# 2022 NRG Trial Portfolio

# NRG Lung Group

## SCLC

- Limited Stage Small Cell
  - LU005: Phase III Randomized Study of Chemoradiation vs. Chemoradiation + Atezolizumab
- Extensive Stage Small Cell
  - LU007: Randomized Phase II/III Trial of Consolidation Radiation + Immunotherapy: RAPTOR Trial

## Mesothelioma

- LU006: Phase III Randomized Trial of Pleurectomy/Decortication + Chemotherapy With or Without Adjuvant Hemithoracic Intensity-Modulated Pleural Radiation Therapy (IMPRINT)

## Early Stage Inoperable NSCLC

- SWOG/NRG Joint Study: Randomized Phase III Trial Induction/ Consolidation Atezolizumab + SBRT vs. SBRT Alone in High Risk, Early Stage NSCLC
- Pacific 4: Durvalumab vs. Placebo + SBRT for early stage unresectable NSCLC

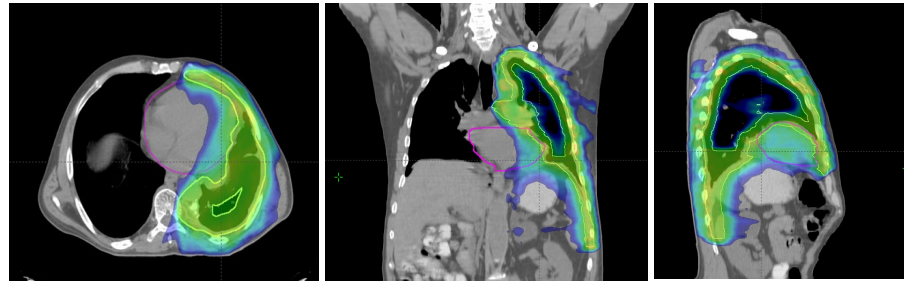
## Unresectable Stage II-III NSCLC

- RTOG-1308: Phase III Randomized Trial Comparing Overall Survival After Photon vs. Proton Chemoradiotherapy for Inoperable Stage II-IIIB NSCLC

## Metastatic NSCLC

- LU002: Maintenance Systemic Therapy Versus Local Consolidative Therapy + Maintenance Therapy For Limited Metastatic NSCLC: A Randomized Phase II/III Trial

# NRG-LU006



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

**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

P/D (MCR)

Pemetrexed (500mg/m2) + Cisplatin (or carboplatin) (75mg/m2)

q21 days x4 cycles

R

1:1
n=150

IMPRINT (50.4/60 Gy in 28 fractions)

No adjuvant IMPRINT

**Permissible alternatives:**
- Neoadjuvant chemo → P/D
- Intensity-Modulated Proton Therapy

# NRG-LU006: Phase III Randomized Trial on IMPRINT for MPM

**Primary Objective:**

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

**Secondary Objectives:**

- Local Failure-Free Survival
- Distant Metastases-Free Survival
- 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

# NRG-LU006: Phase III Randomized Trial on IMPRINT for MPM

## 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 or chemotherapy
- Pregnancy or lactating

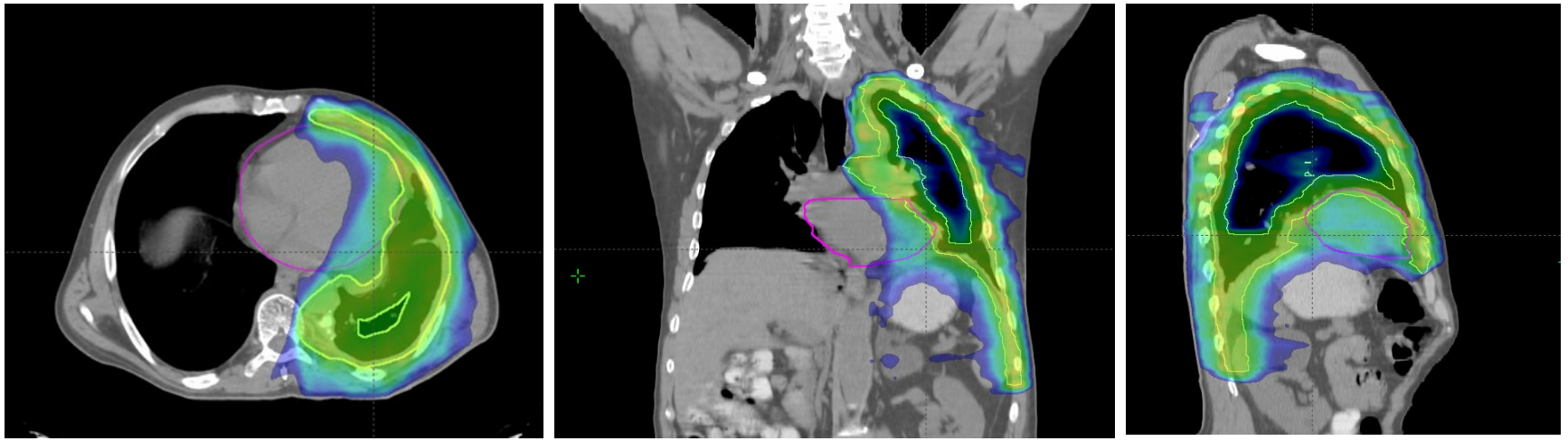
# NRG-LU006: Phase III Randomized Trial on IMPRINT for MPM

## Surgeon Credentialing

- MCR = goal of surgical resection in every patient 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
- Systematic nodal sampling
- >5 MPM surgeries in the past 2 years
- 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



# NRG-LU006: Phase III Randomized Trial on IMPRINT for MPM

## Current Status

- Accrual: 6 patients (1 Alliance, 5 NRG credits)
- Applications for Site Registration: 75
- Sites approved: 20
- Monthly conference calls with participating sites (3rd Friday of the month, 11:00 a.m. EST)

- Main challenge: Surgical volumes for MPM are markedly down nationwide, reasons somewhat unclear (apart from the Covid pandemic)

# NRG-LU006: Phase III Randomized Trial on IMPRINT for MPM

## Planned Changes

- Amendment #1 (to be submitted to CTEP):
  - Allow for neoadjuvant systemic therapy prior to enrollment
  - Allow for chemo/anti-PD-1/L1 therapy or ipilimumab/nivolumab
  - Adjust window for randomization to 0-8 weeks prior to RT
- Selected by the Protocol Operations Monitoring Committee for pilot project
  - Pilot project to improve accrual
  - Reviewed by QuinteT (protocol improvement initiative at the University of Bristol, UK), meeting with QuinteT on 12/16/2021
- Start asking participating centers for quarterly screening logs
- Seminar on treatment planning to be held and recorded

# Potential Trial Idea

## Neoadjuvant durvalumab with or without stereotactic body radiotherapy in patients with early-stage non-small-cell lung cancer: a single-centre, randomised phase 2 trial

*Nasser K Altorki, Timothy E McGraw, Alain C Borczuk, Ashish Saxena, Jeffrey L Port, Brendon M Stiles, Benjamin E Lee, Nicholas J Sanfilippo, Ronald J Scheff, Bradley B Pua, James F Gruden, Paul J Christos, Cat… Karla V Ballman, Silvia C Formenti*


- Single institution phase II randomized, Cornell neoadjuvant durvalumab (2) ± SBRT (8Gy x 3 to $1^0$)
- 60 pt
- MPR: 7% vs. 53%
- Gr 3-4 AE: 17% vs 20%

*Altorki N, Lancet Oncol, 2021*

# Conclusion

- A paucity of trails which include thoracic surgery
- Always looking for new trial ideas
- Innovative ways to choose appropriate therapy for early stage disease or integrate surgery and radiation in locally advanced