# Breast Cancer Tumor Test Lets Many Women Avoid Chemotherapy

Genetic test can help guide decisions about treatment after surgery.

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A test that evaluates 21 tumor genes can show which women are at risk for cancer recurrence after surgery for early breast cancer and which ones can safely skip chemotherapy, according to a large study presented this week at the American Society of Clinical Oncology (ASCO) annual meeting in Chicago. Guided by the test, about 70 percent of women were able to avoid chemotherapy, and they had recurrence and survival rates similar to those of women who used it.

These findings "will transform care immediately, and for the better," said ASCO expert Harold Burstein, MD, PhD, of the Dana-Farber Cancer Institute in Boston. "Practically speaking, this means that thousands of women will be able to avoid chemotherapy, with all of its side effects, while still achieving excellent long-term outcomes."

Breast cancer is classified by the kind of receptors it expresses. A majority of breast cancers carry receptors for estrogen, known as ER-positive, and treatment usually includes hormone-blocking drugs. Other tumors express the HER2 (human epidermal growth factor receptor 2) receptor and can be treated with HER2 inhibitors like Herceptin (trastuzumab). Triple-negative breast cancer doesn't express any of these receptors and is hardest to treat.

About half of women diagnosed with breast cancer—or around 60,000 annually in the United States—have ER-positive, HER2-negative cancer that is confined to the breast. Of these, nearly a third may develop incurable recurrent cancer over 10 years, according to lead researcher Joseph Sparano, MD, of the Albert Einstein Cancer Center and Montefiore Health System in New York City.

Joseph Sparano, MDCourtesy of Albert Einstein College of Medicine

Women with this type of breast cancer usually undergo surgery to remove the tumor and receive drugs that block estrogen, which could promote the growth of any residual cancer cells.

Studies have shown that adding adjuvant (post-surgery preventive) chemotherapy can reduce the risk of recurrence by a small amount (around 3 to 5 percent). In 2000, the National Institutes of Health concluded that adjuvant chemotherapy should be recommended for the majority of women with localized breast cancer, regardless of lymph node, menopause or receptor status. But most women with this type of early breast cancer who receive chemotherapy never would have experienced disease progression without it and therefore needlessly suffer side effects from overtreatment.

The TAILORx study compared outcomes among women with early-stage ER-positive, HER2-negative breast cancer that was confined to the breast and had not spread to axillary (armpit) lymph nodes, with a tumor size of no more than 5 centimeters.

This federally funded Phase III prospective trial evaluated whether a test that predicts the likelihood of cancer recurrence could help women get the most appropriate treatment based on their risk category. This is an example of precision medicine, or individualized treatment—this year's ASCO conference theme.

After surgery, more than 10,000 women had their tumors evaluated using OncoType DX, a test that looks at the expression of 21 tumor genes. Prior studies of the test showed that cancer recurrence is rare with estrogen therapy alone if the recurrence score is low, and adding chemotherapy has a large benefit if the score is high. But it is less clear what to do about

midrange scores.

In TAILORx, low-risk women (recurrence scores of 0 to 10) received estrogen therapy alone, the high-risk group (scores of 26 to 100) received estrogen blockers plus chemotherapy and the midrange group (scores of 11 to 25)—which included two thirds of those tested—were randomly assigned to estrogen therapy with or without added chemotherapy. Participants had to be willing to let their treatment be guided by the test, so the study likely didn't include women with a strong preference for aggressive treatment.

The intermediate group included 6,711 women with a media age of 55; a third were under 50. A majority had a tumor size of 1 to 2 centimeters. For estrogen therapy, most women used aromatase inhibitors or tamoxifen. For chemotherapy, more than half used taxane drugs such as docetaxel while about a third used anthracycline drugs such as doxorubicin.

After nine years of follow-up, 83.3 percent of intermediate-risk women who received estrogen therapy alone and 84.3 of those who received estrogen therapy plus chemotherapy were still alive without distant recurrence, or metastasis, in other parts of the body; recurrence in the same breast or nearby lymph nodes; cancer in the opposite breast; or development of a new type of cancer.

The rates of survival without distant recurrence alone (about 95 percent) and overall survival (about 94 percent) were also about the same in the two treatment arms, Sparano reported.

In an exploratory analysis of the intermediate-risk group, the researchers found that women under 50 and those with recurrence scores of 16 to 25 appeared to get some benefit from adding chemotherapy.

Regarding the other risk groups, only 3 percent of women with low recurrence scores who received estrogen therapy alone developed unexpected distant recurrences. Conversely, 13 percent of those in the high-risk group experienced distance recurrence despite receiving both estrogen blockers and chemotherapy.

Looking at the impact on care, Sparano said the test enabled about 70 percent of women in the full study population to avoid chemotherapy, thus limiting this often poorly tolerated treatment to the 30 percent who will likely benefit from it.

"Any woman with early-stage breast cancer 75 years or younger should have the test and discuss the results of TAILORx with her doctor to guide her decision regarding chemotherapy after surgery to prevent recurrence," he said in an ASCO press release.

The OncoType DX test costs about $4,500 and is generally covered by insurance. A similar type of test known as MammaPrint looks at 70 different tumor genes.

Sparano stressed that TAILORx addresses only women with early-stage breast cancer, not those with Stage II or Stage III disease. Another study, known as RESPONDER, is evaluating a similar

testing strategy for women with cancer that has spread to lymph nodes.

Commenting on the study findings, Lisa Carey, MD, of the University of North Carolina said ER-positive, HER2-negative breast cancer is “ripe for de-escalation.” TAILORx “confirms excellent outcome” without chemotherapy in women with low recurrence scores and “supports omitting chemotherapy” in those with intermediate scores, she concluded.

Click here to read the study abstract.

Click here to read the full study in The New England Journal of Medicine.

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