New treatment regimen shows clinical benefit in advanced colon cancer

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A new treatment regimen for patients with metastatic colon cancer appears to offer clinical benefit even when used after multiple other treatments have failed, say research physicians at Georgetown Lombardi Comprehensive Cancer Center, a part of Georgetown University Medical Center.

The research team found that combining a PARP inhibitor with chemotherapy (temozolomide) offers significant benefit in patients who had no further treatment options. However, the study is small, and does not include a comparison arm, so further investigation is needed, they add. The study will be presented in an oral session on Saturday, June 4th, at the 2011 annual meeting of the American Society of Clinical Oncology in Chicago.

PARP, short for "poly (ADP-ribose) polymerase" is a key part of a cell's DNA repair apparatus, and is important for protecting our normal cells against DNA damage. However, cancer cells become resistant to chemotherapy in part by increasing PARP expression and thus rapidly repairing DNA damage intentionally caused by chemotherapy. PARP inhibitors are designed to overcome a cancer cell's ability to repair the damaged DNA. (They are showing promise in both breast and ovarian cancers, and are being studied in a variety of other cancer types).

In this clinical study, doctors administered a potent DNA-damaging chemotherapy, temozolomide, with a PARP inhibitor called ABT-888. The theory is that ABT-888 will diminish the ability of these cancer cells

to fix the damage that was just inflicted by the temozolomide, pushing the cancer into a death spiral.

"This is a classic one-two punch: the chemotherapy damages the cancer cells and the PARP inhibitor prevents it from fixing itself, leaving the cell to die," says lead author, Michael Pishvaian, M.D., Ph.D., an assistant professor at Georgetown Lombardi.

This single-arm, phase II study enrolled 49 patients with metastatic disease who were not eligible for surgery and had exhausted all of the standard therapies currently used. Despite having advanced cancer, all study participants were still active at work or home. Researchers found the drug combination controlled cancer growth for nearly six months in 23 percent of the patients, with two patients having a significant reduction in their tumor burden (partial response).

Pishvaian explains, "The treatment was extremely well tolerated, so to have a period of six months with no tumor growth, but also no significant side effects was really meaningful for the patients."

In addition, researchers were able to collect samples of the patients' tumors for further molecular analysis. "By testing tissue samples and identifying their molecular fingerprints, perhaps we can identify which patient subgroups are most likely to respond to this new therapeutic combination," concludes Pishvaian.

Provided by Georgetown University Medical Center