Biomarker predicts risk of breast cancer recurrence after tamoxifen treatment

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A biomarker reflecting expression levels of two genes in tumor tissue may be able to predict which women treated for estrogen-receptor (ER)-positive breast cancer should receive a second estrogen-blocking medication after completing tamoxifen treatment. In their report being published online in the *Journal of the National Cancer Institute*, Massachusetts General Hospital (MGH) Cancer Center investigators describe finding that the HOXB13/IL17BR ratio can indicate which women are at risk for cancer recurrence after tamoxifen and which are most likely to benefit from continuing treatment with the aromatase inhibitor letrozole (Femara).

"Most patients with early-stage, ER-positive breast cancer remain cancer-free after five years of tamoxifen treatment, but they remain at risk of recurrence for 15 years or longer after their initial treatment," says Dennis Sgroi, MD, of the MGH Cancer Center and Department of Pathology, lead and corresponding author of the report. "Our biomarker identifies the subgroup of patients who continue to be at risk of recurrence after tamoxifen treatment and who will benefit from extended therapy with letrozole, which should allow many women to avoid unnecessary extended treatment."

Previous research by Sgroi's team, in collaboration with investigators from bioTheranostics Inc., discovered that the ratio between levels of expression of two genes – HOXB13 and IL17BR – in tumor tissue predicted the risk of recurrence of ER-positive, lymph-node-negative breast cancer, whether or not the patient was treated with tamoxifen. The current study of patients from MA.17, the highly successful clinical trial of letrozole, was designed to evaluate the usefulness of the HOXB13/IL17BR ratio for both prognosis – predicting which tamoxifen-treated remained patients at risk of recurrence – and for identifying who could benefit from continued treatment with letrozole.

To answer those questions the investigators analyzed primary tumor samples and patient data from the placebo-controlled MA.17 trial, which confirmed the ability of extended letrozole therapy to improve survival after the completion of tamoxifen treatment. Tissue samples were available from 83 patients whose tumors recurred during the study period – 31 who had received letrozole and 52 in the placebo group – and 166 patients with no recurrence, 91 of whom had received letrozole, with 75 getting the placebo. Analysis of the tumor samples revealed that a high HOXB13/IL17BR ratio – meaning the expression level of HOXB13 is greater than that of IL17BR – predicts an increased risk for tumor recurrence after tamoxifen therapy, but that elevated risk drops significantly if a patient receives letrozole

Paul E. Goss, MD, PhD, director of the Breast Cancer Research Program at the MGH Cancer Center and a co-author of the report, explains, "This discovery means that about 60 percent of women with the most common kind of breast cancer can be spared unnecessary treatment with the concommitant side effects and costs. But more importantly, the 40 percent of patients who are at risk of recurrence can now be identified as needing continued therapy with letrozole, and many will be spared death from breast cancer." He and Sgroi note that their findings need to be validated by additional studies before they can be put into clinical practice.

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