

Olaparib and PI3K inhibitor BKM120 combination active against ovarian and breast cancer subtypes

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Combination treatment with the poly ADP-ribose polymerase (PARP) inhibitor olaparib and the investigational phosphatidylinositol-3-kinase (PI3K) inhibitor BKM120 was safe and yielded evidence of clinical benefit for women with triple-negative breast cancer and for those with high-grade serous ovarian cancer, according to data from a phase I clinical trial presented at the AACR Annual Meeting 2015, held April 18-22.

"Several years ago, my colleagues on the Stand Up To Cancer [SU2C] Targeting the PI3K Pathway in Women's Cancers Dream Team found that olaparib and BKM120 were more effective in mouse models of BRCA-mutant breast cancer and BRCA-wildtype [triple-negative breast cancer](#) than either drug alone," said Ursula A. Matulonis, MD, director and program leader of Medical Gynecologic Oncology in the Susan F. Smith Center for Women's Cancers at the Dana-Farber Cancer Institute in Boston. "Using SU2C funding, we then initiated this clinical trial to test whether the preclinical data would hold true in patients.

"We are reassured that it is possible to combine olaparib and BKM120 and that we have seen responses in women with triple-negative breast cancer as well as in women with high-grade serous [ovarian cancer](#)," continued Matulonis who is also an associate professor of medicine at Harvard Medical School.

In the olaparib/BKM120 dose escalation phase of the clinical trial, Matulonis and colleagues have enrolled 46 patients, 12 with breast cancer and 34 with ovarian cancer. Among these patients, 35 were known to have germline BRCA gene mutations. They then enrolled patients with [breast cancer](#) and ovarian cancer in the dose expansion phase of the trial after the maximally tolerated dose had been determined.

According to Matulonis, 10 different dose level combinations of olaparib and BKM120 were tested and the maximum tolerated dose was found to be 50 milligrams once per day of BKM120 plus 300 milligrams twice per day of olaparib. The dose-limiting toxicities of a grade three depression in one patient and a grade four liver function test in another patient were concerning, Matulonis explained, and meant the researchers were able to escalate BKM120 doses to only half of the single-agent dose.

"It is important that we saw responses against both BRCA-mutant and BRCA-wildtype cancers," said Matulonis. "We need to do further analysis to identify biomarkers that we can use to more effectively identify the patient population that will be most positively affected by the olaparib/BKM120 combination."

Provided by American Association for Cancer Research

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