NRG Trial Update 2021

NRG Lung Cancer Trials

Study	Title	Phase	Disease Site
S1914	SWOG/NRG Joint Study: A Randomized Phase III Trial **of Induction/ Consolidation Atezolizumab (NSC #783608) + SBRT** Versus SBRT Alone in High Risk, Early Stage NSCLC	III	Unresectable High Risk Stage I NSCLC
NRG-LU004	Phase I Trial of **Accelerated or Conventionally Fractionated Radiotherapy** Combined With MEDI4736 (durvalumab) in PD-L1 High Locally Advanced Non-Small Cell Lung Cancer (NSCLC) (ARCHON-1)	I	Unresectable locally advanced NSCLC
RTOG-1308	Phase III Randomized Trial Comparing Overall Survival After **Photon Versus Proton** Chemoradiotherapy for Inoperable Stage II-IIIB NSCLC	III	Unresectable locally advanced NSCLC
NRG-LU002	Maintenance Systemic Therapy Versus **Local Consolidative Therapy (LCT)** Plus Maintenance Systemic Therapy For Limited Metastatic Non-Small Cell Lung Cancer (NSCLC): A Randomized Phase II/III Trial	II/III	Oligometastatic stage IV NSCLC
NRG-LU003	A Biomarker-Driven Protocol for Previously Treated ALK-Positive Non-Squamous NSCLC Patients: The **NCI-NRG ALK Master Protocol**	II	Stage IV NSCLC
NRG-LU005	Limited Stage Small Cell Lung Cancer (LS-SCLC): A Phase II/III Randomized Study of Chemoradiation Versus **Chemoradiation Plus Atezolizumab**	II/III	Limited stage Small Cell
NRG-LU007	Randomized Phase II/III Trial of **Consolidation Radiation + Immunotherapy** for ES-SCLC: RAPTOR Trial	II/III	Extensive stage Small Cell

NRG Mesothelioma Trial

Study	Title	Phase	Disease Site
NRG-LU006	Phase III Randomized Trial of Pleurectomy/Decortication Plus Chemotherapy With or Without **Adjuvant Hemithoracic Intensity-Modulated Pleural Radiation Therapy (IMPRINT)** For Malignant Pleural Mesothelioma (MPM)	III	Mesothelioma

NRG-LU006
Phase III Randomized Trial on IMPRINT for MPM

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**

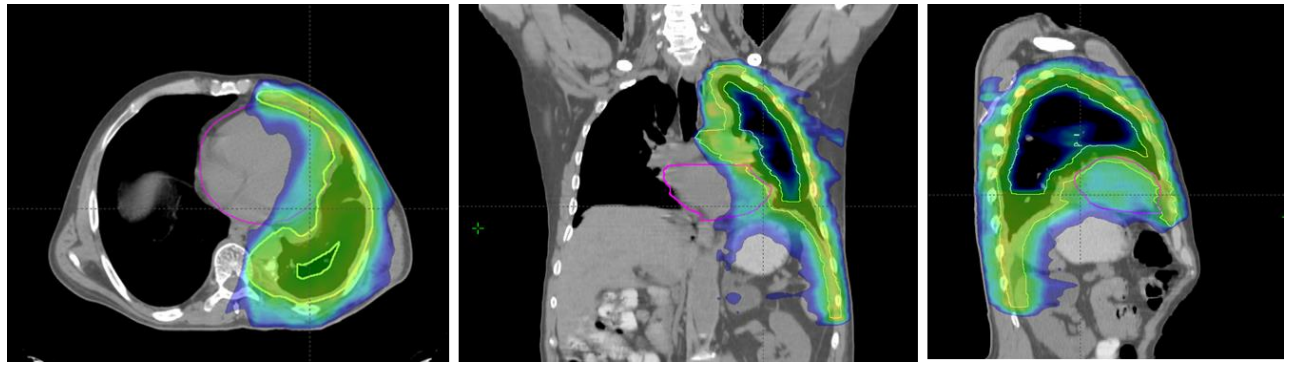
1:1
n=150

→ **IMPRINT (50.4/60 Gy in 28 fractions)**

→ **No adjuvant IMPRINT**

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

Stratification:
- Cell type: Epithelioid vs biphasic
- Macroscopic complete resection: R0/R1 vs R2
- Center patient volume: ≤10 vs >10 P/D's per year

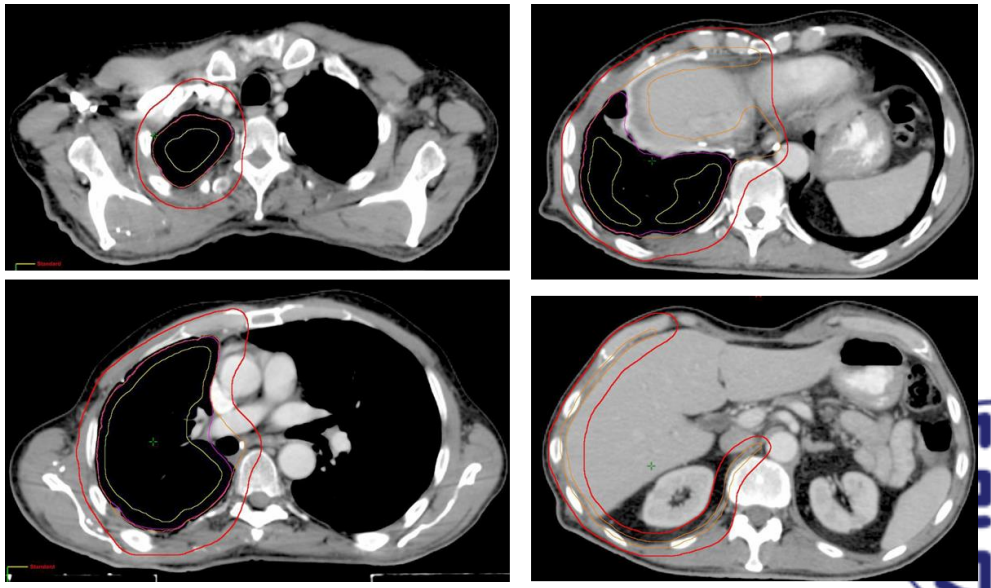


Surgeon Credentialing

- MCR = goal of surgical resection in every patient
- Resection defined 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 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
- Detailed contouring Atlas



NRG Esophageal Cancer Trials

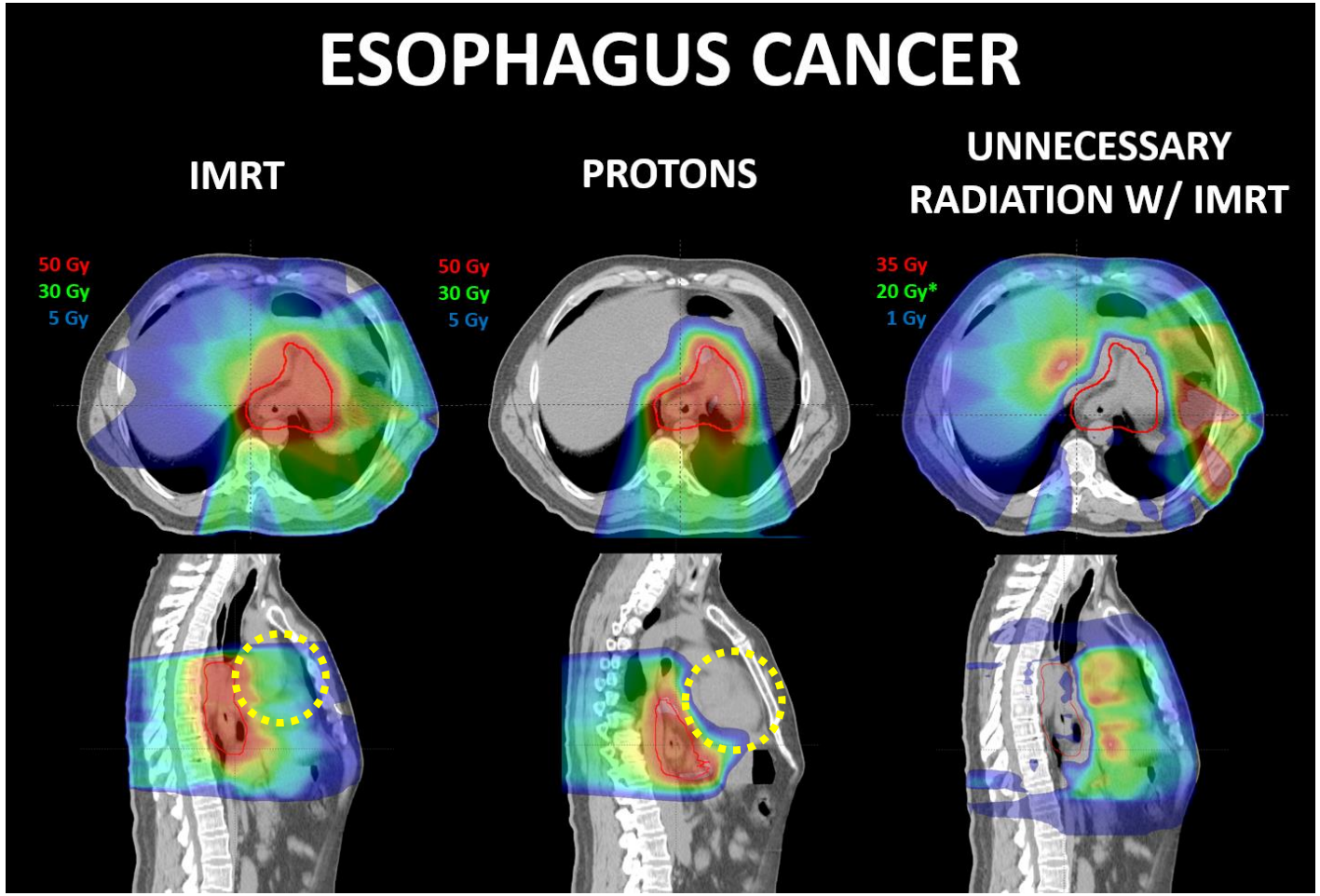
Study	Title	Phase	Disease Site
NRG-GI006	Phase III Randomized Trial of **Proton Beam Therapy (PBT) Versus Intensity Modulated Photon Radiotherapy (IMRT**) for the Treatment of Esophageal Cancer	III	Esophageal
NRG-GI007	Phase I Trial with Expansion Cohort of **OBP-301 (Telomelysin) and Definitive Chemoradiation** for Patients with Locally Advanced Esophageal And Gastroesophageal Adenocarcinoma Who are Not Candidates for Surgery	I	Unresectable locally advanced esophageal cancer

NRG-GI006

Phase III Randomized Trial of Proton Beam Therapy vs. IMRT for Esophageal Cancer

Hypothesis: dosimetric superiority of proton bean compared to IMRT to thoracic organs benefits patients in improving overall survival and/or reduction of grade 3+ cardiopulmonary toxicity burden

Eligibility: mid or distal esophageal or GE jxn cancer (Siewart I-II), stage I-IVA, can go on to resection



NRG-GI006

SCHEMA (05-NOV-2020)

STEP 1 REGISTRATION
Register and work on confirmation of payment coverage for treatment (insurance or other)

↓

STEP 2 RANDOMIZATION*

STRATIFY
- Histology (adenocarcinoma vs. squamous cell carcinoma)
- Stage (I-II vs. III-IVA) per AJCC 8th Edition
- Patient Candidate for Post Chemoradiation Resection (Yes vs. No)
- Type of concurrent chemotherapy (taxane containing vs. oxaliplatin based)

↓

Arm 1
PBT
+
Chemotherapy**

Followed by surgery*** 4-8 weeks after completion of chemoradiation

Arm 2
IMRT
+
Chemotherapy**

Followed by surgery*** 4-8 weeks after completion of chemoradiation

*Randomization is 1:1.
**Chemotherapy regimen will be determined by the individual treating physician per institutional standards at the time of study enrollment, chosen from the following 3 chemotherapy regimens: 1) Carboplatin/Paclitaxel, 2) FOLFOX/CAPOX, 3) Docetaxel/5-FU (with capecitabine an acceptable substitute for 5-FU).
***For patients who are candidates for post chemoradiation resection per Section 5.3.

Co-Primary objectives

- OS is improved *or*
- OS is non-inferior, grade 3+ cardiopulmonary toxicities are better

Secondary objectives

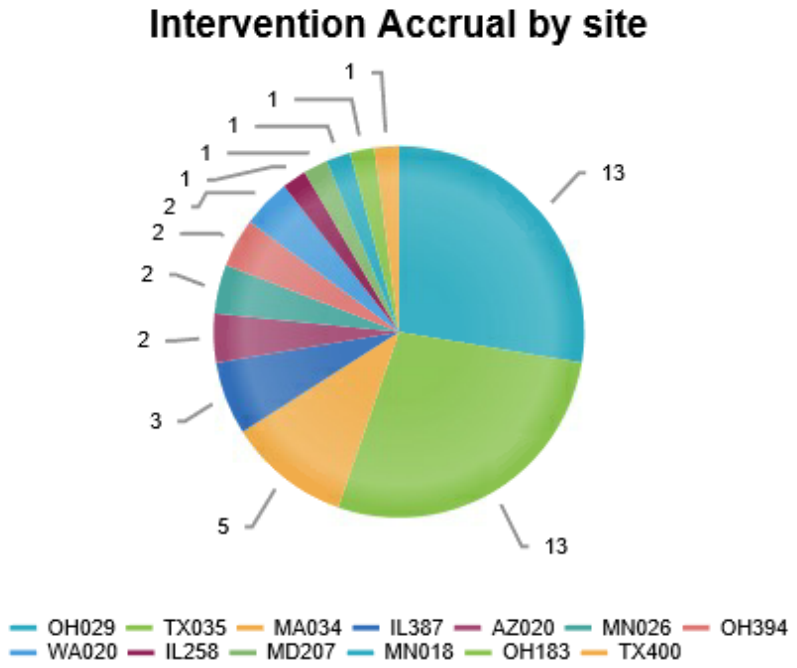
- Symptom burden and QoL
- Quality Adjusted Life Years (QALY)
- Cost-benefit economics analysis
- Length of hospitalization
- Grade 4 lymphopenia risk, and lymphocyte nadir
- Early (< 90 days) and late (≥ 90 days) cardiovascular and pulmonary events
- Total Toxicity Burden based on a composite index of 9 individual cardiopulmonary toxicities.

NRG-GI006: Accrual

Protocol Status:	**ACTIVE**
Protocol Status Date:	06-Mar-2019
Activation Date:	06-Mar-2019
Lead Organization:	**NRG**
NCI Program:	**NCTN**
Phase:	**III**
Country Participation:	

Accrual: As of 14-Jan-2021 08:30:08 AM

Step Type	Step(s)	Planned	Actual
Intervention	2	300	47



Supported By:

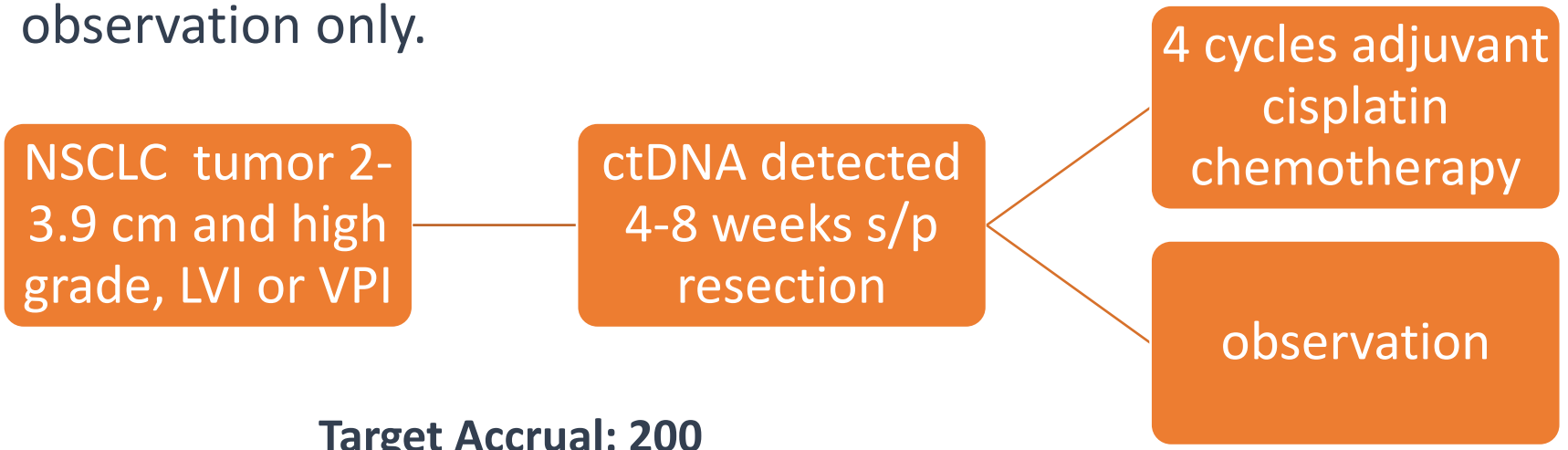
CIRB	DTL	OPEN	Rave	TSDV	IROC/ TRIAD	DQP	ePRO	SAE Int	CM
✓	✗	✓	✓	✓	✓	✓	✓	✗	✗

NRG Lung Cancer Trial Concepts

Study	Title	Phase	Disease Site
NRG-LU2025	Trial of Adjuvant Chemotherapy Based on Molecular Residual Disease in Early Stage NSCLC	II	Resected stage I NSCLC
NRG-LU2027	Radscopal	IIR	Stage IV NSCLC
	SBRT followed by chemo/XRT to involved nodes	IIR	Unresectable locally advanced NSCLC
	Accelerated vs. standard fractionated XRT with concurrent I/O for locally advanced NSCLC	IIR	Unresectable locally advanced NSCLC

NRG 2025
Phase II Trial of Adjuvant Chemotherapy Based on Molecular Residual Disease in Early Stage NSCLC

HYPOTHESIS: improved recurrence-free survival for early stage NSCLCs with high-risk features and molecular residual disease detected by circulating tumor DNA after resection that received adjuvant chemotherapy compared to observation only.



Target Accrual: 200

Primary Outcome:
RFS

Secondary outcomes:
OS
ctDNA clearance rate