Mesothelioma Program

Memorial Sloan Kettering Cancer Center™

2023 Directors' Report

Mesothelioma at a Glance

Types of Mesothelioma

Pleural

Start in the chest, more than 3 out of 4 mesotheliomas are pleural.

Peritoneal

Start in the abdomen.

Pericardial

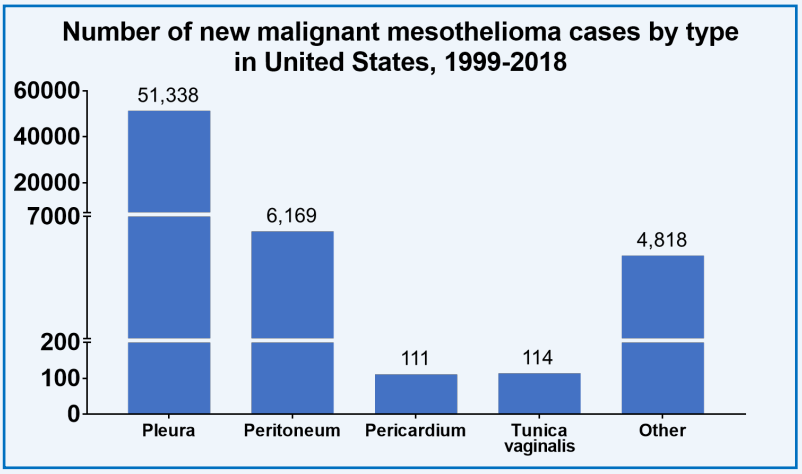
Start in the covering around the heart and are very rare.

Tunica Vaginalis

Very rare tumors that start in the covering layer of the testicles.

Pathological Subtypes

- More than half of mesotheliomas are **epithelioid**. This type tends to have a better prognosis than the other types.
- About 10% to 20% of mesotheliomas are **sarcomatoid**.
- **Mixed (biphasic)** mesotheliomas have both epithelioid and sarcomatoid areas. They make up the remaining 20% to 30% of mesotheliomas.



Source: Centers for Disease Control and Prevention. *Incidence of Malignant Mesothelioma, 1999–2018*. USCS Data Brief, no. 27. Atlanta, GA: Centers for Disease Control and Prevention, US Department of Health and Human Services; 2022.

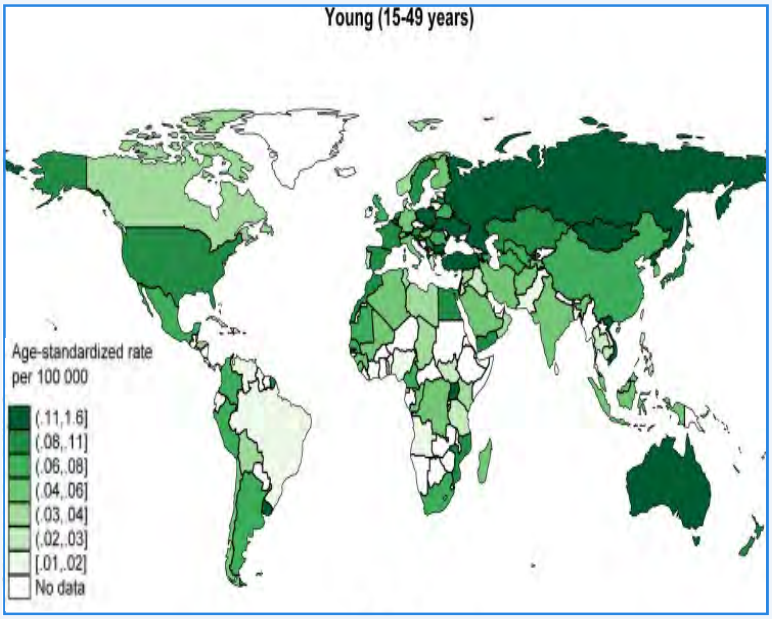
2,500

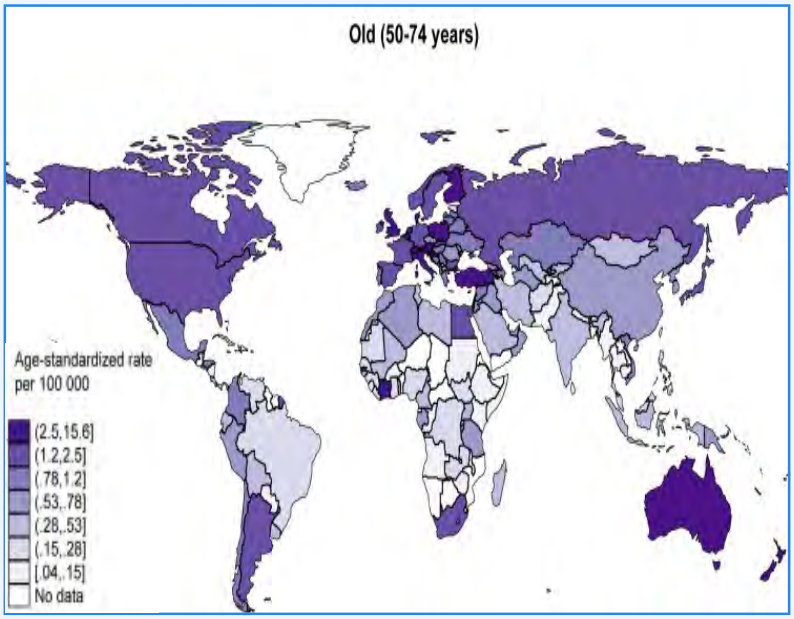
approximate deaths of mesothelioma patients each year in the United States

66,951

Americans were diagnosed with mesothelioma between 1999 and 2019

Global Incidence of Mesothelioma by Age in 2020





Source: (1) Centers for Disease Control and Prevention. *Incidence of Malignant Mesothelioma, 1999–2018*. USCS Data Brief, no. 27. Atlanta, GA: Centers for Disease Control and Prevention, US Department of Health and Human Services; 2022. **(2)** Huang J, ... Withers M, Wong MCS; NCD Global Health Research Group, Association of Pacific Rim Universities (APRU). Global Incidence, Risk Factors, and Temporal Trends of Mesothelioma: A Population-Based Study. *J Thorac Oncol*. 2023 Jun;18(6):792-802. **(3)** Molunari, Linda. *Mesothelioma Statistics. 2022.* https://www.mesothelioma.com/mesothelioma/statistics/

Contents

Letter from the Directors

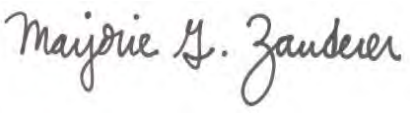
The Mesothelioma Program at Memorial Sloan Kettering Cancer Center (MSK) is one of the longest-serving and busiest clinical, academic, and research programs in the world. While our faculty and staff members have played a key role in optimizing the clinical management of patients with mesothelioma over the decades, we are aware of the current limitations that exist for cancer management. In addition to providing state-of-the-art chemotherapy, surgical resection, thoracic radiation, and immunotherapy, this report reflects the drive and ability of the members of the Mesothelioma Program to conduct research that will not only improve the treatments available to our patients, but also preserve their quality of life.

The Mesothelioma Program Directors' report provides an overview of the clinical care and research performed by mesothelioma specialists and nursing and allied health professionals at MSK during the 2017–2023 academic years. The exceptional multi-disciplinary team of clinicians, nurses, fellows, and staff that has been dedicated to the Mesothelioma Program provides clinical care and meets regularly to coordinate individualized patient care. In addition to those who are dedicated to clinical care, this report recognizes the hardworking staff in research MSK laboratories and their publications that have advanced the understanding of mesothelioma through basic science laboratory research, translational research, clinical trials, and research on patient outcomes and quality of life. This report also recognizes the members who have received research funding from federal and non-federal agencies as well as industry and philanthropic sources.

We specifically acknowledge the faculty members who have contributed to building a strong foundation to advance patient outcomes; these faculty members include Drs. Valerie W. Rusch (Chief of Thoracic Surgery, 2000–2013), Mark G. Kris (Chief of Thoracic Oncology, 1990–2013), Andreas Rimner (Director of Thoracic Radiation Oncology Research, 2019–present), Ellen D. Yorke (Physicist, 1998–present), as well as Charles M. Rudin and David R. Jones (Chiefs of Thoracic Disease Management Team). Finally, we would like to thank and recognize Meg Dooley (Senior Advisor to the Chief Development Officer) from the MSK Office of Development for her exceptional support to the Mesothelioma Program over the years. We are grateful to the patients who have entrusted their care to us.

Prasad S. Adusumilli, MD

Attending, Thoracic Service,
Department of Surgery



Marjorie G. Zauderer, MD

Associate Attending, Thoracic Oncology Service,
Department of Medicine

Mesothelioma Program (2017-2023 Academic Years)

36

FACULTY

17

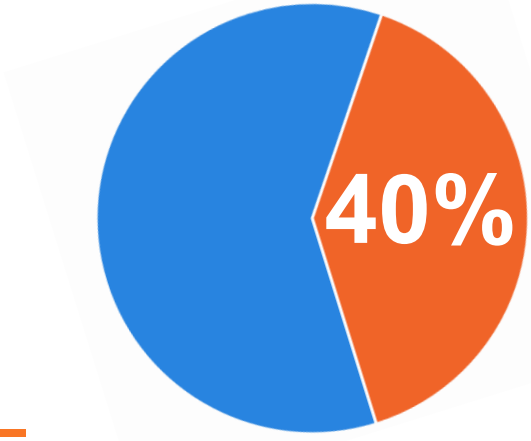
CLINICAL STAFF

46

RESEARCH STAFF

82

PUBLICATIONS



% OF PUBLICATIONS IN JOURNALS WITH AN IMPACT FACTOR (IF) ≥10

32

CLINICAL TRIALS

13

FEDERAL GRANTS

21

FOUNDATION GRANTS

25

INDUSTRY GRANTS

Patient Snapshot (2017-2023)

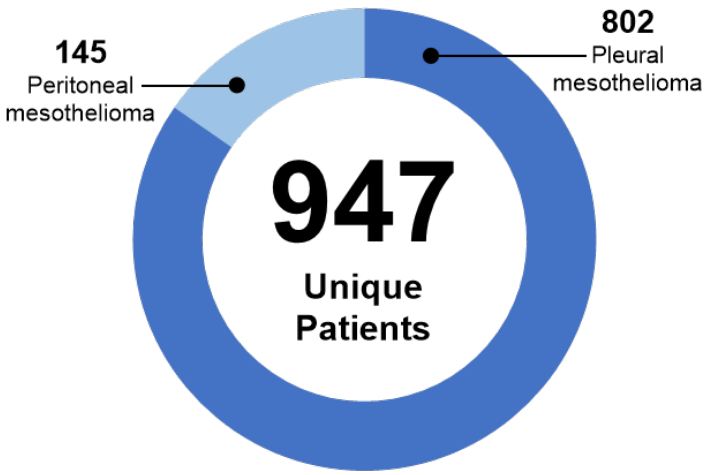
VISITS

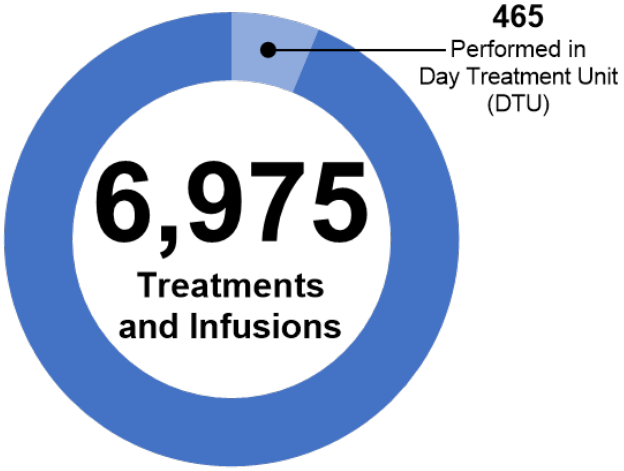
9,145
Clinical visits

1,328
New visits

Enrolled in:
Clinical trial protocols
23%
Biospecimen protocols
55%

POPULATION





TREATMENTS

168
Surgeries performed

120
Radiation regimens initiated

10
Proton regimens initiated

DATABASES

1036 surgically resected mesothelioma patients' database

- **192** data characteristics per patient
- **1 in 4** contributed from MSK to the international database (IASLC) of surgically resected mesothelioma patients

Mesothelioma Patient Treatment Journey

Patient calls referral service

Referral service obtains patient information

- Medical records
- Scans (CT/PET)
- Pathology slides

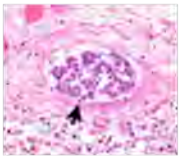
Clinic appointments coordinated for the **same day**

- MDs:
  - Surgery
  - Medical oncology
  - Radiation oncology
- Specialized nursing
- Social worker
- Research team

The management of each patient is discussed in multidisciplinary mesothelioma working group

Radiology review

Pathology review



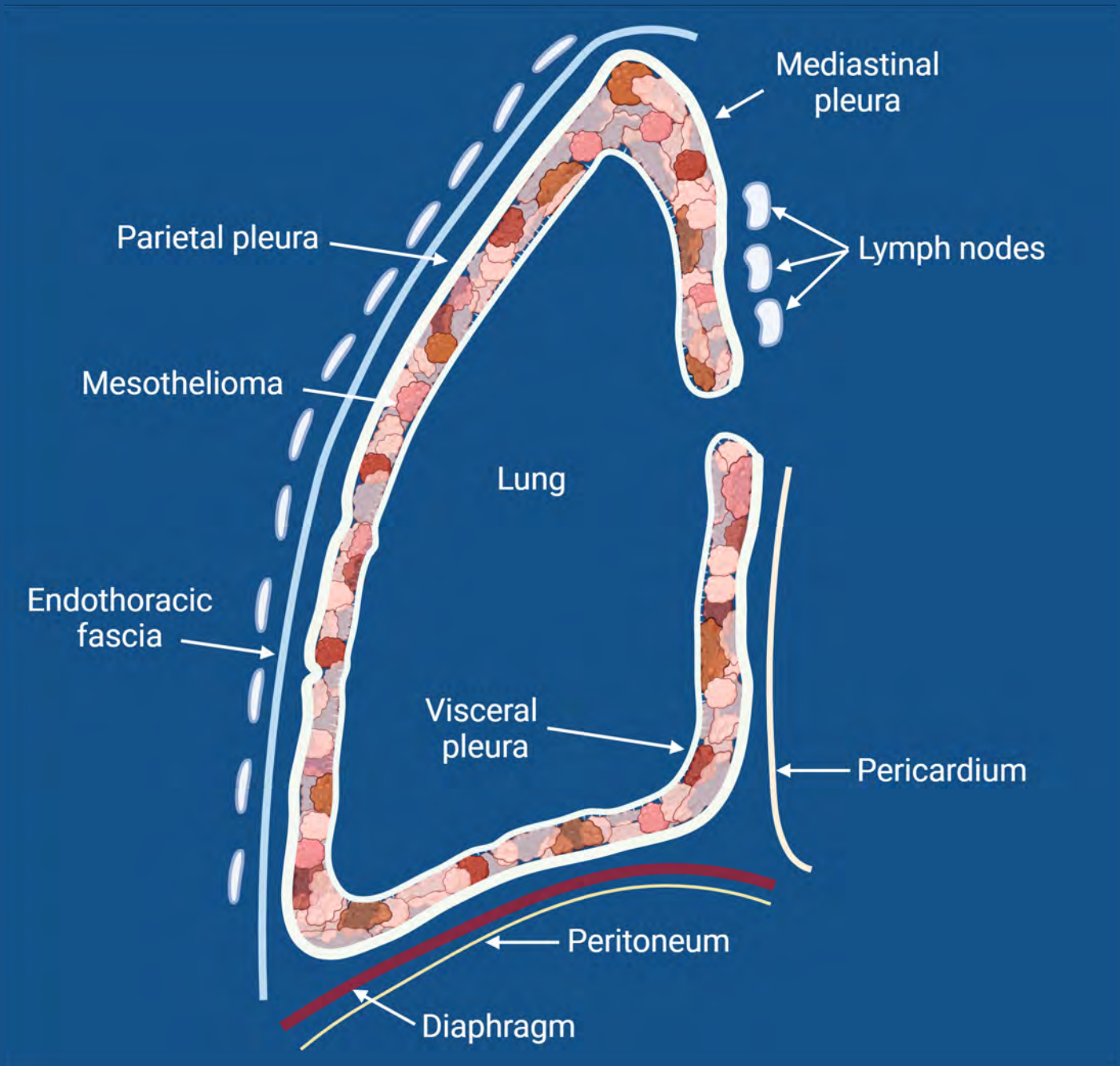
Treatment plan

- Surgery
- Induction chemotherapy → Surgery
- Chemo/immunotherapy

Progress monitored

Continued discussion in multidisciplinary mesothelioma working group

Clinical Faculty



Clinical Faculty

Prasad S. Adusumilli, MD
Deputy Chief and Attending, Thoracic Service; Vice Chair for Translational Research; Co-Director, MSK Mesothelioma Program; Min H. & Yu-Fan C. Kao Chair in Thoracic Cancer

Erica S. Alexander, MD
Assistant Attending Radiologist

Marina K. Baine, MD, PhD
Assistant Attending Pathologist

Manjit S. Bains, MD
Thoracic Surgeon

Mohit Chawla, MD
Chief, Pulmonary Service

Darren R. Feldman, MD
Chair, Quality Assurance, Department of Medicine; Section Head, Germ Cell Cancer

Michelle S. Ginsberg, MD
Vice Chair for Education, Department of Radiology

Robert P. Lee, MD
Section Head, Section of Interventional Pulmonology; Program Director, Interventional Pulmonology Fellowship

Garrett M. Nash, MD
Vice Chair for Quality and Safety, Department of Surgery

Michael D. Offin, MD
Assistant Attending Thoracic Oncologist

Eduardo J. Ortiz Hormaza, MD
Assistant Attending Radiologist

Victor E. Reuter, MD
Vice Chair, Department of Pathology; Director, Genitourinary Pathology Fellowship

Andreas Rimner, MD
Director, Thoracic Radiation Oncology Research

Charles M. Rudin, MD, PhD
Cancer Center Deputy Director; Chief, Thoracic Oncology Service; Co-Director, Druckenmiller Center for Lung Cancer Research; Sylvia Hassenfeld Chair in Lung Cancer Research

Valerie W. Rusch, MD
Vice Chair for Clinical Research, Department of Surgery; Miner Family Chair in Intrathoracic Cancers

Jennifer L. Sauter, MD
Assistant Attending Pathologist

Annemarie Fernandes Shepherd, MD
Director, Proton Therapy for Thoracic Malignancies

Charles B. Simone, MD
Chief Medical Officer, New York Proton Center

Stephen B. Solomon, MD
Chief, Interventional Radiology Service; Enid A. Haupt Chair in Clinical Investigation

William D. Travis, MD
Director, Thoracic Pathology

Soo-Ryum (Stewart) Yang, MD
Assistant Attending Pathologist

Marjorie G. Zauderer, MD
Associate Attending, Thoracic Oncology Service; Co-Director, MSK Mesothelioma Program

Etay Ziv, MD, PhD
Associate Attending Radiologist

Valerie W. Rusch, MD

Dr. Rusch worked as a thoracic surgeon for 35 years at Memorial Sloan Kettering Cancer Center in New York and served as Chief of Thoracic Surgery from 2000 to 2013. During her tenure, she led a multi-disciplinary team in advancing the management of malignant pleural mesothelioma.

A native New Yorker, Dr. Rusch graduated from the Lycée Français de New York and Vassar College and is fluent in both French and English. She received her medical degree from the College of Physicians and Surgeons at Columbia University, then completed residency training in general surgery and cardiothoracic surgery at the University of Washington in Seattle. Subsequently, she spent one year at MD Anderson Cancer Center in Houston for additional training in thoracic oncology prior to joining the faculty at the University of Washington for six years. In 1989, she joined the staff at MSK.

During her tenure as a faculty member and Chief of Thoracic Surgery, Dr. Rusch made sentinel contributions in coordinating multi-disciplinary mesothelioma patient care. These contributions include improving staging, developing standardized techniques for surgical resection of mesothelioma, evaluating outcomes following pleurectomy and decortication, and integrating intensity modulated radiation therapy into standard-of-care for patients with pleural mesothelioma. In addition, she has provided key support for advancing mesothelioma research that investigates genomics, oncolytic viral therapy, and adoptive cell therapy.

In addition to other responsibilities, she currently serves as Chair of the American Board of Thoracic Surgery, a Regent (i.e., member of the Board of Directors) of the American College of Surgeons, Chair of the Lung and Esophagus Task Force of the American Joint Committee on Cancer, and Chair of the Mesothelioma Subcommittee of the International Association for the Study of Lung Cancer's Staging Committee.

Awards:

Pioneer Award for clinical research in malignant mesothelioma, by the Mesothelioma Applied Research Foundation, 2015

Miner Family Chair in Intrathoracic Cancers

Clinical Trials:

Lung Cancer Study Group 1984-1989: Study Chairman for LCSG#851: Malignant Mesothelioma Pilot Study and LCSG#882: A Phase II Study of Intrapleural and Systemic Adjuvant Chemotherapy for Patients with Resected Malignant Mesothelioma

Principal Investigator, Phase I Study of Intra-Pleural Administration of GL-ONC1, a Genetically Modified Vaccinia Virus, In Patients with Malignant Pleural Effusion: Primary, Metastases and Mesothelioma (SK2012-1374; GENELUX IRB 12-169), 2012-present

Principal Investigator, Volumetric CT for the Staging of Malignant Pleural Mesothelioma (Mesothelioma Applied Research Foundation), 2013-2016

Co-Investigator, Phase II Toxicity Study of Pleurectomy/ Decortication Followed by Adjuvant Chemotherapy and Intensity Modulated Radiation Therapy to the Pleura in Patients with Locally Advanced Malignant Pleural Mesothelioma (Cycle for Survival, 2016-2017)

Committees and Organization Work:

President, International Mesothelioma Interest Group, 2002-2005

Chair, International Association for the Study of Lung Cancer (IASLC) Mesothelioma Domain, 2008-present

Member, Scientific Advisory Board, Mesothelioma Applied Research Foundation, 2009-2011

Member, Mesothelioma Dataset Development Panel, International Committee on Cancer Reporting (ICCR), 2014

Member, ASCO Expert Panel on Treatment of Malignant Pleural Mesothelioma, 2016-2018

Leader, Surgical/Early Stage Group, Mesothelioma Working Group, NCI Thoracic Staging Malignancies Committee (NTSM), 2016-present

Surgical Reviewer, Data Safety and Monitoring Committee, MARS 2 trial (A Feasibility Study Comparing (Extended) Pleurectomy Decortication Versus no Pleurectomy Decortication in Patients with Malignant Pleural Mesothelioma), United Kingdom, 2018-present

Co-Chair, IASLC-EURASCAN Multidisciplinary Committee for Mesothelioma Classification, 2018-present

Drs. Jones and Rudin initiated “Mesothelioma Program at MSK” in 2017 and appointed Drs. Adusumilli and Zauderer as Co-Directors of the program.

David R. Jones, MD

Dr. Jones is the Chief of the MSK Thoracic Surgery Service.

Dr. Jones’s research focuses on the mechanisms and drivers of metastases in lung cancer. His research has been funded by the NIH/NCI, Department of Defense, and the American Association for Cancer Research. He has been the principal investigator or co-PI on over 35 funded grants and currently holds two R01 awards from the NCI. He has published over 370 papers and has written over 35 book chapters.

Charles M. Rudin, MD, PhD

In addition to serving as Chief of the Thoracic Oncology Service, Dr. Rudin has led the National Cancer Institute’s Small Cell Lung Cancer Research Consortium since its inception in 2015.

Dr. Rudin’s lab leads research that focuses on the development and testing of novel therapeutic approaches to lung cancer and mesothelioma in preclinical models including patient-derived xenografts. These studies are integrated with early phase clinical trials.

Dr. Rusch’s Selected Publications:

Rusch VW, Saltz L, Venkatraman E. A Phase II trial of pleurectomy/decortication followed by intrapleural and systemic chemotherapy for malignant pleural mesothelioma. J Clin Oncol, 1994;12:1156-1163. PMID: 8201377

Rusch VW, The International Mesothelioma Interest Group. A proposed new international TNM staging system for malignant pleural mesothelioma. Chest 1995;108:1122-28. PMID: 7555126

Rusch VW, Rosenzweig K, Venkatraman E. A phase II trial of surgical resection and adjuvant high dose hemithoracic radiation for malignant pleural mesothelioma. J Thorac Cardiovasc Surg 2001;122:788-795. PMID: 11581615

Flores RM, Krug LM…**Rusch VW**. Induction chemotherapy, extrapleural pneumonectomy, and postoperative high dose radiation for locally advanced malignant pleural mesothelioma: A Phase II trial. J Thorac Oncol 2006;1:289-295. PMID: 17409872

Flores RM, Akhurst T...**Rusch VW**. Positron emission tomography defines metastatic disease but not locoregional disease in patients with malignant pleural mesothelioma. J Thorac Cardiovasc Surg 2003;126:11-16. PMID: 12878934

Flores RM, Zakowski M…**Rusch VW**. Prognostic factors in the treatment of malignant pleural mesothelioma at a large tertiary referral center. J Thorac Oncol 2007;2:957-965. PMID: 17909360

Flores RM, Pass HI…**Rusch VW**. Extrapleural pneumonectomy (EPP) versus pleurectomy/decortication (P/D) in the surgical management of malignant pleural mesothelioma (MPM): Results in 663 patients. J Thorac Cardiovasc Surg 2008;135:620-626. PMID: 18329481

Bott M, Brevet M...**Rusch VW**, Ladanyi M. The nuclear deubiquitinase BAP1 is commonly inactivated by somatic mutations and 3p21.1 losses in malignant pleural mesothelioma. Nature Genetics 2011;43(7):668-72. PMID: 21642991

Rusch VW, Giroux D, Kennedy C. Initial analysis of the International Association for the Study of Lung Cancer (IASLC) mesothelioma database. J Thorac Oncol 2012;7:1631-1639. PMID 23070243

Pass H, Giroux D…**Rusch VW**; Staging and Prognostic Factors Committee, Advisory Boards and Participating Institutions. The IASLC mesothelioma database: Improving staging of a rare disease through international participation. J Thorac Oncol 2016;11(12):2082-2088. PMID: 27670823

Nursing & Allied Healthcare Providers

Proton beam therapy. Photon IMRT.

Linda Ahn
Advanced Practice Provider II

Karen Bartlett
Clinical Nurse II

Elizabeth Blackler, MBE, LCSW-R
Program Manager, Ethics Committee,
Office of Physician-In-Chief

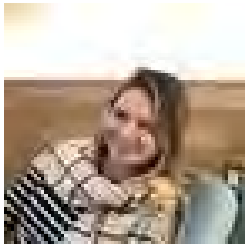
Michelle Colletti
Advanced Practice Provider IV

Joseph George
Clinical Nurse II

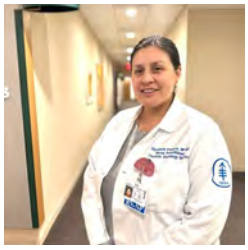
Kathleen Leary
Advanced Practice Provider II

Alison Massey Tanner
Advanced Practice Provider II

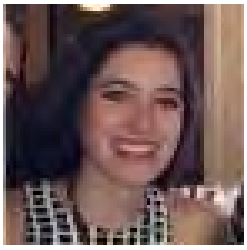
Paige Mullins, MSW
Clinical Social Worker I



Inna Palotsi
Clinical Nurse III



Elizabeth Panora
Clinical Trials Nurse Practitioner



Sarah Permutt
Clinical Nurse III

Rebecca Repetti
Advanced Practice Provider II

Erica Stumpf
Clinical Trials Nurse Practitioner

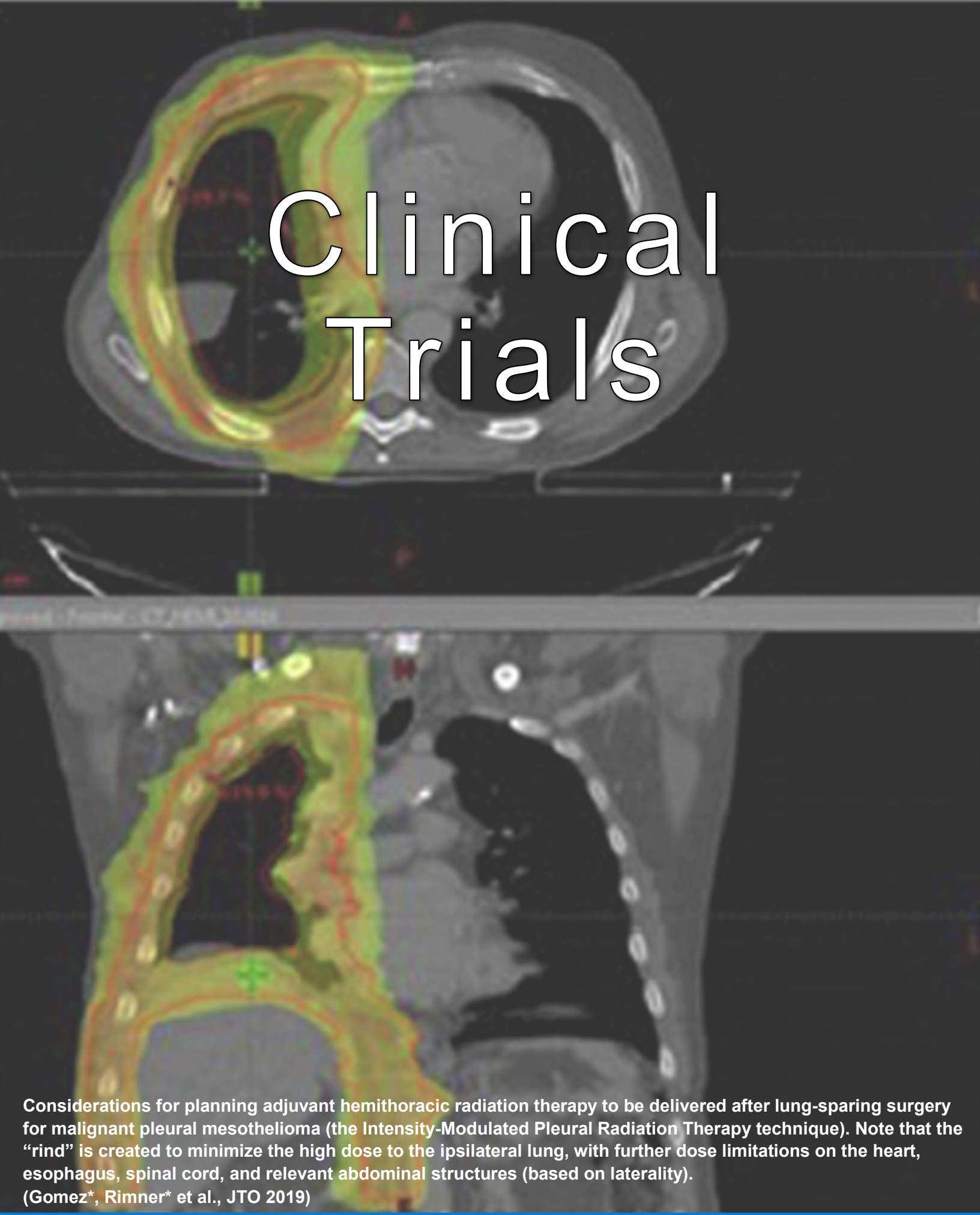
Mark Traynor
Clinical Nurse II

Leslie Tyson
Nurse Practitioner

Jodi Weinberg
Advanced Practice Provider II

Catherine Wickersham
Clinical Nurse IV

Clinical Trials



Considerations for planning adjuvant hemithoracic radiation therapy to be delivered after lung-sparing surgery for malignant pleural mesothelioma (the Intensity-Modulated Pleural Radiation Therapy technique). Note that the "rind" is created to minimize the high dose to the ipsilateral lung, with further dose limitations on the heart, esophagus, spinal cord, and relevant abdominal structures (based on laterality).
(Gomez*, Rimner* et al., JTO 2019)

IRB	Title	PIs
23-197	Phase 1, Multi-Center, Open-Label Study of VT3989 in Patients with Refractory Locally Advanced or Metastatic Solid Tumors Enriched for Tumors Harboring Mutations of the Neurofibromatosis Type 2 Gene (mutant NF2 or mNF2)	Zauderer, Marjorie, MD; Offin, Michael, MD
23-145	ICARuS II (Intraperitoneal Chemotherapy After cytoReductive Surgery): A Multi-center, Randomized Phase II Trial of Normothermic Intraperitoneal Chemotherapy and Intravenous Chemotherapy After Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy for Malignant Peritoneal Mesothelioma	Nash, Garrett, MD; Offin, Michael, MD
23-100	Breathprinting (E-Nose) Technology to Measure Response to Treatment of Malignant Pleural Mesothelioma (MPM) through MPM-Specific Volatile Organic Compounds Detected in Exhalates	Rocco, Gaetano, MD
22-379	A Phase 1/2, Multi-Center, Open-Label Study to Evaluate the Safety, Tolerability, and Preliminary Anti-tumor Activity of TNG908 in Patients with MTAP-deleted Advanced or Metastatic Solid Tumors (TNG908-C101)	Gounder, Mrinal, MD; Zauderer, Marjorie, MD
22-367	A Phase 1, First-in-Human Study of IK-930, an Oral TEAD Inhibitor Targeting the Hippo Pathway in Subjects With Advanced Solid Tumors	Gounder, Mrinal, MD
22-139	A Phase 1/2 Multiple Expansion Cohort Trial of MRTX1719 in Patients with Advanced Solid Tumors with Homozygous MTAP Deletion	Arbour, Kathryn, MD; Offin, Michael, MD
22-092	A Prospective, Non Interventional, Trial Evaluating the Diagnostic Accuracy of FBLN3 for Mesothelioma Pleural Effusions (NYU)	Adusumilli, Prasad, MD; Offin, Michael, MD
21-342	A Phase 1 Study of Pembrolizumab plus Cryoablation in Unresectable Mesotheliomas (funded by the Druckenmiller Lung Cancer Center)	Offin, Michael, MD; Zauderer, Marjorie, MD;
21-302	Phase 1 Study of CI-8993 Anti-VISTA Antibody in Patients with Advanced Solid Tumor Malignancies	Zauderer, Marjorie, MD; Offin, Michael, MD
21-237	DREAM3R: Durvalumab (MEDI4736) with Chemotherapy as First Line Treatment in Advanced Pleural Mesothelioma - A Phase 3 Randomised Trial (WIRB)	Zauderer, Marjorie, MD; Offin, Michael, MD
21-197	Phase I Dose Escalation and Local Control Study of Pembrolizumab + Intensity-Modulated Pleural Radiation Therapy (IMPRINT) for Malignant Pleural Mesothelioma (funded by Merck)	Rimner, Andreas, MD; Offin, Michael, MD; Zauderer, Marjorie, MD
20-328	A Single-Arm, Open-Label, Phase I Trial to Assess the Safety of Genetically Engineered Autologous T Cells Targeting the Cell Surface Antigen Mesothelin with Cell-Intrinsic Checkpoint Inhibition in Patients with Mesothelioma	O'Cearbhaill, Roisin, MD
20-173	Phase III Randomized Trial of Pleurectomy/Decortication Plus Systemic Therapy With or Without Adjuvant Hemithoracic Intensity-Modulated Pleural Radiation Therapy (IMPRINT) for Malignant Pleural Mesothelioma (MPM) (NRG LU006) (CIRB)	Rimner, Andreas, MD; Rusch, Valerie, MD; Zauderer, Marjorie, MD
19-472	A Phase 1/2 Single Arm Open-Label Clinical Trial of Gavocabtagene Autoleucel (GAVO-CEL) in Patients with Advanced Mesothelin-Expressing Cancer	O'Cearbhaill, Roisin, MD; Adusumilli, Prasad, MD
19-460	Assessment of Endogenous and CAR T-Cell Immunity Following Anti-PD-1 Agent as a Transition Step to Phase 2 Combination Immunotherapy	Adusumilli, Prasad, MD; Zauderer, Marjorie, MD
19-272	Feasibility and Safety of Neoadjuvant Nivolumab and Chemotherapy for Resectable Malignant Pleural Mesothelioma (funded by BMS)	Offin, Michael, MD; Adusumilli, Prasad, MD; Zauderer, Marjorie, MD
19-001	A Phase 1, Open-Label, Dose Escalation and Dose Expansion Trial Evaluating the Safety, Pharmacokinetics, Pharmacodynamics, and Clinical Effects of Orally Administered CA-170 in Patients with Advanced Tumors and Lymphomas	Zauderer, Marjorie, MD

IRB	Title	PI
18-268	Tazemetostat Rollover Study (TRuST): An Open-Label, Rollover Study	Zauderer, Marjorie, MD
18-198	A Phase 1 Study of AG-270 in the Treatment of Subjects with Advanced Solid Tumors or Lymphoma with Homozygous Deletion of MTAP	Gounder, Mrinal, MD
18-009	INCAGN 1876-201: A Phase 1/2 Study Exploring the Safety, Tolerability, and Efficacy of INCAGN01876 in Combination With Immune Therapies in Subjects With Advanced or Metastatic Malignancies	Dunn, Lara, MD
17-654	Combining a WT1 Cancer Vaccine (Galinpepimut-S) with Checkpoint Inhibition (Nivolumab) in Patients with WT1-Expressing Malignant Pleural Mesothelioma: A Phase I Study (funded by BMS and Sellas Life Sciences)	Zauderer, Marjorie, MD; Offin, Michael, MD
17-361	Pevonedistat as a Single Agent and in Combination with Chemotherapy in Patients with Malignant Mesothelioma (partially funded by NIH/NCI)	Zauderer, Marjorie, MD
17-358	A Safety Study of Avelumab plus SBRT in Malignant Mesothelioma (MPM)	Rimner, Andreas, MD; Zauderer, Marjorie, MD
17-002	CA209743: A Phase III, Randomized, Open Label Trial of Nivolumab in Combination with Ipilimumab versus Pemetrexed with Cisplatin or Carboplatin as First Line Therapy in Unresectable Pleural Mesothelioma	Zauderer, Marjorie, MD
16-608	A Phase II Trial of BIBF 1120 (Nintedanib) in Recurrent Malignant Pleural Mesothelioma	Zauderer, Marjorie, MD
16-736	Examining the Role of Chromosomal Instability and Molecular Markers of Radiosensitivity, Chemosensitivity and Prognosis in Malignant Mesothelioma	Zauderer, Marjorie, MD; Rimner, Andreas MD
16-1414	POLARIS2015-003: Randomized, Double-Blind, Phase 2/3 Study in Subjects with Malignant Pleural Mesothelioma with Low Argininosuccinate Synthetase 1 Expression to Assess ADI-PEG 20 with Pemetrexed and Cisplatin (ATOMIC-Meso Phase 2/3 Study)	Zauderer, Marjorie, MD
16-1034	A Phase 2, Multicenter Study of the EZH2 Inhibitor Tazemetostat in Adult Subjects with Relapsed or Refractory Malignant Mesothelioma with BAP1 Loss of Function	Zauderer, Marjorie, MD
16-047	Investigating the Tumor Immune Microenvironment in Thoracic Malignancies–Lung Cancer, Mesothelioma, Esophageal Cancer, and Lung Metastasis	Adusumilli, Prasad, MD
15-007	A Phase I/II Clinical Trial of Malignant Pleural Disease Treated with Autologous T Cells Genetically Engineered to Target the Cancer-Cell Surface of Antigen Mesothelin	Zauderer, Marjorie, MD; Adusumilli, Prasad, MD; O'Cearbhaill, Roisin, MD
12-235	Clinical and Histopathologic Characteristics of BAP1 Mutations (funded by the Department of Defense)	Zauderer, Marjorie, MD
10-134	Randomized Phase II Study of Adjuvant WT-1 Analog Peptide Vaccine in Patients with Malignant Pleural Mesothelioma (MPM) After Completion of Combined Modality Therapy (funded by the Department of Defense)	Zauderer, Marjorie, MD; Rusch, Valerie, MD

Mesothelioma Leadership Mentoring

The following former MSK trainees in thoracic surgery went on to develop mesothelioma programs at their own institutions.

Stephen Barnett, MBBS

Consultant Thoracic Surgeon

Austin Hospital, Sir Peter McCallum Cancer Centre,
Royal Melbourne and Western General Hospitals

Melbourne, Australia

Andrea Bille, MD, PhD

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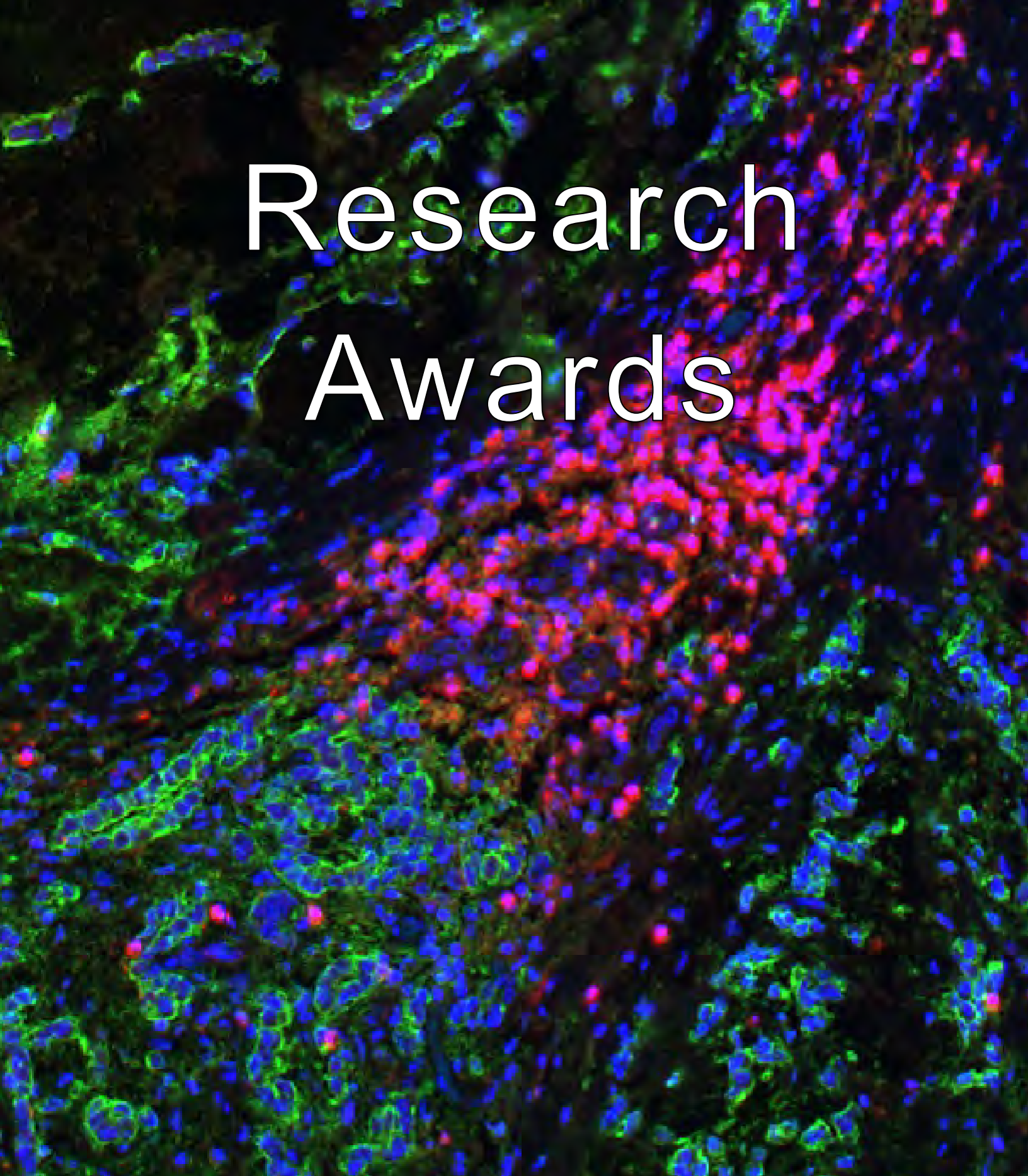
Research Awards



Multiplex immunofluorescence image of human malignant pleural mesothelioma at low magnification. Tumor cells are stained for mesothelin (green), T cells are stained for CD4/CD8 (red), and cell nuclei are stained for DAPI (blue). Scale bar 100mm.

Federal Research Grants (Active During 2017-2023 Academic Years)

Name	Role	Service/ Department	Funding Organization	Name of Grant
Adusumilli, Prasad; Zauderer, Marjorie	Multi-Principal Investigator	Thoracic/Surgery	NIH/NCI R01	A phase I/II combination immunotherapy clinical trial: mesothelin-targeted chimeric antigen receptor T cells and checkpoint blockade agent in pleural mesothelioma
Adusumilli, Prasad	Principal Investigator	Thoracic/Surgery	NIH/NCI R01	Image-guided irreversible electroporation directed CAR T-cell delivery to solid tumors
Adusumilli, Prasad; Zauderer, Marjorie	Multi-Principal Investigator	Thoracic/Surgery	DoD CDMRP	Assessment of endogenous and CAR T-cell immunity following anti-PD-1 agent as a transition step to phase II combination immunotherapy
Adusumilli, Prasad	Principal Investigator	Thoracic/Surgery	DoD CDMRP	Cell-selective, repetitive, irreversible electroporation to augment mesothelioma CAR T-cell therapy
Adusumilli, Prasad	Co-investigator	Thoracic/Surgery	NIH/NCI U01 (New York University School of Medicine)	The EDRN mesothelioma biomarker discovery laboratory
Adusumilli, Prasad	Mentor	Thoracic/Surgery	NIH/NCI T32	Surgical oncology research training grant (Trainee: Jennie Choe, MD)
Adusumilli, Prasad	Mentor	Thoracic/Surgery	NIH/NCI T32	Surgical oncology research training grant (Trainee: Matthew Skovgard, MD)
Adusumilli, Prasad	Mentor	Thoracic/Surgery	NIH/NCI T32	Surgical oncology research training grant (Trainee: Jordan Dozier, MD)
Adusumilli, Prasad	Mentor	Thoracic/Surgery	NIH/NCI T32	Surgical oncology research training grant (Trainee: Zachary Tano, MD)
Ponomarev, Vladimir; Adusumilli, Prasad	Principal Investigator	Thoracic/Surgery	NIH/NCI R21	Imaging the efficacy of TRAIL-enhanced cancer immunotherapy
Zauderer, Marjorie; Giancotti, Filippo G.	Multi-Principal Investigator	Thoracic Oncology/ Medicine	NIH/NCI R01	Therapeutic efficacy of the CRL inhibitor MLN4924 in NF2 mutant mesothelioma
Zauderer, Marjorie	Principal Investigator	Thoracic Oncology/ Medicine	DoD CDMRP	BAP1 mutations in malignant pleural mesothelioma: Biology, clinical phenotypes, radiotherapy response, and target discovery for somatic and germline mutations
Zauderer, Marjorie	Principal Investigator	Thoracic Oncology/ Medicine	DoD CDMRP	Randomized phase II trial of adjuvant WT-1 analog peptide vaccine in patients with malignant pleural mesothelioma after completion of multimodality therapy

Foundation Research Grants (Active During 2017-2023 Academic Years)

Name	Role	Service	Funding Organization	Name of Grant
Adusumilli, Prasad	Principal Investigator	Thoracic/ Surgery	Batishwa Fellowship	Novel therapies for pleural mesothelioma (Trainee: Meriem Taleb, PhD)
Adusumilli, Prasad	Principal Investigator	Thoracic/ Surgery	Batishwa Fellowship	Novel therapies for pleural mesothelioma (Trainee: Yuquan Xiong, MD, PhD)
Adusumilli, Prasad	Principal Investigator	Thoracic/ Surgery	Experimental Therapeutics Center (MSK)	Translational T-cell therapies for solid tumors
Adusumilli, Prasad	Principal Investigator	Thoracic/ Surgery	Mesothelioma Applied Research Foundation	Preclinical mesothelin-targeted adoptive T-cell therapy
Adusumilli, Prasad	Principal Investigator	Thoracic/ Surgery	Mesothelioma Applied Research Foundation	TGF-β resistant CAR T-cell intrinsic strategies for mesothelioma therapy
Adusumilli, Prasad	Principal Investigator	Thoracic/ Surgery	Miner Family Fund	Translational research in pleural mesothelioma
Adusumilli, Prasad	Principal Investigator	Thoracic/ Surgery	Technology Development Fund (MSK)	Exploiting cKIT mutation as a costimulatory domain in CAR T cells
Adusumilli, Prasad	Principal Investigator	Thoracic/ Surgery	The Baker Street Foundation	Novel therapies for pleural mesothelioma
Adusumilli, Prasad	Principal Investigator	Thoracic/ Surgery	Trumbull Foundation	Immunotherapy for mesothelioma
Adusumilli, Prasad	Project Principal Investigator	Thoracic/ Surgery	Experimental Therapeutics Center (MSK)	Innovations in the structures, functions and targets of monoclonal antibody-based drugs for cancer (Project: CAR T cells with cell-intrinsic checkpoint blockade to resist tumor-mediated immunoinhibition in lung cancer)
Adusumilli, Prasad	Co-Investigator	Thoracic/ Surgery	Mesothelioma Applied Research Foundation	Novel CXCR4-targeted theranostic compounds for mesothelioma
Alexander, Erica; Offin, Michel; Solomon, Stephen	Multi-Principal Investigator	Thoracic Oncology/ Medicine	Druckenmiller Center for Lung Cancer Research	An efficacy and safety study of pembrolizumab plus cryoablation in malignant pleural mesothelioma (MPM)
Dozier, Jordan	Recipient	Thoracic/ Surgery	Society of Thoracic Surgeons	Looking to the future scholarship

Name	Role	Service	Funding Organization	Name of Grant
Nash, Garrett	Principal Investigator	Colorectal/ Surgery	Mesothelioma Cancer Research Fund	Mesothelioma cancer research fund
Offin, Michael	Principal Investigator	Thoracic Oncology/ Medicine	MSK	A phase 1 study of pembrolizumab plus cryoablation in unresectable mesotheliomas
Offin, Michael	Principal Investigator	Thoracic Oncology/ Medicine	Ning Zhao & Ge Li Fund for Pathology Research	Adjuvant dose-painting intensity-modulated radiation therapy (IMRT) for malignant pleural mesothelioma (MPM): A randomized, multi-institutional phase II study
Rimner, Andreas; Zauderer, Marjorie	Principal Investigator	Radiation Oncology	Miner Family Fund	A phase I study of concurrent pemetrexed/ cisplatin with pleural intensity modulated radiation therapy for patients with unresectable malignant pleural mesothelioma
Rimner, Andreas	Principal Investigator	Radiation Oncology	Cycle for Survival (MSK)	Adjuvant dose-painting intensity-modulated radiation therapy (IMRT) for malignant pleural mesothelioma (MPM): A randomized, multi-institutional phase II study
Rimner, Andreas	Principal Investigator	Radiation Oncology	MSK	Multicenter phase II study on adjuvant dose-painting intensity-modulated radiation therapy (IMRT) for malignant pleural mesothelioma (MPM)
Sauter, Jennifer	Principal Investigator	Thoracic Pathology	Department of Pathology R&D Grant (MSK)	Utility of MTAP, 5-hmC and BAP1 immunochemistry in the diagnosis of malignant pleural mesothelioma in cytology specimens
Sauter, Jennifer	Principal Investigator	Thoracic Pathology	Valeriani Family Fund	Pathologic and molecular characterization of long -term survivors with pleural mesothelioma

Industry Research Grants (Active During 2017-2023 Academic Years)

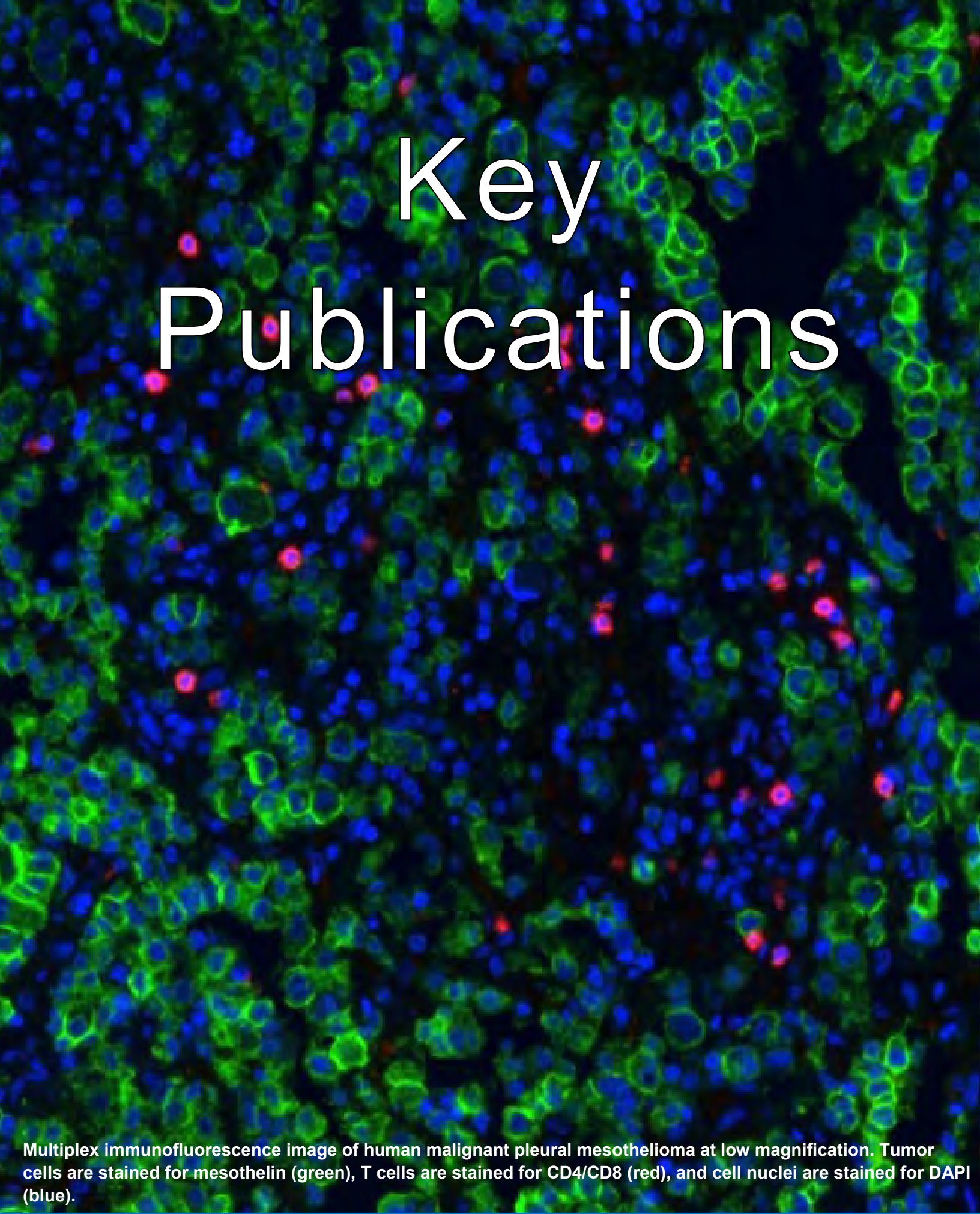
Name	Role	Service	Funding Organization	Name of Grant
Adusumilli, Prasad	Principal Investigator	Thoracic/ Surgery	ACEA Biosciences	Assessment of autologous CAR-T mediated killing in pleural effusions
Adusumilli, Prasad	Principal Investigator	Thoracic/ Surgery	Atara Biotherapeutics	A phase I clinical trial of malignant pleural disease treated with autologous T cells genetically engineered to target the cancer-cell surface antigen mesothelin
Adusumilli, Prasad	Principal Investigator	Thoracic/ Surgery	Atara Biotherapeutics	Development of chimeric antigen receptor T-cells that target mesothelin and encode PD1 dominant negative receptor checkpoint inhibition

Industry Research Grants (continued)

Name	Role	Service	Funding Organization	Name of Grant
Adusumilli, Prasad	Principal Investigator	Thoracic/ Surgery	Atara Biotherapeutics	A single-arm, open-label, phase I trial to assess the safety of genetically engineered autologous T cells targeting the cell surface antigen mesothelin with cell-intrinsic checkpoint inhibition in patients with mesothelioma
Adusumilli, Prasad	Principal Investigator	Thoracic/ Surgery	Juno Therapeutics	Mesothelin-targeted CAR T-cell strategies to overcome immunoinhibition in lung adenocarcinoma
Branch, Kevin	Recipient	Thoracic/ Surgery	Merrill Lynch	Merrill-Lynch training program fund
Offin, Michael	Principal Investigator	Thoracic Oncology/ Medicine	Bristol-Myers Squibb	Feasibility and safety of neoadjuvant nivolumab and chemotherapy for resectable malignant pleural mesothelioma
Offin, Michael	Principal Investigator	Thoracic Oncology/ Medicine	DualityBio, Inc. (Duality)	Duality project proposal: DB-1305 in Malignant Pleural Mesothelioma
Offin, Michael	Principal Investigator	Thoracic Oncology/ Medicine	Harpoon Therapeutics Inc	A phase 1/2a open-label, multicenter, dose escalation and dose expansion study of the safety, tolerability, and pharmacokinetics of HPN536 in patients with advanced cancers associated with mesothelin expression who have failed standard available therapy
Rimner, Andreas; Rusch, Valerie; Zauderer, Marjorie	Multi-Principal Investigator	Radiation Oncology	NRG Oncology	Phase III randomized trial of pleurectomy/ decortication plus systemic therapy with or without adjuvant hemithoracic intensity-modulated pleural radiation therapy (IMPRINT) for malignant pleural mesothelioma (MPM)
Rimner, Andreas	Principal Investigator	Radiation Oncology	Pfizer, Inc.	An efficacy and safety study of avelumab plus SBRT in malignant mesothelioma (MPM)
Rimner, Andreas	Principal Investigator	Radiation Oncology	Pfizer, Inc.	An efficacy and safety study of avelumab plus SBRT in malignant mesothelioma (MPM)
Rusch, Valerie	Principal Investigator	Thoracic/ Surgery	Genelux Corporation	Phase I study of intra-pleural administration of GL-ONC1, a genetically modified vaccinia virus, in patients with malignant pleural effusion: Primary, metastases and mesothelioma
Simone, II, Charles	Principal Investigator	Radiation Oncology	Varian Medical Systems	Investigation of biologically optimized adaptive PBS proton treatment for lung treatment
Zauderer, Marjorie	Principal Investigator	Thoracic Oncology/ Medicine	Bristol-Myers Squibb	CA209743: A phase III, randomized, open label trial of nivolumab in combination with ipilimumab versus pemetrexed with cisplatin or carboplatin as first line therapy in unresectable pleural mesothelioma

Name	Role	Service/ Department	Funding Organization	Name of Grant
Zauderer, Marjorie	Principal Investigator	Thoracic Oncology/ Medicine	Bristol-Myers Squibb	IIT: BMS CA209-9U4: Combining a WT1 cancer vaccine (galinpepimut-S) with checkpoint inhibition (nivolumab) in patients with WT1-expressing malignant pleural mesothelioma: A phase I study
Zauderer, Marjorie; Hellmann, Matthew,	Multi-Principal Investigator	Thoracic Oncology/ Medicine	Curis, Inc.	A phase 1, open-label, dose escalation and dose expansion trial evaluating the safety, pharmacokinetics, pharmacodynamics, and clinical effects of orally administered CA-170 in patients with advanced tumors and lymphomas
Zauderer, Marjorie; Offin, Michael	Multi-Principal Investigator	Thoracic Oncology/ Medicine	Curis, Inc.	Phase 1 study of CI-8993 anti-VISTA antibody in patients with advanced solid tumor malignancies
Zauderer, Marjorie	Principal Investigator	Thoracic Oncology/ Medicine	Epizyme, Inc.	A phase 2, multicenter study of the EZH2 inhibitor tazemetostat in adult subjects with relapsed or refractory malignant mesothelioma with BAP1 loss of function
Zauderer, Marjorie; Paik, Paul	Multi-Principal Investigator	Thoracic Oncology/ Medicine	Epizyme, Inc.	Tazemetostat rollover study (TRuST): an open-label, rollover study
Zauderer, Marjorie; Daly, Robert	Multi-Principal Investigator	Thoracic Oncology/ Medicine	Karmanos Cancer Institute/Wayne State University	A phase II trial of BIBF 1120 (nintedanib) in recurrent malignant pleural mesothelioma
Zauderer, Marjorie	Principal Investigator	Thoracic Oncology/ Medicine	MD Anderson Cancer Center	Therapeutic efficacy of the CRL inhibitor MLN4924 in NF2 mutant mesothelioma
Zauderer, Marjorie	Principal Investigator	Thoracic Oncology/ Medicine	Polaris Pharmaceuticals, Inc.	POLARIS2015-003: Randomized, double-blind, phase 2/3 study in subjects with malignant pleural mesothelioma with low argininosuccinate synthetase 1 expression to assess ADI-PEG 20 with pemetrexed and cisplatin (ATOMIC-Meso phase 2/3 study)
Zauderer, Marjorie; Offin, Michael	Multi-Principal Investigator	Thoracic Oncology/ Medicine	PrECOG, LLC	DREAM3R: DuRvalumab (MEDI4736) with chEmotherapy as first line treAtment in advanced pleural Mesothelioma - A phase 3 Randomised trial (WIRB)
Zauderer, Marjorie; Offin, Michael	Multi-Principal Investigator	Thoracic Oncology/ Medicine	Vivace Therapeutics, Inc.	Phase 1, multi-center, open-label study of VT3989 in patients with refractory locally advanced or metastatic solid tumors enriched for tumors harboring mutations of the neurofibromatosis type 2 gene (mutant NF2 or mNF2)

Key Publications



Multiplex immunofluorescence image of human malignant pleural mesothelioma at low magnification. Tumor cells are stained for mesothelin (green), T cells are stained for CD4/CD8 (red), and cell nuclei are stained for DAPI (blue).

Clinical

Clinical outcomes of stereotactic body radiation therapy for malignant pleural mesothelioma

Shin JY, Offin M, Simone Ii CB, Zhang Z, Shepherd AF, Wu AJ, Shaverdian N, Gelblum DY, Gomez DR, Sauter JL, Ginsberg MS, Adusumilli PS, Rusch VW, Zauderer MG, Rimner A. Clinical outcomes of stereotactic body radiation therapy for malignant pleural mesothelioma. Radiother Oncol. 2023 Dec 15:110057. doi: 10.1016/j.radonc.2023.110057. Epub ahead of print. PMID: 38104783

Background: The objective of this study is to determine the outcomes and toxicities of patients with malignant pleural mesothelioma (MPM) treated with stereotactic body radiotherapy (SBRT).

Materials and Methods: Data were extracted from an institutional tumor registry for patients diagnosed with mesothelioma and treated with SBRT. Kaplan-Meier and Cox regression analyses were employed to determine local control (LC) and overall survival (OS).

Results: Forty-four patients with 59 total treated tumors from December 2006 to April 2022 were identified. Fifty-one (86.4%) cases had oligoprogressive disease (five sites or less). The median prescription dose delivered was 3000 cGy in 5 fractions (range: 2700-6000 cGy in 3-8 fractions). Fifty-one (86.4%) tumors were in the pleura, 4 (6.8%) spine, 2 (3.4%) bone, 1 (1.7%) brain, and 1 (1.7%) pancreas.

The median follow-up from SBRT completion for those alive at last follow-up was 28 months (range: 14-52 months). The most common toxicities were fatigue (50.8%), nausea (22.0%), pain flare (15.3%), esophagitis (6.8%), dermatitis (6.8%), and pneumonitis (5.1%). There were no grade ≥3 acute or late toxicities. There were 2 (3.4%) local failures, one of the pleura and another of the spine. One-year LC was 92.9% (95% CI: 74.6-98.2%) for all lesions and 96.3% (95% CI: 76.5-99.5%) for pleural tumors. One-year LC was 90.9% (95% CI: 68.1-97.6%) for epithelioid tumors and 92.1% (95% CI: 72.1-98.0%) for oligoprogressive tumors. One-year OS from time of SBRT completion was 36.4% (95% CI: 22.6-50.3%). On multivariable analysis, KPS was the lone significant predictor for OS (p=0.029).

Conclusions: Our single-institutional experience on patients with MPM suggests that SBRT is safe with a low toxicity profile and potentially achieve good local control.

Reliability of assessing morphologic features with prognostic significance in cytology specimens of epithelioid diffuse pleural mesothelioma and implications for cytopathology reporting

Li Y, Salama AM, Baine MK, Bodd FM, Offin MD, Rekhtman N, Zauderer MG, Travis WD, Adusumilli PS, Sauter JL. Reliability of assessing morphologic features with prognostic significance in cytology specimens of epithelioid diffuse pleural mesothelioma and implications for cytopathology reporting. Cancer Cytopathol. 2023 Aug;131(8):495-506. doi: 10.1002/cncy.22705. Epub 2023 May 1. PMID: 37127928

Background: The World Health Organization incorporates morphologic features with prognostic significance in the 2021 classification of epithelioid diffuse pleural mesothelioma (E-DPM). Although cytology specimens are often the first and occasionally the only specimen available for patients with DPM, these features have not yet been investigated in cytology.

Methods: Nuclear atypia, pleomorphic features, necrosis, and architectural patterns were retrospectively assessed in 35 paired cytology and concurrent/consecutive surgical pathology specimens of E-DPM. Agreement between pairs was determined via unweighted κ scores. Discordant cases were re-reviewed to determine the reasons for disagreement.

Results: Interpretation of nuclear atypia in cytology was concordant with histology in all cases (κ = 1.000; $p < .001$). The presence of pleomorphic features and necrosis was concordant in 97.1% (κ = 0.842; $p < .001$) and 85.7% (κ = 0.481; $p = .001$) of paired cases, respectively. Assessment of architectural patterns in cytology showed only slight agreement with histology (κ = 0.127; $p = .037$). In cytology cases ($n = 23$) with cell block material available, assessment of nuclear atypia and the presence of pleomorphic features showed perfect agreement (κ = 1.000; $p < .001$, each), the presence of necrosis showed moderate agreement (κ = 0.465; $p = .008$), and assessment of architectural patterns showed slight agreement (κ = 0.162; $p = .15$) in paired specimens. Most disagreements were due to sampling differences between cytology and histology specimens.

Conclusions: Although complete nuclear grading of E-DPM is not possible given the unreliability of mitotic counts in cytology, assessment of nuclear atypia in cytology specimens is shown to be reliable. Identification of pleomorphic features and necrosis is also reliable despite occasional sampling issues. Assessment of architectural patterns is more limited in cytology.

Multimodality therapy in patients with primary pericardial mesothelioma

Offin M, De Silva DL, Sauter JL, Egger JV, Yorke E, Adusumilli PS, Rimner A, Rusch VW, Zauderer MG. Multimodality Therapy in Patients With Primary Pericardial Mesothelioma. J Thorac Oncol. 2022 Dec;17(12):1428-1432. doi: 10.1016/j.jtho.2022.08.017. Epub 2022 Sep 6. PMID: 36075530; PMCID: PMC9691618

Introduction: Primary pericardial mesothelioma (PPM) has no accepted standard-of-care treatment options with management and outcomes often extrapolated from diffuse pleural mesothelioma. Disease-specific research is needed to better define PPM. We report our institutional experience with PPM highlighting the potential role for multimodality therapy.

Methods: Patients with PPM diagnosed by a multidisciplinary team of medical oncologists, thoracic surgeons, thoracic pathologists, and radiologists between January 2011 and January 2022 were followed to February 2022. Clinicopathologic features and treatment outcomes were annotated. Overall survival (OS) was defined from the date of pathologic diagnosis.

Results: The median age at diagnosis of the 12 patients identified with having PPM was 51 (range: 21–71) years old. Most patients were of female sex (n = 8; 67%), 75% of the samples were epithelioid (n = 9), and 25% were nonepithelioid (two sarcomatoid and one biphasic). Most cases (92%, 11 of 12) had expression of at least two mesothelial markers on immunohistochemistry. The median OS of the cohort was 25.9 months. Five patients had an OS greater than 12 months; four of whom received pericardial radiation. Three of the patients who received radiation did so as part of a trimodality approach (surgical resection, adjuvant chemotherapy, and radiation); the OS for patients who received trimodality therapy was 70.3 months versus 8.2 months for those who did not.

Conclusions: PPM represents a distinct disease with no universally accepted treatment options. Our findings suggest that trimodality therapy may improve outcomes in selected patients with PPM.

The 2021 WHO classification of tumors of the pleura: advances since the 2015 classification

Sauter JL, Dacic S, Galateau-Salle F, Attanoos RL, Butnor KJ, Churg A, Husain AN, Kadota K, Khoor A, Nicholson AG, Roggli V, Schmitt F, Tsao MS, Travis WD. The 2021 WHO Classification of Tumors of the Pleura: Advances Since the 2015 Classification. J Thorac Oncol. 2022 May;17(5):608-622. doi: 10.1016/j.jtho.2021.12.014. Epub 2022 Jan 10. PMID: 35026477

Substantial changes in the 2021 WHO Classification of Tumors of the Pleura and Pericardium since the 2015 WHO Classification include the following: (1) pleural and pericardial tumors have been combined in one chapter whereas in the 2015 WHO, pericardial tumors were classified with cardiac tumors; (2) well-differentiated papillary mesothelioma has been renamed well-differentiated papillary mesothelial tumor given growing evidence that these tumors exhibit relatively indolent behavior; (3) localized and diffuse mesothelioma no longer include the term “malignant” as a prefix; (4) mesothelioma in situ has been added to the 2021 classification because these lesions can now be recognized by loss of BAP1 and/or MTAP by immunohistochemistry and/or CDKN2A homozygous deletion by fluorescence in situ hybridization; (5) the three main histologic subtypes (i.e., epithelioid, biphasic, and sarcomatoid) remain the same but architectural patterns and cytologic and stromal features are more formally incorporated into the 2021 classification on the basis of their prognostic significance; (6) nuclear grading for epithelioid diffuse mesothelioma is introduced, and it is recommended to record this and other histologically prognostic features in pathology reports; (7) BAP1, EZH2, and MTAP immunohistochemistry have been found to be useful in separating benign mesothelial proliferations from mesothelioma; (8) biphasic mesothelioma can be diagnosed in small biopsies having both epithelioid and sarcomatoid components even if the amount of one component is less than 10%; and (9) the most frequently altered genes in diffuse pleural mesothelioma include *BAP1, CDKN2A, NF2, TP53, SETD2,* and *SETDB1*.

Divided by an ocean of water but united in an ocean of uncertainty: A transatlantic review of mesothelioma surgery guidelines

Waller DA, Opitz I, Bueno R, Van Schil P, Cardillo G, Harpole D, Adusumilli PS, De Perrot M. Divided by an ocean of water but united in an ocean of uncertainty: A transatlantic review of mesothelioma surgery guidelines. J Thorac Cardiovasc Surg. 2021 Jun;161(6):1922-1925. doi: 10.1016/j.jtcvs.2020.11.001. Epub 2020 Nov 19. PMID: 33223192

Comparison of the most recent guidelines from major professional societies in America and Europe on the surgical management of malignant pleural mesothelioma reveals much agreement. Where differences do occur they reflect areas where good evidence is currently lacking.

The use of a next-generation sequencing-derived machine-learning risk-prediction model (OncoCast-MPM) for malignant pleural mesothelioma: a retrospective study

Zauderer MG, Martin A, Egger J, Rizvi H, Offin M, Rimner A, Adusumilli PS, Rusch VW, Kris MG, Sauter JL, Ladanyi M, Shen R. The use of a next-generation sequencing-derived machine-learning risk-prediction model (OncoCast-MPM) for malignant pleural mesothelioma: a retrospective study. Lancet Digit Health. 2021 Sep;3(9):e565-e576. doi: 10.1016/S2589-7500(21)00104-7. Epub 2021 Jul 28. PMID: 34332931; PMCID: PMC8459747

Background: Current risk stratification for patients with malignant pleural mesothelioma based on disease stage and histology is inadequate. For some individuals with early-stage epithelioid tumours, a good prognosis by current guidelines can progress rapidly; for others with advanced sarcomatoid cancers, a poor prognosis can progress slowly. Therefore, we aimed to develop and validate a machine-learning tool—known as OncoCast-MPM—that could create a model for patient prognosis.

Methods: We did a retrospective study looking at malignant pleural mesothelioma tumours using next-generation sequencing from the Memorial Sloan Kettering Cancer Center-Integrated Mutation Profiling of Actionable Cancer Targets (MSK-IMPACT). We collected clinical, pathological, and routine next-generation sequencing data from consecutive patients with malignant pleural mesothelioma treated at the Memorial Sloan Kettering Cancer Center (New York, NY, USA), as well as the MSK-IMPACT data. Together, these data comprised the MSK-IMPACT cohort. Using OncoCast-MPM, an open-source, web-accessible, machine-learning risk-prediction model, we integrated available data to create risk scores that stratified patients into low-risk and high-risk groups. Risk stratification of the MSK-IMPACT cohort was then validated using publicly available malignant pleural mesothelioma data from The Cancer Genome Atlas (ie, the TCGA cohort).

Findings: Between Feb 15, 2014, and Jan 28, 2019, we collected MSK-IMPACT data from the tumour tissue of 194 patients in the MSK-IMPACT cohort. The median overall survival was higher in the low-risk group than in the high-risk group as determined by OncoCast-MPM (30·8 months [95% CI 22·7–36·2] vs 13·9 months [10·7–18·0]; hazard ratio [HR] 3·0 [95% CI 2·0–4·5]; p<0·0001). No single factor or gene alteration drove risk differentiation. OncoCast-MPM was validated against the TCGA cohort, which consisted of 74 patients. The median overall survival was higher in the low-risk group than in the high-risk group (23·6 months [95% CI 15·1–28·4] vs 13·6 months [9·8–17·9]; HR 2·3 [95% CI 1·3–3·8]; p=0·0019). Although stage-based risk stratification was unable to differentiate survival among risk groups at 3 years in the MSK-IMPACT cohort (31% for early-stage disease vs 30% for advanced-stage disease; p=0·90), the OncoCast-MPM-derived 3-year survival was significantly higher in the low-risk group than in the high-risk group (40% vs 7%; p=0·0052).

Interpretation: OncoCast-MPM generated accurate, individual patient-level risk assessment scores. After prospective validation with the TCGA cohort, OncoCast-MPM might offer new opportunities for enhanced risk stratification of patients with malignant pleural mesothelioma in clinical trials and drug development.

Evolving landscape of initial treatments for patients with malignant pleural mesotheliomas: clinical trials to clinical practice

Offin M, Rusch VW, Rimner A, Adusumilli PS, Zauderer MG. Evolving Landscape of Initial Treatments for Patients with Malignant Pleural Mesotheliomas: Clinical Trials to Clinical Practice. Oncologist. 2022 Aug 5;27(8):610-614. doi: 10.1093/oncolo/oyac113. PMID: 35708504; PMCID: PMC9355824

Malignant pleural mesothelioma (MPM) is the most common form of mesothelioma and the type most often studied in prospective clinical trials. This review reports the trials that have shaped first-line treatment for patients with advanced/unresectable MPM and the real-world integration of first-line immune checkpoint inhibitors into clinical practice.

Malignant mesothelioma of the tunica vaginalis testis: outcomes following surgical management beyond radical orchiectomy

Recabal P, Rosenzweig B, Bazzi WM, Carver BS, Sheinfeld J. Malignant Mesothelioma of the Tunica Vaginalis Testis: Outcomes Following Surgical Management Beyond Radical Orchiectomy. Urology. 2017 Sep;107:166-170. doi: 10.1016/j.urology.2017.04.011. Epub 2017 Apr 14. PMID: 28416299; PMCID: PMC5632754

Objective: To describe clinical management and outcomes of a cohort of patients with malignant mesothelioma of the tunica vaginalis testis (MMTVT) who received treatments beyond radical orchiectomy.

Methods: Patients with confirmed MMTVT at a single tertiary care institution were identified. Treatments, pathologic outcomes, and survival were recorded. Prognostic variables associated with survival were analyzed with a Cox proportional hazards model and Kaplan-Meier curves.

Results: Overall, 15 patients were included. Initial presentation was a scrotal mass in 7 of 15 (47%) and hydrocele in 5 of 15 (33%) patients. Clinical staging revealed enlarged nodes in 5 of 15 (33%) patients. Radical orchiectomy was the initial treatment in 5 of 15 (33%) patients. Positive surgical margins were found in 6 of 14 (43%) radical orchiectomies and were associated with worse survival (P = .007). The most frequent histologic subtype was epithelioid, associated with better survival (P = .048). Additional surgeries were performed on 12 of 15 (80%) patients. Pathologic examination revealed MMTVT in 6 of 12 (50%) hemiscrotectomies, 7 of 8 (88%) retroperitoneal lymph node dissections, 1 of 7 (14%) pelvic lymph node dissections, and 10 of 10 (100%) groin dissections. Five patients received adjuvant chemotherapy. Two also received adjuvant radiation therapy. Three patients with lymph node involvement remain no evidence of disease over 6 years after diagnosis. After a median follow-up of 3.5 years (interquartile range: 1.2-7.2), 5 patients have died, all of MMTVT; the median overall survival has not been reached. Common sites of relapse were lungs (5 of 7) and groin (3 of 7).

Conclusion: The pattern of metastatic spread of MMTVT is predominantly lymphatic. Nodes in the retroperitoneum and the groin are commonly involved. Prognosis is poor, but there may be a role for aggressive surgical resection including hemiscrotectomy, and inguinal and retroperitoneal lymph nodes.

Clinical Trials

A phase 1 safety study of avelumab plus stereotactic body radiation therapy in malignant pleural mesothelioma

Rimner A, Adusumilli PS, Offin MD, Solomon SB, Ziv E, Hayes SA, Ginsberg MS, Sauter JL, Gelblum DY, Shepherd AF, Guttmann DM, Eichholz JE, Zhang Z, Ritter E, Wong P, Iqbal AN, Daly RM, Namakydoust A, Li H, McCune M, Gelb EH, Taunk NK, von Reibnitz D, Tyagi N, Yorke ED, Rusch VW, Zauderer MG. A Phase 1 Safety Study of Avelumab Plus Stereotactic Body Radiation Therapy in Malignant Pleural Mesothelioma. JTO Clin Res Rep. 2022 Dec 1;4(1):100440. doi: 10.1016/j.jtocrr.2022.100440. PMID: 36590015; PMCID: PMC9801123

Introduction: Single-agent monoclonal antibody therapy against programmed death-ligand 1 (PD-L1) has modest effects in malignant pleural mesothelioma. Radiation therapy can enhance the antitumor effects of immunotherapy. Nevertheless, the safety of combining anti-PD-L1 therapy with stereotactic body radiation therapy (SBRT) is unknown. We present the results of a phase 1 trial to evaluate the safety of the anti-PD-L1 antibody avelumab plus SBRT in patients with malignant pleural mesothelioma.

Methods: This was a single-arm, investigator-initiated trial in patients who progressed on prior chemotherapy. Avelumab was delivered every other week, and SBRT was delivered to one lesion in three to five fractions (minimum of 30 Gy) followed by continuation of avelumab up to 24 months or until disease progression. The primary end point of the study was safety on the basis of grade 3+ nonhematologic adverse events (AEs) within 3 months of SBRT.

Results: Thirteen assessable patients received a median of seven cycles (range: 2–26 cycles) of avelumab. There were 27 grade 1, 17 grade 2, four grade 3, and no grade 4 or 5 avelumab-related AEs. The most common were infusion-related allergic reactions (n = 6), anorexia or weight loss (n = 6), fatigue (n = 6), thyroid disorders (n = 5), diarrhea (n = 3), and myalgia or arthralgias (n = 3). There were 10 grade 1, four grade 2, one grade 3, and no grade 4 or 5 SBRT-related AEs. The most common were diarrhea (n = 3), chest pain/myalgia (n = 2), fatigue (n = 2), cough (n = 2), dyspnea (n = 2), and nausea/vomiting (n = 2).

Conclusions: Combination avelumab plus SBRT seems tolerable on the basis of the prespecified toxicity end points of the first stage of this Simon two-stage design phase 1 study.

A phase I trial of regional mesothelin-targeted CAR T-cell therapy in patients with malignant pleural disease, in combination with the anti-PD-1 agent pembrolizumab

Adusumilli PS, Zauderer MG, Rivière I, Solomon SB, Rusch VW, O'Cearbhaill RE, Zhu A, Cheema W, Chintala NK, Halton E, Pineda J, Perez-Johnston R, Tan KS, Daly B, Araujo Filho JA, Ngai D, McGee E, Vincent A, Diamonte C, Sauter JL, Modi S, Sikder D, Senechal B, Wang X, Travis WD, Gönen M, Rudin CM, Brentjens RJ, Jones DR, Sadelain M. A Phase I Trial of Regional Mesothelin-Targeted CAR T-cell Therapy in Patients with Malignant Pleural Disease, in Combination with the Anti-PD-1 Agent Pembrolizumab. Cancer Discov. 2021 Nov;11(11):2748-2763. doi: 10.1158/2159-8290.CD-21-0407. Epub 2021 Jul 15. PMID: 34266984; PMCID: PMC8563385

Malignant pleural diseases, comprising metastatic lung and breast cancers and malignant pleural mesothelioma (MPM), are aggressive solid tumors with poor therapeutic response. We developed and conducted a first-in-human, phase I study of regionally delivered, autologous, mesothelin-targeted chimeric antigen receptor (CAR) T-cell therapy. Intrapleural administration of 0.3M to 60M CAR T cells/kg in 27 patients (25 with MPM) was safe and well tolerated. CAR T cells were detected in peripheral blood for >100 days in 39% of patients. Following our demonstration that PD-1 blockade enhances CAR T-cell function in mice, 18 patients with MPM also received pembrolizumab safely. Among those patients, median overall survival from CAR T-cell infusion was 23.9 months (1-year overall survival, 83%). Stable disease was sustained for ≥6 months in 8 patients; 2 exhibited complete metabolic response on PET scan. Combination immunotherapy with CAR T cells and PD-1 blockade agents should be further evaluated in patients with solid tumors.

Significance: Regional delivery of mesothelin-targeted CAR T-cell therapy followed by pembrolizumab administration is feasible, safe, and demonstrates evidence of antitumor efficacy in patients with malignant pleural diseases. Our data support the investigation of combination immunotherapy with CAR T cells and PD-1 blockade agents in solid tumors.

EZH2 inhibitor tazemetostat in patients with relapsed or refractory, BAP1-inactivated malignant pleural mesothelioma: a multicentre, open-label, phase 2 study

Zauderer MG, Szlosarek PW, Le Moulec S, Popat S, Taylor P, Planchard D, Scherpereel A, Koczywas M, Forster M, Cameron RB, Peikert T, Argon EK, Michaud NR, Szanto A, Yang J, Chen Y, Kansra V, Agarwal S, Fennell DA. EZH2 inhibitor tazemetostat in patients with relapsed or refractory, BAP1-inactivated malignant pleural mesothelioma: a multicentre, open-label, phase 2 study. Lancet Oncol. 2022 Jun;23(6):758-767. doi: 10.1016/S1470-2045(22)00277-7. Epub 2022 May 16. PMID: 35588752

Background: Treatment options for malignant pleural mesothelioma are scarce. Tazemetostat, a selective oral enhancer of zeste homolog 2 (EZH2) inhibitor, has shown antitumour activity in several haematological cancers and solid tumours. We aimed to evaluate the anti-tumour activity and safety of tazemetostat in patients with measurable relapsed or refractory malignant pleural mesothelioma.

Methods: We conducted an open-label, single-arm phase 2 study at 16 hospitals in France, the UK, and the USA. Eligible patients were aged 18 years or older with malignant pleural mesothelioma of any histology that was relapsed or refractory after treatment with at least one pemetrexed-containing regimen, an Eastern Cooperative Oncology Group performance status of 0 or 1, and a life expectancy of greater than 3 months. In part 1 of the study, participants received oral tazemetostat 800 mg once on day 1 and then twice daily from day 2 onwards. In part 2, participants received oral tazemetostat 800 mg twice daily starting on day 1 of cycle 1, using a two-stage Green-Dahlberg design. Tazemetostat was administered in 21-day cycles for approximately 17 cycles. The primary endpoint of part 1 was the pharmacokinetics of tazemetostat and its metabolite at day 15 after administration of 800 mg tazemetostat, as measured by maximum serum concentration (Cmax), time to Cmax (Tmax), area under the concentration-time curve (AUC) to day 15 (AUC0–t), area under the curve from time 0 extrapolated to infinity (AUC0–∞), and the half-life (t1/2) of tazemetostat, assessed in all patients enrolled in part 1. The primary endpoint of part 2 was the disease control rate (the proportion of patients with a complete response, partial response, or stable disease) at week 12 in patients with malignant pleural mesothelioma per protocol with BAP1 inactivation determined by immunohistochemistry. The safety population included all the patients who had at least one post-dose safety assessment. This trial is now complete and is registered with ClinicalTrials.gov, NCT02860286.

Findings: Between July 29, 2016, and June 2, 2017, 74 patients were enrolled (13 in part 1 and 61 in part 2) and received tazemetostat, 73 (99%) of whom had BAP1-inactivated tumours. In part 1, following repeat dosing of tazemetostat at steady state, on day 15 of cycle 1, the mean Cmax was 829 ng/mL (coefficient of variation 56·3%), median Tmax was 2 h (range 1–4), mean AUC0–twas 3310 h·ng/mL (coefficient of variation 50·4%), mean AUC0–∞ was 3180 h·ng/mL (46·6%), and the geometric mean t1/2 was 3·1 h (13·9%). After a median follow-up of 35·9 weeks (IQR 20·6–85·9), the disease control rate in part 2 in patients with BAP1-inactivated malignant pleural mesothelioma was 54% (95% CI 42–67; 33 of 61 patients) at week 12. No patients had a confirmed complete response. Two patients had a confirmed partial response: one had an ongoing partial response with a duration of 18 weeks and the other had a duration of 42 weeks. The most common grade 3–4 treatment-emergent adverse events were hyperglycaemia (five [7%] patients), hyponatraemia (five [7%]), and anaemia (four [5%]); serious adverse events were reported in 25 (34%) of 74 patients. Five (7%) of 74 patients died while on study; no treatment-related deaths occurred.

Image-guided interventional radiological delivery of chimeric antigen receptor (CAR) T cells for pleural malignancies in a phase I/II clinical trial

Ghosn M, Cheema W, Zhu A, Livschitz J, Maybody M, Boas FE, Santos E, Kim D, Beattie JA, Offin M, Rusch VW, Zauderer MG, Adusumilli PS, Solomon SB. Image-guided interventional radiological delivery of chimeric antigen receptor (CAR) T cells for pleural malignancies in a phase I/II clinical trial. Lung Cancer. 2022 Mar;165:1-9. doi: 10.1016/j.lungcan.2022.01.003. Epub 2022 Jan 6. PMID: 35045358; PMCID: PMC9256852

Objectives: We describe techniques and results of image-guided delivery of mesothelin-targeted chimeric antigen receptor (CAR) T cells in patients with pleural malignancies in a phase I/II trial (ClinicalTrials.gov: NCT02414269).

Materials and Methods: Patients without a pleural catheter or who lack effusion for insertion of a catheter (31 of 41) were administered intrapleural CAR T cells by interventional radiologists under image guidance by computed tomography or ultrasound. CAR T cells were administered through a needle in an accessible pleural loculation (intracavitary) or following an induced loculated artificial pneumothorax. In patients where intracavitary infusion was not feasible, CAR T cells were injected via percutaneous approach either surrounding and/or in the pleural nodule/thickening (intratumoral). Pre- and post-procedural clinical, laboratory, and imaging findings were assessed.

Results: CAR T cells were administered intrapleurally in 31 patients (33 procedures, 2 patients were administered a second dose) with successful delivery of planned dose (10–186 mL); 14/33 (42%) intracavitary and 19/33 (58%) intratumoral. All procedures were completed within 2 h of T-cell thawing. There were no procedure-related adverse events greater than grade 1 (1 in 3 patients had prior ipsilateral pleural fusion procedures). The most common imaging finding was ground glass opacities with interlobular septal thickening and/or consolidation, observed in 12/33 (36%) procedures. There was no difference in the incidence of fever, CRP, IL-6, and peak vector copy number in the peripheral blood between infusion methods.

Conclusion: Image-guided intrapleural delivery of CAR T cells using intracavitary or intratumoral routes is feasible, repeatable and safe across anatomically variable pleural cancers.

Phase 1 cohort expansion study of LY3023414, a dual PI3K/mTOR inhibitor, in patients with advanced mesothelioma

Zauderer MG, Alley EW, Bendell J, Capelletto E, Bauer TM, Callies S, Szpurka AM, Kang S, Willard MD, Wacheck V, Varghese AM. Phase 1 cohort expansion study of LY3023414, a dual PI3K/mTOR inhibitor, in patients with advanced mesothelioma. Invest New Drugs. 2021 Aug;39(4):1081-1088. doi: 10.1007/s10637-021-01086-6. Epub 2021 Mar 4. PMID: 33660194; PMCID: PMC8280020

Background: LY3023414 is a selective, ATP competitive inhibitor of class I PI3K isoforms, mTORC1/2 and DNA-PK. A Phase 1 dose escalation, 200 mg twice daily (BID) of LY3023414 was the determined recommended phase 2 dose (RP2D). We report the antitumor activity and safety of LY3023414 monotherapy in patients with advanced mesothelioma.

Methods: Patients enrolled had advanced malignant pleural or peritoneal mesothelioma with measurable disease, ECOG PS 0–1, were refractory or ineligible to receive standard therapies. Patients received LY3023414 200 mg BID. This dose expansion cohort is intended to evaluate preliminary antitumor activity of LY3023414 by overall response rate. Safety, tolerability and pharmacokinetics were assessed. Biomarkers associated with treatment response was an exploratory endpoint.

Results: Forty-two patients received LY3023414 for a median duration of 11.2 weeks (range: 1.1–53.0). One patient had a confirmed partial response (PR) (ORR 2.4%). Three patients had an unconfirmed PR. Seventeen patients had stable disease (SD) (DCR 43%). Most common adverse events (AEs) included fatigue (43%), nausea (43%), decreased appetite (38%), vomiting (33%), and diarrhea (29%). AEs were mostly mild or moderate. Grade ≥ 3 AEs were reported for 21% of patients with fatigue as the most frequent event (10%). Alterations of BAP1 were identified in 11/19 patients as the most common molecular aberration, followed by SETD2 and NF2 alterations. No obvious pattern of genetic changes/mutations in single genes or pathways was associated with anti-tumor activity.

Conclusion: LY3023414 monotherapy (200 mg BID) demonstrated an acceptable and manageable safety profile with limited single-agent activity in patients with advanced mesothelioma. ClinicalTrials.gov identifier: NCT01655225; Date of registration: 19 July 2012.

A randomized phase II trial of adjuvant galinpepimut-S, WT-1 analogue peptide vaccine, after multimodality therapy for patients with malignant pleural mesothelioma

Zauderer MG, Tsao AS, Dao T, Panageas K, Lai WV, Rimner A, Rusch VW, Adusumilli PS, Ginsberg MS, Gomez D, Rice D, Mehran R, Scheinberg DA, Krug LM. A Randomized Phase II Trial of Adjuvant Galinpepimut-S, WT-1 Analogue Peptide Vaccine, After Multimodality Therapy for Patients with Malignant Pleural Mesothelioma. Clin Cancer Res. 2017 Dec 15;23(24):7483-7489. doi: 10.1158/1078-0432.CCR-17-2169. Epub 2017 Sep 28. PMID: 28972039; PMCID: PMC5732877

Purpose: Determine the 1-year progression-free survival (PFS) rate among patients with malignant pleural mesothelioma (MPM) receiving the WT1 peptide vaccine galinpepimut-S after multimodality therapy versus those receiving control adjuvants.

Experimental Design: This double-blind, controlled, two center phase II trial randomized MPM patients after surgery and another treatment modality to galinpepimut-S with GM-CSF and Montanide or GM-CSF and Montanide alone. An improvement in 1-year PFS from 50% to 70% was the predefined efficacy threshold, and 78 patients total were planned. The study was not powered for comparison between the two arms.

Results: Forty-one patients were randomized. Treatment-related adverse events were mild, self-limited, and not clinically significant. On the basis of a stringent prespecified futility analysis (futility = ≥10 of 20 patients on one arm experiencing progression < 1 year), the control arm closed early. The treatment arm was subsequently closed because of the resultant unblinding. The PFS rate at 1 year from beginning study treatment was 33% and 45% in the control and vaccine arms, respectively. Median PFS was 7.4 months versus 10.1 months and median OS was 18.3 months versus 22.8 months in the control and vaccine arms, respectively.

Conclusions: The favorable safety profile was confirmed. PFS and OS were greater in those who received vaccine, but the trial was neither designed nor powered for comparison between the arms. On the basis of these promising results, the investigators are planning a larger randomized trial with greater statistical power to define the optimal use and benefit of galinpepimut-S in the treatment of MPM.

Improved outcomes with modern lung-sparing trimodality therapy in patients with malignant pleural mesothelioma

Shaikh F, Zauderer MG, von Reibnitz D, Wu AJ, Yorke ED, Foster A, Shi W, Zhang Z, Adusumilli PS, Rosenzweig KE, Krug LM, Rusch VW, Rimner A. Improved Outcomes with Modern Lung-Sparing Trimodality Therapy in Patients with Malignant Pleural Mesothelioma. J Thorac Oncol. 2017 Jun;12(6):993-1000. doi: 10.1016/j.jtho.2017.02.026. Epub 2017 Mar 21. PMID: 28341225; PMCID: PMC5499250

Introduction: Higher target conformity and better sparing of organs at risk with modern radiotherapy (RT) may result in higher tumor control and less toxicity. In this study, we compare our institutional multimodality therapy experience of adjuvant chemotherapy and hemithoracic intensity-modulated pleural RT (IMPRINT) with previously used adjuvant conventional RT (CONV) in patients with malignant pleural mesothelioma (MPM) treated with lung-sparing pleurectomy/decortication (P/D).

Methods: We analyzed 209 patients who underwent P/D and adjuvant RT (131 who received CONV and 78 who received IMPRINT) for MPM between 1974 and 2015. The primary end point was overall survival (OS). The Kaplan-Meier method and Cox proportional hazards model were used to calculate OS; competing risks analysis was performed for local failure-free survival and progression-free survival. Univariate analysis and multivariate analysis were performed with relevant clinical and treatment factors.

Results: The median age was 64 years, and 80% of the patients were male. Patients receiving IMPRINT had significantly higher rates of the epithelial histological type, advanced pathological stage, and chemotherapy treatment. OS was significantly higher after IMPRINT (median 20.2 versus 12.3 months, p = 0.001). Higher Karnofsky performance score, epithelioid histological type, macroscopically complete resection, and use of chemotherapy/IMPRINT were found to be significant factors for longer OS in multivariate analysis. No significant predictive factors were identified for local failure or progression. Grade 2 or higher esophagitis developed in fewer patients after IMPRINT than after CONV (23% versus 47%).

Conclusions: Trimodality therapy including adjuvant hemithoracic IMPRINT, chemotherapy, and P/D is associated with promising OS rates and decreased toxicity in patients with MPM. Dose constraints should be applied vigilantly to minimize serious adverse events.

Translational Research

Tumor-targeted nonablative radiation promotes solid tumor CAR T-cell therapy efficacy

Quach HT, Skovgard MS, Villena-Vargas J, Bellis RY, Chintala NK, Amador -Molina A, Bai Y, Banerjee S, Saini J, Xiong Y, Vista WR, Byun AJ, De Biasi A, Zeltsman M, Mayor M, Morello A, Mittal V, Gomez DR, Rimner A, Jones DR, Adusumilli PS. Tumor-Targeted Nonablative Radiation Promotes Solid Tumor CAR T-cell Therapy Efficacy. Cancer Immunol Res. 2023 Oct 4;11(10):1314-1331. doi: 10.1158/2326-6066.CIR-22-0840. PMID: 37540803; PMCID: PMC10592183

Infiltration of tumor by T cells is a prerequisite for successful immunotherapy of solid tumors. In this study, we investigate the influence of tumor-targeted radiation on chimeric antigen receptor (CAR) T-cell therapy tumor infiltration, accumulation, and efficacy in clinically relevant models of pleural mesothelioma and non–small cell lung cancers. We use a nonablative dose of tumor-targeted radiation prior to systemic administration of mesothelin-targeted CAR T cells to assess infiltration, proliferation, antitumor efficacy, and functional persistence of CAR T cells at primary and distant sites of tumor. A tumor-targeted, nonablative dose of radiation promotes early and high infiltration, proliferation, and functional persistence of CAR T cells. Tumor-targeted radiation promotes tumor-chemokine expression and chemokine-receptor expression in infiltrating T cells and results in a subpopulation of higher-intensity CAR-expressing T cells with high coexpression of chemokine receptors that further infiltrate distant sites of disease, enhancing CAR T-cell antitumor efficacy. Enhanced CAR T-cell efficacy is evident in models of both high-mesothelin-expressing mesothelioma and mixed-mesothelin-expressing lung cancer—two thoracic cancers for which radiotherapy is part of the standard of care. Our results strongly suggest that the use of tumor-targeted radiation prior to systemic administration of CAR T cells may substantially improve CAR T-cell therapy efficacy for solid tumors. Building on our observations, we describe a translational strategy of “sandwich” cell therapy for solid tumors that combines sequential metastatic site–targeted radiation and CAR T cells—a regional solution to overcome barriers to systemic delivery of CAR T cells.

Neurofibromatosis type 2-yes-associated protein and transcriptional coactivator with PDZ-binding motif dual immunohistochemistry is a reliable marker for the detection of neurofibromatosis type 2 alterations in diffuse pleural mesothelioma

Li Y, Yang SR, Chen YB, Adusumilli PS, Bialik A, Bodd FM, Ladanyi M, Lopardo J, Offin MD, Rusch VW, Travis WD, Zauderer MG, Chang JC, Sauter JL. Neurofibromatosis Type 2-Yes-Associated Protein and Transcriptional Coactivator With PDZ-Binding Motif Dual Immunohistochemistry Is a Reliable Marker for the Detection of Neurofibromatosis Type 2 Alterations in Diffuse Pleural Mesothelioma. Mod Pathol. 2023 Mar;36(3):100030. doi: 10.1016/j.modpat.2022.100030. Epub 2023 Jan 10. PMID: 36788094; PMCID: PMC10428583

Neurofibromatosis type 2 (NF2) loss occurs in approximately 30% to 50% of diffuse pleural mesothelioma (DPM) with accumulation of yes-associated protein (YAP) 1 and transcriptional coactivator with PDZ-binding motif (TAZ) in tumor nuclei. NF2 and YAP/TAZ represent potential therapeutic targets. We investigated the performance of NF2 -YAP/TAZ dual immunohistochemistry (IHC) in identifying DPM that harbors NF2 alterations and in distinguishing DPM from benign mesothelial proliferations. NF2-YAP/TAZ IHC was subsequently performed in a Discovery cohort of DPMs with (n = 10) or without (n = 10) NF2 alterations detected by next-generation sequencing (NGS) and 9 benign cases. The cutoff values for loss of NF2 expression and YAP/TAZ overexpression using IHC were determined in the Discovery cohort. The performance characteristics of NF2-YAP/TAZ IHC were investigated in a Validation cohort (20 DPMs and 10 benign cases). In the Discovery cohort, all DPMs with NF2 alterations using NGS showed NF2 IHC scores of <2, whereas all NF2-wild-type DPMs showed scores of ≥2. NF2-altered DPMs had significantly higher YAP/TAZ H-scores ($P < .001$) than NF2-wild-type DPM and benign pleura (median H-scores: 237.5 [range, 185-275], 130.0 [range, 40-225], and 10.0 [range, 0-75], respectively). NF2-YAP/TAZ IHC demonstrated 95.2% sensitivity, 100% specificity, 100% positive predictive value, and 95% negative predictive value for detecting NF2 alterations in DPM (n = 40) with NGS as the gold standard and 87.5% sensitivity and 100% specificity for distinguishing DPM (n = 40) from benign mesothelial proliferations (n = 19). NF2-YAP/TAZ IHC has a high sensitivity and specificity for detecting NF2 alterations in DPM and a high specificity for malignancy, highlighting potential utility for guiding NF2-targeted therapies and distinguishing DPM from benign mimics.

Correlative analysis from a phase I clinical trial of intrapleural administration of oncolytic vaccinia virus (Olvi-vec) in patients with malignant pleural mesothelioma

Chintala NK, Choe JK, McGee E, Bellis R, Saini JK, Banerjee S, Moreira AL, Zauderer MG, Adusumilli PS, Rusch VW. Correlative analysis from a phase I clinical trial of intrapleural administration of oncolytic vaccinia virus (Olvi-vec) in patients with malignant pleural mesothelioma. Front Immunol. 2023 Feb 16;14:1112960. doi: 10.3389/fimmu.2023.1112960. PMID: 36875061; PMCID: PMC9977791

Background: The attenuated, genetically engineered vaccinia virus has been shown to be a promising oncolytic virus for the treatment of patients with solid tumors, through both direct cytotoxic and immune-activating effects. Whereas systemically administered oncolytic viruses can be neutralized by pre-existing antibodies, locoregionally administered viruses can infect tumor cells and generate immune responses. We conducted a phase I clinical trial to investigate the safety, feasibility and immune activating effects of intrapleural administration of oncolytic vaccinia virus (NCT01766739).

Methods: Eighteen patients with malignant pleural effusion due to either malignant pleural mesothelioma or metastatic disease (non-small cell lung cancer or breast cancer) underwent intrapleural administration of the oncolytic vaccinia virus using a dose-escalating method, following drainage of malignant pleural effusion. The primary objective of this trial was to determine a recommended dose of attenuated vaccinia virus. The secondary objectives were to assess feasibility, safety and tolerability; evaluate viral presence in the tumor and serum as well as viral shedding in pleural fluid, sputum, and urine; and evaluate anti-vaccinia virus immune response. Correlative analyses were performed on body fluids, peripheral blood, and tumor specimens obtained from pre- and post-treatment timepoints.

Results: Treatment with attenuated vaccinia virus at the dose of 1.00E+07 plaque-forming units (PFU) to 6.00E+09 PFU was feasible and safe, with no treatment-associated mortalities or dose-limiting toxicities. Vaccinia virus was detectable in tumor cells 2-5 days post-treatment, and treatment was associated with a decrease in tumor cell density and an increase in immune cell density as assessed by a pathologist blinded to the clinical observations. An increase in both effector (CD8+, NK, cytotoxic cells) and suppressor (Tregs) immune cell populations was observed following treatment. Dendritic cell and neutrophil populations were also increased, and immune effector and immune checkpoint proteins (granzyme B, perforin, PD-1, PD-L1, and PD-L2) and cytokines (IFN-γ, TNF-α, TGFβ1 and RANTES) were upregulated.

Conclusion: The intrapleural administration of oncolytic vaccinia viral therapy is safe and feasible and generates regional immune response without overt systemic symptoms.

Genomic and transcriptomic analysis of a diffuse pleural mesothelioma patient-derived xenograft library

Offin M, Sauter JL, Tischfield SE, Egger JV, Chavan S, Shah NS, Manoj P, Ventura K, Allaj V, de Stanchina E, Travis W, Ladanyi M, Rimner A, Rusch VW, Adusumilli PS, Poirier JT, Zauderer MG, Rudin CM, Sen T. Genomic and transcriptomic analysis of a diffuse pleural mesothelioma patient-derived xenograft library. Genome Med. 2022 Nov 15;14(1):127. doi: 10.1186/s13073-022-01129-4. PMID: 36380343; PMCID: PMC9667652

Background: Diffuse pleural mesothelioma (DPM) is an aggressive malignancy that, despite recent treatment advances, has unacceptably poor outcomes. Therapeutic research in DPM is inhibited by a paucity of preclinical models that faithfully recapitulate the human disease.

Methods: We established 22 patient-derived xenografts (PDX) from 22 patients with DPM and performed multi-omic analyses to deconvolute the mutational landscapes, global expression profiles, and molecular subtypes of these PDX models and compared features to those of the matched primary patient tumors. Targeted next-generation sequencing (NGS; MSK-IMPACT), immunohistochemistry, and histologic subtyping were performed on all available samples. RNA sequencing was performed on all available PDX samples. Clinical outcomes and treatment history were annotated for all patients. Platinum-doublet progression-free survival (PFS) was determined from the start of chemotherapy until radiographic/clinical progression and grouped into < or ≥ 6 months.

Results: PDX models were established from both treatment naïve and previously treated samples and were noted to closely resemble the histology, genomic landscape, and proteomic profiles of the parent tumor. After establishing the validity of the models, transcriptomic analyses demonstrated overexpression in WNT/β-catenin, hedgehog, and TGF-β signaling and a consistent suppression of immune-related signaling in PDXs derived from patients with worse clinical outcomes.

Conclusions: These data demonstrate that DPM PDX models closely resemble the genotype and phenotype of parental tumors, and identify pathways altered in DPM for future exploration in preclinical studies.

Image-guided interventional radiological delivery of chimeric antigen receptor (CAR) T cells for pleural malignancies in a phase I/II clinical trial

Ghosn M, Cheema W, Zhu A, Livschitz J, Maybody M, Boas FE, Santos E, Kim D, Beattie JA, Offin M, Rusch VW, Zauderer MG, Adusumilli PS, Solomon SB. Image-guided interventional radiological delivery of chimeric antigen receptor (CAR) T cells for pleural malignancies in a phase I/II clinical trial. Lung Cancer. 2022 Mar;165:1-9. doi: 10.1016/j.lungcan.2022.01.003. Epub 2022 Jan 6. PMID: 35045358; PMCID: PMC9256852

Objectives: We describe techniques and results of image-guided delivery of mesothelin-targeted chimeric antigen receptor (CAR) T cells in patients with pleural malignancies in a phase I/II trial (ClinicalTrials.gov: NCT02414269).

Materials and Methods: Patients without a pleural catheter or who lack effusion for insertion of a catheter (31 of 41) were administered intrapleural CAR T cells by interventional radiologists under image guidance by computed tomography or ultrasound. CAR T cells were administered through a needle in an accessible pleural loculation (intracavitary) or following an induced loculated artificial pneumothorax. In patients where intracavitary infusion was not feasible, CAR T cells were injected via percutaneous approach either surrounding and/or in the pleural nodule/thickening (intratumoral). Pre- and post-procedural clinical, laboratory, and imaging findings were assessed.

Results: CAR T cells were administered intrapleurally in 31 patients (33 procedures, 2 patients were administered a second dose) with successful delivery of planned dose (10–186 mL); 14/33 (42%) intracavitary and 19/33 (58%) intratumoral. All procedures were completed within 2 h of T-cell thawing. There were no procedure-related adverse events greater than grade 1 (1 in 3 patients had prior ipsilateral pleural fusion procedures). The most common imaging finding was ground glass opacities with interlobular septal thickening and/or consolidation, observed in 12/33 (36%) procedures. There was no difference in the incidence of fever, CRP, IL-6, and peak vector copy number in the peripheral blood between infusion methods.

Conclusion: Image-guided intrapleural delivery of CAR T cells using intracavitary or intratumoral routes is feasible, repeatable and safe across anatomically variable pleural cancers.

Diffuse pleural mesothelioma: advances in molecular pathogenesis, diagnosis and treatment

Febres-Aldana CA, Fanaroff R, Offin M, Zauderer MG, Sauter JL, Yang SR, Ladanyi M. Diffuse Pleural Mesothelioma: Advances in Molecular Pathogenesis, Diagnosis and Treatment. Annu Rev Pathol. 2023 Sep 18. doi: 10.1146/annurev-pathol-042420-092719. Epub ahead of print. PMID: 37722697

Diffuse pleural mesothelioma (DPM) is a highly aggressive malignant neoplasm arising from the mesothelial cells lining the pleural surfaces. While DPM is a well-recognized disease linked to asbestos exposure, recent advances have expanded our understanding of molecular pathogenesis and transformed our clinical practice. This comprehensive review explores the current concepts and emerging trends in DPM, including risk factors, pathobiology, histologic subtyping, and therapeutic management, with an emphasis on a multidisciplinary approach to this complex disease.

Molecular characterization of peritoneal mesotheliomas

Offin M, Yang SR, Egger J, Jayakumaran G, Spencer RS, Lopardo J, Nash GM, Cercek A, Travis WD, Kris MG, Ladanyi M, Sauter JL, Zauderer MG. Molecular Characterization of Peritoneal Mesotheliomas. J Thorac Oncol. 2022 Mar;17(3):455-460. doi: 10.1016/j.jtho.2021.09.012. Epub 2021 Oct 11. PMID: 34648949; PMCID: PMC8882128

Introduction: Malignant peritoneal mesothelioma (MPeM) is clinically distinct and less studied than malignant pleural mesothelioma. We report the genomic and immunophenotypic features of a prospectively collected MPeM cohort.

Methods: Next-generation sequencing (NGS) was performed on MPeM tumors. Genomic near-haploidization (GNH) was assessed. WT1, BAP1, mesothelin, VISTA, and programmed death-ligand 1 were evaluated by immunohistochemistry (IHC) when tissue was available. Overall survival was stratified by selected genomic and IHC features.

Results: A total of 50 consented patients with MPeM (45 epithelioid, 5 nonepithelioid) were studied exhibiting common alterations in BAP1 (60%; 30 of 50), NF2 (24%; 12 of 50) SETD2 (22%; 11 of 50), and TP53 (16%; 8 of 50). A total of 76% (38 of 50) of specimens were assessable for allele-specific copy number analysis; 8% (3 of 38) had GNH. IHC positivity rates were 93% (37 of 40) for mesothelin, 96% (46 of 48) for WT1, 50% (19 of 38) for programmed death-ligand 1, and 89% (34 of 38) for VISTA. BAP1 loss by IHC was observed in 76% (29 of 38), including five wild-type on NGS. Combining NGS and IHC for BAP1, overall survival was worse with alteration or loss compared with wild-type or retained in all patients (n = 37 versus 13, 43.8 versus 117.3 mo, p = 0.04) Three of 30 patients had a pathogenic germline variant: POT1 I78T, MUTYH R109Y, and BAP1 E402∗.

Conclusions: MPeM has distinct biology and genomic composition. CDKN2A/B alterations were rare in MPeM, whereas BAP1, NF2, TP53, SETD2, and LATS2 were common. BAP1 alteration/loss was associated with shorter survival when all patients were included. A notable minority of specimens had GNH associated with NF2, TP53, and SETDB1 mutations. Pathogenic germline mutations were found in 3 of 30 patients.

V-domain Ig-containing suppressor of T-cell activation (VISTA), a potentially targetable immune checkpoint molecule, is highly expressed in epithelioid malignant pleural mesothelioma

Muller S, Victoria Lai W, Adusumilli PS, Desmeules P, Frosina D, Jungbluth A, Ni A, Eguchi T, Travis WD, Ladanyi M, Zauderer MG, Sauter JL. V-domain Ig-containing suppressor of T-cell activation (VISTA), a potentially targetable immune checkpoint molecule, is highly expressed in epithelioid malignant pleural mesothelioma. Mod Pathol. 2020 Feb;33(2):303-311. doi: 10.1038/s41379-019-0364-z. Epub 2019 Sep 19. PMID: 31537897; PMCID: PMC8366498

V-domain Ig-containing suppressor of T-cell activation (VISTA) is an immune checkpoint gene that inhibits anti-tumor immune responses. Since most malignant pleural mesotheliomas do not respond to anti-programmed cell death(-ligand)1 (PD-(L)1)/cytotoxic T-lymphocyte-associated protein 4 (CTLA4) therapy and given the recent finding of The Cancer Genome Atlas Study that pleural mesothelioma displays the highest expression of VISTA among all cancers studied, we examined VISTA expression in a large pleural mesothelioma cohort. VISTA and PD-L1 immunohistochemistry were performed on tissue microarray of immunotherapy-naive pleural mesotheliomas (254 epithelioid, 24 biphasic and 41 sarcomatoid) and ten whole-tissue sections of benign pleura (VISTA only). Percentages of tumor and inflammatory cells with positive staining were assessed. Optimal prognostic cutoff percentages were determined using maximally selected rank statistics. Overall survival was evaluated using Kaplan–Meier methods and Cox proportional hazard analysis. All benign mesothelium expressed VISTA. Eighty-five percent of 319 and 38% of 304 mesotheliomas expressed VISTA and PD-L1 (88% and 33% of epithelioid, 90% and 43% of biphasic, and 42% and 75% of sarcomatoid), respectively. Median VISTA score was significantly higher in epithelioid (50%) (vs. biphasic [20%] and sarcomatoid [0]) ($p < 0.001$), while median PD-L1 score was significantly higher in sarcomatoid tumors (20%) (vs. biphasic and epithelioid [both 0%]) ($p < 0.001$). VISTA and PD-L1 were expressed in inflammatory cells in 94% ($n = 317$) and 24% ($n = 303$) of mesothelioma, respectively. Optimal prognostic cutoffs for VISTA and PD-L1 were 40% and 30%, respectively. On multivariable analysis, VISTA and PD-L1 expression in mesothelioma were associated with better and worse overall survival ($p = 0.001$ and $p = 0.002$), respectively, independent of histology. In a large cohort of mesothelioma, we report frequent expression of VISTA and infrequent expression of PD-L1 with favorable and unfavorable survival correlations, respectively. These findings may explain poor responses to anti-PD-(L)1 immunotherapy and suggest VISTA as a potential novel target in pleural mesothelioma.

Cancer antigen profiling for malignant pleural mesothelioma immunotherapy: expression and coexpression of mesothelin, cancer antigen 125, and Wilms tumor 1

Eguchi T, Kadota K, Mayor M, Zauderer MG, Rimner A, Rusch VW, Travis WD, Sadelain M, Adusumilli PS. Cancer antigen profiling for malignant pleural mesothelioma immunotherapy: expression and coexpression of mesothelin, cancer antigen 125, and Wilms tumor 1. Oncotarget. 2017 Sep 12;8(44):77872-77882. doi: 10.18632/oncotarget.20845. PMID: 29100432; PMCID: PMC5652821

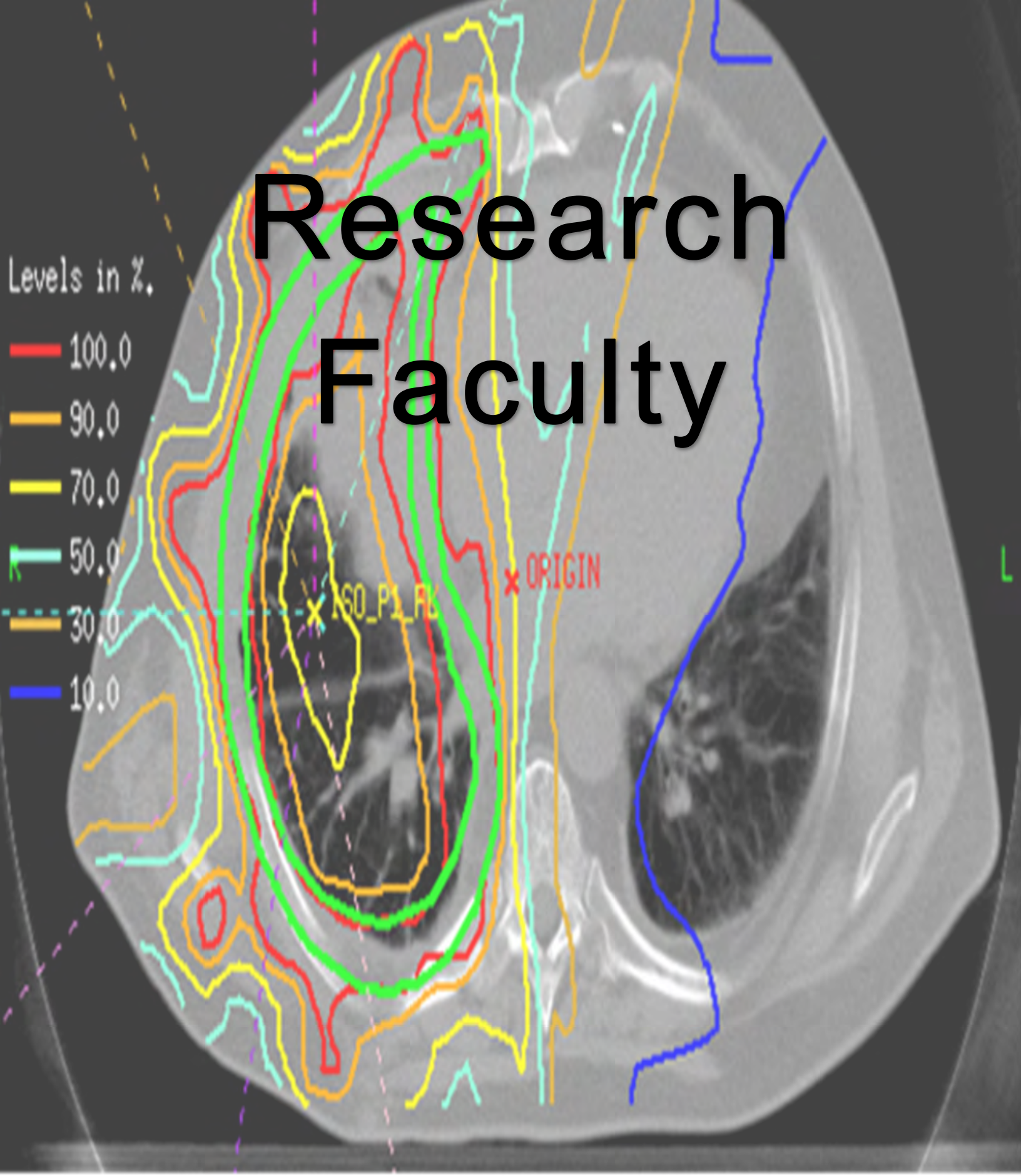
Introduction: Malignant peritoneal mesothelioma (MPeM) is
Background: To develop cancer antigen-targeted immunotherapeutic strategies for malignant pleural mesothelioma (MPM), we investigated the individual and coexpressions of the cancer-associated antigens mesothelin (MSLN), cancer antigen 125 (CA125), and Wilms tumor 1 (WT1) in both epithelioid and non-epithelioid MPM.

Methods: All available hematoxylin and eosin-stained slides from patients who were diagnosed with MPM (1989-2010) were reviewed. We constructed tissue microarrays from 283 patients (epithelioid = 234; non-epithelioid = 49). Intensity and distribution for each antigen were assessed by immunohistochemistry.

Results: Positive expression of MSLN, CA125, and WT1 were demonstrated in 93%, 75%, and 97% of epithelioid MPM cases, and 57%, 33%, and 98% of non-epithelioid MPM cases, respectively. Triple- and double-positive antigen coexpressions were demonstrated in 72% and 23% of epithelioid MPM cases and 29% and 33% of non-epithelioid MPM cases, respectively. Complete absence of expression for all three antigens was demonstrated in <2% of MPM cases. More than two-thirds of MPM cases had ≥50% distribution of MSLN-positive cells and, among the remaining third, half had ≥50% distribution of WT1-positive cells. CA125/MSLN coexpression was observed in more than two-thirds of epithelioid MPM cases and one-third of non-epithelioid MPM cases.

Conclusion: A limited number of cancer-associated antigens can target almost all MPM tumors for immunotherapy.

Conclusions: MPeM has distinct biology and genomic composition. CDKN2A/B alterations were rare in MPeM, whereas BAP1, NF2, TP53, SETD2, and LATS2 were common. BAP1 alteration/loss was associated with shorter survival when all patients were included. A notable minority of specimens had GNH associated with NF2, TP53, and SETDB1 mutations. Pathogenic germline mutations were found in 3 of 30 patients.



Typical isodose distribution using eight angles as part of a pleural intensity modulated radiation therapy (IMRT) treatment plan. These are equally spaced over 200-240 degrees covering the lung on the affected side of the chest. The area within the green lines is the target area.

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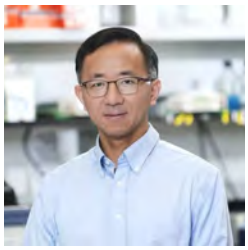

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Laboratories Conducting Mesothelioma Research

Investigation of the tumor immune microenvironment and the development of T-cell–mediated immunotherapy for thoracic malignancies and pleural-based diseases. Dr. Adusumilli's team has championed regional immunotherapy delivery strategies, resulting in translation of mesothelin-targeted CAR T-cell immunotherapy for malignant pleural mesothelioma, lung, and breast cancers.

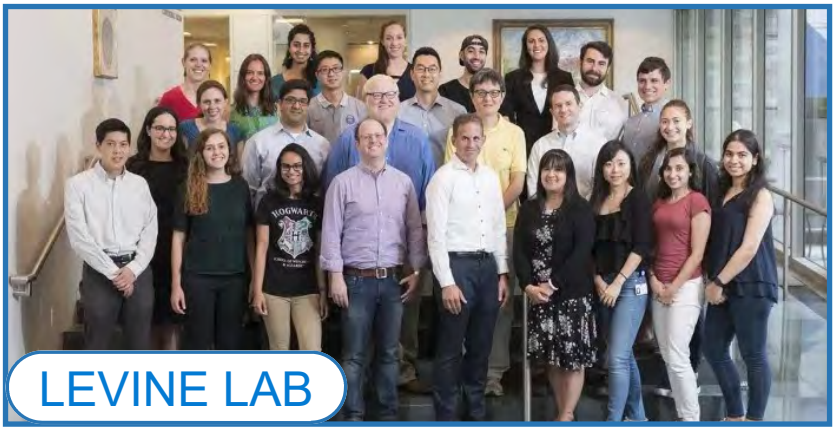
ADUSUMILLI LAB

JIANG LAB

The research of Dr. Jiang's laboratory focuses on two directions highly relevant to cancer biology, (1) the molecular basis of programmed cell death processes (including apoptosis and ferroptosis), and their roles in human disease; and (2) the molecular basis of autophagy and its role in cancer. The lab also studies various cancer signaling and cellular metabolic events, especially those involved in cell death/survival determination.

The research program in the Marc Ladanyi laboratory focuses on the genomics and molecular pathogenesis of sarcomas and thoracic malignancies, with an emphasis on clinical translation of potential diagnostic markers and therapeutic targets. Dr. Ladanyi also co-directs (with Chris Sander) the Genome Data Analysis Center at Memorial Sloan Kettering, which is part of the TCGA project network.

LADANYI LAB



LEVINE LAB

The goal of the research of the Ross Levine laboratory is to improve the understanding of the genetic basis of blood disorders known as myeloid malignancies, and to use this knowledge to improve therapies for patients with these disorders.

Dr. Ponomarev is a physician-scientist who focuses on the development of new multi-modal imaging approaches for specific applications, such as sequential in vivo imaging studies in cancer biology, cancer immunotherapy, and radiation sciences.

PONOMAREV LAB

RUDIN LAB

Physician-scientist Charles M. Rudin, Chief of the Thoracic Oncology Service, leads research that focuses on the development and testing of novel therapeutic approaches to lung cancer in preclinical models including patient-derived xenografts. These studies are integrated with early phase clinical trials.

The Michel Sadelain lab studies the mechanisms governing transgene expression, stem cell engineering, and genetic strategies to enhance immunity against cancer. Dr Michel Sadelain has been awarded the 2024 Breakthrough Prize in Life Sciences. The prestigious prize recognizes Dr. Sadelain for the development of chimeric antigen receptor T cell immunotherapy whereby the patient's T cells are modified to target and kill cancer cells.

SADELAIN LAB

SCHEINBERG LAB

The overall goals of the David Scheinberg laboratory are to develop novel targeted immunotherapies based on effectors of the immune system and to understand their mechanisms of action as well as the mechanisms of resistance to them. This includes antibodies, targeted nano -devices, engineered cells, and active specific agents such vaccines. An important goal is to take these new therapies into human clinical trials for testing.

Research & Laboratory Staff

Hematoxylin and Eosin stained brightfield image showing tubulopapillary histological pattern of the epithelioid subtype of human malignant pleural mesothelioma. Cell nuclei are stained for hematoxylin (blue), and cell cytoplasm and extracellular matrix components are stained for eosin (pink).

Research Fellows, Scholars, & Scientists

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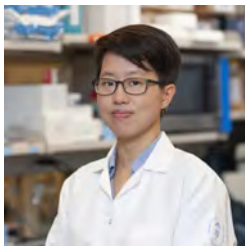

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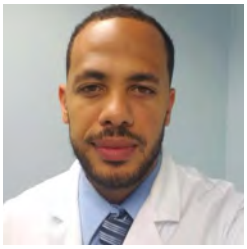

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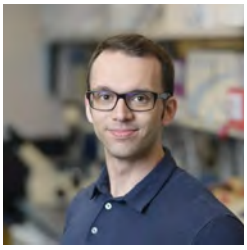

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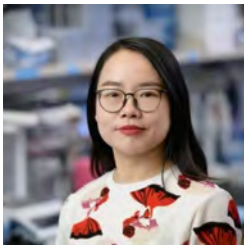

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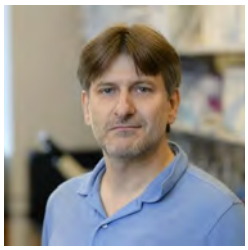

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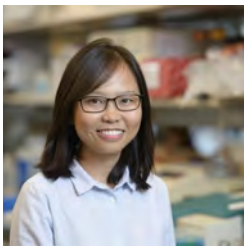

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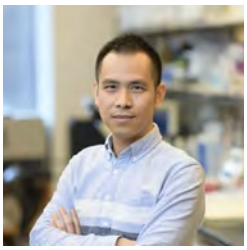

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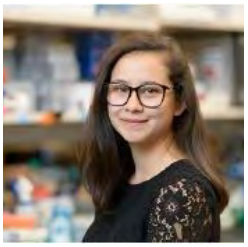

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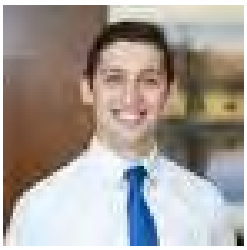

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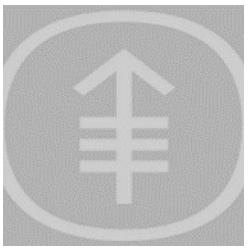

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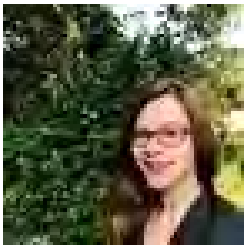

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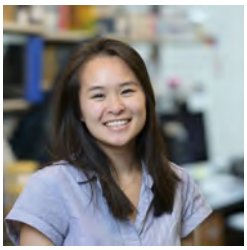

Amy Zhu
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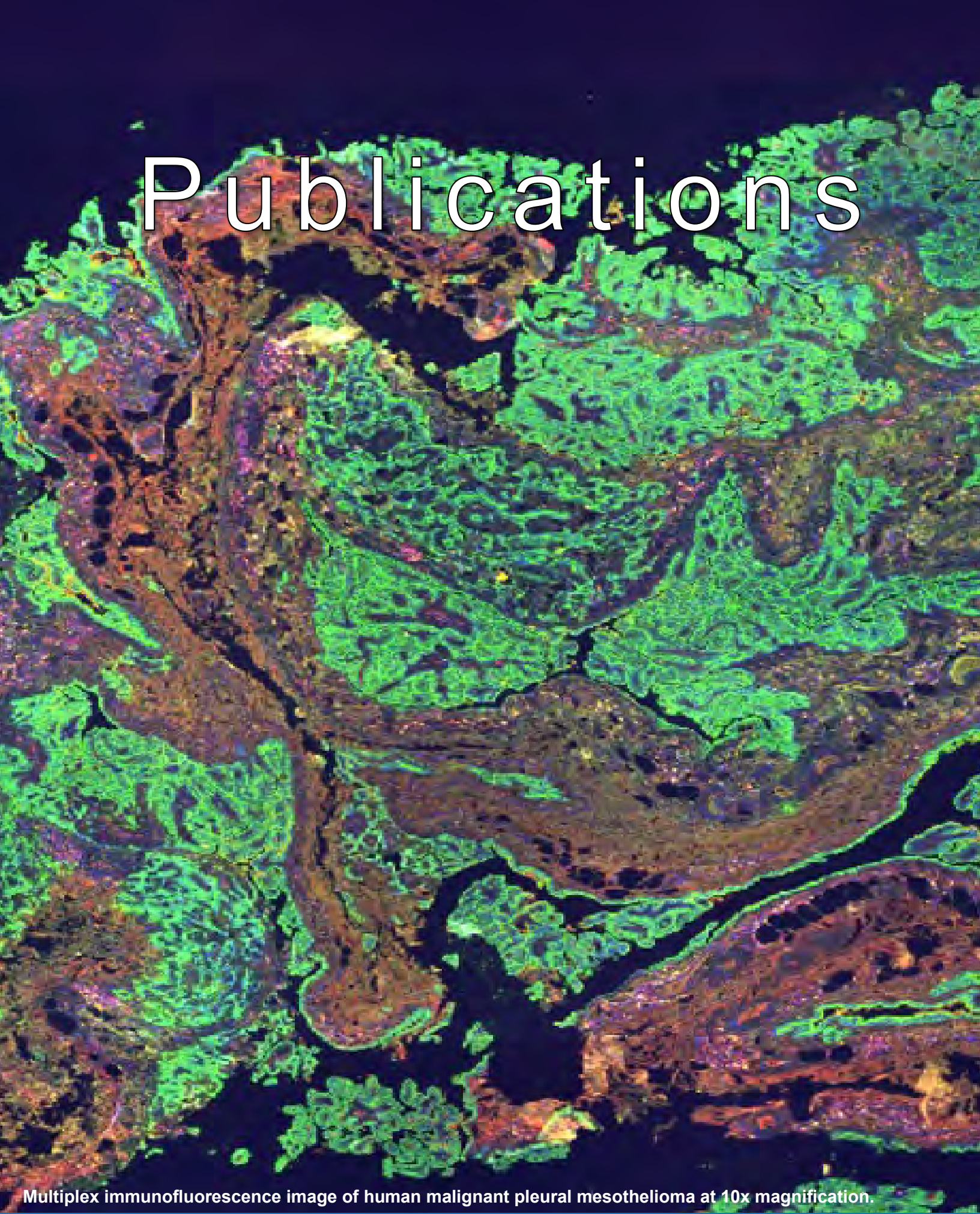
Publications



Multiplex immunofluorescence image of human malignant pleural mesothelioma at 10x magnification.

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*Blue text indicates publications that were published in a journal with an impact factor ≥10

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*Blue text indicates publications that were published in a journal with an impact factor ≥10

National Recognitions & Leadership

Organization	Role	Faculty Members
Mm H. & Yu-Fan C. Kao Chair in Thoracic Cancer	Chair	Adusumilli, Prasad
External Scientific Advisory Board, Immunotherapy Group, Erasmus MC Cancer Institute	Member	Adusumilli, Prasad
Fleischner Society, American Society of Clinical Investigation, and American Surgical Association	Member	Adusumilli, Prasad
Mesothelioma, Thymoma and Other Thoracic Malignancies Track Committee, 2021 World Conference, International Association for the Study of Lung Cancer (**IASLC**)	Member	Adusumilli, Prasad
Thoracic Malignancies Steering Committee, Mesothelioma Working Group, National Cancer Institute (**NCI**)	Member	Adusumilli, Prasad
Mesothelioma Committee, IASLC	Member	Adusumilli, Prasad
Thoracic Malignancy Steering Committee, 2017 & 2018 Mesothelioma Clinical Trials Planning Meeting, National Cancer Institute, Coordinating Center for Clinical Trials	Member	Adusumilli, Prasad
The Rodman E. Sheen and Thomas G. Sheen Award 2023, American College of Surgeons	Recipient	Adusumilli, Prasad
Scientific Advisory Board, Mesothelioma Applied Research Foundation (**MARF**)	Member	Offin, Michael
Young Investigator Award, International Mesothelioma Interest Group	Recipient	Offin, Michael
International Mesothelioma Interest Group	Board Member	Rimner, Andreas
2017/2018 Mesothelioma Clinical Trials Planning Meeting, NCI	Member	Rimner, Andreas
Mesothelioma Committee, IASLC	Member	Rimner, Andreas
NCI Thoracic Malignancy Steering Committee, Mesothelioma Working Group	Member	Rimner, Andreas
Program Committee, 2018 and 2023 IASLC Annual Meeting	Member	Rimner, Andreas
Thymic and Mesothelioma Working Groups, IASLC Staging and Prognostic Factors Committee (**SPFC**)	Member	Rimner, Andreas
Treatment of Malignant Pleural Mesothelioma Guideline Panel, American Society of Clinical Oncology (**ASCO**)	Member	Rimner, Andreas
IASLC	Chair	Rusch, Valerie
IASLC-EURASCAN Multidisciplinary Committee for Mesothelioma Classification	Co-Chair	Rusch, Valerie
Surgical/Early Stage Group, Mesothelioma Working Group, NCI Thoracic Staging Malignancies Committee	Leader	Rusch, Valerie
ASCO Expert Panel on Treatment of Malignant Pleural Mesothelioma	Member	Rusch, Valerie
Advisory Board, Staging and Prognostic Factors Committee, IASLC	Member	Sauter, Jennifer
Management of Pleural Mesothelioma Guideline, Pathology Lead and Expert Panel, ASCO	Member	Sauter, Jennifer
Planning Committee, International Mesothelioma Panel, Pathology Working Group IASLC-EURACAN Multidisciplinary Meeting in Lyon France, July 2018	Member and Secretary to the Chair	Sauter, Jennifer
International Representative for Radiation Oncology, International Mesothelioma Interest Group (**iMig**)	International Representative	Simone, Charles
Biennial Meeting Scientific Abstract Review Committee, iMig	Member	Simone, Charles
Scientific Subcommittee, iMig	Member	Simone, Charles
Board of Directors, MARF	Chair	Zauderer, Marjorie
Annual Meeting Scientific Program Committee, ASCO	Member	Zauderer, Marjorie
Mesothelioma Analysis Working Group, The Cancer Genome Atlas (**TCGA**)	Member	Zauderer, Marjorie
Mesothelioma Committee, IASLC	Member	Zauderer, Marjorie
Mesothelioma Committee, Peritoneal Surface Malignancy Consortium	Member	Zauderer, Marjorie
Thoracic Malignancy Mesothelioma Working Group, NCI	Member	Zauderer, Marjorie

MSK ‘In The News’

CAR Therapy for Solid Tumors Draws Attention at Annual Cancer Conference

Sunday, March 31, 2019

Results from a clinical trial indicate that an experimental CAR therapy for mesothelioma is safe.

Tazemetostat for Pleural Mesothelioma Shows Encouraging Results

Monday, May 16, 2022

A targeted drug shows promise for controlling pleural mesothelioma.

Scientists See Potential in Cellular 'Death by Iron' for Cancer Treatment

Tuesday, August 27, 2019

This form of cell death is called ferroptosis, and certain cancer cells are especially vulnerable to it.

New Design Could Make CAR T Cells a More Effective Immunotherapy for Solid Tumors

Monday, June 19, 2023

Learn how researchers engineered CAR T cells to work better by using a mutation in a gene called c-KIT that drives cancer cell growth

CAR T Cell Therapy Shows Promise for Treating Mesothelioma

Thursday, July 29, 2021

A combination immunotherapy approach using CAR T cells could be an effective new way to treat mesothelioma.

How MSK Is Improving CAR T Cell Therapy for Cancer Treatment

Tuesday, November 7, 2023

Learn how experts at MSK who helped develop CAR T cell therapy to fight cancer are making the treatment stronger, safer, more durable and accessible to more people.

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The Baker Street Foundation

· The President of the Baker Street Foundation is Mary Miner.

· The Baker Street Foundation is the most generous and longstanding donor to mesothelioma research at MSK.

Support

· Largest Gifts to MSK: An outright gift in 2023 and a pledge in 2021 from Mrs. Miner to the Miner Initiative for Innovative Therapies in Mesothelioma; and pledges in both in 2011 and 2017 from Mrs. Miner to support the Miner Fund for Mesothelioma Therapies.

· Most Recent Gift to MSK: 2021 via the Baker Street Foundation to support the Mesothelioma Research Fund

· Other Related Gifts: The Baker Street Foundation created an endowed mesothelioma research fund at MSK in the late 1990s. Other related gifts from the extended Miner family include those from Bob Miner's late sisters, Florence and Gloria Miner, to create the Batishwa Fellowship; those from Florence and Gloria Miner to endow the Miner Family Chair in Intrathoracic Cancers, currently held by Dr. Valerie Rusch; and those from Mary Miner's daughter, Nicola Miner, in honor of Gloria Miner.

Source: Memorial Sloan Kettering Cancer Center. "Annual Update: Mesothelioma Research at Memorial Sloan Kettering Cancer Center: Prepared for the Baker Street Foundation". October 13, 2023.

Mesothelioma Applied Research Foundation

The Mesothelioma Applied Research Foundation is the nonprofit charity organization dedicated to ending mesothelioma, and the suffering caused by this cancer, by:

· funding research to improve treatment options

· providing treatment support and education for patients and their families

· advocating for federal funding of research

Support

· MSK Board Members: Marjorie G. Zauderer, MD, Chair, Board of Directors; Michael Offin, MD, Member, Science Advisory Board

Source: Mesothelioma Applied Research Foundation. "About Us". 2023. https://www.curemeso.org/about-us/

Special Thank You to Our External Partners

Govind Srimathveeravalli, PhD
(University of Massachusetts Amherst)

International Association for the Study of Lung Cancer (IASLC)

Mesothelioma Applied Research Foundation

Steamfitters Local 638 Union

Request Appointment

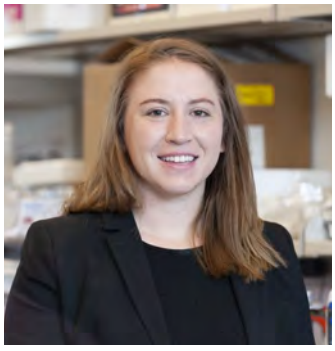
To request an appointment with a MSK mesothelioma expert, please call

646-964-1263

Care Advisors are available Monday through Friday, 8:00 a.m. - 6:00 p.m. (EST)

Report Compilation

Prasad S. Adusumilli, MD



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