Overall E5508 Study Objective

To compare maintenance therapy with bevacizumab, pemetrexed, or a combination of both following 4 cycles of carboplatin, paclitaxel, and bevacizumab with the goal of identifying an optimal maintenance regimen that results in improved survival for patients with advanced-stage, nonsquamous NSCLC

Study Schema

Stratification factors:
- Gender (male vs female)
- Stage (IIIB-T4Nx*/IV M1a vs IV M1b vs recurrent)
- Best response to first-line therapy (CR/PR vs SD)
- Smoking status (never vs ever smokers)

Accrual = 1495.
1 cycle = 21 days.
*Stage IIIB-T4Nx patients must have a nodule in the ipsilateral lung lobe and must not be candidates for combined chemotherapy and radiation.
†Prophylactic treatment for paclitaxel (PC) includes dexamethasone (20 mg PO 12 and 6 h prior to PC infusion), diphenhydramine (50 mg IV, < 1 h prior to PC), and cimetidine (300 mg IV, < 1 h prior to PC).
‡Continue until disease progression or unacceptable toxicity.
§Patients in maintenance arms B and C are to receive premedication consisting of folic acid (400-1000 µg PO, every day × 21 d) and vitamin B12 (1000 µg IM, every 3 cycles) 1 week prior to pemetrexed. One day before pemetrexed, administer dexamethasone (4 mg twice daily × 3 d).
Study Objectives

Primary Objective
- Compare overall survival associated with maintenance therapy with bevacizumab versus pemetrexed versus combination bevacizumab/pemetrexed in patients with advanced-stage NSCLC

Secondary Objectives
- Determine response rate among the 3 maintenance treatment arms
- Evaluate progression-free survival
- Assess safety and potential biomarkers

Main Eligibility Criteria*
- ≥ 18 years of age with cytologically or histologically confirmed nonsquamous NSCLC
- NSCLC classified as IIIB-T4Nx, IV M1a, or IV M1b stage of disease
- ECOG performance status of 0-1
- Adequate laboratory values and organ function
- Measurable or nonmeasurable disease as defined by RECIST criteria
- No uncontrolled hypertension or uncontrolled intercurrent illness (eg, ongoing/active infection, symptomatic congestive heart failure, unstable angina pectoris, serious cardiac arrhythmia, or psychiatric illness)
- Brain metastasis must have been locally treated and not progressed for at least 2 weeks post completion of local therapy, prior to registration
- No pregnancy or breast-feeding
- No prior systemic chemotherapy, including paclitaxel, pemetrexed, or bevacizumab
- No major hemoptysis within 4 weeks prior to study registration (defined as bright red blood of 1/2 teaspoon or more)
- No major surgery (eg, thoracotomy, laparotomy, craniotomy) or significant traumatic injury 6 weeks prior to registration, or history of serious nonhealing wounds
- No abdominal fistula, gastrointestinal perforation, or intra-abdominal abscess within the past 6 months
- No arterial thrombotic events or major bleeding within the past 12 months, significant vascular disease within the past 6 months, clinically significant cardiovascular disease

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