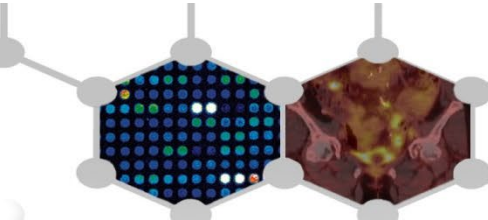

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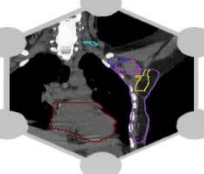

NRG-LU007: Randomized Phase II/III Trial Of Consolidation Radiation + Immunotherapy for ES-SCLC

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Disclosures

- No disclosures

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NRG-LU007: Study Chairs/Leadership/Champions

Quynh-Nhu Nguyen, MD; *MD Anderson Cancer Center*	Principal Investigator
James Welsh, MD; *MD Anderson Cancer Center*	Radiation Oncology Co-Chair
Jeremy Erasmus, MD; *MD Anderson Cancer Center*	Radiology Co-Chair
John Heymach, MD PhD; *MD Anderson Cancer Center*	Medical Oncology Co-Chair
Vinicius Ernani, MD; Mayo Clinic in Arizona	Medical Oncology Co-Chair and Study Champion for The Alliance
Ning Winston Wen, PhD; *Henry Ford Health System*	Medical Physics Co-Chair
Saumil Gandhi, MD; *MD Anderson Cancer Center*	Translational Science Co-Chair
Chen Hu, PhD; *NRG Oncology*	Lead Statistician for Lung Committee
Henry Park, MD, MPH; *Yale School of Medicine*	Study Champion for SWOG
Jeffrey D. Bradley, MD; *Emory Winship Cancer Center*	NRG Lung Committee Chair

NRG-LU007 NRG Operations and SDMC Study Team

For Contact Information (see protocol cover page)	
Data Management	Tammy Bausinger Matthew Novak
Core Services for Radiation Therapy/Dosimetrists	Jennifer Presley
Protocol Development	Fran Bradley
Statistics	Chen Hu Rebecca Paulus
Auditing/Monitoring	Jerome Koss - Auditor

Rationale for the study

Chest RT prolongs PFS, improves 2Y survival, and reduces chest recurrences by more than 50% when given after chemo in ES SCLC in patients with non-PD, and is considered a SOC[1]

Data suggests RT to extrathoracic sites may provide additional benefit

Atezo+EP followed by atezo improved OS & PFS for ES SCLC

Durvab + EP significantly improved OS for ES-SCLC

RT may enhance efficacy of PD1/PD-L1 blockade, studies suggest that the approach of immunotherapy combined with consolidative chest radiotherapy is safe and the efficacy merits further investigation for ES SCLC patients

1. Slotman et al., Lancet 2015
2. Welsh et al., JTO 2019

Schema

PATIENT POPULATION:	**STRATIFY**	**RANDOMIZE***	
Patients with extensive stage small cell lung cancer (ES-SCLC), stable disease (SD) or partial response (PR) after 4-6 cycles of etoposide/platinum (E/P) doublet plus atezolizumab	• Number of sites receiving radiation therapy (fields 1-3 vs >3) • PR vs SD • ECOG Performance Status (0/1 vs 2)		**Arm 1** Atezolizumab maintenance **Arm 2** Standard RT: (Daily up to 5 sites) Thoracic or Liver RT: 45 Gy or 30 Gy Extra-Thoracic RT: 30 Gy or 20 Gy + Atezolizumab maintenance

Target Accrual and Activation

Target Accrual

Phase II = 138 eligible patients

Phase III = 186 patients

Overall sample size of Phase II/III = 324

Activation – August 2020

Study Duration:

The phase II portion accrual is projected to take 30 months (2.5 years).

Another 30 months (2.5 years) from the end of phase II portion will be needed to complete the entire phase III accrual.

The entire phase II/III study is projected to take approximately 80 months (6.7 years) from the phase II portion initiation to reach the required 251 deaths.

Primary Objectives:

Phase II

To compare investigator-assessed progression free survival (PFS) between atezolizumab plus radiotherapy and atezolizumab alone

Phase III

To compare overall survival (OS) between atezolizumab plus radiotherapy and atezolizumab alone

Secondary Objectives

To assess the toxicity between the atezolizumab plus radiotherapy arm and the atezolizumab arm

To assess the impact of adding radiotherapy on PFS and OS in patients with 1-3 visible tumors and >3 visible tumors

To assess the impact of adding radiotherapy on PFS and OS in patients receiving consolidation radiotherapy to all visible disease (“complete consolidation”) and patients who do not receive consolidation radiation to all visible disease (“incomplete consolidation”)

Eligibility Criteria

Pathologically proven diagnosis of ES-SCLC

PR or SD after 4-6 cycles of carbo/cis + etoposide + atezolizumab within 9 weeks of last dose of chemotherapy or 6 weeks from completion of PCI

Patients must have had measurable disease (RECIST) after chemotherapy and prior to randomization and 3 or fewer observable liver metastases

Imaging to include MRI brain with contrast or Brain CT with contrast, CT chest, abdomen and pelvis, or PET/CT scan after the final cycle of chemotherapy + 6 wks prior to registration

Pleural effusion if thoracentesis is negative of if too small sample w/thoracentesis or PET/CT negative

Age ≥ 18

ECOG Performance Status of 0-2 at the time of registration

Laboratory values within 14 days prior to registration

Ineligibility Criteria

Metastatic disease invading the liver (>3 metastases), heart or >10 metastatic sites after induction systemic therapy

Prior thoracic or mediastinal radiation or metastatic site region of study

Prior invasive malignancy

- Except non-melanomatous skin cancer, unless disease free for 5 year prior to randomization

History of autoimmune disease

- Including systemic lupus erythematosus, inflammatory bowel disease, vascular thrombosis associated with antiphospholipid syndrome, Wegener's granulomatosis, Sjögren's syndrome, Guillain-Barré syndrome, multiple sclerosis, vasculitis, or glomerulonephritis.

Severe co-morbidities including: severe liver, renal, COPD, cardiac morbidities

History of recent myocardial infarction

History of allogeneic organ transplant

Patients who have had immunotherapy induced pneumonitis.

Supply of Study Agents

Atezolizumab

Provided free of charge to patients by Genentech/F.Hoffman-La Roche

Distributed by the Pharmaceutical Management Branch (PMB). Requests are processed through the Online Agent Order Processing (OAOP) Application. The Investigator Brochure (IB) is also available via the OAOP.

Radiation Technique

Site Identifier	Anatomic Site	Total Dose and Fractionation Options		
		45 Gy in 15 fractions	30 Gy in 10 fractions	20 Gy in 5 fractions
1	Lung (primary)	x	x	
2	Liver	x	x	x
3	Bone		x	x
4	Spine		x	x
5	Abdomen/Pelvis		x	x
6	Soft Tissue		x	x

RT-specific pre-registration requirements are detailed in section 8.3 protocol

ACCRUAL

- Number Sites Approve 217
- Number of NCORPS approved Enroll: 113
- Acdrual: 34/138 (planned)

- Please open at your site to accrue.
- Please help with research teams with accrual!

Questions

- **For study related questions,** please contact the study chair (***qnnguyen@mdanderson.org***) and/or study project manager
- **For questions concerning eligibility**, please contact the Biostatistics/Data Management Center
- **For radiation therapy-related eligibility questions**, please contact RTQA
- **For all protocol documents visit,** www.ctsu.org

See contact list on protocol title page