

# CLINICAL TRIALS Broadcast

In Focus: Non-Small Cell Lung Cancer

## E1505:

A Phase III Randomized Trial of Adjuvant Chemotherapy With or Without Bevacizumab for Patients With Completely Resected Stage IB–IIIA Non-Small Cell Lung Cancer

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### Background

Adjuvant chemotherapy became the standard of care for completely resected stage II–IIIA non-small cell lung cancer (NSCLC) after three clinical trials confirmed the efficacy of this approach in extending survival.<sup>1–4</sup> The role of this approach in stage IB disease is somewhat controversial, but still widely adopted. However, lung cancer is still the leading cause of cancer death in the United States and worldwide, and 30–60% of patients with resected NSCLC die of their disease.<sup>5,6</sup>

Efforts to improve upon the 4–15% survival advantage conferred by adjuvant chemotherapy following surgical resection are focusing on the incorporation of biologic agents into the adjuvant regimen. The National Cancer Institute of Canada's JBR.19 study of adjuvant gefitinib closed early when other studies of gefitinib showed negative findings.<sup>7</sup> The results of JBR.19 are awaited.

Targeting the vascular endothelial growth factor (VEGF) is another promising strategy to combine with adjuvant chemotherapy. VEGF is the most potent and specific angiogenic factor identified to date, stimulating proliferation of vascular endothelial cells and having increased expression in most tumor cell types as compared to normal tissues.<sup>8</sup> Bevacizumab, a humanized IgG1 monoclonal antibody, binds all active isoforms of human VEGF. Neutralization of VEGF by this agent inhibits VEGF-induced proliferation of human endothelial cells in vitro, and decreases microvessel density and interstitial pressure in vivo.<sup>9</sup>

The Eastern Cooperative Oncology Group (ECOG) study E4599 evaluated carboplatin plus paclitaxel with or without the anti-VEGF agent bevacizumab for the treatment of advanced NSCLC (nonsquamous histology only) in nearly 900 patients. A survival of 10.3 versus 12.3 months ( $P=.003$ ) for the chemotherapy-only and combination arms, respectively, was reported.<sup>10</sup> Given these encouraging results, studying bevacizumab in the adjuvant setting is a compelling research question that will be asked in E1505.

Several chemotherapy regimens have been studied in the adjuvant setting for NSCLC. In the present study, investigators choose one of three chemotherapy options: cisplatin/vinorelbine; cisplatin/docetaxel; and cisplatin/gemcitabine. Patients are randomized to receive bevacizumab starting with the first cycle of chemotherapy and continuing for up to 1 year or chemotherapy without bevacizumab. Only 4 cycles of chemotherapy will be administered. Although cisplatin/vinorelbine is the only regimen with proven efficacy in the adjuvant setting, based on data from advanced stage disease the other options are felt to provide at least equivalent efficacy. Emerging data may lead to adjustments in the protocol as necessary.

Thus far, bevacizumab is the only agent that has been associated with prolonged survival when combined with frontline therapy for advanced NSCLC (E4599). Studying this agent in the treatment of early-stage NSCLC is a logical next step toward improving adjuvant therapy for this disease. In this trial squamous cell histologies will be allowed as there will be no gross tumor and the risk of pulmonary hemorrhage should be absent.

## References

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## Objectives

### Primary

To evaluate overall survival with chemotherapy with or without bevacizumab used in the adjuvant setting in patients with resected stage IB–IIIA NSCLC.

### Secondary

- To evaluate disease-free survival and toxicity with chemotherapy with or without bevacizumab used in the

adjuvant setting in patients with resected stage IB–IIIA NSCLC.

- To perform analyses of tissue and blood to establish factors that predict for clinical outcome in patients receiving chemotherapy, with or without bevacizumab, for resected early-stage NSCLC
- To determine whether smoking status is linked to outcome for patients with resected stage IB–IIIA NSCLC treated with chemotherapy with or without bevacizumab in the adjuvant setting.

## Basic Eligibility Criteria

- Completely resected stage IB–IIIA NSCLC, resected  $\geq 6$  weeks and  $\leq 12$  weeks and completely recovered prior to randomization
- Sufficient pathologic material representative of patient's cancer available for correlative studies and tissue banking for future, unspecified research purposes
- ECOG performance status 0 or 1
- No prior systemic chemotherapy, no prior hormonal cancer or radiation therapy within 5 years of randomization, no history of cancer within 5 years from randomization

## Contact Information

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## Schema

