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)

**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

**Study Schema**

- **Arm A**
  - 1 of 4 chemotherapy regimens (no bevacizumab)
  - Until disease recurrence, unacceptable toxicity, or total of 4 cycles
- **Arm B**
  - 1 of 4 chemotherapy regimens Plus bevacizumab
  - Until disease recurrence, unacceptable toxicity, or total of 4 cycles
  - If no progression, then bevacizumab alone continues after completion of 4 cycles of chemotherapy for up to 1 year from start of treatment

**Stratification Factors**
- **Chemotherapy Type**
  - Vinorelbine/cisplatin vs docetaxel/cisplatin vs gemcitabine/cisplatin vs pemetrexed/cisplatin
- **Stage (AJCC 6th ed)**
  - IB (≥ 4 cm) vs II vs IIIA-N2 vs IIIA-T3N1
- **Histology**
  - Squamous cell histology vs other NSCLC
- **Gender**
  - Male vs female

Follow-up duration: 10 years from date of study registration
Main Eligibility 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

- Surgical resection occurring ≥ 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

- Mediastinal lymph node sampling at specified levels is required 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

- No prior chemotherapy. Exception: 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 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

- No history of cerebral vascular accident or transient ischemic attack; no myocardial infarction or other arterial thrombotic disease < 1 year

- No continued hemoptysis after surgery

- No planned postoperative radiation therapy (PORT)

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

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