Study shows new paradigm in breast cancer research

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The first investigator results from an unprecedented nationwide effort to test promising new breast cancer drugs before the tumor is removed were presented during the 2013 San Antonio Breast Cancer Symposium.

The research initiative, called I-SPY 2, employs an innovative clinical trial design in the curative setting that is enabling researchers to quickly drop drugs and drug combinations that don't work, while fast-tracking effective regimens for further study.

The first drug to graduate out of this innovative research design is veliparib, which was added to standard chemotherapy (carboplatin and paclitaxel) given to women with high-risk breast cancer. Kathy Albain, MD, of Loyola University Medical Center, is among the co-authors of the trial, and Loyola enrolled patients in the trial.

In a traditional clinical trial of treatment after definitive breast cancer surgery, the veliparib/carboplatin/paclitaxel regimen would have been tested on a very large and broad population of high-risk patients whose tumors are designated HER2-. (In a HER2- tumor, the cancer cells do not have a surface receptor protein known as HER2—Human Epidermal growth factor Receptor 2.)

In I-SPY 2, women received the veliparib/carboplatin/paclitaxel combination prior to surgery, and response rates to the drugs were determined by examining tumor specimens removed during surgery. Researchers then used a statistical model to predict which subset of

patients would most likely benefit in a follow-up small Phase 3 clinical trial. In this way, new drugs can get to patients much faster than in the traditional approach.

In this trial, researchers estimated that the subset of patients with "triple negative" breast cancer had the greatest benefit from the addition of veliparib, as well as a 91 percent probability of success in the confirmatory small Phase 3 trial. (Triple negative means that neither HER2, estrogen or progesterone receptors are present on cancer cells.)

By comparison, there was only a 70 percent probability of success for all HER2- patients and only a 16 percent probability of success for HER2- patients whose cancer cells showed estrogen or progesterone.

Researchers concluded that the veliparib/carboplatin/paclitaxel regimen should be further tested in the confirmatory phase 3 trial, but only in patients with triple negative breast cancer. The innovative I SPY 2 design enabled researchers to make this recommendation based on a modest number of subjects – 72 patients who received veliparib/carboplatin/paclitaxel, and 62 patients who were randomly assigned to a control group without veliparib.

"I-SPY 2 is a new paradigm in breast cancer clinical trials," Albain said. "The veliparib/carboplatin/paclitaxel study is a great example of how I-SPY 2 can tell us, as rapidly as possible, which drugs work best on different types of tumors. This could prove to be an enormous benefit to patients, especially women with the most aggressive cancers."

Loyola is one of the I-SPY 2 site locations, and Albain is principal investigator at the Loyola site. Loyola also participated in an I-SPY 2 clinical trial of a second drug, neratinib, that also has graduated for further study.

Provided by Loyola University Health System