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Lung Cancer Workshop

Charles B. Simone II, MD, FACRO
Radiation Oncology Co-Chair of NRG LU-006
Chief Medical Officer New York Proton Center
Professor, Department of Radiation Oncology
Memorial Sloan Kettering Cancer Center

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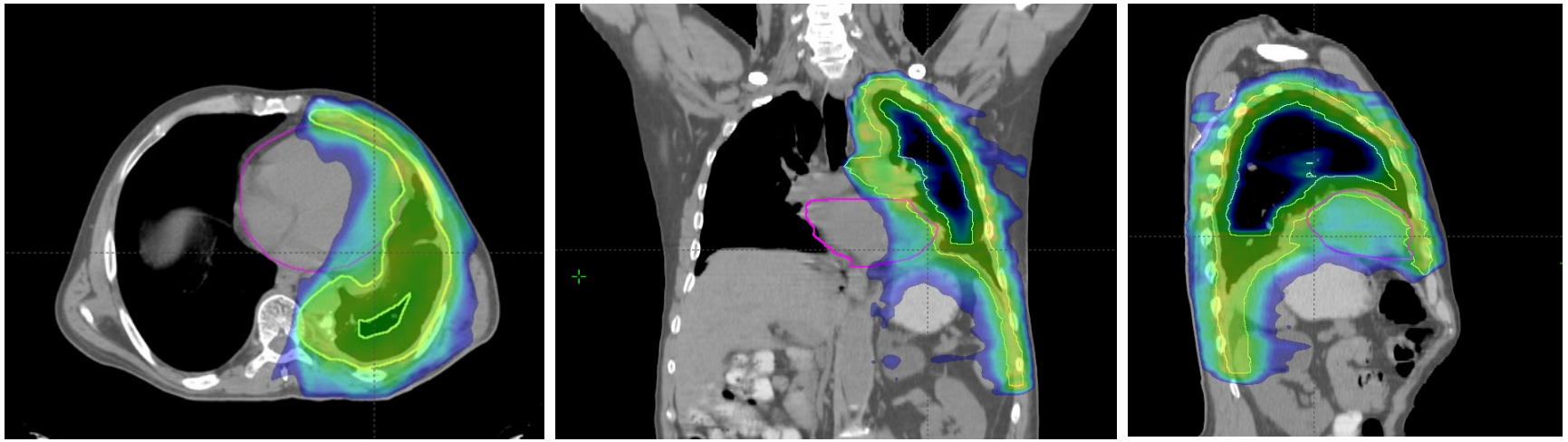
NRG-LU006

NCT04158141 – PI = Andreas Rimner, MD

Phase III Randomized Trial of Pleurectomy/Decortication + Chemotherapy +/- Adjuvant Hemithoracic Intensity-Modulated Pleural Radiation Therapy (IMPRINT) for Malignant Pleural Mesothelioma (MPM)



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Disclosures

- National Institutes of Health
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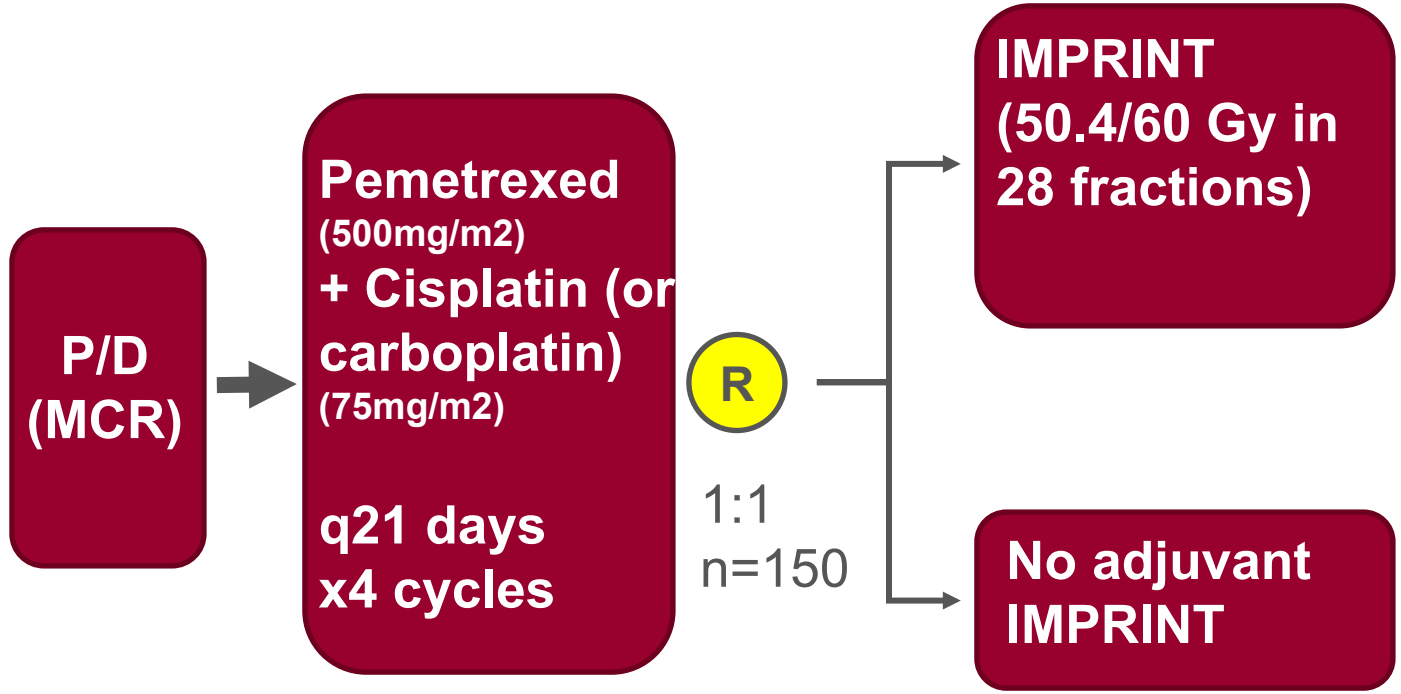
- Varian Medical Systems research grants, honorarium

Background

- Pleurectomy/Decortication (P/D) has become a common lung-sparing surgical approach for MPM
- Chemotherapy (platinum/pemetrexed) may be delivered in the neoadjuvant or adjuvant setting
- Adjuvant hemithoracic intensity-modulated pleural radiation therapy (IMPRINT) was developed at Memorial Sloan Kettering Cancer Center and found to be safe in a multi-institutional phase II study, with promising survival outcomes
- A Phase III randomized National Clinical Trials Network (NCTN) trial (NRG-LU006) was designed to evaluate the efficacy of this lung-sparing trimodality treatment approach for resectable MPM

NRG-LU006 Study Design

Eligibility:
- Stage I-III MPM
- Resectable by lung-sparing P/D
- Epithelioid or biphasic subtype
- Age ≥18 and ≤80 years
- KPS ≥80%
- FEV1 ≥40%, DLCO ≥40% predicted



Stratification:
- Cell type: Epithelioid vs biphasic
- Macroscopic complete resection: R0/R1 vs R2
- Chemotherapy vs chemo/immunotherapy

Permissible alternatives:
- Neoadjuvant chemo → P/D
- Neaodjuvant chemo/immunotherapy or ipilimumab/nivolumab
- Neaodjuvant therapy prior to enrollment
- Intensity-Modulated Proton Therapy

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Objectives

Hypothesis:

Addition of adjuvant IMPRINT is associated with an overall survival benefit compared to surgery + chemotherapy alone.

Primary Objective:

Improvement in median OS from 12 months (null hypothesis) to 20 months (alternative hypothesis) (calculated from the time of randomization)

Secondary Objectives:

- Local Failure-Free, Distant Metastases-Free and Progression-Free Survival
- Toxicities per CTCAE v5.0
- QOL (QLQ-Q30 and LC13) (10-point change at 9 months)

Exploratory Objectives:

- To build a multiparametric prognostic imaging model to improve clinical staging and target delineation
- To identify genomic and immunologic predictive biomarkers of radiation sensitivity and potential future therapeutic targets
- Test RapidPlan model for optimized RT plan development (Mt. Sinai collaboration with Dr. Dumane/Rosenzweig)
- Center patient volume ≤10 vs >10 pleurectomy/decortications per year

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Inclusion/Exclusion Criteria

Inclusion criteria

- Pathologically confirmed stage I-IIIA MPM (epithelioid or biphasic)
- Amenable to P/D as determined by a thoracic surgeon
- Age ≥18 years and ≤80 years
- Karnofsky performance status ≥80%
- FEV1 ≥40%, DLCO ≥40% predicted
- Adequate liver and renal function

Exclusion criteria

- Sarcomatoid histology
- Continuous oxygen use
- Third space fluid that cannot be controlled by drainage
- Serious unstable medical illness (e.g. concurrent active malignancy, active infection, or acute congestive heart failure)
- Prior thoracic radiation therapy
- Pregnancy or lactating

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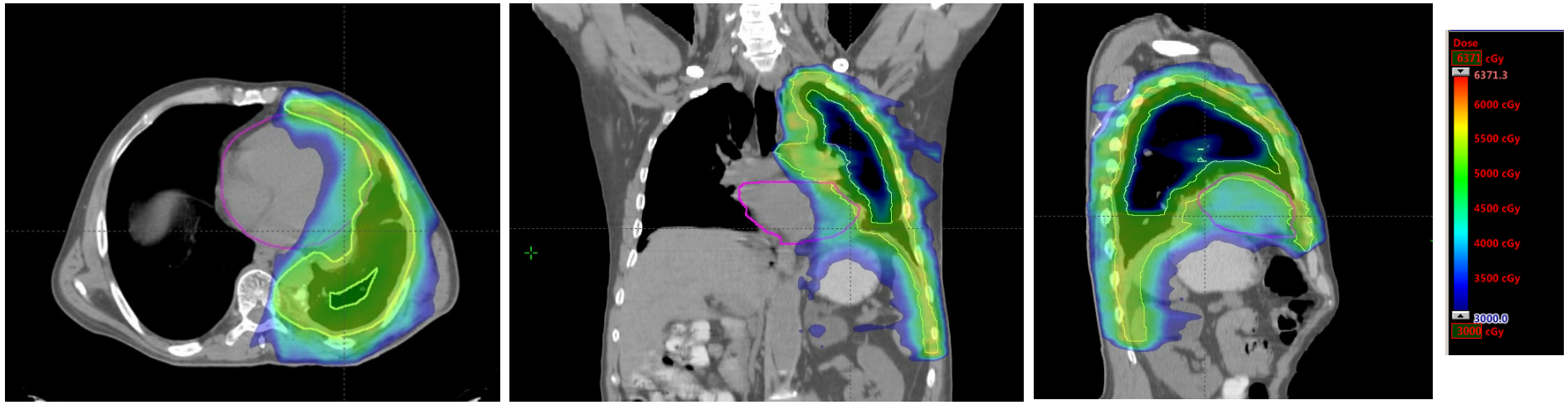
Surgeon Credentialing

- MCR = goal of surgical resection in every patient
- Resection definitions per IASLC/IMIG guidelines
- Documentation of diaphragmatic, pericardial and chest wall invasion for accurate T-staging
- Documentation of unresectable areas + clip placement
- No intraoperative adjunctive therapies, i.e. heated chemotherapy, photodynamic therapy
- Systematic nodal sampling
- Number of MPM surgeries in the past 2 years (must be >5/year)
- Number of grade 4-5 toxicities within 30 days postop in the past 2 years

Central Radiation Oncology Review

- Central review of each patient assigned to IMPRINT arm
  1) Review of target and OAR delineation
  2) Review of radiation treatment plan

- 48-hour turnaround



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Current Status

- Accrual: 8 patients (1 Alliance, 7 NRG credits)
- Applications for Site Registration: 75
- Sites approved: 20 (MDACC and Temple University pending)
- Monthly conference calls with participating sites (3rd Friday of the month, 11:00 a.m. EST), all participating sites are welcome

- Recordings on target delineation and treatment planning on CTSU website
- QuinTeT recommendations incorporated

- Presentation to the International Member Committee at this meeting to recruit additional international sites

Amendment #1&2 Approved on 4/13/2022

Incorporated changes:

- Allow for neoadjuvant systemic therapy prior to enrollment
- Allow for neoadjuvant chemo/anti-PD-1/L1 therapy or ipilimumab/nivolumab
- Adjust window for randomization to 0-8 weeks prior to RT
- Language changes to the consent

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Acknowledgments

NRG-LU006 Study Investigators

Andreas Rimner, MD, *Memorial Sloan Kettering Cancer Center*	PI
Charles B. Simone, II, MD, *New York Proton Center*	Rad. Oncology
Valerie W. Rusch, MD, *Memorial Sloan Kettering Cancer Center*	Surg. Oncology
Marjorie G. Zauderer, MD, *Memorial Sloan Kettering Cancer Center*	Med. Oncology
Ritu R. Gill, MD, *Beth Israel Deaconess Medical Center*	Radiology
Ellen Yorke, PhD, *Memorial Sloan Kettering Cancer Center*	Med. Physics
Zuofeng Li, DSc, *University of Florida College of Medicine*	Proton Physics
Khinh Ranh Voong, MD MPH, *Sidney Kimmel Cancer Center*	Statistics
Tobias Peikert, MD Mayo Clinic Cancer Center	Translational
Ming S. Tao, MD, *Princess Margaret Cancer Center*	Pathology
Chen Hu, PhD, *NRG Oncology Statistical and Data Management Center & John Hopkins University School of Medicine*	Statistics

Champions	
John Varlotto, MD	**ECOG-ACRIN**
Jeremy Brownstein, MD	**Alliance**
Robert Samstein, MD, PhD	**SWOG**

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Acknowledgments
NRG Operations and SDMC Team

For Contact Information see protocol cover page	
Data Management	Sylvia Solakov Jeff Serianni
RTQA	Jennifer Presley
Protocol Development	Fran Bradley
Lung Committee Chair	Jeffrey D. Bradley
Biostatistics	Chen Hu, Rebecca Paulus

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- Patients

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Contact

- Andreas Rimner (rimnera@mskcc.org)
- Fran Bradley

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