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Preoperative Bevacizumab in Combination With Paclitaxel and Carboplatin in Surgically Resectable Non-Small Cell Lung Cancer

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To the Editor

Preoperative chemotherapy is established for stage III (N2 positive) non-small cell lung cancer (NSCLC) and has demonstrated benefit in two studies. In both studies, survival was improved for patients who received chemotherapy (5-year survival 53% vs 24% [1], and median survival 26 vs 8 months [2]). Recently, Pisters and colleagues [3] reported the results of S9900, a trial of preoperative chemotherapy, followed by surgical resection, compared with surgical resection alone in earlier stage NSCLC [3]. Although this trial was stopped before full accrual, it showed a trend toward improved survival in the preoperative chemotherapy arm.

Bevacizumab, an antibody directed to vascular endothelial growth factor, has improved response rates and overall survival when combined with chemotherapy for patients with metastatic lung cancer and is being tested in the adjuvant setting with chemotherapy [4]. Several important toxicities, including bleeding, tracheoesophageal fistulas, and wound healing complications, affect the utility of bevacizumab in the perioperative setting [5].

We designed a trial of induction chemotherapy and bevacizumab for patients with surgically resectable NSCLC. Unfortunately, this National Cancer Institute-sponsored protocol was terminated early due to poor accrual. Although conclusions about the efficacy of this approach cannot be established, we wish to communicate that thoracic operations can be performed safely after bevacizumab-containing chemotherapy.

The trial enrolled 6 men, and most were white. Patients with squamous cell carcinoma were not excluded from treatment; however, patients with central tumors (within the inner one-

third of the chest) and hemoptysis were excluded. Four patients had squamous cell cancers. Planned treatment included two preoperative cycles of carboplatin AUC 6, paclitaxel (200 mg/m²), and bevacizumab (15 mg/kg) on day 1 of a 21-day cycle.

Five patients received two cycles of chemotherapy with bevacizumab; 1 patient received two cycles of chemotherapy, but bevacizumab was discontinued before cycle 2 due to hypertension. Treatment-related toxicity was minimal. There were no significant bleeding events—1 patient had grade 1 epistaxis and another had grade 1 hematuria. The only grade 3 or 4 toxicity observed was neutropenia. Four of the enrolled patients underwent planned surgical resection: three lobectomies and one bilobectomy. The average time between the last dose of bevacizumab and the operation was 48 days (range, 35 to 75 days). Progressive disease was discovered in 2 patients during the preoperative evaluation, and they did not undergo resection.

No postoperative complications attributable to bevacizumab were observed. One patient had atelectasis due to secretions and a persistent air leak. Despite receiving bevacizumab, no significant perioperative bleeding complications were observed. Similarly, none of the patients had wound-healing complications, and there were no fistulas. Furthermore, no perioperative thromboembolic events occurred. Partial pathologic responses were discovered in 2 patients at the time of the operation, as demonstrated by smaller tumors with necrosis.

Improved survival remains the goal of perioperative therapy for early-stage NSCLC. Our limited data provide early signals that bevacizumab can safely be added to preoperative chemotherapy and supports the ongoing Bevacizumab and Chemotherapy for Operable NSCLC (BEACON) study of preoperative chemotherapy and bevacizumab (NCT00130780).

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