Drug combination boost PARP inhibitor response in resistant ovarian cancer

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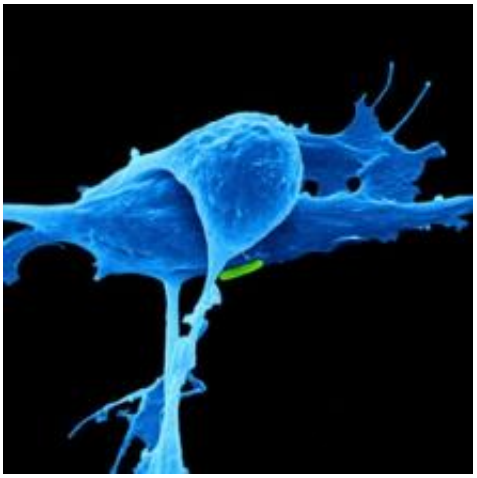

About one-third of patients with ovarian cancer who wouldn't be expected to respond to a PARP inhibitor had partial shrinkage of their tumor when a kinase inhibitor was added to treatment, report scientists from Dana-Farber Cancer Institute.

"When we combined the two drugs, we obtained a very good response rate - as high as 36 percent in patients with ovarian cancer that was resistant to platinum-based chemotherapy," said Panagiotis Konstantinopoulos, MD, PhD, who presented the findings during a clinical trials mini-symposium on Sunday, April 2, 2017 at 3:00 p.m., at the annual meeting of the American Association for Cancer Research

(AACR).

Twenty-eight patients with high-grade serous ovarian cancer received olaparib, a PARP inhibitor, along with an investigational alpha-specific PI3-Kinase inhibitor, BYL719, in the phase I trial. Twenty-six of the 28 had platinum-resistant cancer. In such patients, response to a PARP inhibitor itself is as low as 4 percent, said Konstantinopoulos, a medical oncologist with the Susan F. Smith Center for Women's Cancers at Dana-Farber.

In pre-clinical studies, adding a PI3K inhibitor appeared to sensitize the cancer cells to the effects of the PARP inhibitor, which impairs tumor cells' ability to repair DNA damage. The median duration of the response in the ovarian cancer patients was about 5.5 months, which is "a good duration of response in this patient population," said Konstantinopoulos. Five patients remained on treatment at the time of the presentation.

Olaparib is approved for treatment of platinum-resistant ovarian cancer in women with germline BRCA mutation. However, in the current trial, the response rate was 29 percent in women without germline BRCA mutations - not much lower than the rate of 33 percent in patients without the inherited BRCA mutations.

Overall, the combination was well tolerated, according to the report: Four patients discontinued therapy because of toxicity.

"The activity of this combination in ovarian cancer patients without germline BRCA mutations and with platinum-resistant disease was higher than expected from olaparib monotherapy and warrants further investigation," said Konstantinopoulos.

Medical Xpress

Provided by Dana-Farber Cancer Institute

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