Cancer Research Consortium of West Michigan
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FAST FACTS

NRG LU005 - LIMITED STAGE SMALL CELL LUNG CANCER (LS-SCLC): A PHASE II/III RANDOMIZED STUDY OF CHEMORADIATION VERSUS CHEMORADIATION PLUS ATEZOLIZUMAB

Eligibility Criteria

1. Pathologically (histologically or cytologically) proven diagnosis of limited stage small cell lung cancer (Stage Tx, T1-T4, N0-3, M0, AJCC Staging, 8th Ed.), within 60 days prior to registration;

2. Patients must have received one pre-registration cycle of platinum/etoposide chemotherapy prior to study entry, with study registration required within 21 days from day 1 of the pre-registration cycle of chemotherapy and protocol treatment designed to begin 21 days after. If patient has not recovered from pre-registration cycle chemotherapy toxicities, then an additional 14 days is permitted.

3. Patients must have had measurable disease (per RECIST, version 1.1) prior to the required pre-registration cycle of platinum/etoposide chemotherapy.

4. Minimal staging requirements include:
   • History/physical examination within 30 days prior to registration;
   • PET/CT scan for staging within 45 days prior to registration;
   • CT chest/abdomen with IV contrast (unless contraindicated based on kidney function*) within 45 days prior to registration – this can be obtained as part of PET/CT if CT imaging is of diagnostic quality;
   *Note: If contrast allergy exists, premedication per institutional guidelines should be performed prior to obtaining CT with contrast. The only exception to this is a documented life-threatening allergy.
   - • MRI scan of the brain with contrast (preferred) or CT scan of the brain with contrast (allowable if there is a contraindication with MRI with contrast) within 30 days prior to registration;

5. Age ≥ 18;

6. ECOG Performance Status of 0-2 within 30 days prior to registration;

7. Required Initial Laboratory Values

(pre-registration cycle): ANC	≥1,500/cells/mm3
Platelet Count	≥100,000 cells/mm3
Hemoglobin	≥9 g/dL
Total Bilirubin	≤1.5 x ULN
AST (SGOT) and ALT (SGPT)	≤2.0 x ULN

Adequate renal function within 30 days prior to registration defined as follows:

Glomerular filtration rate (GFR) ≥ 50 mL/min/1.73 m2 (See Appendix III for eGFR calculations)

8. Patients presenting with a pleural effusion will be eligible if thoracentesis is cytologically negative and non-bloody or if pleural fluid is too small a volume to effectively sample by thoracentesis and does not show increased metabolic activity on CT/PET imaging.

9. Negative serum pregnancy test within 14 days of registration for pre-menopausal women of childbearing potential.

10. The patient or a legally authorized representative must provide study-specific informed consent prior to study entry.

Ineligibility Criteria

1. Definitive clinical or radiologic evidence of metastatic disease;

2. Definitive surgical resection of small cell lung cancer;

3. Prior invasive malignancy (except non-melanomatous skin cancer, localized prostate cancer, or any early stage cancer treated with curative intent resection) unless disease free for a minimum of 2 years (carcinoma in situ of the breast, oral cavity, or cervix are all permissible);

4. More than 1 cycle of prior platinum-based chemotherapy for SCLC prior to enrollment; note that prior chemotherapy for a different cancer is allowable;

5. Any prior Atezolizumab or other immunotherapy agent;

6. Prior radiotherapy to the lungs or mediastinum that would result in clinically significant overlap of radiation therapy fields; prior tangent fields for breast cancer with minimal overlap with target volumes are allowed per approval of study PIs.

7. Patients with cytologically positive pleural or pericardial fluid are not eligible.

8. An active, known or suspected autoimmune disease. Patients are permitted to enroll if they have vitiligo, type I diabetes mellitus, residual hypothyroidism due to autoimmune condition only requiring hormone replacement, psoriasis not requiring systemic treatment, or conditions not expected to recur in the absence of an external trigger.

9. Active or prior documented inflammatory bowel disease (e.g., Crohn's disease, ulcerative colitis)

10. History of allogeneic organ transplant

11. History of primary immunodeficiency

12. Severe, active co-morbidity defined as follows:
    - Known clinically significant liver disease, including active viral, alcoholic, or other hepatitis, cirrhosis, fatty liver, and inherited liver disease;
    - Any other diseases, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates

the use of an investigational drug or that may affect the interpretation of the results or render the patient at high risk from treatment complications;

- Active tuberculosis;
- Active hepatitis B (chronic or acute) or hepatitis C infection. Note that if hepatitis status is unknown, hepatitis B/C testing is required.
  o Patients with past or resolved hepatitis B infection (defined as having a negative hepatitis B surface antigen (HBsAg) test, a positive anti-HBc [antibody to hepatitis B core antigen], and a negative viral DNA test (only obtained if HBsAg is found positive) are eligible.
  o Patients positive for HCV antibody are eligible only if polymerase chain reaction (PCR) is negative for HCV RNA. (The HCV RNA test must be performed for patients who have a positive HCV antibody test.)
- Known immunosuppressive disease, for example history of bone marrow transplant or CLL;
- CD4 count < 200 cells/microliter. Note that patients who are HIV positive are eligible, provided they are under treatment with highly active antiretroviral therapy (HAART) and have a CD4 count ≥ 200 cells/microliter within 30 days prior to registration. Note also that HIV testing is not required for eligibility for this protocol.
- COPD requiring chronic oral steroid therapy of > 10 mg prednisone daily or equivalent at the time of registration. Inhaled corticosteroids are not exclusionary;
- Unstable angina and/or congestive heart failure requiring hospitalization within the last 3 months;
- Transmural myocardial infarction within the last 3 months;
- Clinically significant interstitial lung disease

13. A condition requiring systemic treatment with either corticosteroids (> 10 mg daily prednisone equivalents) or other immunosuppressive medications within 14 days of study drug administration. Inhaled or topical steroids and adrenal replacement doses > 10 mg daily prednisone equivalents are permitted in the absence of active autoimmune disease.

14. Pregnancy or women of childbearing potential and men who are sexually active and not willing/able to use medically acceptable forms of contraception for the duration of study treatment and for 180 days after the last dose of study drug (Arm 2); this exclusion is necessary because the treatment involved in this study may be significantly teratogenic.

NRG-LU005
SCHEMA

PATIENT POPULATION:
Limited stage (Tx, T1-T4, N0-3, M0) small cell lung cancer (LS-SCLC)

STRATIFICATION

- Radiation schedule, BID (3 weeks) vs daily (6.5 weeks)
- Chemotherapy (cisplatin vs carboplatin)
- Sex (male vs female)
- ECOG Performance Status (0/1 vs 2)

RANDOMIZE*

Arm 1	**Arm 2**
Platinum**/etoposide q3 weeks x 4 cycles + Thoracic RT 45 Gy bid or 66 Gy daily beginning with cycle 2 of chemotherapy***	Platinum**/etoposide q3 weeks x 4 cycles + Thoracic RT 45 Gy bid or 66 Gy daily beginning with cycle 2 of chemotherapy*** + Atezolizumab q3 weeks x 1 year, beginning with cycle 2 of chemotherapy

* Randomization is 1:1.

** First cycle of chemotherapy must be given prior to study entry for a total of 4 cycles, 3 given on study. Chemotherapy doublets delivered concurrently, cisplatin/etoposide or carboplatin/etoposide, is required. The site/investigator must declare the chemotherapy regimen that the patient will receive prior to the patient's randomization. Patients who develop a contraindication to cisplatin after beginning therapy may receive carboplatin in subsequent cycles. See Section 5.1 and 6 for details.

*** All patients with a complete or near complete response are strongly recommended to receive prophylactic cranial irradiation (PCI), planned within 4-6 weeks from completion of chemoradiotherapy. **Significant chemoradiotherapy toxicities should be resolved to grade 2 or less before beginning PCI.** Patients on Arm 2 who receive PCI will receive it concurrent with atezolizumab.