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# Gene-expression-based biomarker predicts long-term risk of breast cancer recurrence

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A comparison of three methods of predicting the risk of recurrence in women treated for estrogen-receptor (ER)-positive breast cancer finds that only the breast cancer index (BCI) – a biomarker based on the expression levels of seven tumor-specific genes – accurately identifies patients who continue to be at risk after five years of treatment with either tamoxifen or the aromatase inhibitor anastrozole. The study comparing the BCI with two other prognostic tests has been published online in *Lancet Oncology*.

"We have validated a unique 'fingerprint' in the primary tumor of breast cancer patients that can help identify a high or low risk of cancer recurrence," says study co-author Paul Goss, MD, PhD, director of the Breast Cancer Research Program at Massachusetts General Hospital (MGH) Cancer Center. "This should enable us to offer prolonged treatment to patients who remain at risk and, importantly, to avoid the costs and side effects of treatment in those at low risk."

Standard treatment for early-stage, ER-positive breast cancer includes five years of treatment with either tamoxifen or an aromatase inhibitor, drugs that block the action of estrogen. While that approach is sufficient for most patients, some continue to experience recurrence during subsequent years. The study authors note that knowing whether or not a patient continues to be at risk is essential to determining whether prolonged treatment is necessary.

MGH researchers previously developed, in collaboration with

investigators from bioTheranostics, Inc., two biomarkers for recurrence risk assessment – the molecular grade index, which measures expression levels of five genes related to tumor proliferation; and the H/I ratio, which compares expression levels of two other genes. BCI is a combination of both biomarkers and has been shown to identify patients who are at risk of early recurrence despite receiving hormonal treatment.

The current study, led by Dennis Sgroi, MD, of the MGH Cancer Center and Department of Pathology, was designed to compare the ability of the BCI to predict long-term recurrence risk with that of two other gene-expression signatures that can predict risk in the first five years – the Oncotype Dx Recurrence Score, the current gold standard for guiding clinical decision making, and the less frequently used ICH4 gene signature. All three methods were used to analyze primary tumor samples from more than 650 participants in a clinical trial comparing tamoxifen with anastrozole. Assay results were compared with patient records to determine individual rates of recurrence up to 10 years after initial surgical treatment.

While all three methods were able to predict recurrence risk in the first five years, only the BCI was able to accurately assess long-term recurrence risk. In fact, the BCI was able to clearly distinguish 60 percent of patients whose risk was quite low from 40 percent who continued to be at significant long-term risk. "We know that more than half the instances of recurrence in ER-positive breast cancer occur after five years of therapy with tamoxifen or anastrozole, so these findings are highly relevant to clinical management," says Sgroi. "Since the BCI identifies two distinct risk groups, it may provide a much-needed tool in determining those patients who need extended hormonal therapy and those who may be spared its well-known adverse side effects."

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