Two groundbreaking studies reflect new paradigm in breast cancer research

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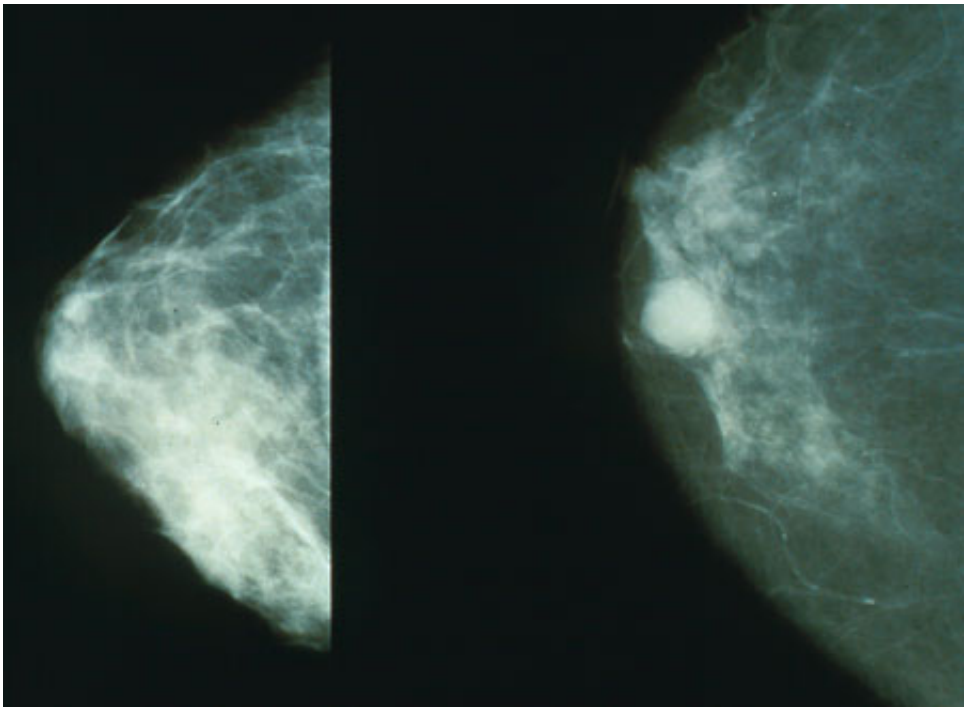

Mammograms showing a normal breast (left) and a breast with cancer (right). Credit: Public Domain

In a new paradigm of breast cancer research, physicians are fast-tracking promising new experimental drugs for further study, while immediately dropping drugs and drug combinations that don't work.

Loyola Medicine oncologist Kathy S. Albain, MD, FACP, FASCO is a co-author of two such studies, published in the July 7, 2016 *New*

England Journal of Medicine. The studies found that patients with specific subtypes of breast cancer, the drug neratinib and the drug combination veliparib plus carboplatin were more effective in eradicating tumors before surgery than standard chemotherapy alone.

The studies are part of a nationwide research initiative called I-SPY2. Dr. Albain is the principal investigator at Loyola, one of only two academic medical centers in Illinois participating in I-SPY2.

"I-SPY2 is employing an exciting new model for testing drugs," Dr. Albain said. "Trials have not been run this way before in breast cancer. Now we can determine much sooner which drugs are active, while minimizing patients' exposure to drugs that do not work - all as the trial progresses from day to day."

Dr. Albain, a professor in the department of medicine, division of hematology/oncology of Loyola University Chicago Stritch School of Medicine, is also a member of the national I-SPY2 New Agents Committee and the lead "chaperone" of another I-SPY2 study for the experimental drug trebananib.

I-SPY2 researchers use biomarker profiles of breast cancer cell genes to determine which investigational drug under study is most suited to a given patient's tumor profile.

"A patient's treatment is targeted, in real time, to the tumor's biology," Dr. Albain said. "I-SPY2 allows us to bring exciting new agents into the curative setting more quickly than the standard way of first testing them extensively in large, multi-year trials."

The I-SPY2 studies were conducted in patients before they underwent surgery. Such studies allow drugs to be tested in smaller trials, with faster results.

Researchers examined whether the experimental treatments resulted in complete eradication of tumors before surgery. Tumor eradication does not necessarily mean a patient is cured, and she still must undergo surgery. But women who do experience tumor eradication before surgery are less likely to relapse or die of breast cancer.

In one of the newly published I-SPY2 studies, researchers examined the drug neratinib, which was highly active in patients with a type of breast cancer known as HER2-positive, hormone-receptor-negative. Fifty-six percent of the patients who were treated with neratinib plus standard treatment experienced tumor eradication before surgery, compared with 33 percent of patients who received standard treatment alone.

The second trial involved patients who had a type of breast cancer called triple negative. Fifty-one percent of the women who received veliparib and carboplatin along with standard treatment experienced tumor eradication before surgery, compared with 26 percent of women who received standard treatment alone.

Based on these results, the experimental drugs are being fast-tracked to large-scale phase 3 trials.

In an accompanying perspective article, researchers from the Dana-Farber Cancer Institute and Harvard's school of public health, who were not involved in the trial, wrote that I-SPY2 is "an important addition to the inventory of trial designs." The perspective authors, David Harrington, PhD and Giovanni Parmigiani, PhD, concluded: "We applaud the use of I-SPY2 described here and urge continued innovation in trial design, especially in both earlier phase 1 and later phase 3 settings."

The studies are titled "Adaptive Randomization of Neratinib in Early Breast Cancer" and "Adaptive Randomization of Veliparib-Carboplatin

Treatment in Breast Cancer."

More information: John W. Park et al, Adaptive Randomization of Neratinib in Early Breast Cancer, *New England Journal of Medicine* (2016). DOI: 10.1056/NEJMoa1513750

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