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Study results offer another boon for PARP inhibitors in treatment of advanced breast cancer

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Patients with certain advanced hereditary breast cancers may have new treatments options on the horizon, according to two studies presented this week at the annual San Antonio Breast Cancer Symposium. Susan Domchek, MD, executive director of the Basser Center for BRCA at Penn's Abramson Cancer Center, will present new results from the Mediola and OlympiAD trials showing continued success of treating BRCA-related metastatic breast cancer with the PARP inhibitor olaparib with limited side effects for patients.

Immunotherapy & PARP Combo Exceeds Disease Control Expectations (PD6-11)

Results of the phase II multicenter Mediola study show that twenty of 25 patients with BRCA-related metastatic breast cancer had disease control 12 weeks after treatment with the combination of olaparib and the immunotherapy drug durvalumab. Results of this study will be presented during Poster Discussion: Immuno Oncology on Thursday, December 7, 2017 at 5:00 p.m. CT/6:00 p.m. ET.

In the study, patients whose disease had not responded to prior therapies were treated with olaparib for four weeks followed by the combination of the PARP inhibitor olaparib and durvalumab until such time as their disease progressed. Tumors were measured and assessed at four weeks and every eight weeks thereafter. Researchers sought to determine

disease control at 12 weeks, as well as the safety and tolerability of the combination. At 28 weeks post-treatment, a secondary measure of the study, 12 of the patients still had disease control.

Overall, the data presented shows that when added to olaparib, durvalumab is well tolerated and the combination, which reached its target 12-week disease control rate, is effective. Researchers say the treatment combinations of targeted and immune therapies are promising and warrant further investigation.

"BRCA-related cancers are notoriously aggressive and difficult to treat, leaving patients with a limited number of treatment options," said Domchek, lead author of the study. "We've gained a lot more insights about how PARP inhibitors work over the years, and are now able to put that knowledge into practice, leveraging our advances with PARP inhibitors to develop new therapies in combination with the rapidly evolving field of cancer immunotherapy."

Though promising, the authors say the limited trial size warrants further investigation to successfully assess the hypothesis that olaparib increases tumor-infiltrating lymphocytes (TILs) in the body; patients with tumors that contain increased numbers of TILs generally survive longer than those with tumors without TILs. Further analysis is ongoing, including immune-related gene expression profiling, genomic sequencing, and T-cell receptor analysis.

PARP Inhibitor Produces Fewer Serious Side Effects for Patients with Advanced Breast Cancer (P5-21-12)

Earlier this year, results of the Phase III OlympiAD trial showed for the first time that olaparib is superior to chemotherapy for tumor control in patients with BRCA-related advanced breast cancer. Now, new results

from the trial detail the side effects seen and demonstrate that olaparib well tolerated by patients and produces fewer side effects compared to chemotherapy in addition to being effective for treatment. Results of the study will be presented during Poster Session 5: Treatment: Advanced therapy - targeted, on Friday, December 8, 2017, at 5:00 p.m. CT/6:00 p.m. ET.

In the study, researchers randomized 302 patients who had metastatic breast cancer to either take 300 mg olaparib twice a day or receive standard chemotherapy until the cancer worsened or the patient developed severe side effects. All of the women had HER2-negative germline BRCA1 or BRCA2-mutated breast cancer and had up to two prior rounds of chemotherapy for their breast cancer.

Building on the trial's initial findings which showed that tumors shrank in about 60 percent of patients who received olaparib, compared with 29 percent of those who received chemotherapy, the new results show that patients taking olaparib were 15 percent less likely to experience serious episodes of side effects such as significant nausea, vomiting, and diarrhea, than patients who received chemotherapy (36.6 percent vs. 50.5 percent, respectively). Notably, of the patients taking olaparib, there were no reported incidents of severe nausea or vomiting. Anemia was experienced more frequently by patients taking olaparib, but rarely led to the need to stop treatment.

"These results show that not only is the PARP inhibitor more effective than standard chemotherapy - which we saw earlier this year - but that patients also tolerate it better, which speaks to their quality of life during treatment," said Domchek. "These patients have particularly aggressive cancers that are difficult to treat. If we can provide a treatment option that gives them a chance to fight their disease and avoid serious side effects so they can continue living their lives, it's another boon to olaparib's advantages over standard chemotherapy."