Medical Xpress

Study examines drug regimen for the treatment of non-small cell lung cancer among older patients

April 17 2012

Analysis of a drug regimen approved by the F.D.A. in 2006 for the treatment of non-small cell lung cancer (bevacizumab added to the standard chemotherapy regimen carboplatin and paclitaxel) finds Medicare insured patients age 65 years and older who received this regimen did not have improved survival compared to patients who received the standard treatment of carboplatin and paclitaxel alone, according to a study in the April 18 issue of *JAMA*, a theme issue on comparative effectiveness research.

Deborah Schrag, M.D., M.P.H., of the Dana-Farber Cancer Institute, Boston, presented the findings of the study at a *JAMA* media briefing at the National Press Club.

"A previous randomized trial demonstrated that adding bevacizumab to carboplatin and paclitaxel improved survival in advanced non-small cell lung cancer (NSCLC). However, longer survival was not observed in the subgroup of patients aged 65 years or older, " according to background information in the article. "Notwithstanding the uncertainty about benefits in the population aged 65 years or older, the Centers for Medicare & Medicaid Services (CMS) has covered bevacizumab therapy for its enrollees subsequent to Food and Drug Administration [FDA] approval. Little is known about how clinicians have interpreted efficacy studies to formulate treatment recommendations, and given that approximately two-thirds of patients with lung cancer receive their

diagnoses at age 65 years or older, establishing the survival advantage of bevacizumab in the Medicare population is a priority for informed decision making."

Dr. Schrag and colleagues conducted a study to examine whether adding bevacizumab to carboplatin-paclitaxel was associated with improved survival in the Medicare population. The researchers used analytic strategies to address confounding (factors that can influence outcomes) and selection bias caused by the lack of treatment randomization in observational studies that may limit the ability to make valid inferences about causality. The study included 4,168 Medicare beneficiaries ages 65 years or older with advanced (stage IIIB or stage IV) non-squamous cell NSCLC diagnosed in 2002-2007. Patients were categorized into 3 cohorts based on diagnosis year and type of initial chemotherapy administered within 4 months of diagnosis: (1) diagnosis in 2006-2007 and bevacizumab-carboplatin-paclitaxel therapy; (2) diagnosis in 2006-2007 and carboplatin-paclitaxel therapy; or (3) diagnosis in 2002-2005 and carboplatin-paclitaxel therapy. The associations between carboplatin-paclitaxel with vs. without bevacizumab and overall survival were compared using various models and analyses.

The researchers found that the median (midpoint) overall survival was 9.7 months for patients receiving the bevacizumab combination compared with 8.9 months for those receiving carboplatin-paclitaxel in 2006-2007, and 8.0 months for those receiving carboplatin-paclitaxel in 2002-2005. The 1-year survival probabilities were 39.6 percent for bevacizumab-carboplatin-paclitaxel vs. 40.1 percent for carboplatin-paclitaxel in 2006-2007 and 35.6 percent for carboplatin-paclitaxel in 2002-2005. Controlling for demographic and clinical characteristics in adjusted models, the authors did not find a significant difference in overall survival between patients treated with bevacizumab and those treated only with carboplatin-paclitaxel in either 2006-2007 or 2002-2005.

None of the 4 propensity score-adjusted models demonstrated any evidence to support the superiority of bevacizumab-carboplatin-paclitaxel to carboplatin-paclitaxel. Also, neither subgroup nor sensitivity analyses changed their finding that bevacizumab was not associated with a survival advantage.

"In the future, for malignancies like NSCLC that disproportionately affect elderly patients or where the CMS covers a large proportion of treatment costs, negotiations with pharmaceutical sponsors of pivotal trials might mandate adequate representation of elderly patients and/or preplanned subgroup analyses relevant to the Medicare population. Absent this information, clinicians will need to rely on efficacy data from subgroup analysis of randomized trials, observational data such as this report, and their clinical judgment to make treatment recommendations. Given that neither subgroup analyses from efficacy studies nor observational data analyses identify a benefit for adding bevacizumab to standard carboplatin-paclitaxel therapy, bevacizumab should not be considered standard of care in this context. Clinicians should exercise caution in making treatment recommendations and should use bevacizumab judiciously for their older patients," the authors conclude.

More information: *JAMA*. 2012;307[15]:1593-1601.

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