DNA repair pathway score for predicting chemotherapy response in ovarian cancer patients

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A DNA repair pathway-focused score has the potential to help determine if first-line platinum based chemotherapy can benefit advanced-stage ovarian cancer patients, according to a study published April 13 in the *Journal of the National Cancer Institute*.

Most ovarian cancer patients are diagnosed with advanced disease (stages III and IV). They undergo surgery to remove as much tumor as possible, and then undergo platinum-based chemotherapy. But tools to predict response to platinum-based chemotherapy in ovarian cancer patients have been inadequate.

In order to determine if a DNA repair pathway-focused score could help predict outcomes for ovarian cancer patients treated with platinum-based chemotherapy, Josephine Kang, M.D., Ph.D., of the Department of Radiation Oncology at Dana Farber Cancer Institute, and colleagues gathered gene expression data from The Cancer Genome Atlas (TCGA) database for patients with advanced stage ovarian cancer, and established a molecular score by looking at the genes involved in platinum-induced DNA damage repair pathways. The patients were placed either into low or high score categories, and the prognostic value of the score for overall survival, recurrence free survival, and progression-free survival was assessed.

The researchers found that patients with high scores showed a

statistically significant improved overall survival compared to the patients with low scores. These patients' score was positively correlated with complete response rate, recurrence-free survival, and progression-free survival. The researchers also found that the patients' scores outperformed other known clinical factors in predicting overall survival in the TCGA dataset as well as in two additional validation sets. "Developing the ability to predict OS and outcomes to chemotherapy using prognostic markers such as the score is critical, particular in ovarian cancer, because there are presently no other good clinical measures to predict response to standard platinum-based chemotherapy," the authors write.

They also note the study's limitations, namely that the score has not yet been tested prospectively in a clinical trial, although they do believe it is ready for testing. "With additional prospective validation in clinical trials, we hope that the score can become a powerful tool that is useful in stratifying advanced-stage ovarian cancer patients toward optimal treatments incorporating new treatment regimens vs. current standard of care," the authors write.

In an accompanying editorial, Elizabeth M. Swisher, M.D., of the Department of Obstetrics and Gynecology at the University of Washington agrees that the score was not adequately validated and is not ready for clinical application. She writes that the study is an important effort, while adding that the "premature application of inadequately validated biomarkers may adversely impact the successful implementation of individualized therapies."

Provided by Journal of the National Cancer Institute

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