Impact of adding bevacizumab to presurgery chemo for triple-negative breast cancer varies with subtype

December 12 2014

Among women with triple-negative breast cancer, the benefit of adding bevacizumab to standard presurgery chemotherapy was greater for those whose cancers were classified as basal-like by gene expression assay compared with those whose cancers were nonbasal-like, according to data presented at the 2014 San Antonio Breast Cancer Symposium, held Dec. 9–13. In contrast, the benefit of adding carboplatin was equivalent across subtypes.

"We found that adding bevacizumab to standard preoperative, or neoadjuvant, chemotherapy increased pathologic complete response rates for women with basal-like cancers—that is, it increased the proportion of women who had no residual cancer detected at surgery—but decreased pathologic complete response rates for women with nonbasal-like cancers," said William M. Sikov, MD, associate director of clinical research for the Program in Women's Oncology at Women and Infants Hospital and associate professor of medicine at the Alpert Medical School of Brown University in Providence, Rhode Island.

Among patients with basal-like disease, adding bevacizumab to standard neoadjuvant chemotherapy increased the pathologic complete response rate from 45 percent to 64 percent. Among those with nonbasal-like disease it decreased the rate from 60 percent to 43 percent.

"In contrast, adding the chemotherapy drug carboplatin to standard neoadjuvant chemotherapy increased pathologic complete response rates equally for women with basal-like and nonbasal-like cancers," said Sikov.

"While these are interesting observations, I don't think that our data will change clinical practice, for two reasons," continued Sikov. "First, we observed a much lower percentage of nonbasal-like triple-negative cancers [13 percent] than we had anticipated based on prior reports. Second, while subtype [basal-like vs. other] may be predictive of response with the addition of bevacizumab, interest in the use of this agent in early-stage triple-negative breast cancer has diminished following disappointing results from a number of phase III studies.

"On the other hand, subtype was not predictive of response with the addition of carboplatin, for which long-term outcomes are not known," added Sikov. "Thus, identification of the relatively small proportion of triple-negative breast cancer patients whose cancers are not basal-like by gene expression array would not appear to be helpful in deciding on the appropriate neoadjuvant treatment regimen.

"We don't understand the reasons for the difference in benefit from bevacizumab experienced by patients with basal-like and nonbasal-like disease," continued Sikov. "With low numbers of triple-negative breast cancer patients with nonbasal-like disease it will be hard to study this."

Sikov and colleagues reported last year that, in a randomized, phase II clinical trial called CALGB/Alliance 40603, adding either bevacizumab or carboplatin to standard neoadjuvant chemotherapy increased pathologic complete response rates for women with triple-negative breast cancer. These latest results are further analysis of data from this clinical trial, in which 443 patients with operable, stage 2 or 3 triple-negative breast cancer were enrolled.

Pretreatment tumor samples from 360 patients for whom pathologic complete response information was available were classified as basal-like or nonbasal-like following mRNA sequencing analysis and comparison of gene expression patterns to a standard panel from The Cancer Genome Atlas. Three hundred and thirteen were classified as basal-like; the other 47 were a mix of subtypes: 25 were normal-like, 14 were HER2-enriched, seven were claudin-low, and one was luminal A.

"We have also looked at expression of various gene signatures in the pretreatment tissue samples to determine if these are predictive of response and increased benefit from the addition of bevacizumab or carboplatin," said Sikov. "Of particular interest is the observation that gene signatures indicating high proliferation rates and low estrogen-receptor signaling, which are both considered characteristics of more aggressive disease, were associated with higher pathologic complete response rates overall and with increased benefit from adding bevacizumab. Many additional correlative studies are now being performed using tissue and blood samples obtained from the patients treated on this study."

Provided by American Association for Cancer Research