. Clearance of 5mm versus 10mm, may be considered an adequate margin, especially in large tumours where resection with >1cm margin is challenging. Adjuvant radiotherapy is not routinely recommended but can potentially reduce LR risk in very select cases. The patterns of care from this series could help guide national guidelines for management and follow up of borderline and malignant PT.



Poster #247 #1818888

VALIDATION OF A NOVEL RISK SCORE TO PREDICT EARLY AND LATE RECURRENCE IN SOLITARY FIBROUS TUMOR

Kjetil Boye, MD, PhD¹; Tatiana Georgiesh, MD¹; Ninna Aggerholm Pedersen, MD, MSc, PhD, Associate professor²; Patrick Schöffski, MD³; Yifan Zhang⁴; Andrea Napolitano, MD, PhD⁵; Judith V.M.G. Bovée, MD PhD⁶; Åse Hjelle, MD⁷; Gordon Tang, MD⁸; Mateusz Spalek, MD, PhD⁹; Margherita Nannini, MD¹⁰; David Swanson, PhD¹; Raf Sciote, MD, PhD¹¹; Asle C. Hesla, MD¹²; Paul Huang, MD, PhD¹³; Desiree Dorleijn, MD⁶; Hans Kristian Haugland, MD, PhD⁷; Maribel Lacambra, MD¹⁴; Jacek Skoczylas, MD⁹; Maria A. A. Pantaleo, MD, PhD¹⁰; Rick L. Haas, MD PhD¹⁵; Anna M. Czarnecka, MD, PhD⁹; Herbert Loong, MBBS, PDipMDPath, MRCP, FRCP Edin, FHKCP, FHKAM(Medicine)¹⁶; Nina L. Jebsen, MD, PhD⁷; Michiel van de Sande, MD PhD⁶; Robin L. Jones, BSc, MBBS, MD¹⁷; Felix Haglund, MD, PhD¹⁸; Iris Timmermans, MD¹⁹; Akmal Safwat, MD, M.Sc., D.M.Sc²⁰; Bodil Bjerkehagen, MD, PhD¹

¹Oslo University Hospital, Oslo, Oslo, NORWAY, ²Aarhus University Hospital, Aarhus, Denmark, Aarhus, Midtjylland, DENMARK, ³General Medical Oncology, University Hospitals Leuven – Campus Gasthuisberg, Leuven, Brabant Wallon, BELGIUM, ⁴Department of Pathology and Cancer Diagnostics, Karolinska University Hospital, Stockholm, Sweden and Department of Oncology-Pathology, Karolinska Institute, Stockholm, Sweden, Solna, Stockholms Lan, SWEDEN, ⁵The Royal Marsden Hospital and The Institute of Cancer Research, London, England, UNITED KINGDOM, ⁶Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ⁷Haukeland University Hospital, Bergen, Hordaland, NORWAY, ⁸Prince of Wales Hospital, Hong Kong SAR, Guangdong, CHINA (PEOPLE'S REPUBLIC), ⁹Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Mazowieckie, POLAND, ¹⁰IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Emilia-Romagna, ITALY, ¹¹Department of Pathology, KU Leuven and University Hospitals Leuven, Leuven, Belgium, Leuven, Vlaams-Brabant, Belgium, ¹²Karolinska University Hospital, Stockholm, Stockholms Lan, SWEDEN, ¹³The Institute of Cancer Research, London, England, UNITED KINGDOM, ¹⁴The Chinese University of Hong Kong, Hong Kong SAR, Guangdong, China (People's Republic), ¹⁵The Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS, ¹⁶The Chinese University of Hong Kong, Hong Kong, HONG KONG, ¹⁷The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, England, UNITED KINGDOM, ¹⁸Department of Pathology and Cancer diagnostics, Karolinska University Hospital, Stockholm, Sweden and Department of Oncology-Pathology, Karolinska Institute, Stockholm, Sweden, Stockholm, Stockholms Lan, SWEDEN, ¹⁹University Hospitals Leuven, Leuven, Vlaams-Brabant, BELGIUM, ²⁰Aarhus University Hospital, Aarhus, Midtjylland, DENMARK

Objective: Solitary fibrous tumor (SFT) is a rare fibroblastic neoplasm characterized by NAB2-STAT6 gene rearrangement. Distant or local recurrence has been reported in 10-30% of localized, extrameningeal SFTs after surgery. Current risk stratification systems have been developed using patient cohorts with short follow-up, and there is a need for prognostic models accounting for both early and late recurrences. We have recently developed a risk model termed G-score based on mitotic count, necrosis and sex, using a cohort with long-term follow-up. The aim of the present study was to validate the G-score in a separate, independent cohort of patients with localized, extrameningeal SFT.

Methods: Data were collected from nine sarcoma reference centers worldwide, as a result of a collaboration formed at the FORTRESS meeting in January 2020. Recurrence-free survival (RFS) was the primary endpoint, and included both distant and local recurrence. Patients without recurrence were censored at the date of last imaging or last clinical follow-up. Survival was estimated using the Kaplan-Meier method and compared using the log-rank test. Survival predictions using G-score were compared with the modified Demicco (mDemicco) score and the SalasOS model, since these were the established risk scores with best performance in our previous study. Kaplan-Meier survival curves and the concordance index (C-index) were used to compare models.

Results: The validation cohort comprised 316 patients. Of these, 288 patients underwent primary surgery and had available follow-up data and were included in the analysis. Median follow-up was 64 months. Ninety-six patients (33.3%) experienced disease recurrence. Local recurrence was the first event in 39 (13.5%), distant metastasis in 43 (14.9%) and combined local and distant recurrence in 14 patients (4.9%). Median time to recurrence was 40 months. Estimated 5- and 10-year RFS was 72% and 50%, respectively, indicating that patients were still at risk of recurrence after 10 years of follow-up (Figure 1A). Data to calculate the G-score were available for 211 patients. Forty-nine patients (23.2%) were classified as low, 90 (42.7%)

as intermediate and 72 (34.1%) as high risk. 10-year RFS was 82% in the low risk group, 50% in intermediate risk and 32% in high risk (Figure 1B; $P < 0.0001$, log-rank test). 10-year RFS using the mDemicco score was 72% for low, 51% for intermediate and 8% for high risk. Using the SalasOS model 10-year RFS was 68% for low, 59% for intermediate and 16% for high risk. The C-index was 0.691 for G-score, 0.748 for mDemicco and 0.670 for SalasOS.

Conclusion: In this large, international cohort of patients with localized, extrameningeal SFTs we demonstrate that late recurrences are common, and that patients are still at risk of recurrence up to 10 years after surgery. G-score was validated as a predictor of early and late recurrence and found to be superior compared to other models to predict patients at low risk of relapse, whereas the mDemicco and SalasOS models performed better to identify patients at high recurrence risk. A less intensive follow-up schedule could be considered for patients at low recurrence risk according to G-score.

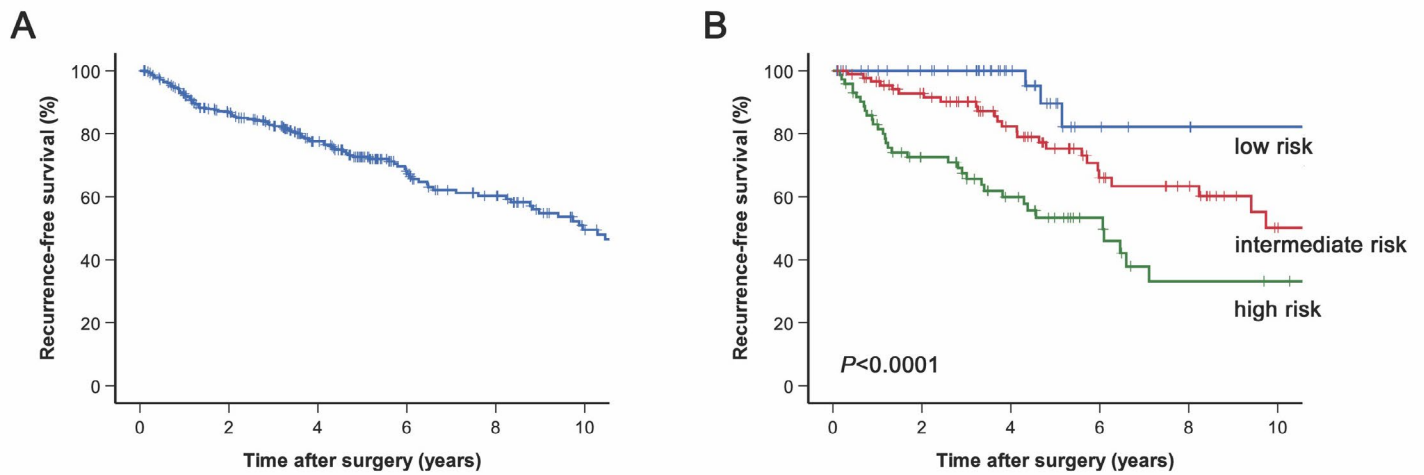


Figure 1. Kaplan-Meier survival curves showing recurrence-free survival. (A) The total study cohort. (B) Stratified by G-score.



Poster #248 #1818964

ACTIVITY OF STANDARD SOFT TISSUE SARCOMA-TYPE SYSTEMIC THERAPY IN CLEAR CELL SARCOMA (CCS): A RETROSPECTIVE INTERNATIONAL SERIES FROM THE WORLD SARCOMA NETWORK (WSN)

Alannah Smrke, MD¹; Anna Maria Frezza, MD²; Claudia Giani, MD³; Neeta Somaiah, MD⁴; Mehdi Brahmi, MD PhD⁵; Anna M. Czarnecka, MD⁶; Piotr Rutkowski, MD, PhD⁷; Winette T. A. van der Graaf, MD PhD⁸; Giacomo Giulio Baldi, MD⁹; Elizabeth Connolly, MBChB MCRPUK FRACP¹⁰; Florence Duffaud, MD¹¹; Hans Gelderblom, MD, PhD¹²; Vivek Bhadri, MD¹³; Peter Grimison, BSc(Med) MBBS(Hons) MPH PhD FRACP¹⁴; Annabelle Mahar, MD¹³; Silvia Stacchiotti, MD²; Robin L. Jones, BSc, MBBS, MD¹⁵

¹BC Cancer, Vancouver, British Columbia, CANADA, ²Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY, ³Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY, ⁴The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁵Cancer Research Centre of Lyon, Lyon, Auvergne, FRANCE, ⁶Maria Sklodowska-Curie National Research Institute of Oncology, Warszawa, Mazowieckie, POLAND, ⁷Department of Soft Tissue/Bone Sarcoma and Melanoma; Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Mazowieckie, POLAND, ⁸Netherlands Cancer Institute, Amsterdam, Noord-Holland, NETHERLANDS, ⁹Department of Medical Oncology, Hospital of Prato, Prato, Italy, Prato, Toscana, ITALY, ¹⁰ProCan®, Children's Medical Research Institute, Faculty of Medicine and Health, The University of Sydney, Chris O'Brien Lifecare Hospital, Sydney, Camperdown, New South Wales, AUSTRALIA, ¹¹Marseille University Hospital Timone, Marseille, Languedoc-Roussillon, FRANCE, ¹²Leiden University Medical Center, Leiden, Zuid-Holland, NETHERLANDS, ¹³Chris O'Brien Lifecare, Camperdown, New South Wales, AUSTRALIA, ¹⁴Chris O'Brien Lifecare, Sydney, New South Wales, AUSTRALIA, ¹⁵The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, England, UNITED KINGDOM

Objective: CCS is an aggressive malignancy with a high incidence of metastases and very poor prognosis. There are very few studies of the efficacy of systemic therapy in CCS. Prospective trials of MET inhibitors, such as crizotinib and tivantinib, have increased our knowledge of this ultra-rare translocated sarcoma type, but there remains a huge unmet medical need. We report on a multi-institutional retrospective study of the outcomes of patients with advanced CCS treated with systemic therapy within the WSN.

Methods: Institutional ethics approval (RMH-SE1020) was obtained prior to study commencement. Patients treated with systemic therapy starting from June 1985 to May 2021 for a diagnosis of locally advanced or metastatic CCS with molecular confirmation of: EWSR1-ATF1, EWSR1-CREB1 or EWSR1 fusion with an unknown partner were included. Baseline demographics and treatment information including response by Response Evaluation Criteria in Solid Tumours (RECIST) 1.1 retrospectively collected by local investigators. Median progression-free survival (mPFS) and overall survival (mOS) were calculated using the Kaplan Meier method. Statistical analyses were performed using SPSS Version 27.

Results: Fifty-five patients from 10 institutions were included. Median follow up was 20.5 months (range 1-334). Median age at diagnosis was 39 (15-73) years, with 49% (n=27/55) female, 47% Caucasian. Most primary tumours were at aponeurosis (n=9/55, 16%) or non-aponeurosis limb sites (n=17/55, 31%). The most common metastatic sites were lung (n=26/55, 47%) and bone (n=20/55, 36%). Thirteen (24%) patients presented with metastatic disease; 42 (76%) patients developed metastatic disease at a median of 15 (range 0-171) months (m) after initial diagnosis. More tumours harboured an EWSR1-ATF1 fusion (n=24/55, 44%), than EWSR1-CREB1 (n=11/55, 20%) or EWSR1 with an unknown fusion partner (n=20/55, 36%). Median number of systemic therapies was 1 (range 1-7). Thirty-four patients were treated with doxorubicin-based therapy, with a RECIST 1.1 response rate (RR) of 12% (n=4/34), mPFS of 3m (95% CI 0.9-4); thirteen received gemcitabine-based with RR 15% (n=2/13), mPFS 3m (95% CI 1.2-4.8); ten had sunitinib with RR 30% (n=3/10), mPFS 4m (95% CI 1.2-6.8-5.6). The response rate to the following treatments was 0%; dacarbazine (n=0/9, mPFS 2m 95%CI NA), pazopanib (n=0/16, mPFS 1m 95% CI 0-2.4), crizotinib (n=0/5, mPFS 2m 95%CI 0.9-3.1), checkpoint inhibitor (n=0/5, mPFS 2m 95%CI 0-5.9), trabectedin (n=0/7, mPFS 1m 95% CI 0-3.6), ifosfamide (n=0/5, mPFS 1 month 95% CI NA). The mOS for patients with advanced/metastatic disease was 15 months (95%CI 3-27).

Conclusion: This is the largest retrospective study of systemic therapy in CCS. Systemic therapy has limited benefit in advanced CCS, with low RRs and short mPFS. Access to early clinical trial enrollment remains key for patients with CCS. International, multi-centre prospective translational studies are required to identify new treatments for this ultra-rare subtype.



Poster #249 #1819024

LURBINECTEDIN INHIBITS THE EWS-WT1 TRANSCRIPTION FACTOR IN DESMOPLASTIC SMALL ROUND CELL TUMOR

Jenna M. Gedminas, MD¹; Rebecca Kaufman, MS²; Elissa Boguslawski¹; Amy Gross³; Marie Adams, MS⁴; Ian Beddows, PhD⁴; Ryan D. Roberts, MD, PhD⁵; Patrick Grohar, MD, PhD⁶

¹Division of Oncology, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, UNITED STATES,

²Childrens Hospital of Philadelphia, Philadelphia, Pennsylvania, UNITED STATES, ³Center for Childhood Cancer,

Nationwide Children's Hospital, The Ohio State University James Comprehensive Cancer Center, Columbus, Ohio,

UNITED STATES, ⁴Van Andel Research Institute, Grand Rapids, Michigan, UNITED STATES, ⁵Nationwide Children's

Hospital, Columbus, Ohio, UNITED STATES, ⁶Division of Oncology, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, UNITED STATES

Objective: DSRCT is a rare pediatric sarcoma with a poor overall survival. This tumor is absolutely dependent on the continued expression and activity of its defining molecular lesion, the EWS-WT1 transcription factor. Unfortunately, the therapeutic targeting of transcription factors is challenging and there is a critical need to identify compounds that inhibit EWS-WT1. In this report we establish the compound lurbinectedin a bona fide inhibitor of EWS-WT1 and candidate for clinical translation for a disease with no effective therapeutic options.

Methods: We use qPCR and western blot to demonstrate the effect of the drug on expression of both EWS-WT1 and its downstream targets. We then use RNA sequencing to characterize the effects on the EWS-WT1 gene signature genome wide. We link these effects to the mechanism of action using confocal microscopy. We determine the consequence of drug exposure on EWS-WT1 binding using chromatin immunoprecipitation sequencing. Finally, we demonstrate the effects on viability both in vitro with cell viability assays and in vivo using xenograft models.

Results: Lurbinectedin inhibits the EWS-WT1 transcription factor by redistributing the protein within the nucleus to the nucleolus. This nucleolar redistribution interferes with the activity and ultimately the expression of EWS-WT1 to reverse expression over 70% of the EWS-WT1 transcriptome. These effects block the oncogenic phenotype and inhibit proliferation at the lowest GI50 ever reported for this compound in any cell type. This translates into the in vivo setting to cause tumor regressions in multiple mice in two different xenograft models.

Conclusion: The effects of lurbinectedin in DSRCT occur at concentrations that are easily achievable in the clinic. This data establishes lurbinectedin as a promising clinical candidate for DSRCT. Importantly, this mechanism of nucleolar redistribution is also seen with wild-type EWSR1 and the related fusion protein EWS-FLI1. This provides evidence for a "class effect" for the more than 18 tumors driven by EWSR1 fusion proteins. Further, it suggests that one approach to target oncogenic fusion proteins is to activate and exploit wild-type functions of one of the fusion protein partners. Most importantly, the data establishes lurbinectedin as a promising clinical candidate for DSRCT.



Poster #250 #1818945

ACTIVITY OF PAN-RAF INHIBITOR DAY101 IN A PEDIATRIC PATIENT WITH A RECURRENT SPINDLE CELL SARCOMA HARBORING A NOVEL SNX8:BRFV GENE FUSION

Katharine Offer, MD¹; Michael McGuire, MD²; Eleni Venetsanakos, PhD³; Samuel C. Blackman, MD, PhD³; Kunchang Song, MD⁴; Michael Goldfischer, MD⁴; Michael C. Cox, PharmD³

¹Joseph M. Sanzari Children's Hospital, Hackensack Meridian Health, Hackensack, New Jersey, UNITED STATES,

²Department of Radiology, Hackensack Meridian School of Medicine, Hackensack, New Jersey, UNITED STATES,

³Day One Biopharmaceuticals, South San Francisco, California, UNITED STATES, ⁴Department of Pathology, Hackensack Meridian Health, Hackensack, New Jersey, UNITED STATES

Objective: Genomic alterations and dysregulation of the MAPK pathway including BRAF fusions, point mutations and in-frame deletions have been described in many different types of pediatric and adult malignancies. BRAF fusions and mutations have recently been reported in mesenchymal tumors with infantile fibrosarcoma (IFS)-like morphology (Penning et al., *Modern Path* 2021). DAY101 is an oral, highly selective, CNS-penetrant, type II panRAF inhibitor that is being developed for cancers harboring an activating BRAF alteration. In an ongoing pediatric phase 1 study, DAY101 was well tolerated and induced rapid, durable responses in 5 of 8 pediatric patients (3 PRs and 2 CRs, based on RANO criteria) with low-grade glioma harboring a BRAF or CRAF fusion (Wright et al., *SNO* 2020). We explored whether DAY101 might be an effective treatment option for a child with recurrent spindle cell sarcoma harboring a novel SNX8:BRFV gene fusion who had exhausted all treatment options including trametinib, a MEK inhibitor.

Methods: A male patient, aged 5 years, presented in January 2019 with a 1-week history of fever, cough and respiratory distress. Following worsening shortness of breath and tachypnea, MRI confirmed an 11.2 x 9.4 x 11.9 cm dominant right lower hemithorax mass partially encasing the aorta, and likely arising from the posterior mediastinum. Biopsy of the mediastinal mass revealed a diagnosis of spindle cell sarcoma and FISH analysis indicated the presence of a BRAF fusion. He was treated with 3 cycles of ifosfamide, doxorubicin and dexrazoxane. In April 2019, he underwent a right thoracotomy with subtotal resection of the right chest mass leaving a 2.1 x 2.7 cm residual soft tissue mass. Whole exome sequencing of the tumor revealed a novel SNX8:BRFV fusion. The patient was consequently started on the MEK inhibitor trametinib in May 2019. Following the first month of treatment there was a decrease in size of residual tumor and hypervascularity resolved. CT was repeated 2 months later and showed no evidence of measurable tumor at the primary site. However, CT in January 2021 showed a new recurrence of a 4.0 x 3.7 x 4.6 cm left posterior mediastinal mass extending circumferentially around the aorta and impressing on the left atrium and pulmonary veins as well as abutting the T7-T8 disc space. Pending molecular test results, which again identified the SNX8:BRFV fusion, the patient started gemcitabine and docetaxel as second-line therapy for recurrent disease. Following 2 cycles, there was no objective response on imaging and symptoms persisted. Given the novel nature of the BRAF fusion, the patient was not considered eligible for an ERK inhibitor on a clinical trial. The pan-RAF inhibitor DAY101 was subsequently initiated at 420 mg/m², administered once weekly, in 28-day cycles on a compassionate use basis.

Results: Following 2 cycles of DAY101, symptoms had resolved, and MRI showed no evidence of measurable disease at the site of previously visualized tumor and only a trace amount of non-enhancing soft tissue surrounding the descending thoracic aorta. The patient developed grade 2 rash after the first dose of DAY101, which resolved in 1 day after a dose of diphenhydramine. He continues treatment on DAY101 and follow-up is ongoing.

Conclusion: Tumors with IFS-like morphology need to undergo comprehensive genomic profiling to identify novel oncogenic fusions. DAY101 is potentially an effective treatment in pediatric patients with soft tissue sarcomas harboring BRAF fusions and warrants further investigation in other BRAF fusion-driven solid tumors.



Poster #251 #1818916

BCOR ALTERED SOFT TISSUE SARCOMAS

Sarah Whittle, MD, MS; Rajkumar Venkatramani, MD
Baylor College of Medicine, Houston, Texas, UNITED STATES

Objective: BCOR altered sarcomas are a heterogeneous group of tumors characterized by recurring genomic alterations involving the BCOR gene. These alterations include internal tandem duplications (ITD) in BCOR as well as recurring fusions with CCNB3, ZC3H7B, and other rare fusion partners. With widespread use of genomic testing, recognition of these alterations are now commonly associated with diagnoses such as Ewing-like sarcoma (BCOR-CCNB3), clear cell sarcoma of the kidney (BCOR-ITD) and high grade endometrial stromal sarcoma (ZC3H7B-BCOR). We sought to summarize the available literature on soft tissue BCOR altered sarcomas.

Methods: A PubMed search was performed using the keywords "Sarcoma (AND) BCOR". Publications that described clinical information regarding one or more of tumor location, size, treatment, and outcome were included. Papers that described pathologic findings only without clinical data were not included. Demographic information including age, sex, tumor location, tumor size, presence of metastatic disease was collected as well as treatment data related to surgical resection, chemotherapy and radiation therapy and outcome data including relapse, death, follow up time, and survival time. BCOR altered soft tissue sarcomas were included, and bone and brain primary tumors excluded. Summary statistics and outcome data were calculated using STATA v12.1.

Results: Thirty-eight publications met criteria for inclusion. These publications described 161 patients with BCOR altered soft tissue sarcomas. BCOR-CCNB3 fusion was the most common alteration (46.5%), followed by BCOR ITD (41.6%), ZCH3H7B-BCOR fusion (8%), and other BCOR alterations (3.7%). BCOR-CCNB3 fusion tumors most commonly occurred in males (83%), while tumors harboring ZCH3H7B-BCOR fusions were mostly in females (89%). BCOR-ITD tumors were not different between males (54%) and females (46%). BCOR-ITD associated tumors occurred in infants (median 0.9 y, range 0-61 y), while BCOR-CCNB3 was most common in teens (median 14 y, range 1-47 y), and ZCH3H7B-BCOR only in adults (median 45 y, range 36-71). The most common site for BCOR-CCNB3 fused tumors were extremity (29%) and pelvic/sacral (20%), while BCOR ITD tumors were most commonly renal tumors (31%). ZCH3H7B-BCOR tumors were predominantly uterine (78%). Metastasis was rare in patients with BCOR-CCNB3 fused tumors (14%), and more common in those with BCOR-ITD (31%) and ZCH3H7B-BCOR (50%). Regardless of alteration, the majority of patients underwent surgical resection (90%), and chemotherapy (83%), while only 38% received radiation therapy. Relapse data was only available for 33% of the reported cases. Relapse occurred in 93% of patients with ZCH3H7B-BCOR fusions, 68% of BCOR-ITD, and 40% of BCOR-CCNB3 fusions. The median follow up time for entire cohort was 26 months. Vital status information was available for 55% of cases. 5 year overall survival was 68% (46-83 95% CI) for patients with BCOR-CCNB3, 35% (15-56 95% CI) for BCOR-ITD, and 41% (11-71 95% CI) for ZCH3H7B-BCOR.

Conclusion: BCOR altered soft tissue sarcomas are a newly identified group of sarcomas with at least three distinct recurring alterations. BCOR-ITD associated tumors are most often renal tumors in occurring young children, and are associated with high rates of relapse, with approximately 50% of affected patients dying of disease. BCOR-CCNB3 fusion tumors occur most often in teenaged male patients, have low rates of metastatic disease and relapse, and are associated with a favorable prognosis. Tumors harboring ZCH3H7B-BCOR fusions are reported exclusively in adults, most commonly in women with uterine sarcomas, and are associated with high rates of relapse and death from disease. Collaborative efforts are need to identify optimal treatment and to improve outcomes for these patients.



Poster #252 #1818903

LAROTRECTINIB IN ADULT PATIENTS WITH TRK FUSION SARCOMAS: UPDATED EFFICACY AND SAFETY

Shivaani Kummar, MD¹; Lin Shen, MD²; David S. Hong, MD³; Ray McDermott, M.B. B.Ch. B.A.O., PhD, M.B.A., F.R.C.P.I.⁴; Vicki L. Keedy, MD, MScF⁵; Michela Casanova, MD⁶; George D. Demetri, MD⁷; Afshin Dowlati, MD⁸; Soledad Gallego Melcon, MD, PhD⁹; Ulrik N. Lassen, MD, PhD¹⁰; Serge Levyraz, MD¹¹; Tianshu Liu, MD¹²; Victor Moreno, MD, PhD¹³; Christine Bestvina, MD¹⁴; Tejas Patil, MD¹⁵; Atrayee BasuMallick, MD¹⁶; Nuno Sousa, MD¹⁷; Makoto Tahara, MD, PhD¹⁸; David S. Ziegler, MBBS, BSc (Med), FRACP, MD¹⁹; Ricarda Norenberg, MS²⁰; Pierre Avis, MD²¹; Nicoletta Brega, MD²²; Alexander Drilon, MD²³; Daniel S.W. Tan, MD²⁴

¹Knight Cancer Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES, ²Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Peking University Cancer Hospital & Institute, Beijing, Beijing, CHINA (PEOPLE'S REPUBLIC), ³The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁴St Vincent's University Hospital and Cancer Trials Ireland, Dublin, Dublin, IRELAND, ⁵Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES, ⁶Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ⁷Dana-Farber Cancer Institute and Ludwig Center at Harvard University, Boston, Massachusetts, UNITED STATES, ⁸University Hospitals Ahuja Medical Center, Beachwood, Ohio, UNITED STATES, ⁹Pediatric Oncology and Hematology, Vall d'Hebron Children's Hospital, Barcelona, Catalonia, SPAIN, ¹⁰Department of Oncology, Rigshospitalet, Copenhagen, Hovedstaden, DENMARK, ¹¹Charité – Universitätsmedizin, Berlin, Berlin, Berlin, GERMANY, ¹²Zhongshan Hospital-Fudan University, Fudan, Shanghai, CHINA (PEOPLE'S REPUBLIC), ¹³Department of Medical Oncology, Hospital Fundación Jimenez Diaz, Madrid, Madrid, SPAIN, ¹⁴Northwestern University, Chicago, Illinois, UNITED STATES, ¹⁵Department of Medicine, Division of Medical Oncology, University of Colorado, Denver, Aurora, Colorado, UNITED STATES, ¹⁶Sidney Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, Pennsylvania, UNITED STATES, ¹⁷Instituto Portugues de Oncologia do Porto Francisco Gentil, Porto, Porto, PORTUGAL, ¹⁸National Cancer Center Hospital East, Kashiwa, Ibaraki, JAPAN, ¹⁹Sydney Children's Hospital, Randwick, NSW, Australia and School of Women's and Children's Health, University of New South Wales Sydney, Sydney, New South Wales, AUSTRALIA, ²⁰Chrestos Concept GmbH & Co. KG, Essen, Nordrhein-Westfalen, GERMANY, ²¹Bayer Pharmaceuticals, Lille, Nord-Pas-de-Calais, FRANCE, ²²Bayer Pharmaceuticals, Milan, Lombardia, ITALY, ²³Memorial Sloan Kettering Cancer Center, New York, NY, USA and Weill Cornell Medical College, New York, New York, UNITED STATES, ²⁴Division of Medical Oncology, National Cancer Centre Singapore, Duke-NUS Medical School, Singapore, SINGAPORE

Objective: Neurotrophic tyrosine receptor kinase (NTRK) gene fusions are oncogenic drivers in a diverse range of tumor types. Larotrectinib is a first-in-class, highly selective, central nervous system (CNS)-active tropomyosin receptor kinase (TRK) inhibitor approved to treat adult and pediatric patients with TRK fusion cancer, with an objective response rate (ORR) of 75% in 206 evaluable adult and pediatric patients with various non-primary CNS solid tumors (Hong et al, ASCO 2021). Here, we report the updated efficacy and safety of larotrectinib in adult patients with TRK fusion sarcomas from an expanded dataset.

Methods: Adult patients (≥18 years old) with sarcomas harboring NTRK gene fusions and treated with larotrectinib were identified from three clinical trials (NCT02122913, NCT02576431, NCT02637687). Patients received 100 mg larotrectinib twice daily (one patient received 150 mg twice daily). Response was investigator assessed per Response Evaluation Criteria In Solid Tumors (RECIST) version 1.1. Data cut-off date was July 20, 2020.

Results: At the data cut-off date, 33 adult patients with locally advanced or metastatic TRK fusion sarcomas (Table 1) had initiated larotrectinib treatment, with 31 evaluable for efficacy. Two patients had bone sarcomas, four had gastrointestinal stromal tumors (GISTs), and 27 had soft tissue sarcomas: not otherwise specified (n=8), malignant peripheral nerve sheath tumor (n=4), epithelioid spindle sarcoma (n=3), spindle cell sarcoma (n=3), myopericytoma (n=2), stromal tumor (n=2), inflammatory myofibroblastic tumor (n=2), and dedifferentiated liposarcoma, fibrosarcoma, and synovial sarcoma (n=1 each). Median age was 41 (range 19–69) years. Ten patients (30%) were treatment-naïve, nine (27%) had received one prior systemic therapy, and 14 (42%) had received ≥2 prior systemic therapies.

ORR was 65% (95% confidence interval [CI] 45–81): 6 (19%) patients had complete responses and 14 (45%) had partial responses (pending confirmation in one; Table 2). Median time to response was 1.8 months (range 0.9–3.5). The 24-month duration of response rate was 68% (95% CI 46–89) and the 24-month progression-free survival rate was 55% (95% CI 35–74). Median overall survival (OS) was not reached (95% CI 44.4 months–not estimable) at a median follow-up of 24.1 months. The 36-month OS rate was 78% (95% CI 60–96).

Duration of treatment ranged from 0.03+ to 55.7 months. Adverse events (AEs) were mostly Grade 1–2, with only one (3%) Grade ≥3 larotrectinib-related AE reported (increased weight). There were two Grade 5 AEs, neither of which were considered related to larotrectinib. No patients discontinued treatment due to a larotrectinib-related AE.

Conclusion: Larotrectinib demonstrated robust and durable responses, extended survival benefit, and a favorable safety profile in adult patients with TRK fusion sarcomas. These data highlight the importance of testing for NTRK gene fusions in patients with sarcomas, especially in those with no identified genomic drivers, to identify patients who may benefit from TRK inhibitors.

Table 1: NTRK gene fusions by sarcoma type

	STS (n=27)	GISTs (n=4)	Bone sarcomas (n=2)	All sarcomas (N=33)
NTRK1	16	0	1	17
NTRK2	0	0	1	1
NTRK3	11	4	0	15

GIST, gastrointestinal stromal tumor; NTRK, neurotrophic tyrosine receptor kinase; STS, soft tissue sarcoma.

Table 2: Response to treatment by sarcoma type

	STS (n=27)	GISTs (n=4)	Bone sarcomas (n=2)	All sarcomas (N=33)
Evaluable patients, n	25	4	2	31
ORR, % (95% CI)	60 (39–79)	100 (40–100)	50 (1–99)	65 (45–81)
Best overall response, n (%)				
Complete response	5 (20)	1 (25)	0	6 (19)
Partial response	10 (40)*	3 (75)	1 (50)	14 (45)*
Stable disease	7 (28)	0	1 (50)	8 (26)
Progressive disease	2 (8)	0	0	2 (6)
Not determined	1 (4)	0	0	1 (3)

*Includes one STS patient with a partial response pending confirmation.
CI, confidence interval; GIST, gastrointestinal stromal tumor; ORR, objective response rate; STS, soft tissue sarcoma.



Poster #253 #1819054

ULTRA-RARE AND OTHER RARE ADVANCED SARCOMA TREATED WITH TRABECTEDIN: A POST-HOC ANALYSIS OF A NON-INTERVENTIONAL, RETROSPECTIVE, MULTICENTER STUDY OF THE ITALIAN SARCOMA GROUP

Emanuela Palmerini, MD¹; Roberta Sanfilippo, MD²; Giovanni Grignani, MD³; Angela Buonadonna, MD⁴; Antonella Romanini, MD⁵; Giuseppe Badalamenti, MD, PhD⁶; Virginia Ferraresi, MD⁷; Bruno Vincenzi, MD, PhD⁸; Alessandro Comandone, MD⁹; Antonio Pzzolorusso, MD¹⁰; Antonella Brunello, MD¹¹; Fabio Gelsomino, MD¹²; Tommaso De Pas, MD¹³; Toni Ibrhaim, MD, PhD¹; Lorena Guerrieri, MD¹⁴; Federica Grosso, MD¹⁵; Francesca Zanelli, MD¹⁶; Maria A. A. Pantaleo, MD, PhD¹⁷; Laura Milesi, MD¹⁸; Libero Ciuffreda, MD¹⁹; Vittorio Ferrari, MD²⁰; Emanuela Marchesi, PhD²¹; Irene Quattrini, PhD¹; Alberto Righi, MD²²; Elisabetta Setola, MD, PhD²³; Elisa Carretta, PhD¹; Paolo G. Casali, MD²⁴; Pero Picci, MD²¹; Stefano Ferrari, MD¹

¹IRCCS Istituto Ortopedico Rizzoli, Bologna, Emilia-Romagna, ITALY, ²Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ³Department of Medical Oncology-Sarcoma Unit, Candiolo Cancer Institute FPO-IRCCS, Candiolo (TO), Italy, Candiolo, Piemonte, ITALY, ⁴Centro di Riferimento Oncologico di Aviano (CRO Aviano), Aviano, Friuli-Venezia Giulia, ITALY, ⁵Azienda Ospedaliero-Universitaria Pisana, Pisa, Toscana, ITALY, ⁶Department of Medical Oncology, Policlinico "Paolo Giaccone", University of Palermo, Palermo, Italy, Palermo, Sicilia, ITALY, ⁷IRCCS Regina Elena National Cancer Institute – Division of Medical Oncology, Rome, Lazio, ITALY, ⁸Department of Medical Oncology, Università Campus Bio-Medico di Roma, Rome, Italy, Roma, Lazio, ITALY, ⁹SC Oncologia ASL Città di Torino, Torino, Piemonte, ITALY, ¹⁰Istituto Nazionale Tumori IRCCS "Fondazione G. Pascale", Napoli, Campania, ITALY, ¹¹Istituto Oncologico Veneto IOV - IRCCS, Padova, Veneto, ITALY, ¹²Department of Oncology and Hematology, University Hospital of Modena, Modena, Emilia-Romagna, ITALY, ¹³Unit of medical oncology Sarcomas, Thymomas and rare tumors, European Institute of Oncology, IRCCS, Milan, Lombardia, ITALY, ¹⁴IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) "Dino Amadori, Meldola, Emilia-Romagna, ITALY, ¹⁵Mesothelioma and Rare Cancer Unit, Azienda Ospedaliera SS. Antonio e Biagio General Hospital, Alessandria, Piemonte, ITALY, ¹⁶Arcispedale Santa Maria Nuova IRCCS Reggio Emilia, Reggio Emilia, Emilia-Romagna, ITALY, ¹⁷IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Emilia-Romagna, ITALY, ¹⁸Department of Oncology, ASST. Papa Giovanni XXIII Hospital, Bergamo, Lombardia, ITALY, ¹⁹Azienda Ospedaliero Universitaria San Giovanni Battista, Molinette, Torino, Piemonte, ITALY, ²⁰Oncologia Medica, Università degli Studi di Brescia, Brescia, Lombardia, ITALY, ²¹Italian Sarcoma Group, Bologna, Emilia-Romagna, ITALY, ²²Rizzoli Orthopaedic Institute, Bologna, Emilia-Romagna, ITALY, ²³Alma Mater Studiorum, University of Bologna, Bologna, Emilia-Romagna, ITALY, ²⁴Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY

Objective: Among sarcomas, which are rare cancers with an incidence of <6 per 100.000 cases, ultra-rare sarcomas accounts for roughly 20% of all soft tissue and bone sarcomas. As agreed by the Connective Tissue Oncology Society (CTOS) consensus, ultra-rare sarcomas are considered those with an incidence of approximately ≤ 1 per 1,000,000 cases, comprising 56 soft tissue sarcoma (STS) types and 21 bone sarcoma types. Herein, we aimed to evaluate the efficacy and safety of trabectedin (Yondelis®) for the treatment of patients with ultra-rare and other rare STS.

Methods: The Italian Sarcoma Group has recently performed a non-interventional, retrospective, multicenter TrObs study (NCT02793050) with data from 512 pretreated patients with advanced multiple sarcoma histologies and treated with trabectedin (Palmerini, Cancers 2021). The study was aimed to provide insights of the real-world efficacy, toxicity and management of patients treated with trabectedin in clinical practice across Italy. A post-hoc analysis was carried out to evaluate overall response rate (ORR), disease control rate (DCR) and progression-free survival (PFS) after trabectedin among patients with ultra-rare and other rare (excluding L-sarcoma, synovial sarcoma and undifferentiated pleomorphic sarcoma) sarcomas in routine clinical practice.

Results: From January 2010 to December 2015 a total of 36 patients (18 women) with ultra-rare and other rare sarcoma were included in the analysis set. Patients had a median age of 53.0 years (range: 22-81) and an Eastern Cooperative Oncology Group performance status score of 0/1 was recorded in 30 patients (83.3%). Most patients had solitary fibrous tumor (SFT; n=11) following by epithelioid sarcoma (n=5), malignant peripheral nerve sheath tumor (MPNST; n=4), Extraskeletal Myxoid Chondrosarcoma (EMC; n 3) and Desmoplastic small round cell tumor (DSRC3; n = 3) (Table 1). Nearly all patients had metastatic disease (n=35) and received trabectedin as a second-line treatment (63.9%).

Among 35 patients evaluable for response, four patients obtained objective responses, reaching the ORR of 18.2% (95% confidence interval [CI]: 4.6-50.7%) in patients with SFT (2 PR partial responses, PRs, among 11 patients), 33.3% in patients with (DSRC3 (1/3 complete response, CR) and 50% in patients with alveolar soft part sarcoma (1/2 PR). In addition, 12 patients (34.3%) had stable disease (SD) as a best result: 4/11 SFT, for a disease control rate (DCR) of 54.4%; 3/5 epithelioid sarcoma (DCR=60%), 2/3 EMC (DCR n= 66.7%), and 1/4 MPNST, 1/2 alveolar part sarcoma (ASPS) and 1/1 myoepithelioma, for a DCR of 25%, 100% and 100% respectively. After a median follow-up of 24.0 months (interquartile range: 8.5-26.0 months) median PFS was 5.7 (0.7-nr) months with 45.7% (14.3-73) of patients free from progression at 6 months after treatment for SFT (Table 2). PFS results per sarcoma subtype in responders and in all series are shown in Table 2 and Fig. 1 (per patient). Nine out of 36 patients (25.0%) had at least one grade \geq 4 adverse event, mostly being bone marrow toxicity (n=6, 66.7%).

Conclusion: This analysis showed that trabectedin was used in patients with multiple other rare and ultra-rare STS histotypes. A manageable safety profile comparable with those previously reported in the overall population from the TrObs study was confirmed. The activity described in some ultra-rare and other rare sarcoma, confirms the activity of trabectedin in some translocation-related sarcoma and warrant further histotype-specific study.

Table 1. Patient and disease characteristics at baseline

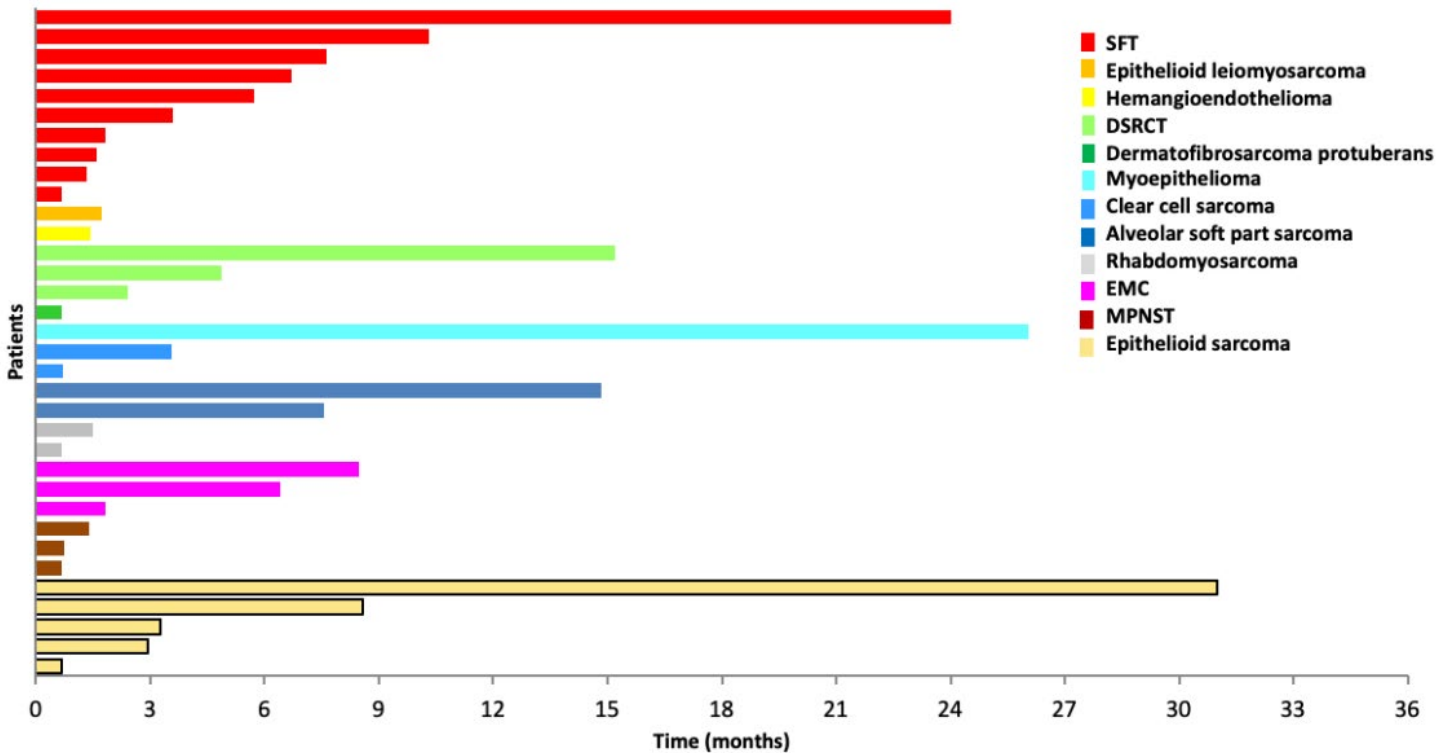
Patients (n)	Analysis set: 36 patients		
Age at study entry (years)	Median	53.0	
	Range (Min-Max)	22.0-81.0	
Histology			
Other rare	Solitary fibrous tumor (SFT)	11 (30.6%)	
	Malignant peripheral nerve sheath tumor (MPNST)	4 (11.1%)	
	Desmoplastic small round cell tumor (DSRCT)	3 (8.3%)	
Ultra-rare	Epithelioid sarcoma	5 (13.9%)	
	Extraskeletal myxoid chondrosarcoma (EMC)	3 (8.3%)	
	Rhabdomyosarcoma	2 (5.6%)	
	Alveolar soft part sarcoma	2 (5.6%)	
	Clear cell sarcoma	2 (5.6%)	
	Myoepithelioma	1 (2.8%)	
	Dermatofibrosarcoma protuberans	1 (2.8%)	
	Hemangioendothelioma	1 (2.8%)	
	Epithelioid leiomyosarcoma	1 (2.8%)	
	Site of primary tumor at first diagnosis	Lower extremity	10 (27.8%)
Intra-abdominal		4 (11.1%)	
Trunk		3 (8.3%)	
Visceral		3 (8.3%)	
Thoracic (non-lung)		3 (8.3%)	
Head and neck		3 (8.3%)	
Thoracic (lung)		2 (5.6%)	
Upper extremity		2 (5.6%)	
Visceral gynecological		2 (5.6%)	
Sacrum level		1 (2.8%)	
Missing		3 (8.3%)	
Eastern Cooperative Oncology Group (ECOG) performance status		0	18 (50.0%)
		1	12 (33.3%)
	2	4 (11.1%)	
	Missing	2 (5.6%)	
Tumor stage at study entry	Locally advanced	1 (2.8%)	
	Metastatic	35 (97.2%)	
	Lung metastases	22 (61.1%)	
	Bone metastases	10 (27.8%)	
	Other metastases	26 (72.2%)	
No. of lines of prior chemotherapy	1 line	23 (63.9%)	
	2 lines	5 (13.9%)	
	\geq 3 lines	8 (22.2%)	

Table 2. Progression-free survival and univariate analyses

	n	Median (95%CI)	PFS	PFS rate at 6 months (95%CI)	Log rank test
All patients	36	3.3 (1.5-6.4)		36.9% (21-51.9)	
By histology in patient with OR					
Alveolar soft part sarcoma (ASFS)	2	11.2 (7.6-nr)		100%	0.9358
Solitary fibrous tumor (SFT)	11	5.7 (0.7-nr)		45.7% (14.3-73)	
Desmoplastic small round cell tumor (DSRCT)	3	4.9 (2.4-nr)		33.3% (9.0-77.4)	

OR objective response; nr, not reached

Figure 1. Progression-free survival by sarcoma subtype and patient





Poster #254 #1819056

ETV4/5 DRIVE SYNOVIAL SARCOMA THROUGH CONTROL OF THE CELL CYCLE AND THE DUX4 EMBRYONIC PATHWAY

Josiane E. Eid, MD¹; Joanna Desalvo, Sr. Research Associate²; Yuguang Ban, PhD²; Luyuan Li, PhD¹; Xiaodian Sun, PhD²; Zhijie Jiang, PhD²; Darcy A. Kerr, MD²; Mahsa Khanlari, MD³; Maria Boulina, PhD²; Mario R. Capecchi, PhD⁴; Juha M. Partanen, PhD⁵; Lin Chen, PhD⁶; Tadashi Kondo, MD, Ph.D⁷; David M. Ornitz, MD, PhD⁸; Jonathan C. Trent, MD, PhD⁹

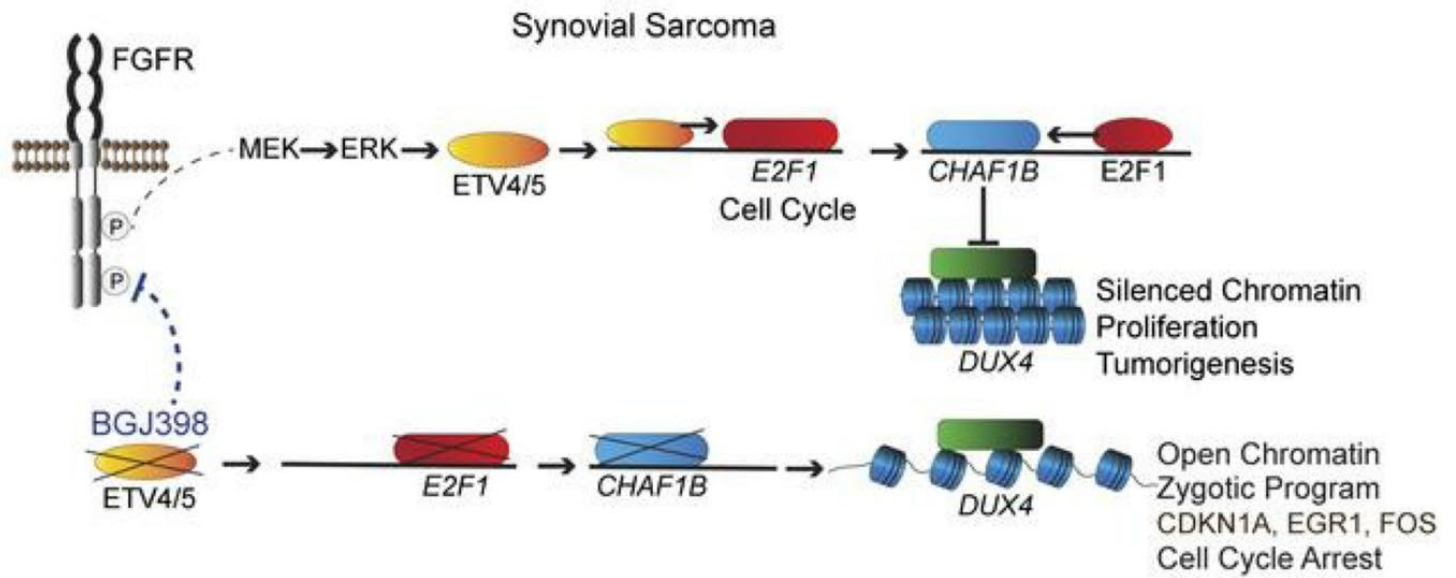
¹Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES, ²University of Miami, Miller School of Medicine, Miami, Florida, UNITED STATES, ³MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ⁴University of Utah School of Medicine, Salt Lake City, Utah, UNITED STATES, ⁵University of Helsinki, Helsinki, Kainuu, FINLAND, ⁶Army Medical University, Chongqing, Chongqing, CHINA (PEOPLE'S REPUBLIC), ⁷Division of Rare Cancer Research, National Cancer Center Research Institute, Chuo-ku, Tokyo, JAPAN, ⁸Washington University School of Medicine, St. Louis, Missouri, UNITED STATES, ⁹Sylvester Comprehensive Cancer Center, Miami, Florida, UNITED STATES

Objective: Advanced synovial sarcoma (SS) is an aggressive malignancy which often affects adolescents and young adults. There are no effective therapeutic options for SS patients after failure of standard treatments. The SS fusion, SS18-SSX, recruits the SWI/SNF-BAF chromatin remodeling and polycomb repressive complexes, drives SS tumorigenesis via a mechanism which remains incompletely understood. We sought to gain additional insight into the downstream effects of the SS18-SSX SS fusion and to identify potential therapeutic targets.

Methods: The SYO-1, HS-SY-II were authenticated through detection of the SS18-SSX fusion. C2C12 cell lines were obtained from the American Type Culture Collection. CDS-X1 and CDS-S2 cells were authenticated by detection of the CIC-DUX4 fusion oncoprotein. The triple knockout FGFR 1,2,3fl/fl mice were obtained from the Ornitz laboratory. SSM2+ and MYF5-Cre+ transgenic mice (SM2) were obtained from the Capecchi laboratory. C57BL6/J mice used for the generation of FGFR-1fl/fl, FGFR2fl/fl, and FGFR3fl/fl and the NU/J mice were acquired from the Jackson Laboratory. Detection, counting, and measurement of tumors in the SM2, SMF1 (FGFR1 KO), SMF2 (FGFR2 KO), SMF3 (FGFR3 KO), and in the BGJ398-treated SM2 mice were performed post-euthanasia. The xenograft SS models (BGJ398-treated tumors and shETV4/5-tumors) were generated with subcutaneous injection of 8x10⁶ SYO-1 cells in the right flank of NU/J mice. The mean, SEM, and SD were calculated in R or Excel. P values were calculated in R, based on two-tailed t test. P values ≤ 0.05 were considered significant. In the RT-qPCR graphs, individual CT (crossing threshold) values were normalized against GAPDH average CT, and SDs between two experimental groups were derived from average ddCT. Fold change was calculated as FC = 2^{-(ddCT)}. In the CHIP-qPCR graphs, the average CT of input chromatin was adjusted to 2% of total chromatin. dCTs of the antibody were adjusted to the new average CT of the input. % input of individual antibody dCTs was calculated as 100*2^{-(dCT)}. P values were derived from SDs based on average dCTs of experimental groups.

Results: In genetic FGFR knockout models, culture, and xenograft synovial sarcoma models treated with the FGFR inhibitor BGJ398, we show that FGFR1, FGFR2, and FGFR3 were crucial for tumor growth. Remarkably, knockout of both FGFR alleles in synovial sarcoma transgenic mice led to substantial attenuation of tumor incidence and number, as 35% of 20 FGFR1 homozygous KO mice, 10% of 20 FGFR2 homozygous KO mice, and 35% of 23 FGFR3 homozygous KO mice developed visible tumors. Transcriptome analyses of BGJ398-treated cells, histological and expression analyses of mouse and human synovial sarcoma tumors revealed prevalent expression of two ETS factors and FGFR targets, ETV4 and ETV5. In a lentiviral shRNA knockdown model in SYO-1 and HS-SY-II synovial sarcoma cell lines, we found that ETV4 expression was markedly diminished upon depletion of any one of the three FGFRs, while ETV5 levels were decreased by FGFR2 knockdown alone. We further demonstrate that ETV4 and ETV5 acted as drivers of synovial sarcoma growth, most likely through control of the cell cycle. We observed that suppression of either ETV4 or ETV5 led to significant inhibition of SS cell proliferation. Furthermore, individual loss of either ETV4 or ETV5 impeded the ability of SYO-1 and HS-SY-II cells to form sarcospheres in serum-free culture media. Upon ETV4 and ETV5 knockdown, we observed a striking upregulation of DUX4 and its transcriptional targets that activate the zygotic genome and drives the atrophy program in facioscapulohumeral dystrophy (FSHD) patients.

Conclusion: In addition to demonstrating the importance of inhibiting all three FGFRs, the current findings reveal ETV4 and ETV5 as well as the DUX4 embryonic pathway to be novel biomarkers and potential therapeutic targets, as a promising approach to abrogate synovial sarcoma tumorigenesis.





Poster #255 #1818860

PRECISION ONCOLOGY IN SARCOMA DRUG DEVELOPMENT: IMPACT OF BIOMARKER MATCHING ON OUTCOMES IN PHASE I CLINICAL TRIALS

Roberto Carmagnani Pestana, MD¹; Justin Moyers, MD²; Nelson Hamerschlag, MD, PhD¹; Jason Roszik, PhD²; Shiraj Sen, MD, PhD³; David S. Hong, MD²; Aung Naing, MD²; Cynthia Herzog, MD²; Siqing Fu, MD, PhD²; Vinod Ravi, MD²; Shreyaskumar Patel, MD⁴; J Andrew Livingston, MD⁵; Neeta Somaiah, MD²; Anthony P. Conley, MD⁵; Funda Meric-Bernstam, MD²; Vivek Subbiah, MD²

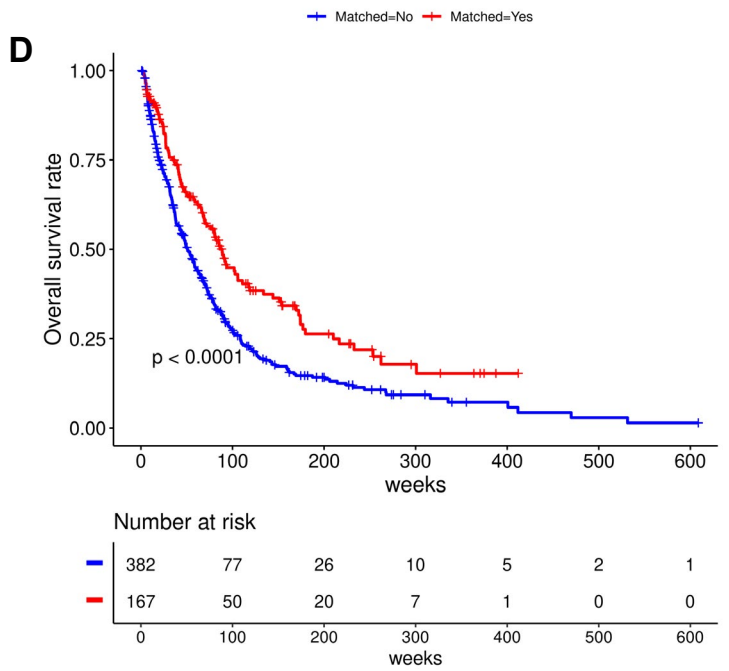
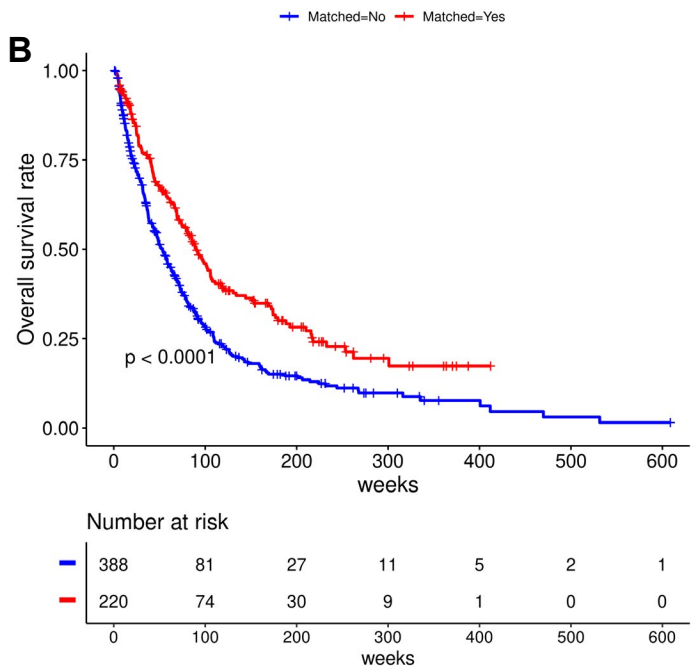
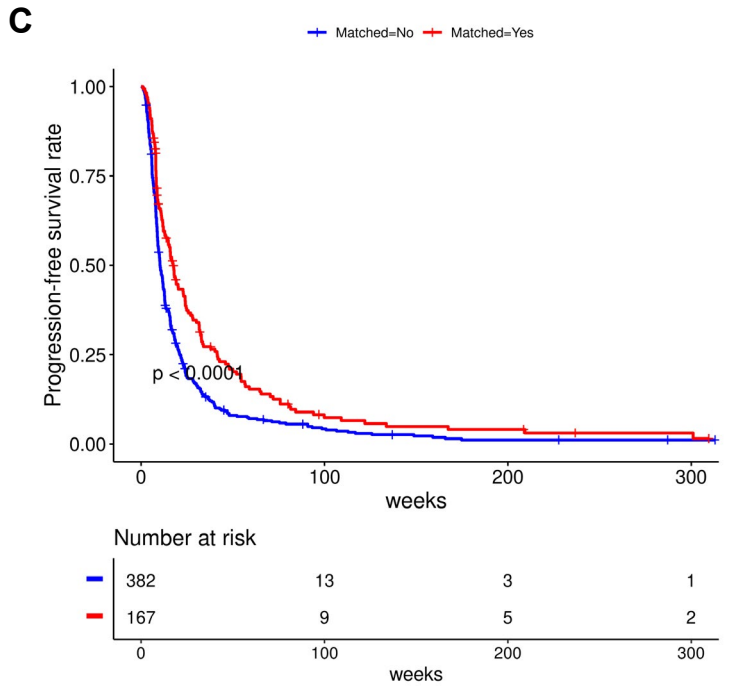
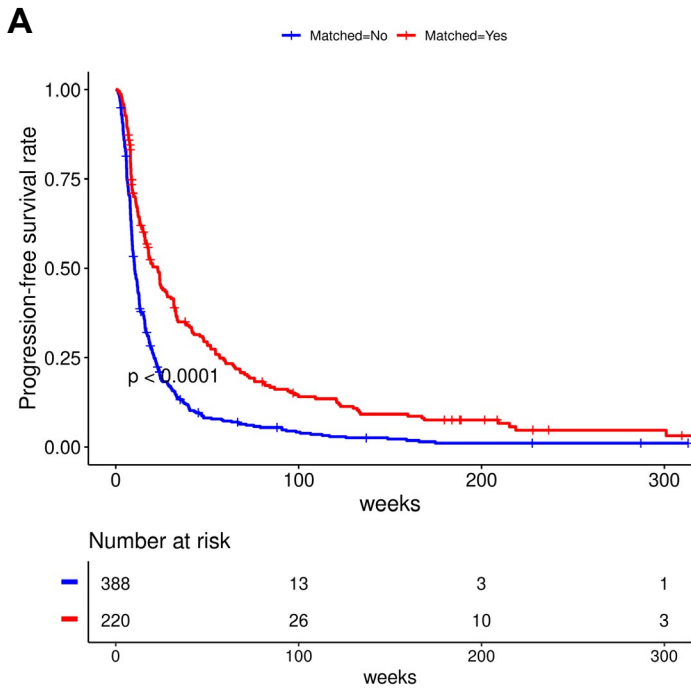
¹Hospital Israelita Albert Einstein, São Paulo, Sao Paulo, BRAZIL, ²The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES, ³Sarah Cannon Research Institute, Denver, Colorado, UNITED STATES, ⁴MDACC, Houston, Texas, UNITED STATES, ⁵MD Anderson Cancer Center, Houston, Texas, UNITED STATES

Objective: Objectives Given the limited efficacy of second- and later- line agents, patients with sarcoma are often enrolled in phase 1 clinical trials, and next-generation sequencing (NGS) analyses have revealed potentially actionable alterations across subtypes. With the exception of targeting KIT/PDGFR in gastrointestinal stromal tumors (GIST), NTRK for fusion-positive stromal tumors, and EZH2 in epithelioid sarcoma, no biomarker-driven targeted therapy currently is approved for sarcomas. Although many published clinical and preclinical studies with novel targeted agents have provided a rationale for using this strategy in a clinical setting, whether sarcoma patients enrolled on matched early phase trials have improved outcomes over unmatched trials remains unknown. The aim of this study was to update on the previous data (J Clin Oncol 37, 2019 (suppl; abstr 11018) the impact of enrollment in biomarker-matched phase I clinical trials in the outcome of patients with advanced sarcoma.

Methods: We analyzed clinical and genomic data from sarcoma patients treated on phase 1 trials at MD Anderson Cancer Center (MDACC) from May, 2006 to May, 2021 and compared overall response rate (ORR), clinical benefit rate, progression-free survival (PFS), and overall survival (OS) in patients enrolled on biomarker-matched versus unmatched trials.

Results: 609 patients with advanced sarcomas (488 soft tissue, 121 bone) were included; median age was 54.5 (range: 11 – 86), 48% were female, and patients had a median of 3 prior lines of therapy (range: 0-9). Most commonly treated subtypes included leiomyosarcoma (n = 103; 17%), liposarcoma (n= 83; 14%), GIST (n=59; 10%), chondrosarcoma (n=45; 7%), Ewing's sarcoma (n=45; 7%), osteosarcoma (n=39; 6%), and synovial sarcoma (n=19; 3%). NGS data was available for 495 patients (81.2%), and 220 patients (36% of total; 44% of those with NGS) were treated on biomarker-matched trials. Objective responses were seen in 12.2% (n=27) matched compared to 5.1% (n=20) of unmatched patients (p=0.002). The clinical benefit rate for biomarker matched trials vs unmatched was 45.5% v 18.5% (<0.001). PFS was significantly longer for patients enrolled on matched trials (median = 23.0 vs 10.3 weeks; p<0.0001; Figure 1A). OS was also superior in patients enrolled on matched trials (median = 90.3 vs 53.4 weeks; p<0.0001; Figure 1B). Benefit in PFS and OS for matched trials was maintained when GIST patients were excluded from the analysis (Figure 1C-D). Objective responses were seen for patients matched to treatments with KIT/PDGFR alpha (n=7), MDM2 (n=5), TRK (N=3), VEGF (n=2), cMET (N=2), MAGE-A4 (n=2), Aurora Kinase (n=1), FGFR (=1) EED inhibitor (n=1), PARP inhibitor (n=1), and mTOR inhibitor (n=1).

Conclusion: Enrollment in biomarker-matched phase I trials continues to be associated with a statistically significant improvement in ORR, clinical benefit rate, PFS, and OS in heavily pretreated patients with metastatic soft-tissue and bone sarcoma. Clinical benefit was observed in patients with multiple histologies receiving targeted therapies with diverse targets, and further refine drug development for these orphan malignancies. NGS of tumors from metastatic patients with consideration for biomarker-matched prospective trials are warranted.





Poster #256 #1818991

RESULTS OF THE PHASE 1B SOFT TISSUE SARCOMA PORTION OF A GLOBAL RANDOMIZED DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF TAZEMETOSTAT PLUS DOXORUBICIN AS FRONTLINE THERAPY FOR ADVANCED EPITHELIOID SARCOMA

Sant P. Chawla, MD¹; Gerald Falchook, MD²; Melissa Burgess, MD³; James L. Chen, MD⁴; Robin L. Jones, BSc, MBBS, MD⁵; Victoria T. Chua-Alcala, MD¹; Coya Tapia, MD, PhD⁶; Jessica Ainscough, BA⁶; Anthony Hamlett, PhD⁶; Melinda S. Merchant, MD, PhD⁶; Rashmi Chugh, MD⁷

¹Sarcoma Oncology Research Center, Santa Monica, California, UNITED STATES, ²Sarah Cannon Research Institute at HealthONE, Denver, Colorado, UNITED STATES, ³University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES, ⁴Ohio State University, Columbus, Ohio, UNITED STATES, ⁵The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, England, UNITED KINGDOM, ⁶Epizyme, Inc., Cambridge, Massachusetts, UNITED STATES, ⁷University of Michigan, Ann Arbor, Michigan, UNITED STATES

Objective: Epithelioid sarcoma (ES) is a rare, aggressive subtype of soft tissue sarcoma (STS). Tazemetostat (TAZ), an FDA-approved EZH2 inhibitor, has shown single-agent clinical activity and a favorable safety profile in patients with metastatic or locally advanced ES. In preclinical studies, TAZ has shown synergistic antitumor activity with doxorubicin (DOX), which is often used as frontline treatment for STS. Here, we present results of the phase 1b study (NCT04204941), designed to assess the recommended phase 3 dose (RP3D), safety, and efficacy of TAZ + DOX in patients with advanced STS.

Methods: The open-label, phase 1b portion of this study enrolled adult patients with previously untreated advanced STS. A standard 3 + 3 dose escalation design was used to assess TAZ 400 mg, 600 mg, and 800 mg orally twice daily in combination with DOX (75 mg/m² intravenously on day 1 of each cycle, for up to 6 cycles) as frontline therapy. Dose-limiting toxicities (DLTs) were predefined in the protocol. The RP3D of TAZ was determined by the Safety Review Committee review of the safety and pharmacokinetic data from the phase 1b escalation portion, with a target DLT rate of <33%.

Results: As of February 23, 2021, 18 patients were enrolled, including 2 with ES; 11 patients are still receiving TAZ + DOX and 7 have discontinued (5 due to disease progression, 1 due to patient refusal of further treatment, and 1 due to death attributed to disease progression). The median age was 52.5 years (range, 29–82) and all had unresectable STS. Median (range) time on treatment was 12.4 (0.1–54.1) weeks across all dose levels evaluated. Two DLTs, both of febrile neutropenia, were observed, 1 in the TAZ 600 mg + DOX cohort (n=1/6, 17%), and 1 in the TAZ 800 mg + DOX cohort (n=1/6, 17%). When used in combination with DOX, the RP3D of TAZ was 800 mg. Grade 3 or 4 treatment-related treatment-emergent adverse events (TR-TEAEs) occurred in 15/18 (83.3%) patients. The most common (≥20%) TR-TEAEs were neutropenia (n=12, 66.7%), anemia (n=10, 55.6%), fatigue (n=10, 55.6%), nausea (n=10, 55.6%), stomatitis (n=9, 50%), febrile neutropenia (n=7, 38.9%), vomiting (n=7, 38.9%), constipation (n=6, 33.3%), and decreased appetite (n=5, 27.8%). TR-TEAEs were defined as attributable to either study agent. Of the 18 patients enrolled, 2 patients achieved sufficient disease shrinkage to have tumor resection. Two patients (1 in each of the 600 mg and 800 mg dose cohorts) achieved a partial response and 8 (44%) patients achieved a best response of stable disease.

Conclusion: The combination of TAZ + DOX was generally well tolerated in this dose finding study in patients with advanced STS. The RP3D to be assessed in the phase 3 randomized, double blind, placebo-controlled portion of the study is TAZ 800 mg twice daily + DOX 75 mg/m². The safety profile of this combination is consistent with the respective safety information for TAZ and for DOX. The TR-TEAEs include known toxicities of DOX or TAZ. Further comparison with DOX + placebo in the phase 3 trial will aid in assessing efficacy and safety of the combination of TAZ + DOX. The global phase 3 confirmatory trial will enroll patients with ES who have unresectable disease and have had no prior systemic therapy.



Poster #257 #1819000

A MULTICENTER, RETROSPECTIVE ANALYSIS OF CLINICAL CHARACTERISTICS AND TREATMENT PATTERNS FOR SPINDLE CELL AND SCLEROSING RHABDOMYOSARCOMA

 Elizabeth J. Davis, MD¹; Sheima Farag, MD²; Hilary Dietz, MD³; Angela C. Hirbe, MD, PhD⁴; Michael J. Wagner, MD⁵; Kristen N. Ganjoo, MD⁶; Robin Jones, MD²; Vicki L. Keedy, MD, MSCI¹; Nam Bui, MD⁷
¹Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES, ²Royal Marsden Hospital, London, England, UNITED KINGDOM, ³Washington University St. Louis, St. Louis, Missouri, UNITED STATES, ⁴Washington University School of Medicine, St. Louis, Missouri, UNITED STATES, ⁵University of Washington/Fred Hutch/Seattle Cancer Care Alliance, Seattle, Washington, UNITED STATES, ⁶Stanford Cancer Center, Stanford, California, UNITED STATES, ⁷Stanford University Department of Oncology, Stanford, California, UNITED STATES

Objective: Spindle cell and sclerosing rhabdomyosarcoma (sRMS/scRMS) were first recognized as distinct subtypes of RMS in 2013 by the World Health Organization. Prior to this, these subtypes were classified under the embryonal variant of RMS. These tumors comprise 5-10% of all RMS cases. Recent studies have suggested that spindle cell and sclerosing subtypes may confer a more aggressive clinical course. MYOD1 mutations have been associated with worse clinical outcomes while VGLL2-related fusions in infantile cases are associated with improved outcomes. However, the literature discussing optimal treatment patterns for these subtypes is sparse. We sought to understand in an international, multi-institutional, retrospective study the treatment patterns and outcomes for patients with sRMS/scRMS.

Methods: We identified cases of sRMS/scRMS treated at five academic sarcoma centers in the United States and the United Kingdom from June 1, 1998-June 1, 2021. Patient data including age at diagnosis, sex, race, site/size/grade of primary disease, treatment rendered, disease status including recurrence, and date of last follow-up were collected. Overall survival (OS) was defined as time from diagnosis to death from any cause.

Results: 41 patients with sRMS/scRMS were identified. Patient and tumor characteristics are described in Table 1. The median age at diagnosis was 34 (0.1-79) years. Most patients (83%) had localized disease at diagnosis. Genomic testing was available for 39% of cases. 24% of tumors had a MYOD1 mutation. Median follow-up was 18.7 months. Median OS was not yet reached. 5-year overall survival was 56% (Figure 1). For patients with localized disease at diagnosis, 5-year survival was 66.5% versus 14% for those with metastatic disease at diagnosis (Figure 2). Treatment patterns are detailed in Table 2. Most patients underwent surgery (78%), radiation (66%), and chemotherapy (71%). 54% of patients received neo/adjuvant chemotherapy. Chemotherapy selections included pediatric and adult soft tissue sarcoma regimens with various combinations of doxorubicin and dactinomycin based-regimens. Vincristine, dactinomycin, cyclophosphamide (VAC) was the most common regimen. Complete responses were seen in two patients, one receiving VAC and one receiving doxorubicin and ifosfamide. A partial response and prolonged (21 weeks) stable disease was also seen with pazopanib.

Conclusion: There is a paucity of literature to guide management of sRMS/scRMS. Our study shows that the clinical behavior of sRMS/scRMS is significantly different from embryonal/alveolar RMS with significantly worse response to first-line chemotherapy and worse overall prognosis. To our knowledge, this is the most comprehensive evaluation of clinical and molecular characteristics as well as treatment patterns in this patient population. Our study also shows that multi-institutional collaboration is feasible and fills a knowledge gap in a rare cancer. Prospective studies are needed to determine optimal systemic therapy for these patients and to evaluate potential molecular predictive and prognostic biomarkers.

Table 1. Patient and tumor characteristics

Patient characteristic	All patients n=41
Age at diagnosis, median in years, (range)	34 (0.1-79)
Sex	
Men	24 (59%)
Women	17 (41%)
Race	
White	22 (54%)
Black	2 (5%)
Asian	2 (5%)
Unknown	15 (37%)
Tumor characteristic	
Histology	
Spindle cell	32 (78%)
Sclerosing	9 (22%)
Tumor site	
Extremity	14 (34%)
Head/Neck	8 (19.5%)
Abdomen/pelvis	8 (19.5%)
Chest	5 (12%)
Genitourinary	4 (10%)
Other	2 (5%)
Median tumor size in cm, (range)	8 (1.7-20)
Grade	
High	19 (46%)
Not reported	22 (54%)
Extent of disease at diagnosis	
Localized	34 (83%)
Metastatic	7 (17%)
Genomic findings	
MYOD1 mutation	10 (24%)
Other	6 (15%)
Unknown	30 (61%)

Figure 1. 5-year overall survival for all patients

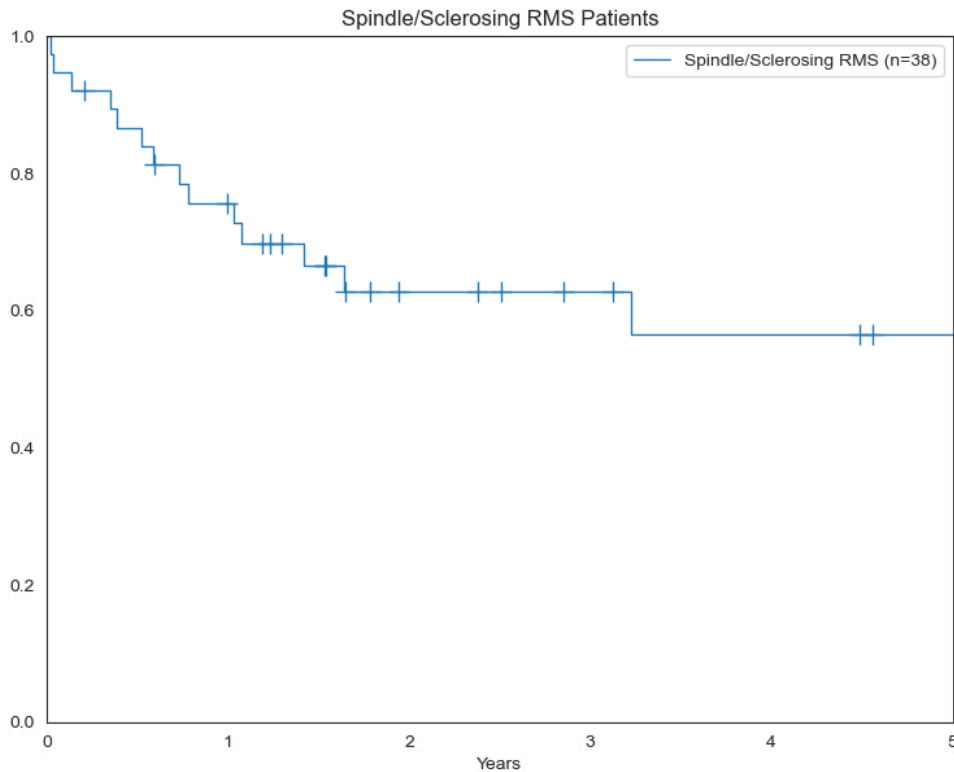


Figure 2. 5-year overall survival by extent of disease at diagnosis

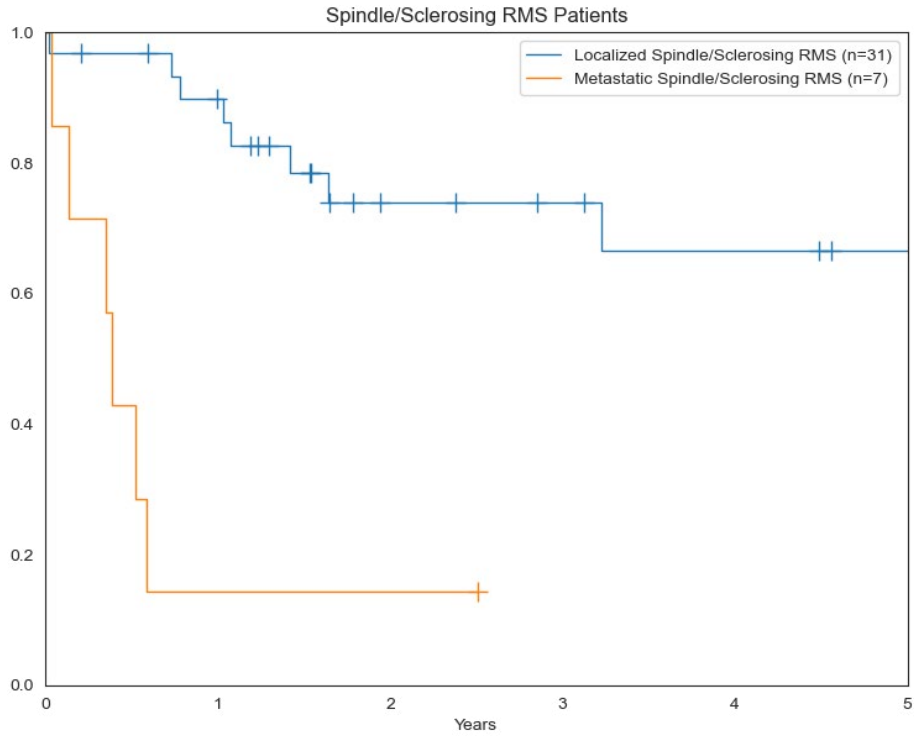


Table 2. Treatment characteristics

Treatment	N=41
Treatment	
Surgery	32 (78%)
Radiation	27 (66%)
Systemic therapy	29 (71%)
Timing of first systemic therapy	
Neo/adjuvant	22 (54%)
Recurrent/metastatic	7 (17%)
First-line systemic therapy regimens	N=29
Vincristine/dactinomycin/cyclophosphamide (VAC)	9
Doxorubicin/ifosfamide	6
Vincristine/doxorubicin/cyclophosphamide (VDC)	4
VAC/vincristine/irinotecan (VI)	3
VDC/ifosfamide/etoposide (IE)	2
VDC/IE/VI	1
Vincristine/doxorubicin/ifosfamide	1
Vincristine/doxorubicin/dactinomycin/ifosfamide	1
Etoposide/vincristine/ doxorubicin/ifosfamide/dactinomycin	1
Pazopanib	1
Response to first-line therapy	N=17
Complete response	2
Partial response	4
Stable disease	6
Progressive disease	5
Second-line systemic therapy	N=10
Cyclophosphamide/topotecan	1
Doxorubicin	1
Doxorubicin/olaratumab	1
Gemcitabine/docetaxel	1
Ifosfamide	1
IE	1
Pazopanib	1
Trabectedin	1
VDC/IE	1
Temozolomide/vinorelbine/cyclophosphamide	1
Response to second-line therapy	
Stable disease	1
Progressive disease	7
Not reported	2



Poster #258 #1819019

PRIMARY SARCOMAS OF THE BREAST-SINGLE INSTITUTION EXPERIENCE

 Hanna Kosela-Paterczyk, MD PhD¹; Anna Mariuk-Jarema, MD¹; Paweł Teterycz, MD PhD¹; Michał Kunkiel, MD²; Maria Krotewicz, MD¹; Joanna Placzke, MD¹; Zbigniew Nowecki, MD PhD²; Piotr Rutkowski, MD, PhD³
¹Maria Skłodowska-Curie Institute - Oncology Center; Department of Soft Tissue/Bone Sarcoma and Melanoma, Warsaw, Mazowieckie, POLAND, ²Department of Breast Cancer and Reconstructive Surgery, Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Mazowieckie, POLAND, ³Department of Soft Tissue/Bone Sarcoma and Melanoma; Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Mazowieckie, POLAND

Objective: Primary sarcomas of the breast constitute less than 5% of all soft tissue sarcomas and less than 1% of all breast tumors. Occurrence of breast sarcoma (most commonly angiosarcoma) can be a consequence of the previous radiotherapy due to breast cancer, or they develop as a sporadic type of cancer. Our study aims to analyze the outcome of patients treated for primary breast sarcoma in one institution.

Methods: In this retrospective study, we included 157 female patients treated in our institution between the years 2000-2021. Kaplan-Meier estimator with log-rank test was used for survival analysis. Overall survival (OS) was calculated from the time of diagnosis to the date of death. Disease-free survival (DFS) was calculated from the time of diagnosis to the date of disease recurrence. Median follow-up was 35 months (95%CI 27-50.5). The mean age at diagnosis was 54 years (SD 13.8). Histological subtypes were Malignant phyllodes tumors (MPT) in 70 patients (44.6%), angiosarcoma (AS) in 49 patients (32.2%), undifferentiated pleomorphic sarcoma in 8 patients (5.1%), other less common subtypes in 30 patients (19.1%). 34 patients (21.7%) had previous locoregional treatment for breast cancer, most often (53.1%) in the AS group. The mean time from breast cancer treatment to sarcoma diagnosis was 6.6 years (SD 3.3). 51 patients (53.7%) had high-grade lesions; in 13 (23.4%) it was low grade, in the remaining grade is unknown. The mean size of the tumor was 8 cm (SD 6.7). The largest lesions were found in the UPS group – mean 11 cm (SD 6.8). 86% of the patients were treated with a radical intention, and the remaining had metastatic disease at diagnosis. 105 patients (66%) underwent perioperative radiotherapy, and 31% had adjuvant chemotherapy. The most common adjuvant chemotherapy in AS was paclitaxel, while in remaining subtypes, doxorubicin-based schemes. 30 patients (23.4%) underwent breast-conserving surgery, and the remaining group had a radical mastectomy. 116 patients (95%) had an R0 resection.

Results: At the time of the analysis, 46 patients died. Median OS for the whole group is 90 months (95% CI 52.2- not reached). Median DFS for the whole group was not reached (95% CI: 21 – not reached). Because the outcome of the most common AS and MPT differ significantly, we decided to present both groups separately. Median OS for AS reached 33.3 months (95% CI: 24.0 – not reached), 5-year OS rate was 31% (95% CI: 18-54). Factors impacting OS in univariate analysis were perioperative chemotherapy (positive effect), perioperative radiotherapy (negative effect), and history of previous breast cancer (positive effect). In the multivariate model, only perioperative chemotherapy positively impacted the OS, while other variables lost their meaning. Median OS for MPT was not reached; the 5-year survival rate was 73% (95% CI: 60-89). The most important factor impacting OS in the univariable analysis was tumor size – HR: 1.07 per 1 cm change (95% CI: 1.00 – 1.14, p = 0.049).

Conclusion: Primary sarcomas of the breast are a heterogeneous group of tumors and require multidisciplinary treatment in a specialized center. Special care should be focused on angiosarcoma patients.



Poster #259 #1818987

INFLAMMATORY MYOFIBROBLASTIC TUMOR- REVISITING A RARE DISEASE IN A REFERENCE CENTER
Inês C. Oliveira, MD¹; Emanuel Gouveia, MD²; Teresa Alexandre, MD²; Isália Miguel, MD²; Hugo Vasques, MD²; Maria Manuel Lemos, MD²; Nuno Abecasis, MD²; Margarida Ferreira, MD²
¹Instituto Português de Oncologia de Lisboa Francisco Gentil, Setúbal, Setubal, PORTUGAL, ²Instituto Português de Oncologia de Lisboa Francisco Gentil, Lisboa, Lisboa, PORTUGAL

Objective: Inflammatory myofibroblastic tumor (IMT) is a rare disease and is described as an intermediate soft tissue tumor. ALK rearrangements are identified in 50% of IMT and ROS, ETV6 and NTRK translocations have been described in ALK-negative IMT. IMT can occur anywhere in the body and despite similar pathological findings, different clinical patterns and outcomes are reported. The objective of this study is to characterize the epidemiological and clinical features of IMT patients (pts) and their outcomes.

Methods: Retrospective study reviewing all pts diagnosed with IMT in our institution in the last 16 years (yrs). Overall (OS) and progression free survival (PFS) were calculated by the Kaplan-Meier method.

Results: From June-2005 to June-2021, 17 pts were diagnosed with IMT. Male-to-female ratio was 1,83 and median age at diagnosis was 45 yrs (12-80). ALK rearrangements were identified in 5 pts (29,4%), ROS translocation in 1 pt (5,9%) and 4 pts (23,5%) lacked immunohistochemistry information. IMT primary sites were heterogeneous (lung IMT were the most frequent: 3 pts, 17,6%) and 2 pts (11,8%) had metastatic disease at diagnosis. Surgery was the selected treatment in 11 pts (64,7%) and local recurrence was documented in 3 of them (27,3%). From the 6 pts (35,3%) with unresectable or metastatic disease, 2 pts were treated with steroids (33,3%); 1 pt was treated with chemotherapy (16,7%; doxorubicin); and 3 pts (50%) lacked treatment information. Disease progression was seen in 3 of these 6 pts (50%). At disease progression 1 ROS-positive pt was treated with crizotinib and then lorlatinib upon progression, with response. Two patients were lost to follow-up (excluded from statistical analysis). Median PFS was 49,9 months (26,6-73,2) and no difference was found between ALK-positive and ALK-negative pts (p value = 0,093). Two pts died (13,3%). Median OS was 61,1 months (44,9-77,2). No difference was documented between ALK-positive and ALK negative pts (p value = 0,564).

Conclusion: IMT are rare tumors described as being more frequent in children and young adults but we also report IMT diagnosis in pts with 60-80 yrs. Heterogeneity of primary site origin was documented, as described in other studies. ALK rearrangements were identified in only 29,4% but information was not available in 4 pts (23,5%) and the patient population is limited. ALK status did not influence PFS and OS in our study but the number of patients may be a limiting factor. More studies are needed on IMT.



Poster #260 #1818992

CHANCES OF LONG-TERM EVENT-FREE SURVIVAL FOR PATIENTS WITH DESMOPLASTIC SMALL ROUND CELL TUMOR (DSRCT)

Claudia Giani, MD¹; Silvia Stacchiotti, MD²; Salvatore Provenzano, MD²; Anna Maria Frezza, MD²; Sandro Pasquali, MD, PhD³; Rossella Maria Bertulli, MD⁴; Michela Casanova, MD⁴; Stefano Chiaravalli, MD⁴; Paola Collini, MD⁵; Gianpaolo Dagrada, MD⁴; Lorenza Gandola, MD⁴; Carlo Morosi, MD⁶; Stefano Radaelli, MD⁴; Claudia Sangalli, MD⁴; Paolo G. Casali, MD²; Andrea Ferrari, MD⁴; Alessandro Gronchi, MD⁷

¹Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY, ²Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Lombardia, ITALY, ³Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ⁴Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Lombardia, ITALY, ⁵Department of Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Lombardia, ITALY, ⁶Department of Radiology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, Milan, Lombardia, ITALY, ⁷Sarcoma Service, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, Milan, Lombardia, ITALY

Objective: DSRCT is a well-defined, ultra-rare sarcoma marked by the presence of EWSR1-WT1 fusion. Although treatment approach exploits the combination of surgery, chemotherapy and radiotherapy, patient outcome remains unsatisfactory and the best treatment strategy is left to be defined. We analyzed our institutional series, in an effort to characterize pts who experienced long-term survival without disease recurrence.

Methods: Data of all consecutive pts treated at our institution for a primary DSRCT between 2000 and 2021 were retrospectively collected. All pts underwent a multimodal approach including multiagent chemotherapy (ChT) (anthracyclines +/- alkylating agents +/- vinca alkaloids +/- etoposide +/- cisplatin +/- irinotecan), +/- surgery +/- HIPEC +/- abdominal radiation therapy (RT) +/- high-dose ChT. Pts were stratified based on disease extent at diagnosis: single or multiple peritoneal nodules, peritoneal nodule(s) + lymph nodes involvement, liver metastases, supra-diaphragmatic disease. Surgery was classified as macroscopically complete (R1) or incomplete (R2). Response to first-line ChT was retrospectively assessed by RECIST 1.1. Survival analysis was performed by Kaplan-Meier method; event-free survival (EFS) was defined as the time from diagnosis to disease relapse, first progression or death; overall survival (OS) was defined as the time from diagnosis to death or last follow-up (FUP). Pts alive and with no evidence of disease at a minimum of 36 mos from diagnosis were defined as long-term survivors.

Results: Thirty-nine pts with a median age at diagnosis of 26 years (range 7-67) were identified; 5 (16%) were long-term survivors. All 39 pts received multiagent ChT, 28/39 (72%) underwent surgery (in 7/28 [25%] HIPEC was performed), and 9/39 (23%) received RT.

There were 31 pts evaluable for response, of whom 17 (55%) achieved a partial response (PR), 13 (42%) had stable disease (SD) and 1 (3%) progressed. Among pts who underwent surgery, 6/28 (21%) had an R2 resection and 22/28 (79%) an R1 resection. RT was administered in 7 pts (32%) after a R1 resection, and in 2 (33%) after a R2 resection.

With a median (m-) FUP of 37 (range 5-209) mos, the overall m-EFS and m-OS were 15 (range 2-209) and 37 (range 5-209) mos, respectively. All relapses/progressions occurred within 35 mos from diagnosis. In pts who underwent surgery, the m-EFS and m-OS were 19 (range 4-209) and 37 (range 9-209) mos, respectively, 23 (range 9-209) and 43 (range 9-209) mos after R1 resection, and 10 (range 4-22) and 19 (range 9-37) mos after R2 resection, respectively. In the subgroup of R1 patients, in those who received also abdominal RT (7/22, [32%]) m-EFS was 27 (15-209) and m-OS was not reached (range 18-209) mos, while in those who did not have RT m-EFS and m-OS were 16 (range 9-53) and 43 (range 9-83) mos, respectively.

Long-term survivors were all treated by multimodal therapy including R1 resection (5/22, [23%]). Their m-age was 32 years (range 11-49). The disease extent at onset was peritoneal only in 3 (3/13 with peritoneal disease, [23%]) and peritoneal + subdiaphragmatic lymph nodes in 2 (2/10 with peritoneal + lymph nodes involvement, [20%]), while none had liver or extra-abdominal metastasis. Best response to ChT was PR in 2 pts, SD in 1 pt, not evaluable in 2 pts (adjuvant ChT). Three/5 pts received abdominal RT, 1/5 high-dose ChT, none HIPEC. At the m-FUP of 53 (range 37-209) mos, no further event was observed and these pts are alive at 37, 39, 53, 64 and 209 mos from diagnosis.

Conclusion: Although the outcome of pts with DSRCT is clearly unsatisfactory, in our series cure was likely achieved in a subset (16%; 25% in completely resected pts). All our long-term event-free survivors did not have liver/extra-abdominal extension, and all received multiagent ChT and complete surgical resection, while 3/5 had abdominal RT.

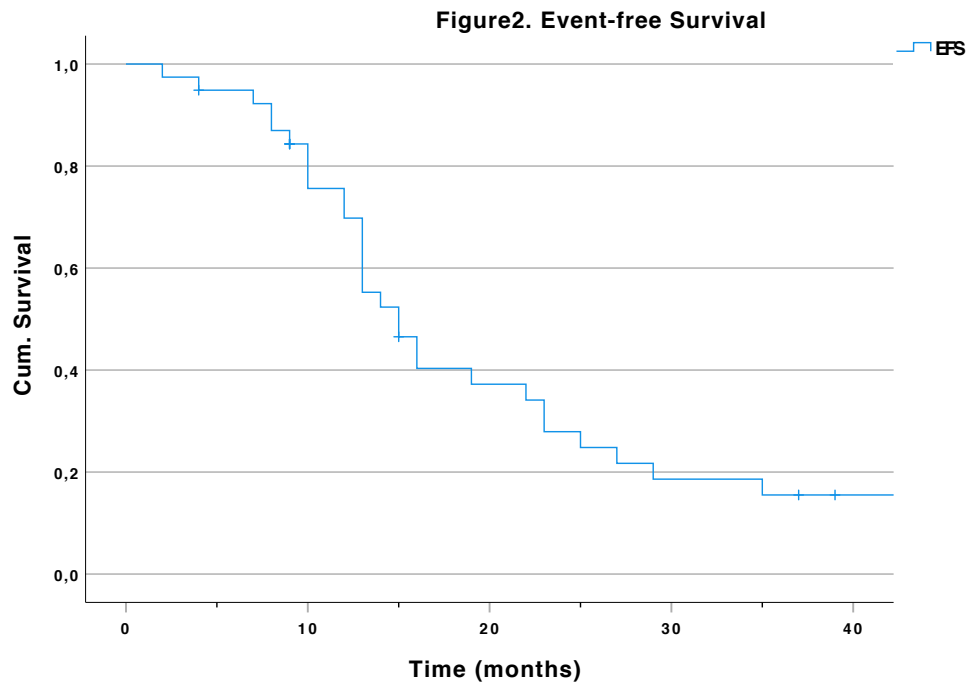
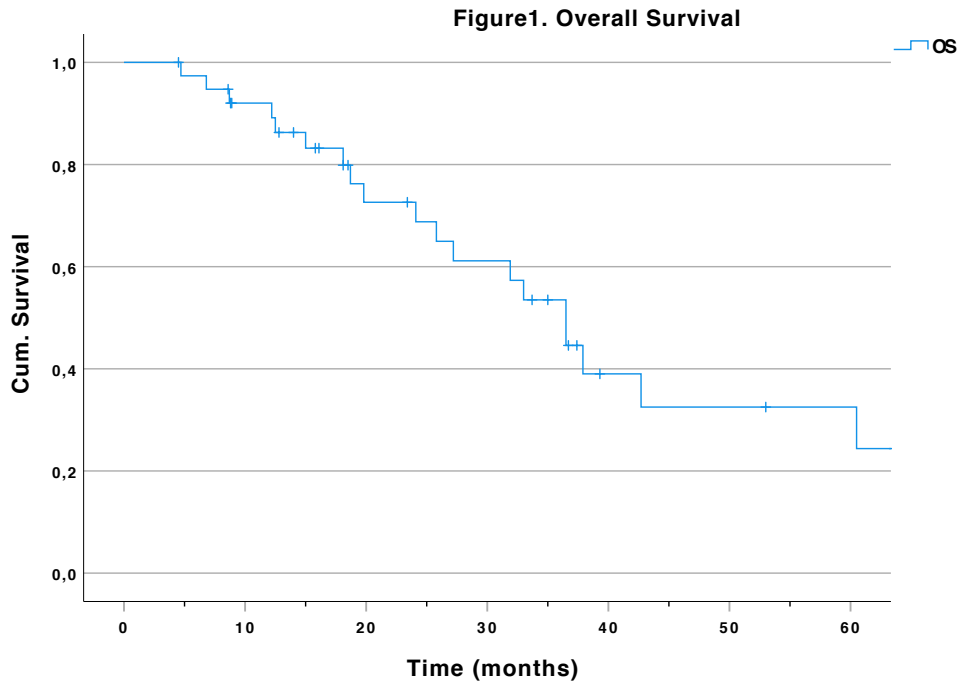


Figure3. EFS according to Surgery

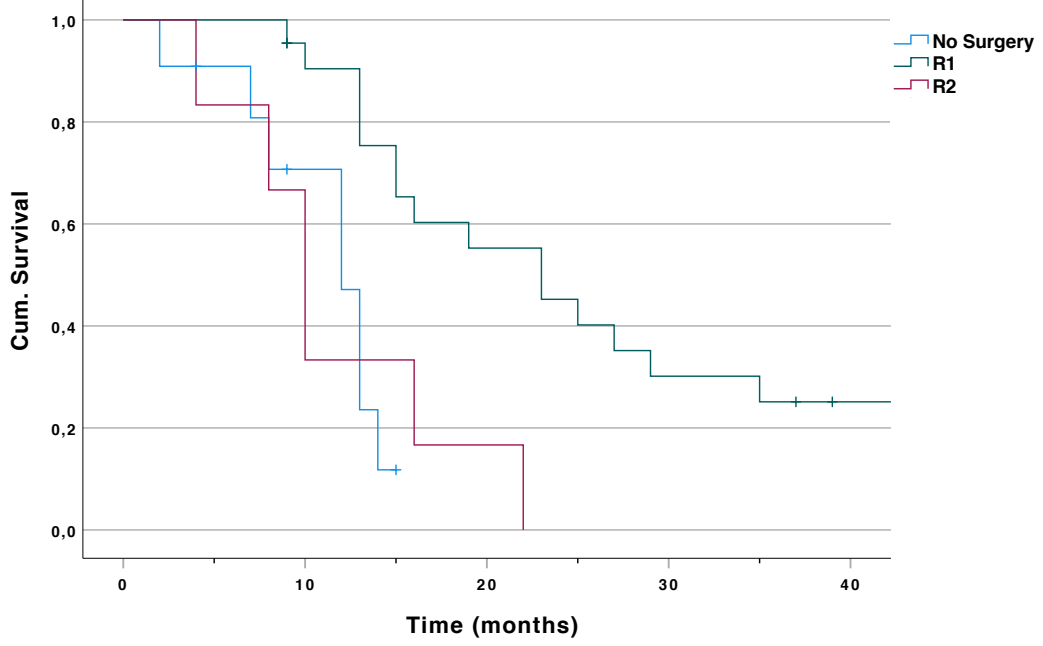
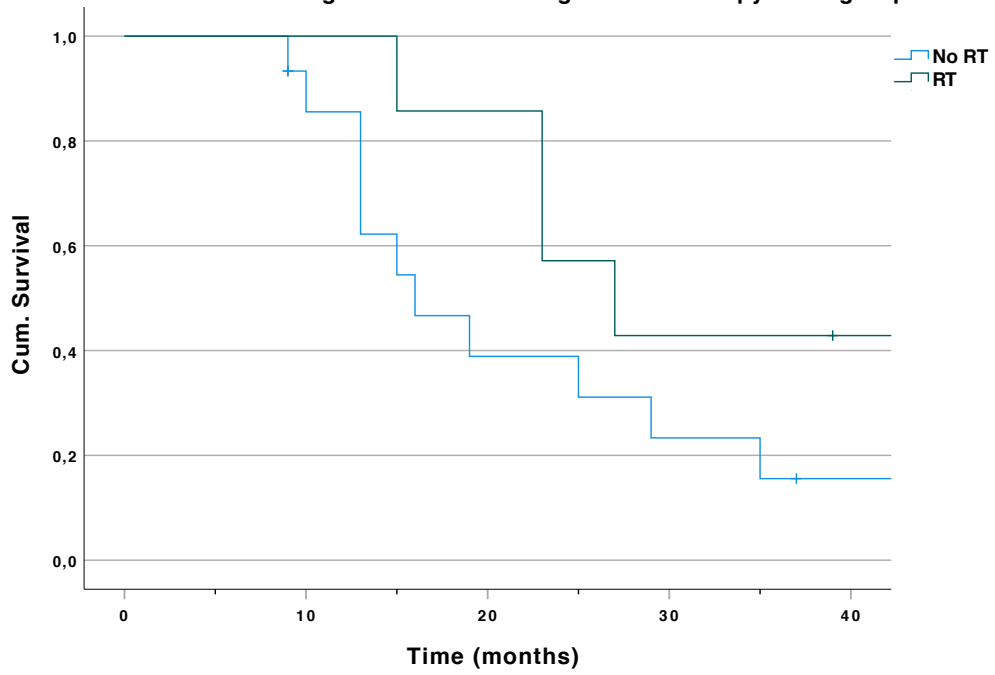


Figure4. EFS according to Radiotherapy in R1 group





Poster #261 #1818873

WHAT ARE PREOPERATIVE RISK FACTORS FOR FIBROSARCOMATOUS TRANSFORMATION IN DERMATOFIBROSARCOMA PROTUBERANS (DFSP)

Matthew T. Houdek, MD¹; Kim M. Tsoi, MD, PhD²; Sarah Almubarak, BS²; Matthew R. Claxton, BS¹; Katerine Mallett, MD¹; Peter C. Ferguson, MD²; Peter S. Rose, MD¹; Jay S. Wunder, MD²

¹Mayo Clinic, Rochester, Minnesota, UNITED STATES, ²University of Toronto, Mount Sinai Hospital, Toronto, Ontario, CANADA

Objective: Dermatofibrosarcoma protuberans (DFSP) is a rare, often superficial soft tissue sarcoma. This tumor has been classified as one that has a high risk of local tumor recurrence, however typically never metastasizes. Rarely, DFSP can transform into a high-grade fibrosarcoma (DFSP-FS) which has a risk of metastatic disease. Currently treatment for DFSP includes Moh’s micrographic surgery, however this technique is not recommended for DFSP-FS. Often the transformation to a DFSP-FS is not recognized until the final histological diagnosis, and re-excision of the previous Moh’s surgery sites can be morbid. As such analyzing risk factors for DFSP-FS transformation are important in order to appropriately manage patients with a Moh’s micrographic surgery versus a wide local excision. The purpose of the current study was to analyze our institutions experience treating DFSP and DFSP-FS to analyze preoperative risk factors which may suggest a diagnosis of DFSP-FS.

Methods: Patients and Methods: We reviewed 368 (174 female, 194 male) patients with a mean age of 42±16 years at the time of presentation from 2 tertiary sarcoma centers in North America. Of these, 319 (87%) of patients had a history of DFSP and 49 (13%) had a history of DFSP-FS. Preoperative patient characteristics were compared in order to identify risk factors for DFSP-FS.

Results: The mean tumor size was 4±3 cm, and 57 (15%) had a history of a painful mass, with 75 (20%) patients reporting the mass they had present for a period of time rapidly started to grow.

When comparing patients with a DFSP to those with a DFSP-FS, patients with a DFSP-FS were more likely to be older (49 vs. 41 years, p<0.01), female (p=0.01) and have larger tumors (6 vs. 4 cm, p<0.01) compared to patients with DFSP. A history of painful mass (OR 2.63, 95% CI 1.30-5.30, p<0.01) and a rapidly enlarging mass (OR 22.2, 95% CI 9.61-51.5, p<0.01) were strongly associated with DFSP-FS.

Conclusion: The results of the current study reveal factors which could assist with the decision-making process to perform Moh’s versus WLE for DFSP. Since DFSP-FS is often not diagnosed until the final pathology with sectioning of the entire tumor, dermatologist performing Moh’s should consider referral of older, female patients with larger tumor displaying either rapid tumor growth or a painful tumor for consideration for WLE. Although Moh’s micrographic surgery can provide local tumor control in DFSP, a microscopic margin around DFSP-FS is likely not adequate for tumor control. As such patients who present with a history of these symptoms should be referred to an orthopedic oncologist for a wide local excision.

Table 1: Comparison of Patient Characteristics

Preoperative Characteristic	All Patients (n=368)	DFSP (n=319)	DFSP-FS (n=49)	P Value
Patient Age	41±16 years	41±15 years	49±18 years	<0.01
Male Gender	174 (44%)	159 (50%)	15 (33%)	0.01
Female Gender	194 (56%)	160 (50%)	34 (67%)	
Tumor Size	4±3 cm	4±2 cm	6±5 cm	<0.01
Painful Mass	57 (15%)	41 (13%)	16 (40%)	<0.01
Rapidly Enlarging Mass	75 (20%)	39 (12%)	36 (73%)	<0.01



PO #01 #1897714

ADULT FIBROSARCOMA IN THE EXTREMITIES: DEMOGRAPHIC AND ONCOLOGICAL OUTCOMES. A SEER-DATABASE RETROSPECTIVE STUDY

Jose M. Ramirez, BS¹; Yonghoon Lee, BA¹; Michael P. Guertin, BS²; Sheila Conway, MD³; Gina D'Amato, MD⁴; Juan Pretell-Mazzini, MD⁵

¹University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES, ²University of Miami Miller School of Medicine, Miramar, Florida, UNITED STATES, ³University of Miami/Jackson Memorial Hospital, Miami, Florida, UNITED STATES, ⁴Medical Oncology, Sylvester Comprehensive Cancer Center/University of Miami, Miami, Florida, UNITED STATES, ⁵Miller School of Medicine - University of Miami, Miami, Florida, UNITED STATES

Objective: Adult Fibrosarcoma (FS) is a rare tumor of mesenchymal origin that is typically a diagnosis of exclusion, common in middle age and older patients. The scarcity of this tumor makes demographics and oncological outcomes difficult to analyze with great statistical power. This project aims to use the Surveillance, Epidemiology, and End Results (SEER) database to determine demographics and survival outcomes of this tumor using a database of a large population of patients.

Methods: The SEER database was used to conduct a retrospective review of adult FS cases from 1975 to 2017. Only tumors in the extremities were included. Patients were classified by gender, age, race/ethnicity, and year of diagnosis. Three time periods (1975-1989, 1990-2004, and 2005-2019) were established to compare interval survival outcomes. Treatment options included surgery, chemotherapy, and radiation. The main oncological outcome analyzed was overall survival. The data was analyzed using SPSS (version 27). The estimated mean survival was determined using Kaplan-Meier survival and the log rank test was used to determine significance. Life tables were also created on SPSS to compare the proportion of patients surviving each year post diagnosis.

Results: 425 patients with adult FS in the extremities were included in this study. The mean follow-up time was 167.8 months (range 0-515 months). There was no difference in gender distribution, but it was most common among people of white race. (79.5%). Tumors were more commonly diagnosed as Stage I or Stage II (36.8% each). Tumors were more common in the lower limbs (63.3%) and most tumors were found in the soft tissues (88.9%). 53 patients (12.5%) underwent chemotherapy (69.3% of patients were Stage 3 or 4). Only 8 patients (1.9%) had metastasis at diagnosis (75% of these patients underwent chemotherapy).

Undergoing surgery with no chemotherapy provided a significant increase in overall survival (estimated mean survival 406.9 months, +/- 23.03, $p < 0.001$). Higher stage at diagnosis had lower estimated mean survival (stage 4 was 56.57 months +/- 38.37 vs Stage 1 tumors were 145.6 months +/- 21.38; $p = 0.002$) as well as presence of metastasis at diagnosis (44.13 months +/- 36.18 vs 326 months +/- 14.23; $p < 0.001$). Estimated mean survival was lower amongst patients who received chemotherapy (154.4 months +/- 58.10 vs 391.1 months +/- 23.11; $p < 0.001$). There was no significant difference in survival outcomes based on year of diagnosis, sex, race, tumor location, or tumor laterality. Life table analysis showed that 91% of adult FS patients survive the first year with a plateau at 4 years post-diagnosis. Chemotherapy had worst survival for the first 4 years post-diagnosis, with almost identical outcomes to those who didn't undergo chemotherapy past this time.

Conclusion: Adult FS it is a rare soft tissue sarcoma that is most found among white people and in lower extremities without gender or race preference. Metastasis at diagnosis and higher stage are associated with decreased survival. Chemotherapy appeared to have worse survival outcomes; however, it is of note that most patients who underwent chemotherapy had higher stage tumors. Surgical excision is associated with significant increase in survival. Life table analysis showed that 91% of patients survive the first year with a plateau at 98% 4 years after diagnosis.

Table 1

Fibrosarcoma characteristics and estimated mean overall survival			
Characteristics	Number of patients with percentage of total	Estimated mean overall survival in months	P value
Sex			P=0.407
Male	231 (54.4%)	353.2 +/- 31.99	
Female	194 (45.6%)	369.7 +/- 31.72	
Race			P=0.790
White	338 (79.5%)	356.4 +/- 26.09	
Black	53 (12.2%)	371.6 +/- 62.64	
Other (American Indian/AK native, Asian/Pacific Islander)	30 (7.1%)	369.2 +/- 87.35	
Tumor Location			P=0.084
Upper limb	156 (36.7%)		
Lower Limb	269 (63.3%)	385.6 +/- 35.36 346.824 +/- 29.89	
Laterality			P=0.565
Not a paired site	50 (11.8%)	331.2 +/- 68.42	
Right	195 (45.9%)	363.4 +/- 33.97	
Left	159 (37.4%)	344.3 +/- 36.40	
Metastasis			P <0.001
No	417 (98.1%)	367.2 +/- 22.98	
Yes	8 (1.9%)	44.13 +/- 36.18	
Year of diagnosis			P=0.555
1975-1989	224 (52.7%)	353.045 +/- 31.34	
1990-2004	131 (30.8%)	247.852 +/- 23.45	
2005-2019	70 (16.5%)	116.0 +/- 15.55	
Tumor Stage			P=0.002
Stage I	21 (4.9%)	147.6 +/- 21.38	
Stage II	21 (4.9%)	123.9 +/- 30.06	
Stage III	6 (1.4%)	73.67 +/- 46.32	
Stage IV	9 (2.1%)	56.57 +/- 38.37	
Unknown stage	368 (86.6%)	N/A	
Chemotherapy			P<0.001
Yes	53 (12.5%)	155.4 +/- 58.10	
No	372 (87.5%)	391.1 +/- 23.11	



PO #02 #1897701

**BRAIN METASTASIS IN HIGH-GRADE BONE AND SOFT TISSUE SARCOMA:
AN ANALYSIS OF CLINICOPATHOLOGICAL CHARACTERISTICS AND SURVIVAL DATA**

Charles A. Gusho, BS¹; Linus Lee, BE²; Alan T. Blank, MD, MS²; Marta Batus, MD²

¹Rush University Medical Center, Milwaukee, Wisconsin, UNITED STATES, ²Rush University Medical Center, Chicago, Illinois, UNITED STATES

Objective: Brain metastases (BM) in sarcoma are exceedingly rare, with few published series documenting ranges from 1% to 8%. The purpose of this investigation was to describe the incidence, clinical characteristics, and outcomes of these patients.

Methods: This study was a retrospective review using the Surveillance, Epidemiology, and End Results (SEER) database from 1975 to 2016. Kaplan and Meier methods were used to estimate and compare survival, and a Cox regression was used to identify prognostic factors of disease-specific survival (DSS) in BM patients only.

Results: Five-thousand nine-hundred thirty-three patients were identified. BM occurred in 0.7% (n = 44), and the median age of BM patients was 55.5 years (range, 4-88 years). The median DSS with BM was six months (95% CI, 3-9 months), with an estimated one-year probability of 24.5% (SE: 8.0%). On univariable analysis, there was no DSS influence of chemotherapy (HR, 0.670; 95% CI, 0.3-1.5; p = 0.326) nor radiation (HR, 1.308; 95% CI, 0.6-2.9; p = 0.517). However, surgery appeared to increase the disease-specific mortality risk (HR 2.492; 95% CI, 1.0-6.0; p = 0.042), and no multivariable model was conducted as this was the only significant factor.

Conclusion: BM in high-grade sarcoma is rare, portends a dismal prognosis, and frequently coexist with other sites of metastasis. The current study failed to prognosticate any survival influence with use of adjuvant therapy.



PO #03 #1897703

COMPARISON OF CLINICOPATHOLOGICAL FEATURES AND OUTCOMES BETWEEN PATIENTS WITH UNDIFFERENTIATED PLEOMORPHIC SARCOMA OF BONE AND SOFT TISSUE

Charles A. Gusho, BS¹; Jonathan Guntin, BS²; Linus Lee, BE²; Alan T. Blank, MD, MS²

¹Rush University Medical Center, Milwaukee, Wisconsin, UNITED STATES, ²Rush University Medical Center, Chicago, Illinois, UNITED STATES

Objective: This investigation sought to compare outcomes of patients with undifferentiated pleomorphic sarcoma of soft tissue (UPS-S) to undifferentiated pleomorphic sarcoma of bone (UPS-B).

Methods: This was a review of the Surveillance, Epidemiology, and End Results database from 1975 to 2016. Kaplan-Meier methods were used to estimate disease-free survival (DFS), and a Cox regression model was used to identify prognostic factors of DFS.

Results: The median age (IQR) of patients with UPS-S was 67 (54;78) years compared to 55 (40;69) years for UPS-B patients ($p < 0.001$). For UPS-S, the median DFS was 317 months compared to 70 for UPS-B ($p=0.020$). On multivariable analysis for UPS-S, age (HR, 1.018; 95% CI, 1.01-1.03; $p<0.001$), non-extremity tumors (HR, 1.490; 95% CI 1.14-1.95; $p=0.004$), and AJCC Stage 3 (HR, 2.238; 95% CI 1.2-4.17; $p=0.011$), and Stage 4 (HR, 9.388; 95% CI 4.69-18.79; $p<0.001$) disease were negative prognostic factors, while surgery (HR 0.234; 95% CI, 0.16-0.34; $p<0.001$) was a positive prognostic factor. For UPS-B, tumor size > 8 cm (HR, 3.101; 95% CI, 1.09-8.75; $p=0.033$) was the only prognostic factor identified.

Conclusion: The current study found no survival association of surgery with and without adjuvant chemotherapy or radiation for patients with UPS-B. Further research is needed to reliably inform the optimal treatment of these patients.



PO #04 #1897704

DEMOGRAPHIC AND PATHOLOGIC FACTORS IMPACTING PROGNOSIS IN BONE SARCOMAS OF THE HAND: SEER DATABASE REVIEW

Muhammad U. Jawad, MD; Christopher O. Bayne, MD; Saif Farhan, MD; Max R. Haffner, MD; Janai Carr-Ascher, MD, PhD; Elysia Alvarez, MD, MPH; Steven W. Thorpe, MD; R. Lor Randall, MD
¹University of California, Davis, Sacramento, California, UNITED STATES

Objective: Primary osseous malignancies of the hand and wrist are extremely rare and are associated with significant morbidity. Anatomical and biomechanical complexity of hand and wrist, with critical neurovascular elements adjacent to osseous and musculo-tendinous structures constitute unique surgical challenges. Surgical challenges include preservation of essential anatomy to maintain function and dexterity while achieving local tumor control with negative margins. The data regarding epidemiology and prognostic factors governing the outcomes for bone sarcomas of the hand and wrist is scarce. Given the rarity of the disease, most of the data is limited to small case series emanating from single-centers. Data from single-center studies is susceptible to selection bias. Population based registries have been employed to elaborate the epidemiological features of soft tissue sarcoma affecting the upper extremity in the US and Europe. The National Cancer Database (NCDB) has also been utilized to investigate the characteristics of osteosarcoma affecting the upper extremity. However, population-based data regarding osseous sarcoma of the hand is lacking. Osteosarcoma, chondrosarcoma, Ewing sarcoma and malignant giant cell tumor of bone (GCTB) constitutes the majority of malignancies affecting the osseous structures of hand and wrist. In the current study we have queried National cancer institute's (NCI) Surveillance, Epidemiology and End Result (SEER) database to extract and analyze the data regarding bone sarcomas of the hand and wrist in the US from 1975-2017. SEER is the only comprehensive source of population-based data in the US and is regarded as a standard of quality among the cancer registries around the world with a case completeness of 98%. We have limited our analysis to the hand and wrist in order to elucidate the unique characteristics of the disease process affecting this intricate anatomical area.

Methods: We isolated a total of 237 cases with primary location as 'small bones of the upper limb' and histologic ICD-O-3 codes for osteosarcoma, chondrosarcoma, malignant giant cell tumor of bone and Ewing sarcoma. The information was extracted from three different datasets within the SEER database. Information regarding patient demographics, grade, stage, size, cause of death, year of diagnosis, surgical and radiation treatment, and survival time until death or loss to follow-up was identified. Information regarding socioeconomic status (SES) and insurance was extracted. Patients with no insurance were grouped together with patients on Medicaid. This was done as patients presenting with no insurance to a healthcare facility are enrolled in Medicaid. Patients with missing data were excluded from each respective univariate and multivariate analysis. Patient age was converted to a categorical variable (0-14, 15-40, 40-59, ≥60) for the purpose of analysis. We chose this stratification to align with adolescent and young adult population demographics being defined at 15-3926, 27. Staging categories of local, regional and distant disease were used according to SEER staging system²⁸. Tumor size was also converted into a categorical variable (≤6 cm, >6 cm) considering the distribution of tumor size in the cohort. SEER* Stat software (version 8.3.8, NCI) was used to analyze incidence rates which were age adjusted and normalized using the 2000 US Standard population using the dataset '9 registries 1975-2017'. Statistical analysis was performed using SPSS Statistical package version 27.0 (SPSS Inc., Chicago, IL). Chi-square test was used to make correlations between categorical variables. Log-rank test was utilized for categorical values to gauge the effects of demographic, clinical, pathological and treatment variables. A multivariate analysis was carried out for determination of independent prognostic factors using the Cox proportional hazards model.

Results: A total of 237 patients were extracted from the SEER database from 1975-2017. The incidence of bone sarcoma of hand and wrist was 0.017 cases per 100,000 persons in 2017 and has not changed significantly since 1975. Annual percentage change (APC) could not be calculated (Figure 1A). Age adjusted incidence shows a late peak after 60 years of age (Figure 1 B). The five and ten-years disease specific survival for the entire cohort was 90% and 84% respectively (Supplemental Table 2, Figure 2A). Stratified by the year of diagnosis, 10-year DSS improved from ~75% for 1975-1994 to ~90% for 1995-2017 (Supplemental Table 2). Univariate and multivariate analyses of the entire cohort are summarized in Supplemental Table 2 and 3 respectively. Of note, osteosarcoma arising from hand and wrist was found to have better prognosis when compared to osteosarcoma arising from the rest of the axial skeleton. On univariate analysis, 'female' sex ($p=0.016$), 'white' race ($p=0.032$), 'low' grade ($p < 0.001$), 'localized' stage ($p < 0.001$), histological subtype of chondrosarcoma or malignant

giant cell tumor ($p < 0.001$), and surgical resection ($p < 0.001$) were significantly associated with improved survival. Of note SES or insurance status are of no prognostic significance for patient with bone sarcoma of hand and wrist. On multivariate analysis (Supplemental Table 3), 'others' race, 'undifferentiated' grade, histopathologic subtype of 'osteosarcoma', and size of primary tumor ' $\geq 6\text{cm}$ ' were independent predictors of worse outcomes. Corresponding Kaplan-Meier curves are shown in Figure 2B & C and Figure 3 A&B. A cross table was made between race and other prognostic factors achieving significance to analyze the racial disparity in outcomes (Supplemental Table 4). Chi square was used to assess the correlation. A significant association was observed between race and stage, size, histology and surgical resection.

Conclusion: Bone sarcomas of the hand and wrist are rare but have been associated with significant morbidity. One of the predictors of improved outcome was Caucasian race when compared to 'others' ($p=0.032$, Table 3). This is a novel finding that has not been reported in the literature to the best of our knowledge. All the confounding factors were controlled for in the multivariate analysis, and 'white' race was still an independent predictor of improved survival. Socioeconomic status as a composite measure and the insurance status were not found to be of prognostic significance (Table 2). Chondrosarcoma was the most common histopathological subtype in our cohort. Most of the chondrosarcoma cases in our cohort were either well differentiated / low grade (59/130) or moderately differentiated (56/130). The stage was 'distant' in only 3 out of 141 cases for which the data was available. Chi Square test revealed a p-value of 0.001 and 0.002 respectively, upon cross-tabulation (data not shown). This finding highlights the significant association between histopathological diagnosis of chondrosarcoma and lack of poorly or undifferentiated grade and distant stage. Osteosarcoma was the second most common histological diagnosis in the cohort of cases with hand and wrist osseous malignancies (Table 1). It was also an independent predictor of poor outcomes on multivariate analysis (Table 3). The five- and ten- years survival for patients with osteogenic sarcoma of the hand and wrist was markedly better as compared to other locations. A higher proportion of patients with 'well differentiated/ low' or 'moderately differentiated' grade was seen in the cohort of patients with hand and wrist osteosarcoma compared to patients with osteogenic sarcoma in other locations (38.1% vs. 17.4%, data not shown). Despite improved survival when compared to other locations for osteogenic sarcoma, it was independently associated with poor outcomes in the cohort of patients with hand and wrist malignancies.



PO #05 #1897716

**EPIDEMIOLOGY AND SURVIVAL FACTORS IN APPENDICULAR MYXOFIBROSARCOMA:
A SEER-RETROSPECTIVE STUDY**

Yonghoon Lee, BA¹; Michael P. Guertin, BS²; Alvin Nguyen, BA³; Jose M. Ramirez, BS¹; Gina D'Amato, MD¹;
Juan Pretell-Mazzini, MD⁴

¹University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES, ²University of Miami Miller School of Medicine, Miramar, Florida, UNITED STATES, ³University of Illinois College of Medicine, Chicago, Illinois, UNITED STATES, ⁴Miller School of Medicine - University of Miami, Miami, Florida, UNITED STATES

Objective: Soft tissue sarcomas are a group of heterogeneous mesenchymal tumors that vary considerably from one another in terms of clinical behavior and treatment. Myxofibrosarcoma (MFS) is a rare subtype of soft tissue sarcoma with a relatively high rate of recurrence and metastasis. However, low incidence of these tumors makes studies with large sample sizes and high power difficult to achieve, thereby, limiting generalizability. Therefore, this study utilized the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database to better understand the epidemiology and factors associated with overall survival on patients with myxofibrosarcoma.

Methods: A retrospective review of MFS cases was performed using the latest version of the SEER database, released in April 2021, to assess cases from January 2000 to December 2015 for a minimum 5-year survival rate. Patients were selected with ICD-O-3 code 8811/3. Tumors only in the extremities were included. Patients were classified demographically by age, gender, race/ethnicity, and year of diagnosis; tumor characteristics were classified by primary site, tumor size, location, depth, grade, laterality, staging (AJCC 6th and 7th edition), radiation, chemotherapy, metastasis at diagnosis; and overall survival was assessed. For comparison with all soft tissue sarcomas (STS), patients were selected with the AYA site recode 2008 "Soft Tissue Sarcomas", with Kaposi Sarcoma excluded, and the same inclusion/exclusion criteria as MFS was applied. All variables were analyzed with SPSS (version 26). Categorical variables were compared using Pearson's Chi-Square test and Cramer V. Kaplan-Meier curves were used to analyze overall survival rates. Hazard ratios (HRs) that compared the risk of death between categorical variables were assessed via Cox regression analysis.

Results: There were 1444 patients with MFS in the extremities. The median age was 62 years (standard deviation, 19); with 46% females and 54% males and a majority (70%) was non-Hispanic and white. The median age of all STS was 56 years (standard deviation, 21) with 46% females and 54% males. The mean tumor size was 75 mm (range, 2-987mm) and most (91%) patients had an excision to remove the tumor. Almost half of the patients received radiation and only 9% had chemotherapy. Three percent of the patients had metastasis at time of diagnosis. Median survival or follow-up time was 64 months (range, 0-215 months) since diagnosis. The 5-year survival rate from MFS was 88% and the overall survival rate was 86%. The 5-year survival rate from all appendicular STS was 68% and overall survival rate was 67%. There are significant increases for risk of death HRs when comparing those under 30s to those between 30 to 70 (HR 3.63, 95% confidence interval (CI) 1.33-9.89, $p=0.012$) and over 70 (HR 7.49, 95% CI 2.75-20.38, $p<0.001$). No patients with tumor in the skin or peripheral nerves died, but the difference in survival rate is not statistically significant compared to subcutaneous or soft tissue invasion ($p=0.30$). Factors that increased the risk of death were: increased stage at diagnosis (HR 2.13, 95% CI 1.80-2.51, $p<0.001$), radiation (HR 1.37, 95% CI 1.03-1.82, $p=0.03$), grade (HR 1.92, 95% CI 1.66-2.21, $p<0.001$) and metastasis found at diagnosis (HR 10.24, 95% CI 7.07-14.83, $p<0.001$). Chemotherapy was associated with an increased risk of death in only those patients diagnosed with tumors in stage IV (HR 4.29, 95% CI 1.15-15.98, $p=0.03$), but trended towards increased survival for tumors in stage II. There is no overall change in survival in patients who underwent chemotherapy and radiotherapy. Compared to non-operative measures, excision decreases the risk of death (HR 0.21, 95% CI 0.14-0.32, $p<0.001$) more so than amputations (HR 0.46, 95% CI 0.24-0.88, $p=0.02$).

Conclusion: MFS occurs later in older adults when compared to all STS. They are more prevalent in the lower extremities and slightly more in males than females. Compared to other STS, it has a high overall survival rate. Decreased survival was most associated with age over 70, no surgery, metastasis at diagnosis, grade 4 and stage IV tumors. Patients under 30 and those with tumor in the skin or peripheral nerves had very high survival rates. There is no clear evidence of improved survival when using chemotherapy and radiotherapy.



PO #06 #1897710

ESTABLISHMENT AND CHARACTERIZATION OF A NOVEL PATIENT-DERIVED CELL LINE FROM GIANT CELL TUMOR OF BONE

Takuya Ono, graduate student¹; Rei Noguchi, MD, PhD²; Yuki Yoshimatsu, PhD³; Yooksil Sin, PhD⁴; Ryuto Tsuchiya, MD¹; Yu Kuwata, Research Associate³; Kaoru Hirabayashi, MD⁵; Kazutaka Kikuta, MD, PhD⁶; Iwao Ozawa, MD⁷; Tadashi Kondo, MD, PhD¹

¹Division of Rare Cancer Research, National Cancer Center Research Institute, Chuo-ku, Tokyo, JAPAN, ²Division of Rare Cancer Research, National Cancer Center Research Institute, Tokyo, Tokyo, Japan, ³Division of Rare Cancer Research, National Cancer Center Research Institute, 5-1-1 Tsukiji, Chuo-ku, Tokyo, JAPAN, ⁴Division of Rare Cancer Research, National Cancer Center Research Institute, Chuo-ku, Tokyo, JAPAN, ⁵Division of Diagnostic Pathology, Tochigi Cancer Center, Utsunomiya-shi, Tochigi, JAPAN, ⁶Division of Musculoskeletal Oncology and Orthopaedic Surgery, Tochigi Cancer Center, Utsunomiya-shi, Tochigi, JAPAN, ⁷Division of Hepato-Biliary-Pancreatic Surgery, Tochigi Cancer Center, Utsunomiya-shi, Tochigi, JAPAN

Objective: Giant cell tumor of bone (GCTB) is an osteolytic intermediate bone tumor that harbours pathogenic H3F3A gene mutations and shows non-neoplastic osteoclast-like giant cells. The estimated incidence of GCTB which accounts for 5% of all primary bone tumors is 1.2-1.7 cases per 1 million person-years. 80% of GCTB occurs in patients between 20 and 40 years of age. The complete surgical resection is the standard curative treatment in GCTB. As GCTB can develop aggressive behaviors associated with local recurrence and distant metastasis, we need effective multidisciplinary treatments. Although patient-derived cancer cell lines are critical tool for preclinical and basic research, there are only 11 cell lines of GCTB according to the cell line database Cellosaurus. Thus, this study aimed to establish a novel patient-derived GCTB cell line.

Methods: Surgically resected tumor tissues from a 52-year-old male patient with GCTB were dissected into small pieces using scissors and incubated with collagenase type II. When the cells from the tumor tissues reached sub-confluence, they were detached with trypsin-EDTA solution and transferred to a culture plate. The cells were maintained in the medium with 10% fetal bovine serum at 37° in a humidified atmosphere with 5% CO₂. Using the cells from GCTB specimens, we performed Sanger sequencing to detect typical genetic mutation. To measure cell proliferation, we counted the number of cells at multiple time points, and calculated the doubling time based on the growth curve. The capability of the invasion was assessed with Matrigel-coated membrane. Spheroid formation was observed with low attachment round bottom plates. We conducted high-throughput screening of 214 anti-cancer agents with the cells.

Results: Using surgically resected tumor tissue from a patient with GCTB, we established the cell line and named it NCC-GCTB4-C1. The H3F3A gene mutation was detected in NCC-GCTB4-C1 cells by Sanger sequencing. The cells showed constant proliferation with population doubling times of 66 h calculated according to the growth curves. NCC-GCTB4-C1 cells displayed invasive ability as a result of in vitro assay with Matrigel-coated membrane. We found that the spheroids fabricated with the cell line included giant cells, which is typical character of GCTB. In drug screening using 214 anti-cancer agents, the seven agents with the lowest IC₅₀ value were doxorubicin, bortezomib, camptothecin, homoharringtonine, mitoxantrone, romidepsin and vinblastine sulfate. Notably, NCC-GCTB1-C1, NCC-GCTB2-C1 and NCC-GCTB3-C1 cell lines that had already established in our laboratory also showed a high sensitivity against doxorubicin, homoharringtonine, mitoxantrone and romidepsin.

Conclusion: These results indicate that the established NCC-GCTB4-C1 cell line has a great potential for preclinical and basic research for GCTB.



PO #07 #1897708

FEASIBILITY AND ADVANTAGE OF PREOPERATIVE RADIOTHERAPY FOR RETROPERITONEAL SARCOMA

Kyo Won Lee, MD, PhD; Jae Berm Park, MD, PhD

Samsung Medical Center, Seoul, Seoul-t'ukpyolsi, REPUBLIC OF KOREA

Objective: High local recurrence rate is the major hurdle to overcome in treatment of retroperitoneal sarcoma (RPS). Many studies have shown improved local recurrence rate with adjuvant radiotherapy. However, radiation can cause toxicity and adjuvant radiation for RPS is frequently dose-limited by the multiple radiosensitive organs that occupy the resected tumor bed (e.g., bowel, kidney, liver). Preoperative radiotherapy (preRTx) is an option to avoid the radiation toxicity and gain the improved local recurrence rate. However, preRTx had concerns about the risk of post-operative complications. Therefore, we tried to figure out the safety and effectiveness of preoperative radiotherapy for RPS.

Methods: We have reviewed the medical records of 199 patients with RPS who had treated by surgery and radiotherapy in our center from October of 2001 to February 2020. They are divided according to the radiotherapy strategy; preRTx group (n=23), postoperative radiotherapy without tissue expander group (postRTx, n=89), and postoperative radiotherapy with tissue expander group (postRTx+TE, n=86). We compared intra-operative characteristics, post-operative complications and radiotherapy characteristics according to groups.

Results: In terms of safety, preRTx did not increase R2 resection rate, operation time, estimated blood loss, and intraoperative transfusion. preRTx group showed higher incidence of post-operative transfusion and intensive care unit care. ($p=0.013$ and 0.036 , respectively) However, severe postoperative complication (CD class > III) rate and reoperation rate were not significantly different among groups. Three patients required operative management for complications in preRTx group and among them, in two patients, complication developed after discharge. In terms of effectiveness, radiation dose was highest in preRTx group ($p < 0.001$). However, there was no significant different in patient survival rate and local recurrence rate among groups.

Conclusion: preRTx is safe and possible option to reduce the local recurrence of RPS. With preRTx, radiation dose elevation can be achieved. However, long term advantage of preRTx need to be assessed with further studies.



PO #08 #1897711

FEMALE PRESENTING TRENDS IN ONCOLOGY ORTHOPEDICS: AN ANALYSIS OF THE PAST 5 YEARS

*Roselle Okubo, RN; Sarah Joseph, MD; Ana C. Belzarena, MD
Miami Cancer Institute, Miami, Florida, UNITED STATE*

Objective: Background: Even though the number of females in medicine has increased in the past few years, still remains low in orthopedic surgery with only 10-15% of females. Looking at the numbers per subspecialty, oncology orthopedics is also not a very popular choice among females who apparently choose more hand, foot and ankle or pediatric orthopedics more. The number of females in oncology orthopedics has also remained low at 6-7.6%. Previous studies, in other areas of medicine, have shown that even when the female numbers increase, female colleagues continued to be underrepresented in leadership positions as well as when presenting in conferences. The proportion of females presenting, as guest speakers and as senior authors are inferior to the number they represent in the workforce, leading to the idea that females are usually seen as just co-authors but not as research leaders. Questions/Purposes: The purpose of this study is to assess if women were proportionally represented in the percentage of presenting authors, senior authors and guest speaker roles in Oncology Orthopedics conferences. Additionally, the study aims at assessing if there were any changes in the trend of those numbers in the past five years.

Methods: Patients and Methods: The final conference programs of the most important oncology orthopedics conferences, from 2015-2019 were analyzed. Final programs of the conference were assessed for number of females presenting, female senior authors, female moderators and female guest speakers. For the year 2015, MSTS was combined with ISOLS, thus the combined program was used for analysis. Observed proportions of women in leadership positions compared with the expected proportion of overall faculty were assessed. Rates of representation of women across each year based on the presence or absence of a woman in research leadership positions were compared.

Results: Results: Over 350 papers presented in the last 5 years (2015-2019) were assessed. The percentage of female co-authors has varied over the years, with 2017 being the year with least females in research papers, only 13.4%. The same occurred with females as first authors, with only 6 of the 47 papers being presented by a woman in 2017. The percentage of female moderators has remained stable over time, with a maximum of 33.3% in 2016 versus 22.2% in 2017. The number of females as senior authors in the papers presented, continued the trend with a minimum in 2017 with only 6.4% of the manuscripts. Unfortunately, in the past 5 years none of the conference president or chair were females. The percentage of females as coauthors, first author, senior author and presenter has improved since 2017, with higher percentages in the last conference in 2019. The only category that did not show an improvement since the low numbers in 2017, was the percentage of female moderators. For the percentage of female oncology orthopedists, the numbers do not show an underrepresentation in most categories except conference chair and conference president.

Conclusion: Conclusions: Gender disparity exists the academic practice locations in many areas of medicine, which is magnified at the research production level. The impact that can be attained from using the potential of women in leadership roles is currently under appreciated in many areas of this field. Even though females are underrepresented in orthopedic surgery (10-15%) and even more in oncology orthopedics (6-6.7%) compared to the male counterparts, they attain higher percentage of representation in conference leadership positions.



PO #09 #1897715

IMPACT OF CONSERVATIVE AND RADICAL SURGICAL APPROACHES ON APPENDICULAR SARCOMAS IN A NATIONAL REFERENCE CENTER OF EUROPE - SEARCHING FOR PROGNOSTIC FACTORS

Miguel Esperança-Martins, Master's Degree¹; Joaquim Soares-do-Brito, Master's Degree²; Tiago Dias-Domingues, Master's Degree³; Raquel L. Lopes-Brás, Master's Degree²; Cecília Melo-Alvim, Master's Degree²; Luís Costa, PhD²; Isabel Fernandes, PhD²

¹Centro Hospitalar Universitário Lisboa Norte, Lisboa, Lisboa, PORTUGAL, ²Centro Hospitalar Universitário Lisboa Norte, Lisbon, Lisboa, PORTUGAL, ³Faculdade de Ciências da Universidade de Lisboa, Lisboa, Lisboa, PORTUGAL

Objective: Sarcomas are rare and heterogenous neoplasms of mesenchymal origin. Most of them develops from soft tissues (75%) (STS) and a smaller proportion develops from bone (10%) (BS). Topographically, they may be divided as extremity or trunk sarcomas. The identification of factors that influence survival and recurrence of sarcoma patients may be helpful, guiding the future selection of patients for neoadjuvant or adjuvant trials and primary therapy. Specific histologic types, tumor grade, mitotic activity and tumor size are known prognostic factors for survival, while microscopically positive margin is a prognostic factor for local recurrence among extremity STS patients [1]. Tumor grade and tumor size also influence survival in different BS types [2]. The identification of further factors that impact the prognosis of these patients is particularly relevant. Our center, despite being a European center, has unique characteristics treating an heterogenous population composed by patients evacuated from the former Portuguese African colonies (commonly with a diagnostic delay and typically presenting with high-volume sarcomas) and by patients diagnosed and referred to our center from different healthcare centers in Portugal. In the cases of extremity sarcomas with significant dimensions, frequently an amputation is proposed as part of the surgical management, in full compliance with the international gold-standard recommendations. Considering the singularity of our center population, we aim to retrospectively examine and compare the impact of limb conservative surgery and amputation on survival and recurrence of the extremity sarcoma patients operated and followed-up in our center between January 2009 and May 2021 and to evaluate the main influencing factors (histopathological, volumetric and surgery related) on survival and recurrence of both resected and amputated extremity sarcoma patients.

Methods: Retrospective cohort study of all the extremity sarcoma patients operated and followed-up in our center between January 2009 and May 2021. Demographic data, data relative to histologic types, histopathologic characteristics of the surgical samples (necrosis degree, angioinvasion, lymphoinvasion, sample margins), tumors dimensions, tumors volumes, types of surgeries performed, dates of surgeries, dates of local or distant recurrence diagnosis, dates of last follow-ups and dates of deaths were collected. For quantitative data, mean \pm standard deviation is presented. For qualitative data, respective absolute and relative frequencies are presented. The comparison between two independent groups, in the case of continuous variables, was performed using the Mann-Whitney test. Kaplan-Meier non-parametric estimator was used for overall survival (OS) and disease-free survival (DFS) estimation. The survival curves of different groups were compared using the log-rank test. The Cox regression model was used to evaluate the influence of a group of different covariables on OS and DFS of the amputated patients. All the results with a p-value inferior to 0.05 were considered statistically significant. Data analysis was performed using SPSS (Statistical Package for Social Sciences) version 26.

Results: An initial number of 228 patients was found, but only 60 patients had concomitant curative intent and made the entire diagnostic march in our center. The 60 patients were involved in this analysis. Thirty-two (53.3%) patients were male and 28 (46.7%) were female. Median age at diagnosis was 46.23 ± 21.17 . No statistically significant differences were found between males and females, respectively, relatively to age (Mann-Whitney test; median: 41.5 vs. 48.0; $p=0.078$). Most of these patients had STS ($n=32$, 53.3%), while 28 patients (46.7%) had BS. Thirty-one patients (51.7%) had confirmed local recurrence or distant metastasis development during the follow-up period and 27 (45%) died. Estimated OS of these patients was 58 months (CI 95%: 27.0-88.9) (Graph 1). Estimated DFS of these patients was 18 months (CI 95%: 8.4-27.6) (Graph 2). Forty-five (75%) of these patients had limb conservative surgery, while 15 (25%) were amputated. Statistically significant differences were found between the OS of patients submitted to limb conservative surgery and the OS of amputated patients, respectively (median 76 months vs. 21 months; log-rank test: $p<0.01$) (Graph 3). No statistically significant differences were found between the DFS of these two groups of patients (median: 19 months vs. 9 months; log-rank test: $p=0.403$) (Graph 4). An adjustment of a Cox regression model was performed to evaluate the influence of a group of covariables in the respective survival times (OS and DFS). Angioinvasion (HR 6.563; CI 95%: 0.978-1.023; $p=0.028$) and surgical procedure

(HR 19.134; CI 95%: 3.171-115.442; $p=0.001$) influenced OS among this group of extremity sarcoma patients (Table 1). The risk proportionality assumption wasn't verified regarding the multivariate analysis for DFS.

Conclusion: The early diagnosis of extremity sarcomas is of paramount importance, allowing a prompt and less radical surgical approach, possibly reducing the probability of an unfavorable biological evolution with an increase on the frequency of tumor aggressivity features, impacting survival and recurrence in these sarcoma patients. The remarkable heterogeneity of the population of our center allows the identification of two different groups of patients with different survival profiles, with biological characteristics of sarcomas (like angioinvasion) and clinical consequences of higher mutilating surgery procedures (like amputation) shaping these differences. Extremity sarcomas remain a group of mesenchymal neoplasms with a dismal prognosis, portrayed by modest OS and DFS median times. The search for easily and readily accessible prognostic factors is still far from being complete, with important gaps that need to be filled in. This task is of utmost importance with probable important reflexes on future patient selection for trials in different contexts and for primary therapy.



PO #10 #1897713

MANAGEMENT OF SOFT TISSUE TUMOR WITH A SIZE OF 2 TO 5 CM

Yoshihiro Araki¹; Norio Yamamoto²; Katsuhiko Hayashi²; Akihiko Takeuchi²; Shinji Miwa²; Kentaro Igarashi²; Takashi Higuchi¹; Hirotaka Yonezawa²; Sei Morinaga²; Yohei Asano²; Hiroyuki Tsuchiya²

¹Kanazawa Red Cross Hospital, Kanazawa City, Ishikawa, JAPAN, ²Department of Orthopedic Surgery, Kanazawa University School of Medicine, Kanazawa, Ishikawa, JAPAN

Objective: Excisional biopsy of soft tissue tumors ≤ 2 cm is conditionally permitted in the Soft Tissue Tumor Treatment Guideline 2020 in Japan, while preoperative biopsy is recommended for soft tissue tumors ≥ 5 cm. However, the management of soft tissue tumors with a size of 2-5 cm is not specified. Therefore, we examined the cases of 2-5 cm soft tissue tumors experienced at our hospital.

Methods: A total of 73 cases diagnosed as soft tissue tumors at our hospital from March 2014 to April 2021 were retrospectively reviewed, and 27 cases with a maximum length of 2-5 cm on images at presentation were enrolled. The histology, tumor size, tumor location, depth, symptoms, magnetic resonance imaging (MRI), needle biopsy, excisional biopsy, follow-up period, and recurrence were investigated.

Results: The histological types were lipoma (n=12), atheroma (n=5), angioleiomyoma (n=2), schwannoma (n=2), fibroma (n=2), ganglion (n=1), and angiomyofibroblastoma (n=1) as benign, and leiomyosarcoma (n=2) as malignancy. The mean size was 33 mm (range, 21-49 mm), the location was lower limbs (n=15), upper limbs (n=7), and trunk (n=5). The depth was superficial (n=22) and deep (n=5). Symptoms were a mass (n=11), an increasing mass (n=11), a painful mass (n=4), and asymptomatic (n=1). MRI was performed on 26 cases (5 cases with contrast enhanced MRI), excluding 1 case of claustrophobia. Needle biopsy and excisional biopsy were performed in 11 and 16 cases, respectively. The mean follow-up periods were 7 months (1-58 months), and no recurrence was observed.

Conclusion: 2-5cm malignant soft tissue tumors rarely exists (2/27 [7%]). The conditions recommended by the guidelines for excisional biopsy (MRI findings for benign tumor, being superficial, being apart from important organs), also apply to 2-5 cm soft tissue tumors. In cases that do not meet this condition, it is important to consider the management including pathological diagnosis by needle biopsy so as not to result in unplanned excision.



PO #11 #1897712

NCC-PLPS1-C1: A NOVEL PATIENT-DERIVED CELL LINE OF PLEOMORPHIC LIPOSARCOMA

Rei Noguchi, MD, PhD¹; Yuki Yoshimatsu, PhD²; Takuya Ono, graduate student³; Kaoru Hirabayashi, MD⁴; Kazutaka Kikuta, MD, PhD⁵; Iwao Ozawa, MD⁶; Tadashi Kondo, MD, PhD³,

¹Division of Rare Cancer Research, National Cancer Center Research Institute, Tokyo, Tokyo, JAPAN, ²Division of Rare Cancer Research, National Cancer Center Research Institute, 5-1-1 Tsukiji, Chuo-ku, Tokyo, JAPAN, ³Division of Rare Cancer Research, National Cancer Center Research Institute, Chuo-ku, Tokyo, JAPAN, ⁴Division of Diagnostic Pathology, Tochigi Cancer Center, Utsunomiya-shi, Tochigi, JAPAN, ⁵Division of Musculoskeletal Oncology and Orthopaedic Surgery, Tochigi Cancer Center, Utsunomiya-shi, Tochigi, JAPAN, ⁶Division of Hepato-Biliary-Pancreatic Surgery, Tochigi Cancer Center, Utsunomiya-shi, Tochigi, JAPAN

Objective: Pleomorphic liposarcoma (PLPS) is a rare, high-grade subtype of liposarcoma. Histologically, PLPS is characterized by the presence of a variable proportion of pleomorphic lipoblasts present within high-grade undifferentiated sarcoma. It accounts for less than 5% of all liposarcomas. Curative treatment for localized disease is local excision with clear surgical margin, whereas the first-line of therapy for the advanced stage consists of anthracycline-based regimens. Effective treatment is not available for patients with inoperable conditions and resistance to chemotherapeutics. Although drugs targeting molecules are approved for the treatment of sarcomas, the effective molecular targeted drugs have not been developed for PLPS. PLPS is an aggressive sarcoma that exhibits frequent local recurrence and metastasis, with an overall 5-year survival rate of 60%. Distant metastases that are unresponsive to chemotherapy or radiotherapy develop in 30-50% of patients, and up to 50% of patients show tumor-associated mortality. Thus, novel therapies have long been required to treat PLPS. However, a paucity of adequate cell lines hinders the progress of research and treatments in PLPS. Presently, one cell line (LiSa-2) has been reported according to the world's largest cell line database Cellosaurus, and it is unavailable from public cell banks. Thus, there is a need to establish additional patient-derived cancer cell lines of PLPS. We aimed to establish and characterize a novel patient-derived cell line of PLPS.

Methods: Surgically resected tumor tissue was obtained from Tochigi Cancer Center Hospital. The tumor tissue was treated with collagenase and seeded onto the tissue culture plates. The tumor cells were maintained under the conventional tissue culture conditions until they grow well. The tumor cells were authenticated with examination of the short tandem repeat (STR) loci using the GenePrint 10 system. Copy number variants (CNV) of the tumor cells were examined using SNP (single nucleotide polymorphism) array genotyping with an Infinium PmniExpressExome-8. Their capability of proliferation, spheroid formation, and invasion were assessed in the tumor cells. We screened 214 anticancer drugs and examined kinase activity in the tumor cells by in vitro kinase assay (PamStation12).

Results: Using surgically resected tumor tissue from a 71-year-old male patient with PLPS, we established the NCC-PLPS1-C1 cell line. The cells were maintained for more than 8 months and passaged ~40 times in the tissue culture condition. The STR patterns of NCC-PLPS1-C1 cells did not match those of cell lines in the public cell banks using Cellosaurus, indicating that the NCC-PLPS1-C1 cell-line is a novel PLPS cell line. Genotyping analysis revealed multiple allelic deletions in chromosomal arms 2q, 4p, 9p, 12p, 13q, 16pq, and 17q. Amplifications such as MDM2 proto-oncogene, MDM2 in chr12 were not identified in NCC-PLPS1-C1 cells. Loss of neurofibromin1, NF1, a gene linked to neurofibromatosis type1 and known as a cancer-related gene, was identified from focal CNV. NCC-PLPS1-C1 cells showed rapid growth, spheroid formation, and invasive potential. Through the screen of the anti-cancer drugs, the proliferation of NCC-PLPS1-C1 cells was reduced by bortezomib, gemcitabine, romidepsin, topotecan, and vinblastine. The NCC-PLPS1-C1 cells and the original tumor tissue shared similar kinase activity profiles for FES and PDGFR- β .

Conclusion: We established a patient-derived cell line of PLPS and named it as NCC-PLPS1-C1. NCC-PLPS1-C1 is available for in vivo experiments such as high-throughput drug screening and kinase activity assay. Even though we established NCC-PLPS1-C1 cell line as a novel PLPS cell line, the paucity of the PLPS cell line has not been solved. Thus, establishment of multiple PLPS cell lines should be continued to promote research and develop novel drugs for patients with PLPS.



PO #12 #1897709

NECESSITY AND SAFETY OF PREOPERATIVE CORE NEEDLE BIOPSY FOR RETROPERITONEAL SARCOMA

Kyo Won Lee, MD, PhD; Jae Berm Park, MD, PhD

Samsung Medical Center, Seoul, Seoul-t'ukpyolsi, REPUBLIC OF KOREA

Objective: Several types of tumor can be arisen in retroperitoneal space. Among them, retroperitoneal sarcoma (RPS) requires aggressive treatment strategy such as wide excision including organs which are adjacent and not invaded by tumor, adjuvant radiotherapy, and adjuvant chemotherapy to reduce the local recurrence rate. Therefore, clinicians need to know the pathologic status of retroperitoneal tumor and perform a core needle biopsy (CNB) for it. However, there are concerns about the CNB including complications of the procedure, disruption of the operation field, needle tract tumor recurrence and risk of sarcomatosis. Therefore, we tried to figure out the necessity and safety of CNB for RPS.

Methods: We have reviewed the medical records of 274 patients with primary RPS who had treated in our center from October of 2001 to February 2020. Patients who got the excisional biopsy or fine needle aspiration and with inappropriate information were excluded. 269 patients were enrolled and among them, 64 patients treated after CNB (preOP biopsy group) and 205 patients treated without CNB (no biopsy group). We compared intra-operative characteristics, immediate post-operative complications, and patterns of tumor recurrence to confirm the safety of CNB for RPS. We also compared treatment outcomes to find out the necessity of it.

Results: In our center, false negative rate of RPS was 15.62%. Patient characteristics were similar in both groups. FNCLCC grade I tumor was more prevalent in no biopsy group (36.9% vs. 22.2%, $p = 0.05$) and follow up duration was longer in no biopsy (1634 days vs. 929 days, $p < 0.001$). In terms of safety, preOP biopsy did not increase the risk of R2 resection, post-operative complications, needle tract tumor recurrence, and tumor recurrence with sarcomatosis pattern. In terms of necessity, preOP biopsy increased chance of pre-operative radiotherapy or chemotherapy ($p < 0.001$ and $= 0.01$, respectively). Among patients got radiotherapy, patients in preOP biopsy group were treated with higher dose of radiation (59.7 Gy vs. 55.3 Gy, $p = 0.006$). However, patient survival rate and tumor local recurrence rate were not different between two groups.

Conclusion: CNB for RPS is safe way to find out the tumor character of RPS and necessary for prepare the treatment strategy for RPS. Even though patient survival and local recurrence rate were note different between groups, preOP biopsy increased the chance of adjuvant therapy with potential advantage.



PO #13 #1897707

RESPONSE TO CEMIPIMAB IN SYNCHRONOUS METASTATIC PLEOMORPHIC DERMAL SARCOMA AND SQUAMOUS CELL CARCINOMA OF THE SKIN

Juliana Beal, MD; Diogo Pereira, MD; Renee Zon Filippi, MD; Murilo Marques, MD; Rene Gansl, MD; Nelson Hamerschlak, MD, PhD; Roberto Carmagnani Pestana, MD
Hospital Israelita Albert Einstein, São Paulo, Sao Paulo, BRAZIL

Objective: Pleomorphic dermal sarcoma (PDS) is a neoplasm of soft tissues that has a higher incidence in the eighth decade of life, most commonly affects men (7:1 ratio) and is frequently found in areas of sun exposure (mainly scalp). Formerly known as malignant fibrous histiocytoma, it was categorized by the World Health Organization together with atypical fibroxanthoma until 2013. Histological differentiation between these entities is done through the depth of invasion into the subcutaneous tissue, presence of cellular infiltrate and lymphovascular/perineural invasion and the presence of necrosis; findings that in a scenario of a skin tumor suggests the diagnosis of dermal sarcoma. It has an aggressive behavior, with local recurrence estimated in 20-38% and distant metastases in 10-20% of the cases, most commonly to skin, lymph nodes and lung. As it is a rare subtype of sarcoma, there is no defined guidelines for treatment - currently, evidence for this disease is based primarily on a few case series, and there is a growing body of evidence suggesting activity of checkpoint inhibitors.

Skin squamous cell carcinoma (SCC) is the second most common skin cancer, responsible for 20% of deaths from skin cancer, with mortality rates reported in up to 70% of cases with distant metastases, in addition to recurrence rates of 15 to 28%. Risk factors for SCC are similar to those for PDS, such as exposure to ultraviolet radiation, advanced age and immunosuppression. Other characteristics in common between these skin malignancies are hallmarks that may suggest benefits with the use of immunotherapy, such as high tumor mutation load, inactivation of tumor suppressor genes and changes in DNA repair genes.

The objective of this case report is to describe a partial response of synchronous metastatic PDS and SCC after 10 cycles of cemiplimab.

Methods: Our report illustrates the case of a patient with two metastatic primary synchronic tumors, with different histological origins, treated with cemiplimab.

Results: A 72-year-old man with a previous history of diffuse B-cell lymphoma treated in 2011 with R-CHOP, with no evidence of relapse since then, underwent excision of two scalp lesions. On the right, biopsy was consistent with PDS, and on the left, consistent with SCC. The patient subsequently presented with palpable cervical masses, and a PET-CT demonstrated the presence of bilateral enlarged cervical lymph nodes with FDG uptake in addition to the presence of multiple pulmonary nodules (up to 8 mm). Bilateral lymph node biopsies were performed with findings suggesting: on the right metastatic PDS, and on the left metastatic SCC. The pulmonary nodules were not biopsied due to their subcentimetric size. PDS had a high immunoexpression of 90% of PD-L1 receptor (22C3 Dako test).

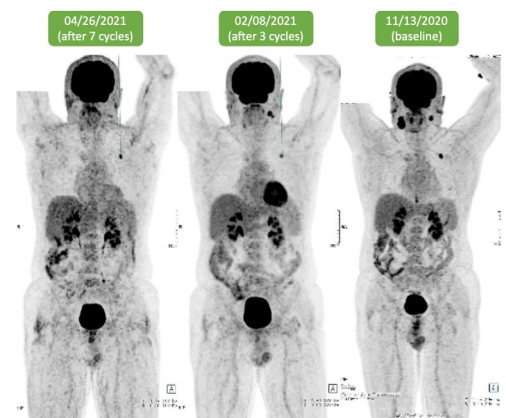
Systemic treatment with cemiplimab was initiated in December 2020 and the patient had a partial response of both metastatic lymph node lesions and major regression in scalp lesions after cycle 3.

Currently the patient is still on therapy, after having received 10 cycles, with sustained partial response (Figure 1).

Conclusion: PDS is a rare entity for which the role of systemic chemotherapy is not well defined. There are few reports of efficacy, however, and no prospective data establishes the best systemic treatment in the context of locally advanced, recurrent or metastatic disease, although there are reports of successful treatment with immune checkpoint inhibitors.

This case report illustrates the clinical response of a patient with two metastatic primary synchronic skin tumors to distant lymph nodes when treated with cemiplimab in the first line, in view of being a therapeutic option with significant activity for metastatic skin SCC and with potential activity for metastatic PDS.

As there is an absence of good prospective data to allow a better approach to PDS, we believe that the present report can assist in the management of other patients diagnosed with the same malignancy.





PO #14 #1897706

RISK FACTORS FOR POSITIVE MARGINS AFTER SURGICAL RESECTION OF PEDIATRIC NON-RHABDOMYOMATOUS SOFT TISSUE SARCOMA

Bryce Beyer, BS¹; Beth McCarville, MD²; Xiaoqing Wang, PhD³; Zhaohua Lu, PhD³; Christopher Tinkle, MD²; Matthew Krasin, MD²; Michael Bishop, MD³; Alberto Pappo, MD³; Teresa Santiago, MD²; Andrew Murphy, MD²; Andrew Davidoff, MD²; Lindsay J. Talbot, MD³; Hafeez Abdelhafeez, MD⁴

¹University of Tennessee School of Medicine, Memphis, Tennessee, UNITED STATES, ²St Jude Children's Research Hospital, Memphis, Tennessee, UNITED STATES, ³St. Jude Children's Research Hospital, Memphis, Tennessee, UNITED STATES, ⁴St. Jude Children's Research Hospital, Memphis, Tennessee, UNITED STATES

Objective: Non-rhabdomyomatous soft tissue sarcomas (NRSTS) are a heterogeneous group of rare mesenchymal tumors that comprise greater than 35 distinct histologic subtypes and affect pediatric patients to a greater degree than adults. While treatment strategies differ based on histology chemosensitivity and radiosensitivity, which can vary substantially between histologies, surgical resection is the cornerstone of treatment for most histologies of NRSTS. Complete (R0) resection is the primary goal for local control, and positive surgical margins have been shown to be the most important contributing factor in local recurrence. In this study, we sought to examine the clinical features associated with positive surgical margins in pediatric patients undergoing primary oncologic resection with intent to cure for NRSTS.

Methods: We conducted a retrospective review of all patients undergoing primary resection for NRSTS at a single tertiary pediatric oncology center between January 2009 and April 2019. Inclusion criteria were age < 21 years, patients undergoing initial operation with curative intent for NRSTS, and the availability of an adequate preoperative MRI for evaluation. Exclusion criteria included resections performed for biopsy or recurrent tumor and lack of adequate preoperative MRI. We collected demographic data including age, sex, and race; tumor-specific data including histology, grade, TNM stage, site, and size; imaging characteristics including infiltrative pattern, presence of tumor-associated edema, and proximity to critical structures, and treatment specific data including neoadjuvant chemotherapy or radiation treatment. Operative reports were additionally examined for the surgeon's assessment of proximity to critical structures (neurovascular bundles, prostatic urethra, chest wall, etc.) precluding R0 resection and the presence of gross residual disease. Positive microscopic surgical margin (R1 resection) was defined as tumor on ink at pathologic examination, and positive macroscopic margin (R2 resection) was defined as tumor on ink with associated confirmation of gross residual disease as determined by the surgical operative report. Descriptive statistics were determined and univariate analysis was performed for all variables between patients with positive surgical margins versus negative surgical margins on final pathology. A p value of < 0.05 was considered significant.

Results: A total of 35 patients met inclusion criteria. Descriptive statistics and univariate analysis are shown in Table 1. We identified 23/35 patients (65.7%) with positive surgical margins after resection. There were no differences observed between patients with negative versus positive surgical margins with regard to age, sex, race, histology, grade, TNM stage, site, size, imaging characteristics, or receipt of neoadjuvant therapy. On univariate analysis, intraoperative surgeon assessment of proximity to vital structures precluding R0 resection was statistically significant between groups, with positive surgical margins associated with a higher likelihood of preclusive proximity to vital structures (73.9% vs 50%; p = 0.031).

Conclusion: NRSTS tumors carry a high risk of local recurrence when positive surgical margins are present after resection. In this study, we have shown that surgeon's intraoperative assessment of proximity to vital structures predicted margin positivity. This study highlights the importance of developing enhanced ability to determine intraoperative margin status and of thorough marking of surgical beds with radio-opaque clips when intraoperative proximity to vital structures is encountered to assist in appropriate postoperative radiotherapy administration. Further evaluation of this critical question should be performed within multicenter collaborative groups.

Table 1. Demographic, tumor-specific, imaging, and operative data.

	Negative Margins N (%)	Positive margins N (%)	P-value	
	N = 12	N = 23		
Demographics				
Age				
<5 years	0	6 (26.1%)	0.958	
5 – 9 years	2 (16.7%)	1 (4.3%)		
10 – 14 years	8 (66.7%)	7 (30.4%)		
15 – 19 years	2 (16.7%)	7 (30.4%)		
>20 years	0	2 (8.7%)		
Sex				
Female	6 (50.0%)	8 (34.8%)	0.685	
Male	6 (50.0%)	15 (65.2%)		
Race				
White non-Hispanic	6 (50.0%)	14 (60.9%)	0.889	
Black	4 (33.3%)	6 (26.1%)		
Other	2 (16.7%)	3 (13.0%)		
Tumor Characteristics				
Histology				
Alveolar Soft Part Sarcoma (ASPS)	1	1	0.664	
Clear Cell Sarcoma	0	2		
Dermatofibrosarcoma Protuberans	1	2		
Epithelioid Sarcoma	0	1		
Fibromyxoid sarcoma	1	2		
Hemangiopericytoma	0	1		
Histiocytoma (Fibrous & Angiomatoid)	2	1		
Infantile Fibrosarcoma	0	2		
Malignant Peripheral Nerve Sheath Tumor	1	1		
Myxoid Liposarcoma	3	1		
Spindle Cell Sarcoma	0	2		
Synovial Sarcoma	1	4		
Undifferentiated Sarcoma	2	3		
Grade				
1	7 (58.3%)	9 (39.1%)		0.664
2	0	1 (4.3%)		
3	5 (41.7%)	12 (52.2%)		
Undetermined	0	1 (4.3%)		
TNM Stage				
1	7 (58.3%)	11 (47.8%)	0.953	
2	2 (16.7%)	3 (13.0%)		
3	2 (16.7%)	5 (21.7%)		
4	1 (8.3%)	4 (17.4%)		
Site				
Trunk	2 (16.7%)	9 (39.1%)	0.456	
Extremities (w/ buttocks and shoulder girdle)	8 (66.7%)	12 (52.2%)		
Head & Neck	2 (16.7%)	2 (8.7%)		
Size				
≤5 cm	5 (41.7%)	7 (30.4%)	0.709	
>5 cm	7 (58.3%)	16 (69.6%)		
Imaging Characteristics				
Infiltrative Pattern				
Infiltrative	6 (50.0%)	14 (60.9%)	0.721	
Non-infiltrative	6 (50.0%)	9 (39.1%)		
Tumor edema				
Edematous	5 (41.7%)	13 (56.5%)	0.489	
Non-edematous	7 (58.3%)	10 (43.5%)		
Near vital structures				
No	6 (50.0%)	11 (47.8%)	1.000	
Yes	6 (50.0%)	12 (52.2%)		
Treatment Specific Data				
Neoadjuvant Chemotherapy				
Yes	3 (25.0%)	12 (52.2%)	0.163	
No	9 (75.0%)	11 (47.8%)		
Neoadjuvant Radiation				
Yes	2 (16.7%)	4 (17.4%)	1.000	
No	10 (83.3%)	19 (82.6%)		
Operative findings				
Tumor not proximal to vital structures	6 (50.0%)	6 (26.1%)	0.031*	
Tumor proximal to vital structures	6 (50.0%)	17 (73.9%)		



PO #15 #1897702

**TOLL LIKE RECEPTOR MEDIATED ACTIVATION OF UNFOLDED PROTEIN RESPONSE TARGETS
CHONDROSARCOMA STEM CELLS**

Karina Galoian, PhD¹; Beatrice Becker, BS/MS²; Anil Sedani, MD³; Alexandra Moran, MD³; Andres Perez, MD³;
Jeffrey Brown, MD⁴; Aaron Hoyt, MD⁴; Viktoria Dahl, MD⁴

¹University of Miami, Miller School of Medicine, Department of Orthopedic Surgery, Miami, Florida, UNITED STATES,
²University of Miami Department of Orthopedics, Miami, Florida, UNITED STATES, ³University of Miami, Miller School of
Medicine, Miami, Florida, UNITED STATES, ⁴University of Miami Miller School of Medicine, Miami, Florida,
UNITED STATES

Objective: Objective: Chondrosarcoma is the second most common primary malignancy of bone and one of most difficult tumors to diagnose and treat. Proline rich polypeptide 1,(PRP-1),mTORC1 inhibitor, innate immunity Toll like receptor (TLR1/2,6) ligand on chondrosarcoma cells, targets and drastically inhibits cancer stem cells and inhibits efficiently the growth of chondrosarcoma The signaling mechanisms leading to such effect needed to be identified.

Methods: Methods: Tissue culture, polyacrylamide gel electrophoresis, western and immunoblot, sarcosphere (cancer stem cell) formation and renewal assay, cell lysate preparation.

Results: Results: PRP-1(10µg/ml) leads to activation of the unfolded protein response (UPR) branches PERK- peIF2α -ATF4-CHOP and IRE1α -XBP1 signaling in chondrosarcoma 3D sarcosphere lysates and its counterpart ,ALDH high fractions, in monolayer lysates when treated with 20-40µg/ml PRP-1. The inhibition of BAFF complexes by PRP-1 was observed as well. Inhibition of both subunits of the esBAF complex (BRG1 and BRM), which possess oncogenic properties in chondrosarcoma and depletion of BAF170 (SMARCC2) was manifested.

Conclusion: Conclusion: PRP-1 was reported previously by us to be a ligand for innate immunity Toll like receptors present in chondrosarcoma. Our experimental results indicated uncharacterised before PRP-1 triggered activation of UPR branches in both in 2D ALDHhigh and 3D cell human chondrosarcoma cell cultures. The unfolded protein response is a stress signaling pathway of the endoplasmic reticulum. We assume that activation of PERK- peIF2α -ATF4-CHOP UPR branch led to activation of IRE1α -XBP1 axis; they were shown in literature to be organ tissue specific and was associated with the loss of stemness. While PRP-1 treatment leads to activation of UPR, the BAFF chromatin remodeling complexes were inhibited in stem cell fractions . BAFF is known to increase the stemness. We assume that PRP-1 induced activation of ER/UPR conformational stress response and, inhibition of BAFF complexes is necessary to trigger drastic decrease of chondrosarcoma stem cells. The interconnection between UPR and BAFF complexes needs to be further explored.



PO #16 #1897705

TRABECTEDIN FOR METASTATIC LIPOSARCOMA AND LEIOMYOSARCOMA: COMPARISON OF OUTCOMES FROM REAL WORLD EXPERIENCE IN AN AUSTRALIA SARCOMA SPECIALIST CENTRE TO PIVOTAL CLINICAL TRIAL RESULTS

Deborah Zhou, Bachelor of Medical Studies/Doctor of Medicine¹; Daniel King, M.Pharm B.MedSci, Pharmacist, Quality use of Medicines pharmacist²; Katie Thomson, RN, BN(Hons), Post grad Cancer & Haematology Nursing, Sarcoma Clinical Nurse Specialist²; Peter Grimison, BSc(Med) MBBS(Hons) MPH PhD FRACP³

¹Chris O'Brien Lifecare, Sydney, Australia, New South Wales, AUSTRALIA, ²Chris O'Brien Lifecare, Sydney, New South Wales, AUSTRALIA, ³Chris O'Brien Lifecare, Sydney, New South Wales, AUSTRALIA

Objective: Trabectedin is a novel marine derived antineoplastic agent with complex mechanisms of action including cytotoxic, immunological and targeted effects. It was only recently approved by the Therapeutics Goods Administration (TGA) in Australia for the treatment of patients with unresectable or metastatic liposarcoma or leiomyosarcoma who received a prior anthracycline-containing regimen. The TGA approval considered the pivotal open-label ET743-SAR-3007 clinical trial (NCT01343277), which randomised patients to trabectedin or dacarbazine, and demonstrated a statistically significant improvement in progression-free survival (median 4.2 vs 1.5 months respectively, HR 0.55, $p < 0.001$). The aim of this study was to compare the baseline characteristics and dosing and disease outcomes of trabectedin in a single Australian sarcoma specialist centre to published results from the pivotal ET743-SAR-3007 trial, and to document adverse events.

Methods: Data from patients who commenced trabectedin for liposarcoma or leiomyosarcoma at Chris O'Brien Lifecare, Sydney Australia between April 2019 and April 2021 were identified via a pharmacy generated report. A comprehensive retrospective paper and electronic chart review was conducted to evaluate the baseline characteristics, dosing schedules, adverse events, progression free survival (PFS) and overall survival (OS). Relevant comparative data for the trabectedin arm of the ET743-SAR-3007 clinical trial were derived from published reports (Patel et al Cancer 2019).

Results: A total of 6 patients were identified to have received trabectedin. Trabectedin was administered every 21 days via a continuous infusion over 24 hours in the outpatient setting. Baseline characteristics are shown in the table: compared to the pivotal trial, there were more myxoid liposarcoma but less non-myxoid liposarcoma, worse performance status, more previous lines of therapy, and more baseline hepatic impairment. Treatment details are shown in the table: compared to the pivotal trial, there were more baseline dose modifications (because of hepatic impairment), and less chemotherapy cycles received. Disease outcomes are shown in the table: compared to the pivotal trial, there was shorter PFS, and one-third of patients dying within 60 days of commencing trabectedin. Common grade 1-2 toxicity included: lethargy, dysgeusia, nausea, vomiting and peripheral oedema. There were 4 grade 3/4 haematological toxicities and 1 grade 3/4 non-haematological toxicity. 1 patient had asymptomatic decrease of left ventricular ejection fraction but there were no cases of rhabdomyolysis or capillary leak syndrome. 1 patient died of sepsis following one cycle of trabectedin.

Conclusion: We have described a real world experience of 6 patients who have been treated with trabectedin for metastatic liposarcoma and leiomyosarcoma. Trabectedin was safely administered in the outpatient setting with a toxicity profile broadly consistent with published data. However compared to the pivotal trial, our patients received less cycles of chemotherapy, were more likely to die within 60 days of commencing treatment, and had much shorter PFS and OS. Worse outcomes could be explained by differences in baseline characteristics with our patients more extensively pretreated, having worse performance status, and worse organ function. Careful assessment of baseline characteristics is important when counselling patients about the anticipated benefits and risk-profile of trabectedin therapy.

		Real World Experience (n=6)	ET743-SAR-3007 clinical trial Patel et al 2019 (n=384)
Histology			
Leiomyosarcoma – Uterine		2 (33%)	144 (38%)
Leiomyosarcoma – Non-uterine		2 (33%)	138 (36%)
Liposarcoma – Myxoid		2 (33%)	42 (11%)
Liposarcoma – Pleomorphic		0	11 (3%)
Liposarcoma – Dedifferentiated		0	49 (13%)
Baseline characteristics			
Gender	Male	2 (33%)	122 (32%)
	Female	4 (66%)	262 (68%)
Age	Median (Range)	56 (43-60)	57 (18-81)
Performance status	0	0	184 (46%)
	1	5 (83%)	200 (52%)
	2	1 (17%)	0
Previous lines of therapy	1	0	46 (12)
	2	0	176 (46%)
	3	3 (50%)	99 (26%)
	4	1 (17%)	39 (10%)
	> 4	2 (33%)	24 (6%)
Hepatic impairment	No	4 (67%)	384 (100%)
	Yes	2 (33%)	0
Treatment details			
Baseline dose modification	No	4 (67%)	340 (89%)
	Yes	2 (33%)	5 (0.01%)
	Unknown		39 (10%)
Chemotherapy cycles received	Median	2.5	4
	< 6	67%	56%
	≥ 6	33%	42%
Disease outcomes			
Progression free survival	Median 3-month rate	1.25 33%	Not provided
Death within 60 days of 1 st dose of study drug		33%	7%



ctos[®] |

Bringing together the
world's sarcoma specialists[®]

The Connective Tissue Oncology Society

For more information,
Please visit the CTOS website:
www.ctos.org

P.O. Box 320574
Alexandria, VA 22320
Phone: 301/502-7371
e-mail: ctos@ctos.org

Barbara Rapp, Executive Director



ctos[®]

Bringing together the
world's sarcoma specialists[®]

Save the Date

2022 Annual Meeting

November 16-19, 2022

Vancouver Convention Centre

Vancouver, Canada

The Connective Tissue Oncology Society

P.O. Box 320574 Alexandria, VA 22320

phone: 301/502-7371

| website: www.ctos.org

| e-mail: ctos@ctos.org