Immune therapy tested in study of women with triple-negative breast cancer

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Early data in a preliminary human study show that an experimental immune system drug is generally safe and well tolerated in women with metastatic, triple-negative breast cancer, a persistently difficult form of the disease to treat.

Results of the early-phase clinical trial of the therapy, called MPDL3280A, which aims to restore the immune system's ability to recognize and attack cancer cells, are expected to be presented at the American Association for Cancer Research's 2015 Annual Meeting in Philadelphia from April 18-22. Triple-negative breast cancer cells lack expression of estrogen receptor, progesterone receptor and HER2 protein, the established targets for breast cancer therapies.

The small study was conducted on 54 patients treated at the Johns Hopkins Kimmel Cancer Center and several other institutions.

"Early data in this trial show that the drug is generally safe and well-tolerated, and it appears to be able to control disease in some of these patients," says Leisha Emens, M.D., Ph.D., an associate professor of oncology at the Johns Hopkins University School of Medicine. "Now we'll need to test it further in more patients and compare it with standard therapies to establish its therapeutic value."

Specifically, the researchers say the drug is designed to disrupt a pathway that hides tumor cells from immune system cells capable of attacking cancer cells. Among the components of the pathway are two

proteins called programmed death-1 (PD-1), expressed on the surface of immune cells, and programmed death ligand-1 (PD-L1), expressed on cancer cells and some immune cells. When the two proteins bind together, the biochemical pairing decreases the activity of the immune system, disarming its ability to attack cancer cells. Cancer is characterized by cells that get around the normal cell death process that is programmed into living cells. MPDL3280A binds to the PD-L1 protein and disrupts the connection with PD-1 proteins on immune cells.

Of the 54 patients with triple-negative breast cancer evaluated, 37 had evidence of PD-L1 proteins on at least 5 percent of immune cells found within samples of the patients' tumors. Most of the patients in the trial experienced at least one low-grade side effect, such as nausea, diarrhea, fatigue, fever and decreased appetite. Six patients experienced more severe side effects, including vomiting, anemia and low white cell counts. No deaths among the patients have been connected to side effects of the drug thus far, the researchers say, although two deaths in the group are being evaluated.

Of the 37 PD-L1-positive patients, 21 underwent evaluation to assess the possible impact of the drug on disease control. Six patients survived at least 24 weeks without progression of their breast cancer, a finding not typical of most patients with metastatic, triple-negative disease, according to Emens. Two of those patients had complete responses, indicating their tumors shrunk completely, and another two had partial responses. Patients in the trial have been followed for an average of 40 weeks.

"Identifying a way to predict ahead of treatment which patients are more likely to respond is also important. There are ongoing efforts to identify biomarkers for cancer patients who are more likely to respond to this therapy," says Emens.

Patients with triple-negative breast cancer generally have worse prognosis than other breast cancer patients, according to Emens. Besides surgery and radiation, drug treatments have been limited to standard chemotherapy agents.

The investigators say they chose to test this type of immunotherapy in this patient group because other studies have shown that patients' triple-negative breast tumors may contain more PD-L1 proteins and certain cancer-fighting immune cells within them than other breast cancer subtypes. Triple-negative breast cancers also mutate at a higher rate than other cancers, she says, which increases the likelihood that cancer cells will create abnormal proteins foreign to the immune system and raise the alarm for destruction by the immune system.

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