

**SWOG S0819** - A Randomized, Phase III Study Comparing Carboplatin/Paclitaxel or Carboplatin/Paclitaxel/Bevacizumab with or without Concurrent Cetuximab in Patients with Advanced Non-Small Cell Lung Cancer (NSCLC)

*Fast Facts*

**Cetuximab provided.**

**Uses 7<sup>th</sup> edition of AJCC Cancer Staging Handbook**

**ELIGIBILITY CRITERIA**

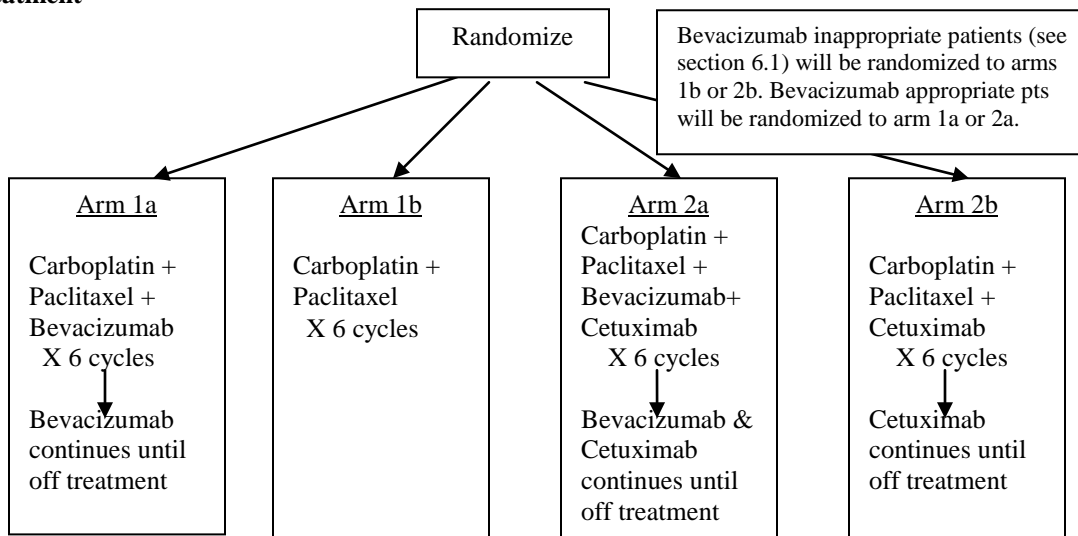
1. Patients must have histologically or cytologically proven newly diagnosed Stage IV, as defined in Section 4.0, advanced primary non-small cell lung cancer (adenocarcinoma, large cell carcinoma, squamous or unspecified) or recurrent disease after previous surgery and/or irradiation. Patients with additional lesions in an ipsilateral non-primary lobe without M1<sub>a</sub>, or M1<sub>b</sub> disease will not be considered to have Stage IV disease and are not eligible.
2. Patients must have a CT or MRI scan of the brain to evaluate for CNS disease within 42 days prior to registration. Patient must not have brain metastases unless: (1) metastases have been treated and have remained controlled for at least two months following treatment, AND (2) patient has no residual neurological dysfunction off corticosteroids.
3. Patients may have measurable or non-measurable disease (see Section 10.1) documented by CT or MRI. The CT from a combined PET/CT may be used to document only non-measurable disease unless it is of diagnostic quality as defined in Section 10.1a. Measurable disease must be assessed within 28 days prior to registration. Pleural effusions, ascites and laboratory parameters are not acceptable as the only evidence of disease. Non-measurable disease must be assessed within 42 days prior to registration. All disease must be assessed and documented on the Baseline Tumor assessment Form (Form #848). See Sections 15.2 and 19.6 for guidelines and submission instructions for required central radiology review.
4. Patients must agree to submission of specimens for EGFR FISH testing and other translational medicine studies as outlined in Section 15.0. Patients must be offered participation in banking for future research.
5. Patients must not have received for any purpose prior chemotherapy. Patients must not have received any cetuximab, gefitinib, erlotinib or other investigational agents that target the EGFR pathway. Patients must not have received for any purpose prior bevacizumab or other VEGF-related agents. Patients must not have received for any purpose prior chimerized or murine monoclonal antibody therapy or have documented presence of human anti-mouse antibodies (HAMA).
6. Prior radiation is permitted; however, patients must have recovered from all associate toxicities at time of registration. In order to qualify as measurable per Section 10.1a measurable disease must be outside the previous radiation field or must have progressed.
7. At least 28 days must have elapsed since surgery (thoracic or other major surgeries), open biopsy or significant traumatic injury and patients must have recovered from all associated toxicities at the time of registration. There must be no anticipation of need for major surgical procedures during protocol treatment. Patients must not have had a core biopsy within 7 days prior to registration.
8. Patients must have an ANC  $\geq$  1,500/mcl, platelet count  $\geq$  100,000/mcl, and hemoglobin  $\geq$  9 g/dL obtained within 14 days prior to registration.
9. Patients must have a serum creatinine  $\leq$  institutional upper limit of normal (IULN) AND calculated or measured creatinine clearance  $\geq$  50 cc/min using the Cockcroft- Gault formula. These tests must have been performed within 14 days prior to registration.
10. Urine protein must be screened by urine analysis for Urine Protein Creatinine (UPC) ratio. For UPC ratio  $>$  0.5, 24-hour urine protein must be obtained and the level must be  $<$  1,000 mg for patient enrollment. The urine protein used to calculate the UPC ratio must be obtained within 14 days prior to registration. Note: UPC ratio of spot urine is an estimation of the 24-hour urine protein excretion – a UPC ratio of 1 is roughly equivalent to a 24-hour urine protein of 1 gm.
11. Patients must have adequate hepatic function documented by serum bilirubin  $\leq$  2 x IULN and either SGOT or SGPT  $\leq$  2 x IULN within 14 days prior to registration (if both SGOT and SGPT are done, both must be  $\leq$  2 x IULN). For patients with liver metastases, bilirubin and either SGOT or SGPT must be  $\leq$  5 x IULN.
12. All patients must have a Zubrod Performance Status of 0-1 (see Section 10.4).
13. Patients must not have  $\geq$  Grade 2 symptomatic neuropathy-sensory
14. Patients must not have documented evidence of acute hepatitis or have an active or uncontrolled infection.

15. Patients must not have the following: history (within past 6 months) of CVA, myocardial infarction or unstable angina; uncontrolled hypertension; New York Heart Association Grade 2 or greater congestive heart failure (see Appendix 19.3); serious cardiac arrhythmia requiring medication; or clinically significant peripheral vascular disease.
16. Patients must have no known hypersensitivity to Chinese hamster ovary cell products or other recombinant human antibodies [examples include trastuzumab (Herceptin) and epoetin alpha].
17. Patients must be willing to provide prior smoking history as required on the **S0819** Prestudy Form (Form #22270).
18. No other prior malignancy is allowed except for the following: adequately treated basal cell or squamous cell skin cancer, in situ cervical cancer, adequately treated Stage I or II cancer from which the patient is currently in complete remission, or any other cancer from which the patient has been disease-free for 5 years.
19. Pregnant or nursing women are not eligible for this trial because of the increased risk of fetal harm including fetal death from the chemotherapeutic agents. Women/men of reproductive potential must not participate unless they have agreed to use an effective contraceptive method during protocol treatment and for at least 6 months following completion of bevacizumab treatment.
20. Patients must be informed of the investigational nature of this study and must sign and give written informed consent in accordance with institutional and federal guidelines.
21. At the time of patient registration, the treating institution's name and ID number must be provided to the Data Operations Center in Seattle in order to ensure that the current (within 365 days) date of institutional review board approval for this study has been entered into the data base.

### Pre-Study Parameters

1. History and physical including weight, performance status, and disease assessment
2. Labs including CBC with differential and platelets, calculated or measured CrCL, serum creatinine, bilirubin, SGOT or SGPT, UPC ratio and INR. Suggested labs include Alk phos, Albumin, LDH, serum Na, Ca, Mg
3. Scans as needed for disease assessment, Brain MRI/CT, Bone scan (suggested or if clinically indicated), EKG (suggested)

### Treatment



See section 7.0 for complete tx plan including pre-medications.  
Cetuximab provided.