

TYPE OF CANCER: Non-Small Cell Lung Cancer
TYPE OF TRIAL: Phase III
TRIAL SPONSOR: RTOG

PRINCIPAL INVESTIGATOR: Anita Pomerantz, M.D.
CONTACT PERSON: Therica Miller
(702) 822-5293

STUDY SUMMARY

A RANDOMIZED PHASE III COMPARISON OF STANDARD- DOSE (60 Gy) VERSUS HIGHDOSE (74 Gy) CONFORMAL RADIOTHERAPY WITH CONCURRENT AND CONSOLIDATION CARBOPLATIN/PACLITAXEL IN PATIENTS WITH STAGE IIIA/IIIB NON-SMALL CELL LUNG CANCER

STUDY OVERVIEW

Compare the overall survival of treated with high does versus standard dose conformal radiotherapy with concurrent and consolidation chemotherapy. The study also compares the tumor free survival, local regional control, and tumor response of patients treated with high vs. standard conformal radiotherapy. The study will also compare toxicity, assess quality of life and correlate outcomes.

PRETREATMENT ASSESMENT

- Informed consent
- Inclusion/exclusion criteria
- Medical history
- Physical Examination
- Vital signs (height, weight, Zubrod)
- tumor biopsy/cytology
- FDG-PET (or bone scan) PET/CT
- CT/MRI of chest, upper abdomen and liver
- MRI brain/CT
- PFTs (including DLCO and FEV1)
- Alkaline Phosphate, glucose, Creatinine, AST + ALT, Total Bilirubin
- Swallowing diary
- Creatinine clearance
- CBC with differentials and ANC
- Adverse events
- QOL:FACT-TOL, EQ-5D

ENTRANCE CRITERIA FOR PARTICIPATION IN TRIAL

Inclusion Criteria

1. Pathologically proven (either histologic or cytologic) diagnosis of Stage IIIA or IIIB non-small cell lung cancer; excluding patients with N3 disease based on supraclavicular or contralateral hilar adenopathy, [according to AJCC Staging, 6th edition; see appendix III] within 12 weeks of registration.
2. Patients must be considered unresectable or inoperable
3. Stage III A or B disease, including no distant metastases, based upon the following minimum diagnostic workup are acceptable:
4. History/physical examination within 8 weeks prior to registration.
5. Computed tomographic (CT)/MRI imaging of the lung and upper abdomen through the liver within 6 weeks prior to registration
6. An MRI of the brain with contrast (or CT if MRI is medically contraindicated) within 6 weeks prior to registration
7. Whole-body FDG-PET or PET/CT or if no PET is available, a bone scan is required within 6 weeks prior to registration. Participation in our two ongoing FDG-PET studies in patients with lung cancer is encouraged (RTOG 0235/ACRIN 6668 and RTOG 0515).
8. If a pleural effusion is present, the following criteria must be met to exclude malignant involvement (incurable T4 disease):
9. When pleural fluid is visible on both the CT scan and on a chest x-ray, a pleuracentesis is required to confirm that the pleural fluid is cytologically negative
10. Exudative pleural effusions are excluded, regardless of cytology
11. Effusions that are minimal (i.e. not visible on chest x-ray) that are too small to safely tap are eligible
12. Patients must have measurable or evaluable disease.
13. Patients with post-obstructive pneumonia are eligible.
14. Patients must be at least 3 weeks from prior thoracotomy (if performed)
15. Zubrod Performance Status 0-1.
16. Age \geq 18.
17. FEV1: best value obtained pre- or post bronchodilator must be \geq 1.5 liters/second.
18. CBC/differential obtained within 2 weeks prior to registration on study, with adequate bone marrow function defined as follows:
 - Absolute neutrophil count (ANC) \geq 1,800 cells/mm³
 - Platelets \geq 100,000 cells/mm³
 - Hemoglobin \geq 10.0 g/dl (Note: The use of transfusion or other intervention to achieve Hgb \geq 10.0 g/dl is acceptable.)
19. Serum creatinine within normal institutional limits or creatinine clearance \geq 60 ml/min
20. Bilirubin within normal institutional limits
21. AST and ALT $<$ 2.5 x the IULN
22. Patient must sign study specific informed consent prior to study entry.

Exclusion Criteria

Conditions for Patient Ineligibility

1. N3 supraclavicular disease

2. Greater than minimal, exudative, or cytologically positive pleural effusions
3. Pancoast tumors
4. Involved contralateral hilar nodes (i.e. greater than 1.5 cm on short axis or positive on PET scan)
5. $\geq 10\%$ weight loss within the past month
6. Prior invasive malignancy (except non-melanomatous skin cancer) unless disease free for a minimum of 3 years. Non-invasive conditions such as carcinoma in situ of the breast, oral cavity, or cervix are all permissible.
7. Prior systemic chemotherapy for the study cancer; note that prior chemotherapy for a different cancer is allowable.
8. Prior radiotherapy to the region of the study cancer that would result in overlap of radiation therapy fields
9. Severe, active co-morbidity, defined as follows:
 10. Unstable angina and/or congestive heart failure requiring hospitalization within the last 6 months
 11. Transmural myocardial infarction within the last 6 months
 12. Acute bacterial or fungal infection requiring intravenous antibiotics at the time of registration
 13. Chronic Obstructive Pulmonary Disease exacerbation or other respiratory illness requiring hospitalization or precluding study therapy within 30 days before registration
 14. Hepatic insufficiency resulting in clinical jaundice and/or coagulation defects; note, however, that laboratory tests for liver function and coagulation parameters are not required for entry into this protocol.
 15. Acquired Immune Deficiency Syndrome (AIDS) based upon current CDC definition; note, however, that HIV testing is not required for entry into this protocol. The need to exclude patients with AIDS from this protocol is necessary because the treatments involved in this protocol may be significantly immunosuppressive. Protocol-specific requirements may also exclude immunocompromised patients.
 16. Pregnancy or women of childbearing potential and men who are sexually active and not willing/able to use medically acceptable forms of contraception; this exclusion is necessary because the treatment involved in this study may be significantly teratogenic.
 17. Any history of allergic reaction to paclitaxel or other taxanes, or to carboplatin.
 18. Uncontrolled neuropathy grade 2 or greater regardless of cause.