

## Advanced lung cancer in the older patient: is there a role for bevacizumab?

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There is ongoing discussion about the most appropriate treatment for lung cancer in elderly patients. Many trials exclude this age group; and those that include elderly, often do not distinguish between age groups. The advent of targeted agents in cancer therapy has raised the hope that older cancer patients could be treated as effectively as younger patients and without added toxicities.

Bevacizumab, a monoclonal antibody which targets vascular endothelial growth factor (VEGF), attained FDA-approval for the use in non-squamous non-small cell lung cancers in 2006 after the ECOG (Eastern Cooperative Oncology Group) 4599 trial demonstrated a survival benefit for patients with advanced stage disease (stage IIIB and IV) when combined with carboplatin and paclitaxel (1). There was a 2-month improvement in overall survival in the entire cohort, while there was a 4 month advantage in patients with adenocarcinoma histology. Approximately 42-44% of patients who were randomized in the trial were over 65 years of age at time of enrollment. A subset analysis of patients at least 70 years of age who were treated on ECOG 4599 showed that although older patients who received bevacizumab had a trend towards higher response rate and progression-free survival, there was no improvement in overall survival (11.3 vs. 12.1 months) (2). In fact, the only statistically significant difference seen in this analysis was a higher rate of grade 3 to 5 toxicities in the bevacizumab-containing arm (3).

In a meta-analysis of four studies involving 2,101 patients, Yang and associates looked at the safety and effectiveness of

bevacizumab for advanced stage non-small cell lung cancer (4). They reported improved progression-free survival, response rate, and 2 year overall survival with bevacizumab; however there was no statistically significant difference in 1-year survival. There also was a significantly increased risk of treatment-related death (hazard ratio: 2.07; 95% CI, 1.19, 3.59) in the bevacizumab-containing treatment groups. Interestingly, this analysis included patients over and under the age of 65.

In the present study, Zhu *et al.* conducted a retrospective review of Medicare patients over the age of 65 who were treated with and without bevacizumab in combination with carboplatin and paclitaxel, as based on the ECOG 4599 trial protocol (5). Data was obtained from the SEER database (Surveillance, Epidemiology, and End Results) as was linked to claims to Medicare. Three different cohorts were evaluated. These included: patients treated 2006-2007 with carboplatin and paclitaxel, patients treated 2006-2007 with carboplatin, paclitaxel, and bevacizumab, and patients treated 2002-2005 with carboplatin and paclitaxel (years prior to bevacizumab approval). The latter group was included in the trial to help avoid selection bias of healthier patients potentially being more likely to be given bevacizumab. This was a well-conducted study and although it suffers from the limitations seen with a retrospective analysis, it nonetheless provides a more real-world view of the impact of bevacizumab in advanced NSCLC. The results of Zhu's retrospective analysis support the previous reported findings that the addition of bevacizumab to carboplatin and paclitaxel does not improve overall survival for patients over the age of 65. Toxicity and safety data were not included in this current study.

These results in combination with the previous analyses clearly suggest that older patients may not benefit from the use of bevacizumab. Careful thought should be given before including bevacizumab in the treatment plan for adults over 65 years of age. Given that more than two-thirds of patients diagnosed with lung carcinoma are over the age of 65, it is vital that this be better defined (6). Prospective studies looking at treatment options for older adults with advanced non-small cell lung cancer should be conducted. Until better options become available, platinum-

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based doublet chemotherapy remains the standard of care in older patients with a good functional status. It has been well documented that while older patients have increased incidence of toxicity, they receive benefit from doublet therapy over monotherapy (7).

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### References

1. Sandler A, Gray R, Perry MC, et al. Paclitaxel-carboplatin alone or with bevacizumab for non-small-cell lung cancer. *N Engl J Med* 2006;355:2542-50.
2. Sandler A, Yi J, Dahlberg S, et al. Treatment outcomes by tumor histology in Eastern Cooperative Group Study E4599 of bevacizumab with paclitaxel/carboplatin for advanced non-small cell lung cancer. *J Thorac Oncol* 2010;5:1416-23.
3. Ramalingam SS, Dahlberg SE, Langer CJ, et al. 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. *J Clin Oncol* 2008;26:60-5.

4. Yang K, Wang YJ, Chen XR, et al. Effectiveness and safety of bevacizumab for unresectable non-small-cell lung cancer: a meta-analysis. *Clin Drug Investig* 2010;30:229-41.
5. Zhu J, Sharma DB, Gray SW, et al. Carboplatin and paclitaxel with vs without bevacizumab in older patients with advanced non-small cell lung cancer. *JAMA* 2012;307:1593-601.
6. Altekruse SE, Kosary CL, Krapcho M, et al. National Cancer Institute. SEER cancer statistics review 1975-2007. Available online: [http://www.seer.cancer.gov/csr/1975\\_2007/results\\_merged/topic\\_age\\_dist.pdf](http://www.seer.cancer.gov/csr/1975_2007/results_merged/topic_age_dist.pdf). Accessed September 2012.
7. Quoix E, Zalcman G, Oster JP, et al. Carboplatin and weekly paclitaxel doublet chemotherapy compared with monotherapy in elderly patients with advanced non-small-cell lung cancer: IFCT-0501 randomised, phase 3 trial. *Lancet* 2011;378:1079-88.



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