New cancer drugs such as bevacizumab (BEV) provide hope for patients worldwide. These opportunities—accompanied by expensive price tags—require evaluations of benefits, toxicities, and costs. One aspect is that not all toxicities are created equal; some patients who experience toxicities are treated as inpatients and others are not. Carroll et al address this concept as they report on patterns of use, clinical toxicities, and hospitalizations associated with carboplatin, paclitaxel, and BEV (CPB) treatment administered to persons with stages IIIB/IV non–small-cell lung cancer (NSCLC). These patients received care at four health maintenance organizations (HMOs) participating in the HMO cancer research network. During the study period, 198 patients with stage IIIB/IV NSCLC received CPB and 911 patients with NSCLC received carboplatinum and paclitaxel (CP) at four HMOs. BEV toxicity is important to assess, since the approval by the US Food and Drug Administration of the CPB regimen was based on identification of a median 2-month improvement in cancer survival relative to the CP regimen.

The observational study by Carroll et al presents several important findings. First, as expected, the CPB-treated patients were significantly younger than the CP-treated patients and had significantly fewer comorbid conditions. Second, consistent with clinical trial reports, CPB-treated patients experienced more episodes of bleeding, proteinuria, and GI perforations. What is novel here is that the study reports on hospitalizations that occurred as a result of clinical toxicity. Although CPB-treated patients experienced significantly more toxicities, they were only half as likely to be hospitalized and had fewer total hospitalizations and hospital days compared with CP-treated patients. How is this possible?

The key here is patient selection. On one hand, the four HMOs preferentially avoided administering BEV to the elderly and to those with cardiovascular disease, diabetes, or a bleeding disorder, presumably because of concerns of increased toxicity risks. On the other hand, the HMOs frequently added BEV to those with cardiovascular disease, diabetes, or a bleeding disorder, presumably because of concerns of increased toxicity. HMOs preferentially avoided administering BEV to the elderly patients. How is this possible?

What is novel here is that the study reports on hospitalizations associated with CPB and their incremental cost-effectiveness ratio relative to CP. One could postulate that more toxicities, and more hospitalizations for toxicity management, could have occurred in other health care settings. On an ironic note, this study demonstrates that when CPB therapy is administered to patients without specific contraindications to BEV, BEV still causes serious adverse drug reactions.

NSCLC imposes a substantial burden on patients and health care systems as a result of its high incidence rate and poor survival rates. Carboplatin and paclitaxel are inexpensive, especially when compared with BEV. In a recent systematic review of first-line treatment of advanced NSCLC, BEV had an incremental cost-effectiveness ratio greater than $150,000 per quality-adjusted life-year, far higher than the generally agreed-upon threshold of $50,000 to $100,000 per quality-adjusted life-year. Resources are limited in every country, and it is likely that only developed countries with large health care budgets can afford to offer CPB treatment broadly for persons with advanced NSCLC. Carroll et al also suggested that even in well-resourced settings such as the United States, CPB treatment should be judiciously administered such that if toxicity occurs, it can be managed on an outpatient basis.

The findings of Carroll et al have international implications, building on analyses of toxicities and costs recently reported for targeted cancer therapies. Whereas toxicities associated with CPB may be relatively constant from country to country, therapy-related hospitalizations will differ because of variations both between and within health systems. Although this study is directed toward oncologists and decision makers in the United States, other audiences will benefit from it. The authors have made a terrific beginning in analyzing the impact of a new cancer regimen for NSCLC in a community setting in the United States. Updates are essential as experience with this regimen matures internationally and as new NSCLC regimens are introduced. For the time being, caveat emptor to clinicians who choose to administer CPB therapy to patients with NSCLC; toxicities are significant with this regimen even among younger patients with few comorbid illnesses.

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AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Adding Bevacizumab to the Treatment of Patients With Non–Small-Cell Lung Cancer: Caveat Emptor

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