LATEST ONCOLOGY UPDATES
Lung Cancer Update for Oncologyeducation.ca Jan 2008

Title:
Outcomes for Elderly, Advanced-Stage Non-Small-Cell Lung Cancer Patients Treated with Bevacizumab in Combination with Carboplatin and Paclitaxel: Analysis of Eastern Cooperative Oncology Group Trial 4599.
JCO. Jan 1 2008; 26(1): 60-5.

Background:
This is a retrospective, post-hoc, subgroup analysis of the ECOG 4599 trial. That trial randomized patients with advanced NSCL cancer to receive first line therapy with Carboplatin (AUC 6) and Paclitaxel (200 mg/m2) with (PCB) or without (PC) bevacizumab (15mg/kg Day 1). Previous ECOG trial comparing 4 platin based regimens (ECOG 1594) suggested similar benefit without excess clinical toxicity in elderly. Since almost 50% of patients with NSCL cancer are 70 years or older, it is important to assess toxicities and efficacy of new treatments in this subgroup. This is particularly important for bevacizumab because of the increase risk factors for bevacizumab toxicity in the elderly.

Study design:
ECOG 4599 enrolled 878 patients. These patients were already selected for good PS (ECOG 0,1) and were excluded if squamous histology, major hemoptysis, brain mets, recent history of bleeding or thrombotic events, uncontrolled hypertension, and use of therapeutic anticoagulation.

224 patients (26%) were considered elderly based on age 70 years or older. This is the highest percentage of elderly patients in any ECOG trial. They compared patient characteristics, efficacy and toxicity between treatment arms in the elderly group as well as between the elderly and younger patients.

Study results:
Toxicity was found to be significantly higher in the elderly patients receiving PCB versus PC, grade 3-5 toxicity 87% versus 61% (p.001). Hemorrhagic events and febrile neutropenia were particularly increased in the PCB arm and there were more treatment related deaths in the PCB arm, 6.8% versus 1.8% (p.1). Similarly, elderly patients receiving PCB experienced more toxicity than younger patients receiving PCB, 87% versus 71% grade 3-5 (p<.001). Treatment related deaths were also higher in the elderly receiving PCB versus younger patients, 6.3% versus 2.6 %.

Although there was a trend toward higher response rate with PCB versus PC in the elderly, 29% versus 17% (p.067), the PR + SD was no different 68% versus 67%. Although there was a trend in favor of increased PFS with PCB versus PC in the elderly,

5.9 m versus 4.9 m (p.063), there was no difference in OS, 11.3 m PCB versus 12.1 m PC.

Bottomline for Canadian medical oncologists:
Although bevacizumab is not routinely used in combination with chemotherapy in advanced NSCL cancer in Canada, this option is discussed with many patients. Given the modest survival benefit seen in ECOG 4599, the toxicities of PCB become even more important. This is particularly so in the elderly population of NSCL cancer patients who have many risk factors for bevacizumab toxicity. While this paper reports post hoc, retrospective data and thus suffers from the usual criticisms of such an approach, it does provide meaningful information in determining the therapeutic index of chemotherapy plus bevacizumab in elderly patients with NSCL cancer. Despite the highly selected nature of the patients in ECOG 4599, elderly patients who received bevacizumab in addition to chemotherapy experienced significantly more toxicity, including hemorrhagic events and febrile neutropenia and a treatment related death rate (6.8%) that I would consider as unacceptable in a palliative setting. Furthermore, while there was a trend toward improved response rate with bevacizumab, there was no difference if one considers response plus stable disease. Most importantly there did not appear to be any improvement in overall survival with the addition of bevacizumab. All medical oncologists discussing treatment options for patients with advanced NSCL cancer needs to be aware of this data and should incorporate this in their discussion with elderly patients with NSCL cancer.