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I-SPY trial offers key insights into locally advanced breast cancer

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Scientists are reporting two findings that could influence the way researchers screen for, treat and assess prognosis for women with locally advanced breast cancer, an aggressive form of the disease. One finding offers a critical message regarding treatment strategy, they say.

"Women with locally advanced breast cancer and their clinicians need to be aware that a growing breast mass should not be ignored even if someone has had a recent normal mammogram," says Laura Esserman, MD, UCSF professor of surgery and radiology and director of the UCSF Carol Franc Buck Breast Care Center.

The findings emerged from I-SPY, a multi-center clinical trial designed to evaluate the impact of chemotherapy before surgery on patients with locally advanced breast cancer. Assessments in the trial focus on biological markers as predictors of pathological complete response and survival. Locally advanced breast cancer tumors develop in younger patients, have a worse prognosis and are large (min. 3 cm.).

The results were reported at the American Society of Clinical Oncology annual meeting on Saturday, May 30, 2009.

One study revealed that most locally advanced breast cancers are discovered in the interval between routine mammogram exams, which are conducted every one or two years. Of the women who were receiving regular screening mammograms, 83 percent had developed such so-called interval cancers.

"This finding suggests that the growth rate of locally advanced breast cancers precludes early detection by conventional screening," says the senior author of the study, Laura Esserman, MD, UCSF professor of surgery and radiology and director of the UCSF Carol Franc Buck Breast Care Center.

"We need to develop a better understanding of the molecular signatures of these tumors. Understanding their biology will be important for developing better strategies for prevention and early detection."

The study, led by Cheryl Lin, MD, postdoctoral research fellow in surgery, contains a critical message, says Esserman. "For these faster growing cancers, patients with' interval cancers' should explore the potential of standard chemotherapy and/or clinical studies that add novel agents in addition to standard therapy in advance of surgery (so called neoadjuvant chemotherapy), which is increasingly the standard of care in this set of patients, says Esserman.

In another report of the findings from the I SPY trial, scientists determined that the molecular profiles of locally advanced breast cancer tumors predicted the response of the tumors to chemotherapy drugs given in advance of surgery. The scientists identified one subset of patients who fared well regardless of how they responded to the chemotherapy treatment. The team also determined that in those patients with poor prognosis profiles response to the chemotherapy was a very good predictor of long term outcome.

"The study demonstrated that locally advanced breast cancers have aggressive biology," says first author Esserman. "Response to therapy and outcome can be predicted by many biomarkers. The I-SPY data set provides a platform to study marker signatures to tailor therapy and demonstrates the power of the neoadjuvant setting."

The response to therapy of the 216 patients examined was measured by serial magnetic resonance imaging, pathologic complete response and residual cancer burden. The study revealed that residual cancer burden was a more refined way to measure pathologic complete response .The study also revealed that magnetic resonance volume is highly predictive of pathologic complete response and residual cancer burden (reported in Sunday Poster Discussion (Local/Regional Breast Cancer).

I-SPY 1, the first phase of a longer term clinical study series, is a collaboration of numerous cancer centers nationwide, and the National Cancer Institute. The second phase, I-SPY 2, now in development, is a collaboration of the NIH Foundation, Food and Drug Administration, NCI, and pharmaceutical and biotechnology companies.

I-SPY 2 is designed to efficiently screen multiple novel agents to see if their addition to standard chemotherapy will improve outcomes. The trial will test a number of new concepts, including "adaptive design" in which drugs are assessed over the course of months - rather than decades - and the information used in real time to direct the course of a trial. It also will test the qualification of biomarkers to help accelerate the path to the identification and availability of successful tailored treatment options for women with locally advanced breast cancer..

The I-SPY series is designed to accelerate and improve the efficiency with which experimental breast cancer therapies are assessed. The goals are to establish a clinical trials model that supports the identification of drugs targeting the molecular profiles of aggressive breast cancers, and to reduce the duration of the drug-assessment process from the current 15 to 20 years down to a few years.

Source: University of California - San Francisco