

**LUN 144: PHASE II TRIAL OF PREOPERATIVE CHEMOTHERAPY AND
BEVACIZUMAB IN PATIENTS WITH STAGE IB (>4 CM), II, OR SELECT STAGE III
NON-SMALL CELL LUNG CANCER**

Fast Facts

Provided Drug: BEVACIZUMAB

Inclusion Criteria

1. Age \geq 18 years.
2. Histologically-confirmed NSCLC (adenocarcinoma, large cell, and undifferentiated). Patients with squamous histology are not eligible unless approved by the study chair.
3. Life expectancy of at least 12 weeks.
4. Patients with the following stages of NSCLC:
 - **T2 N0 tumors:** Limited to tumors \geq 4 cm.
 - **T1-2 N1 tumors.**
 - **T3 N0-1 tumors (excluding superior sulcus tumors):** Including tumors involving the chest wall, proximal airway, or mediastinal pleura where preoperative radiotherapy is not planned.
 - **T1-2 N2 tumors:** For patients with N2 disease involving one zone (Upper zone (R), AP zone (L), subcarinal zone, or lower zone) and nodes \leq 2 cm in diameter.
 - **T4 N0-1 tumors (excluding superior sulcus tumors):** T4 lesions, other than malignant effusions where radiotherapy is not planned.
5. Patients with clinical N2 involvement must have histologic confirmation by mediastinoscopy (or alternate biopsy procedure).
6. Tumors should be considered potentially resectable.
7. No evidence of extrathoracic metastatic disease.
8. Patients must have measurable disease by RECIST version 1.1 criteria (see Section 9).
9. Patients must be candidates (medically) for chemotherapy followed by surgical resection.
10. Adequate recovery from recent surgery. At least 1 week must have elapsed from the time of a minor surgery (with the exception of portacath or other central access catheter placement); at least 4 weeks must have elapsed from the time of a major surgery.
11. Laboratory values as follows:
 - Absolute neutrophil count (ANC) \geq 1500/ μ L
 - Hemoglobin (Hgb) \geq 9 g/dL
 - Platelets \geq 100,000/uL
 - AST/SGOT and ALT/SGPT within normal limits (WNL)
 - Total bilirubin within normal limits (WNL)
 - Creatinine \leq 1.5 mg/dL
12. ECOG Performance Status grade 0 or 1 (see Appendix B).
13. Women of childbearing potential must have a negative serum or urine pregnancy test performed within 7 days prior to start of treatment. Women of childbearing potential or men with partners of childbearing potential must use effective birth control measures during treatment. If a woman becomes pregnant or suspects she is pregnant while participating in this study, she must agree to inform her treating physician immediately.
14. Patient must be accessible for treatment and follow-up.
15. Patients must be able to understand the investigational nature of this study and give written informed consent prior to study entry.

Exclusion Criteria

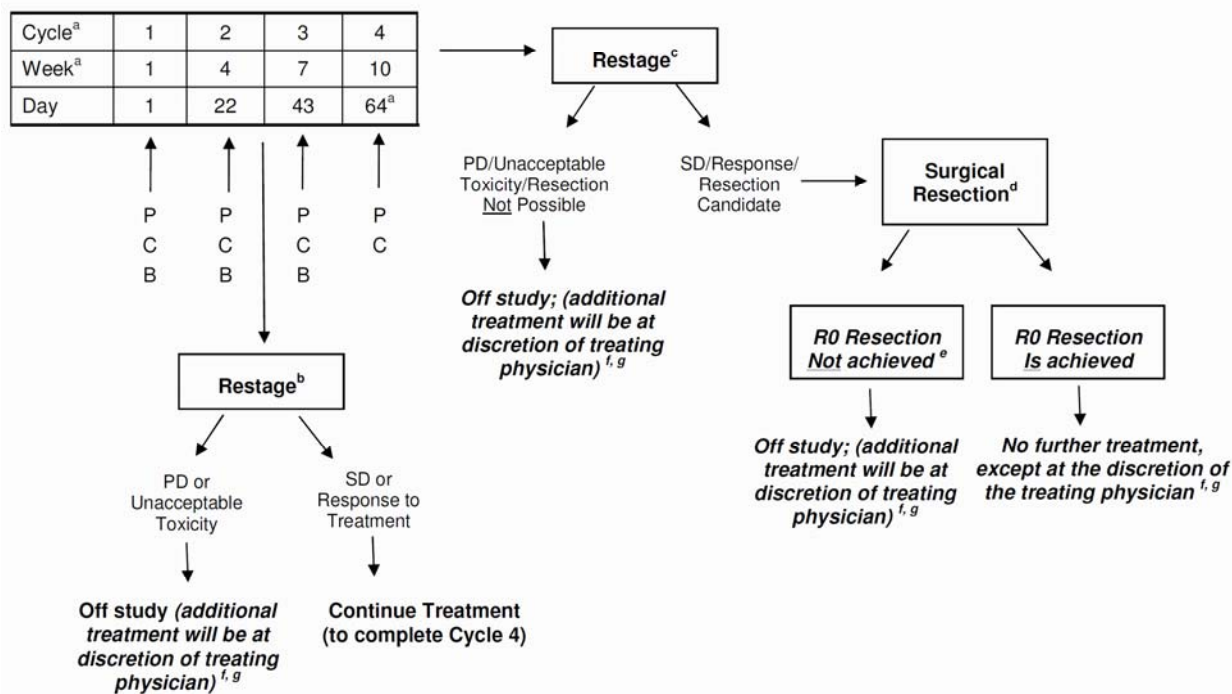
1. Mixed small-cell and non-small cell histologies.
2. Pulmonary carcinoid tumors.
3. History of prior malignancy within 3 years, with the exception of non-melanoma skin cancer or carcinoma in situ.
4. Peripheral neuropathy \geq grade 1.
5. Patients receiving thrombolytic therapy within 10 days of starting study treatment are ineligible. Therapeutic anticoagulation is allowed if the anticoagulant dosing is stable.
6. History of acute myocardial infarction or unstable angina within 6 months prior to Day 1 of study treatment.
7. History of stroke or ischemic attack within 6 months prior to Day 1 of study treatment.
8. Inadequately controlled hypertension (defined as systolic blood pressure $>$ 150 mmHg and/or diastolic blood pressure $>$ 100 mmHg) in spite of medical management.

9. New York Heart Association (NYHA) class II or greater congestive heart failure (CHF) (see Appendix C).
10. Patients with significant vascular disease (e.g., aortic aneurysm requiring surgical repair, or recent peripheral arterial thrombosis) within 6 months prior to Day 1 of study treatment.
11. Any prior history of hypertensive crisis or hypertensive encephalopathy.
12. Patients with hematemesis or hemoptysis ($\geq 1/2$ teaspoon of bright red blood per episode) within 1 month prior to Day 1 of study treatment.
13. Proteinuria at screening, as demonstrated by either:
 - Urine protein: creatinine (UPC) ratio ≥ 1.0 (see Appendix A) at screening, or
 - Urine dipstick for proteinuria $\geq 2+$ (patients discovered to have $\geq 2+$ proteinuria on dipstick analysis should undergo a 24-hour urine collection and must have $\leq 1\text{g}$ of protein in 24 hours to be eligible).
14. Patients with a serious non-healing wound, active ulcer, or untreated bone fracture.
15. Patients with evidence of bleeding diathesis or coagulopathy (in the absence of therapeutic anticoagulation).
16. History of abdominal fistula, gastrointestinal perforation, or intra-abdominal abscess within 6 months prior to Day 1 of study treatment.
17. Women who are pregnant (positive pregnancy test) or lactating.
18. Use of any non-approved or investigational agent within 28 days of administration of the first dose of study drug.
19. Patients may not receive any other investigational or anti-cancer treatments while participating in this study.
20. Concurrent severe, intercurrent illness including, but not limited to, ongoing or active infection, or psychiatric illness/social situations that would limit compliance with study requirements.
21. History of hypersensitivity to active or inactive excipients of any component of treatment.
22. Inability to comply with study and/or follow-up procedures.

Pre-Study Parameters

1. History, PE, vitals, Ht, Weight, PS, AE evaluation and medication review
2. Tumor measurement/Disease assessment
3. LABS: CBC, including diff. and platelets, CMP, PT/PTT/INR, Urinalysis, Serum pregnancy test (childbearing potential only)
4. Staging: CT of chest/abdomen, CT or MRI of the brain, PET or Bone Scan

Treatment Schema for LUN 144



P = Paclitaxel: 200 mg/m² IV on Day 1 of every 3-week (21-day) treatment cycle for a total of 4 cycles (12 weeks).

C = Carboplatin: AUC=6 IV on Day 1 of every 3-week (21-day) treatment cycle for a total of 4 cycles (12 weeks).

B = Bevacizumab: 15 mg/kg IV on Days 1, 22, and 43 (Note: bevacizumab will not be administered on Day 64 of preoperative treatment).