

**RTOG 0813 - Seamless Phase I/II Study of Stereotactic Lung Radiotherapy (SBRT) for Early Stage, Centrally Located Non-Small Cell Lung Cancer (NSCLC) in Medically Inoperable Patients**

*Fast Facts*

**Patient Eligibility**

1. Pathologically (histologically or cytologically) proven diagnosis of non-small cell lung cancer (NSCLC);
2. Stage T1-2, N0, M0 (AJCC Staging, 6th Ed.), tumor size  $\leq 5$  cm, prior to registration, based upon the following minimum diagnostic workup:
  - a. History/physical examination within 4 weeks prior to registration;
  - b. Evaluation by an experienced thoracic cancer surgeon within 12 weeks prior to registration; the primary tumor must be deemed technically resectable by an experienced thoracic cancer clinician, with a reasonable possibility of obtaining a gross total resection with negative margins, defined as a potentially curative resection (PCR). However, the patient must have underlying physiological medical problems that would prohibit a PCR due to a low probability of tolerating general anesthesia, the operation, the post-operative recovery period, or the removal of adjacent functioning lung. These types of patients with severe underlying health problems are deemed "medically inoperable." Standard justification for deeming a patient medically inoperable based on pulmonary function for surgical resection of NSCLC will include any of the following: Baseline FEV1  $< 40\%$  predicted, post-operative FEV1  $< 30\%$  predicted; severely reduced diffusion capacity; baseline hypoxemia and/or hypercapnia; exercise oxygen consumption  $< 50\%$  predicted; severe pulmonary hypertension; diabetes mellitus with severe end organ damage; severe cerebral, cardiac, or peripheral vascular disease; or severe chronic heart disease.
  - c. Imaging as follows:
    - i. CT scan with contrast (unless medically contraindicated) within 8 weeks of registration. The CT scan will include the entirety of both lungs, the mediastinum, liver and adrenal glands; the primary tumor dimensions will be measured on CT. **Note:** Patients with lesions that cannot be visualized by CT scan are not eligible for the study.
    - ii. Whole body positron emission tomography (PET) scan within 8 weeks of registration, using FDG with adequate visualization of the primary tumor and draining lymph node Basins in the hilar and mediastinal regions. Patients with hilar or mediastinal lymph nodes  $\leq 1$  cm and no abnormal hilar or mediastinal uptake on PET will be considered N0. Mediastinal lymph node sampling by any technique is allowed but not required  
 Patients with  $> 1$  cm hilar or mediastinal lymph nodes on CT or abnormal PET (including suspicious but nondiagnostic uptake) may still be eligible if directed tissue biopsies of all abnormally identified areas are negative for cancer.
3. Zubrod Performance Status 0-2 within 4 weeks prior to registration;
4. Age  $\geq 18$ ;
5. Tumor within or touching the zone of the proximal bronchial tree, defined as a volume 2 cm in all directions around the proximal bronchial tree (carina, right and left main bronchi, right and left upper lobe bronchi, intermedius bronchus, right middle lobe bronchus, lingular bronchus right and left lower lobe bronchi). [See figure in section 3.1.5 in protocol] Tumors that are immediately adjacent to mediastinal or pericardial pleura (PVT touching the pleura) also are considered central tumors and are eligible for this protocol.
6. Patients must have measurable disease.
7. Routine spirometry, lung volumes, diffusion capacity, and arterial blood gases within 12 weeks prior to registration;
8. Pleural effusion, if present, must be deemed too small to tap under CT guidance and must not be evident on chest x-ray. Pleural effusion that appears on chest x-ray will be permitted only after thoracotomy or other invasive procedure(s).
9. Negative serum or urine pregnancy test within 72 hours prior to registration for women of childbearing potential;

10. Women of childbearing potential and male participants must agree to use a medically effective means of birth control throughout their participation in the treatment phase of the study (until at least 60 days following the last study treatment);
11. Patients must provide study-specific informed consent prior to any protocol specified procedures.

#### **Patient Ineligibility**

1. Prior invasive malignancy (except non-melanomatous skin cancer) unless disease free for a minimum of 2 years (e.g., carcinomas *in situ* of the breast, oral cavity, or cervix are permissible); previous lung cancer, if the patient is disease-free for a minimum of 2 years is permitted.
2. Prior radiotherapy to the region of the study cancer that would result in overlap of radiation therapy fields;
3. Prior chemotherapy for the study cancer;
4. Plans for the patient to receive other local therapy (including standard fractionated radiotherapy and/or surgery) while on this study, except at disease progression;
5. Plans for the patient to receive systemic therapy (including standard or biologic targeted agents), while on this study, except at disease progression.

#### **Pre-Study Parameters**

1. H&P, weight, performance status and documentation of extent of weight loss in previous 3 months, to be done within 4 weeks prior to treatment;
2. Chest x-ray within 2 weeks prior to treatment; CT and PET within 8 week prior to study treatment;
3. Routine spirometry, lung volumes, diffusion capacity, and arterial blood gases within 12 weeks prior to treatment;
4. CBC/differential and ANC obtained within 8 weeks prior to treatment; pregnancy test within 72 hours prior to treatment (if applicable)
5. Charlson Comorbidity Index (CCI) and hospitalization history (see Section 11.4 and Appendix V) within 12 weeks prior to start of treatment.
6. Thoracic surgeon evaluation within 12 weeks of registration.
7. Patients must be offered the opportunity to participate in the tissue/specimen component of the study. If the patient consents to participate in this component, the site is required to submit the patient's specimens as specified in Section 10.0

#### **Treatment**

Escalating dose levels; at all levels, patients will receive q 2 day fractionation x 5 fractions over 1½ - 2 weeks

<b>Dose Level</b>	Level 1	Level 2	Level 3	Level 4	<b>Level 5*</b>	Level 6	Level 7	Level 8	Level 9
<b>Dose per fraction</b>	8 Gy	8.5 Gy	9 Gy	9.5 Gy	<b>10 Gy</b>	10.5 Gy	11 Gy	11.5 Gy	12 Gy
<b>Total Dose</b>	40 Gy	42.5 Gy	45 Gy	47.5 Gy	<b>50 Gy</b>	52.5 Gy	55 Gy	57.5 Gy	60 Gy

**\*Protocol treatment begins at Level 5. Levels 1-4 will be employed if dose-limiting toxicity is seen with the Level 5 (10 Gy) starting dose.**

See section 5.0 for pre-registration requirements; see section 6.0 for details of radiation therapy planning and delivery.