Pathologic complete response to presurgery chemo improves survival for patients with TNBC

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Patients with stage 2 or stage 3 triple-negative breast cancer (TNBC) who had a pathologic complete response (pCR) after presurgery chemotherapy had increased event-free and overall survival compared with those who had more than minimal residual invasive disease at surgery following presurgery chemotherapy, according to results from the randomized phase II CALGB/Alliance 40603 clinical trial presented at the 2015 San Antonio Breast Cancer Symposium, held Dec. 8-12.

Many patients with TNBC, especially those with breast tumors larger than 2 cm or evidence that the cancer has spread to lymph nodes in the axilla (underarm), receive chemotherapy before surgery, a treatment approach called neoadjuvant chemotherapy. Previously published results from the CALGB/Alliance 40603 clinical trial showed that adding carboplatin or bevacizumab to standard neoadjuvant chemotherapy increased the number of patients with stage 2 or stage 3 TNBC who had a pCR, meaning that they had no residual invasive cancer detectable in breast tissue and lymph nodes removed during surgery, explained William Sikov, MD, associate director of clinical research in the Program in Women's Oncology at Women and Infants Hospital of Rhode Island, and associate professor of medicine and obstetrics and gynecology at the Warren Alpert Medical School of Brown University in Providence, Rhode Island.

"Our new data show that patients on any arm of this study who had a

pCR had far superior outcomes compared with those who did not have a pCR," said Sikov. "After three years of follow-up, only 9 percent of patients who had a pCR had developed a distant recurrence and only 6 percent had died, compared to 27 percent and 25 percent, respectively, of patients who did not have a pCR.

"While this is important, our study was not sufficiently large to have the statistical power to determine whether adding carboplatin or bevacizumab to standard neoadjuvant chemotherapy improved event-free and overall survival," continued Sikov. "On the basis of these results, at the present time, neither carboplatin nor bevacizumab should be considered part of the standard neoadjuvant chemotherapy regimen for stage 2 or 3 TNBC."

The CALGB/Alliance 40603 clinical trial enrolled 443 patients with operable stage 2 or 3 TNBC. Patients were randomly assigned to standard neoadjuvant chemotherapy, standard neoadjuvant chemotherapy plus carboplatin, standard neoadjuvant chemotherapy plus bevacizumab, or standard neoadjuvant chemotherapy plus carboplatin and bevacizumab. Surgery was performed from four to eight weeks after the completion of neoadjuvant treatment.

Sikov and colleagues found that, at three years after starting the study treatment, patients who had no residual invasive cancer detected in either breast tissue or lymph nodes had a 70 percent reduced risk of disease recurrence and an 80 percent reduced risk of death compared with those who did not have a pCR in both the breast and lymph nodes. Including in the analysis both patients with minimal residual invasive disease in either the breast or lymph nodes, as defined by the Residual Cancer Burden method, and those who achieved a pCR in both the breast and lymph nodes, did not significantly alter outcomes: Risk of disease recurrence was reduced by 71 percent and risk of death was reduced by 79 percent.

No significant differences in event-free and overall survival were observed when the researchers evaluated whether adding carboplatin or bevacizumab to standard neoadjuvant chemotherapy affected these outcomes.

"In regards to the question as to whether there is a benefit to adding either carboplatin or bevacizumab to standard chemotherapy for stage 2 or 3 TNBC, it is important to highlight that this is not a negative study," said Sikov. "Rather, it is underpowered, meaning that it was not designed to be large enough to prove or disprove a benefit for either agent. Our results need to be considered alongside data from prior and ongoing studies with these agents in TNBC. Going forward, the question is whether we want to commit the additional patients and resources necessary to answer this question or instead focus our research efforts in TNBC on other opportunities to improve outcomes."

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