

Some patients with incurable tumors and BRCA mutations respond to new two-drug combination

April 7 2013, by Richard Saltus

A novel combination of two drugs has shown anti-cancer activity in patients who had incurable solid tumors and carried a germline mutation in their BRCA genes, Dana-Farber Cancer Institute researchers are reporting at the American Association for Cancer Research annual meeting in Washington, April 6-10.

The two oral drugs, sapacitabine and seliciclib, were given sequentially in a phase 1 clinical trial that is mainly enrolling [patients](#) whose tumors lack BRCA function because of an inherited mutation.

"We have seen several responses among these patients, as well as instances of prolonged stable disease lasting more than a year," said Geoffrey Shapiro, MD, PhD, director of Dana-Farber's Early Drug Development Center (EDDC). As a result, he said that a BRCA mutation may be a potential biomarker that identifies patients who are more likely to respond to the drug combination.

Sixteen patients enrolled in the trial carried an inherited BRCA mutation. Four of these patients had partial responses – a 30 percent or greater shrinkage of tumor mass – including one with pancreatic, two with breast, and one with [ovarian cancer](#). Three patients were continuing to have a partial response at the time of presentation of the data, with the longest lasting more than 78 weeks. Two additional BRCA mutation carriers, with breast and ovarian cancer, experienced stable disease for

21 and 64 weeks, respectively. Of the remaining 22 patients enrolled in the trial, six experienced stable disease for 12 weeks or more.

Sapacitabine is toxic to [cancer cells](#) by causing damage to their DNA, which, if not repaired, causes the cells to self-destruct. The BRCA protein is essential for repair of the [DNA damage](#) caused by sapacitabine, so patients with [mutations](#) that inactivate BRCA may be more sensitive to the drug's activity.

The second drug, seliciclib, is an inhibitor of cyclin-dependent kinases (CDKs), enzymes that have multiple cellular functions, including a role in [DNA repair](#), further augmenting the effects of sapacitabine. The patients in the trial received sapacitabine twice daily for seven days, followed by seliciclib twice daily for three days. Adverse events were mild to moderate in intensity, the study found.

Shapiro and colleagues are continuing to enroll BRCA mutation carriers in the trial, and hope to determine if the mutations may serve as a biomarker for response. He said that these drugs may prove to be an important treatment alternative for patients with BRCA-deficient cancers.

Provided by Dana-Farber Cancer Institute

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