A Phase III Randomized Trial of Adjuvant Chemotherapy With or Without Bevacizumab for Patients With Completely Resected Stage IB (≥ 4 cm)–IIIA Non–Small Cell Lung Cancer (NSCLC)

Overall Study Objective

To examine if bevacizumab can improve survival when combined with a cisplatin-based adjuvant chemotherapy regimen compared with chemotherapy alone in patients with surgically resected stage IB (≥ 4 cm)–IIIA NSCLC

Study Schema

Table 1. Cisplatin-Based Chemotherapy Regimen Choices*

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Cisplatin 75 mg/m² IV, day 1, Plus</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Vinorelbine 30 mg/m² IV push, days 1 and 8</td>
</tr>
<tr>
<td>2</td>
<td>Docetaxel 75 mg/m² IV, day 1</td>
</tr>
<tr>
<td>3</td>
<td>Gemcitabine 1200 mg/m² IV, days 1 and 8</td>
</tr>
<tr>
<td>4</td>
<td>Pemetrexed 500 mg/m² IV, day 1 (nonsquamous cell NSCLC only)</td>
</tr>
</tbody>
</table>

*Combination selection based on physician discretion.

Study Objectives

Primary Objective

- Overall survival with adjuvant chemotherapy with or without bevacizumab

Secondary Objectives

- Disease-free survival and toxicity
- Tissue and blood analyses to establish predictive factors for clinical outcome in patients with resected early-stage NSCLC
- Potential correlation between smoking status and clinical outcome
Eligibility Criteria*

Main Inclusion Criteria

- **Aged ≥ 18 years with stage IB (≥ 4 cm) through IIIA NSCLC**
  
  *Note:* A new risk of ovarian failure has been added; accrual of premenopausal women should be suspended until a revised consent adding this risk is reviewed and approved by the IRB

- **Mediastinal lymph node sampling at specified levels preoperatively (mediastinoscopy) or intraoperatively (levels 7 and 4 for right-sided tumors; levels 7 and 5 and/or 6 for left-sided tumors)**
  
  - **Sampling at specific levels is not required with pathologically confirmed metastasis in any N2 node**

- **Surgical resection occurs ≥ 42 days and ≤ 84 days prior to randomization (includes lobectomy, sleeve lobectomy, bilobectomy, or pneumonectomy; excludes segmentectomy and wedge resection)**

- **ECOG performance status 0-1 and adequate laboratory values**

- **No prior chemotherapy. Exclusion: Low-dose methotrexate for nonmalignant conditions with last dose at least 2 weeks prior to randomization will be allowed. Refer to protocol “Selection of Patients”**

- **No hormonal cancer or radiation therapy within 5 years of randomization**

- **No history of cancer within 5 years of randomization**

- **Stable regimen of therapeutic anticoagulation (INR ≤ 3); see protocol for prohibited medications**

- **No planned postoperative radiation therapy (PORT)**

- **Patients assigned to pemetrexed/cisplatin therapy must not have squamous cell histology**

Main Exclusion Criteria

- **Serious nonhealing wounds**

- **Recent major surgical procedure (< 28 days) or core biopsy (< 7 days)**

- **Uncontrolled hypertension (required level of control, ≤ 150/90) within 28 days of registration. Patients with known hypertension must be on a stable regimen of antihypertensive therapy**

- **History < 1 year of myocardial infarction or other arterial thrombotic disease**

- **Any history of cerebral vascular accident or transient ischemic attack**

- **Continued hemoptysis after surgery**

*When evaluating patients for this study, please refer to the full protocol for the complete list of eligibility criteria.

For Further Study Information

- For more information about the E1505 study, please contact/see the following:
  
  - ClinicalTrials.gov registration number: NCT00324805; [http://clinicaltrials.gov/ct/show/NCT00324805](http://clinicaltrials.gov/ct/show/NCT00324805)
  - For more information about ECOG, visit [http://www.ecog.org/](http://www.ecog.org/)