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Adding Veliparib to chemotherapy improved response rates among patients with BRCA-mutant breast cancer

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Adding the investigational poly(ADP-ribose) polymerase (PARP) inhibitor veliparib to carboplatin and paclitaxel chemotherapy improved the overall response rate without increasing adverse events among patients who had locally recurrent or metastatic breast cancer with BRCA1 or BRCA2 mutations, according to data from a phase II clinical trial presented at the 2016 San Antonio Breast Cancer Symposium, held Dec. 6–10.

"People who inherit mutations in BRCA1 or BRCA2 are at increased risk of developing various malignancies, including breast cancer and ovarian cancer," said Heather S. Han, MD, associate member at the Moffitt Cancer Center in Tampa, Florida. "Cancer cells that harbor BRCA1 or BRCA2 mutations have a decreased ability to repair DNA. Preclinical studies have shown that blocking a second DNA repair pathway in BRCA-mutant cancer cells using a PARP inhibitor makes the cells more susceptible to the effects of chemotherapeutics such as carboplatin.

"We were pleased to see that adding veliparib to chemotherapy significantly improved the overall response rate among patients with BRCA-mutant breast cancer and did not increase adverse events," continued Han. "Although the improvements in progression-free and overall survival were not statistically significant, the study supports further investigation of veliparib in combination with chemotherapy as a

potential treatment for this group of patients. The ongoing phase III BROCADE 3 clinical trial will provide more definitive answers as to whether this PARP inhibitor should become part of routine clinical care."

In the phase II trial, the researchers randomized 290 patients with BRCA1 or BRCA2 mutation to three arms: 97 were randomized to veliparib plus carboplatin and paclitaxel, 99 to placebo plus carboplatin and paclitaxel, and 94 to veliparib plus temozolomide. Here, Han and colleagues report the findings from the carboplatin and paclitaxel with veliparib or placebo arms. More than 50 percent of the patients in these arms of the trial had hormone receptor–positive breast cancer, about 40 percent had triple-negative breast cancer, and a few had HER2-positive breast cancer. Disease characteristics were balanced between the two arms.

Patients assigned placebo, carboplatin, and paclitaxel received a median of 10 cycles of treatment. Those assigned veliparib, carboplatin, and paclitaxel received a median of 12 treatment cycles.

The overall response rate for the veliparib arm was 77.8 percent compared with 61.3 percent for the placebo arm. The improvement in progression-free survival in the veliparib arm (14.1 months versus 12.3 months) was not statistically significant. The trend to improved overall survival was also not statistically significant (28.3 months versus 25.9 months).

There was no significant increase in toxicity with the addition of veliparib. The most common grade 3 or higher adverse events were neutropenia, which was seen in 55 percent of patients assigned placebo compared with 56 percent of patients assigned veliparib; and thrombocytopenia, which was seen in 26 percent of patients assigned placebo compared with 31 percent of patients assigned veliparib.

Han explained that the main limitation of the study was that the number of patients was not sufficient to power the study to detect nondramatic improvements in progression-free survival. However, she noted that an ongoing phase III study will have the power to address this issue.

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