Bevacizumab Combination Improves PFS, but Not OS, in Extensive-Disease SCLC

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The addition of bevacizumab to a first-line regimen of cisplatin and etoposide improved progression-free survival (PFS) in patients with extensive-disease small-cell lung cancer (SCLC), according to a new randomized trial. This did not translate, however, into a significant improvement in overall survival (OS).

“Despite its initial sensitivity to chemotherapy and radiotherapy, extensive-disease SCLC remains an incurable tumor,” wrote study authors led by Marcello Tiseo, MD, of Azienda Ospedaliero-Universitaria in Parma, Italy. Cisplatin plus etoposide has been the standard of care for this malignancy since the early 1980s, and newer strategies have not yielded any step forward. Previous work has suggested that the anti-VEGF agent bevacizumab could be effective.

The trial was a phase III study that randomized treatment-naive extensive-disease SCLC patients to either cisplatin and etoposide (103 patients) or that regimen plus bevacizumab (101 patients). The study was conducted at 29 Italian centers, and there was a median follow-up of 34.9 months; the results were published online ahead of print in the *Journal of Clinical Oncology*.

The median PFS was 6.7 months with bevacizumab and 5.7 months without it, for a hazard ratio (HR) of 0.72 (95% CI, 0.54–0.97; *P* = .030). The difference in median OS, however, was not significant, at 9.8 months and 8.9 months, respectively, for an HR of 0.78 (95% CI, 0.58–1.06; *P* = .113). The response rate with bevacizumab was 58.4%, compared with 55.3% without it, for an odds ratio of 1.13 (95% CI, 0.65–1.97; *P* = .657).

Among 96 eligible bevacizumab patients, 41 continued on with bevacizumab maintenance therapy for a median of 4 cycles. The study found a significant effect of the maintenance therapy on OS, with an HR of 0.60 (95% CI, 0.40–0.91; likelihood ratio test, *P* = .011); there was “only a borderline effect,” however, on PFS, with an HR of 0.72 (95% CI, 0.48–1.07; likelihood ratio test, *P* = .095).

A subgroup analysis revealed that bevacizumab’s effect was dependent on gender. The addition of the agent led to an HR for survival in men of 0.55 and possibly to a detrimental effect in women, with an HR of 1.55 (interaction test, *P* = .003).

There were more grade 3–5 adverse events in the cisplatin/etoposide group (62.1%) than with bevacizumab (54.7%), but this did not reach significance (*P* = .291). More patients receiving bevacizumab (14.7% vs 6.8%) required treatment interruption. There were no differences with regard to hematologic toxicity; grade 3 or 4 hypertension was more common with bevacizumab (6.3% vs 1%; *P* = .57).

“The results of our trial, together with the available knowledge in this field, overall support the conclusion that combining bevacizumab with standard platinum plus etoposide chemotherapy does not lead to meaningful survival improvement in extensive-disease SCLC,” the authors concluded. The PFS improvement, however, suggests further studies with other antiangiogenic agents is warranted in this malignancy, especially in the maintenance setting.