Breast Tumor Profile Fortifies Risk Gene Panel in Younger Patients

BY KURT SAMSON

Combining classic clinical tumor characteristics with the 21-gene breast cancer recurrence score (RS) more accurately predicts which premenopausal patients may safely forego adjuvant therapy than the gene assay alone, researchers have found. Results from a pre-specified secondary endpoint analysis of data from the landmark Trial Assigning Individualized Options for Treatment (Rx), or TAILORx—the largest breast cancer treatment trial to date—were first reported at the 2019 ASCO Annual Meeting and published in the New England Journal of Medicine (2019;380:2395-2405).

The primary endpoint findings of the TAILORx trial, published in 2018, showed that about 70 percent of women with hormone receptor (HR)-positive, HER2-negative, axillary lymph node–negative breast cancer, the most common form of the disease, have a low enough distant relapse risk that, when guided by the RS assay, they may not require chemotherapy.

In the new analysis, hazard ratios for distant recurrence among women at high clinical risk were about 2.5-3 times higher than for those at low clinical risk, regardless of endocrine therapy, either alone or with chemotherapy. Combining classic clinical features could also be used to identify which younger patients will most likely benefit from more effective anti-estrogen therapy, the researchers said.

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Clinical risk features were prognostic in women with an intermediate RS of 11-25 who were randomly assigned to endocrine monotherapy or combined with chemotherapy for women with higher recurrence scores.

After 9 years, the estimated rate of distant recurrence was less than 5 percent for patients 50 years of age or younger who received endocrine therapy alone and had an RS of 10 or less, regardless of clinical risk, and around 4.7 percent of low clinical risk and an intermediate RS. The estimated 9-year recurrence rate was above 10 percent among patients with high clinical risk features treated with endocrine monotherapy, and in women with a high RS who received both chemo and endocrine therapy.

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Although clinical risk features added prognostic value across all groups, disease-free survival and distant recurrence-free interval rates were similar with or without chemotherapy in the entire RS 11-25 group, regardless of clinical risk. However, clinical risk alone was not predictive of chemotherapy benefits, and this proved true for two-thirds of the subjects over age 50 or older.

Editorial

"Readers may be surprised to learn that the classic prognostic markers were not directly analyzed in the 2018 article, unsurprised to learn that they contribute prognostic information, and curious as to why it took two articles in the Journal, published almost a year apart, to impart this information," wrote NEJM Deputy Editor Dan L. Longo, MD, Dana-Farber Cancer Institute, and statistician David J. Hunter, MB, BS, University of Oxford, U.K. (N Engl J Med 2019;380:2472-2474)

The answers lie in how clinical trials are conducted and reported, and affirm the need to incorporate new research findings into practice, they explained.

On the basis of previous studies, they observed, the authors indicate that adding ovarian suppression and an aromatase inhibitor might reduce risk equivalent to that of adjuvant chemotherapy.

"Thus, practice-changing suggestions are being made on the basis of a subgroup analysis of a secondary objective in the trial, published as a follow-up to the report of the primary objective."

"The promise of precision medicine has collided with the rather messier world of using all available evidence to try and make educated guesses to improve patient outcomes," according to the editorial.

"To then view this data set as the test of a single hypothesis would be wasteful of the opportunity to incorporate secondary objectives or even post hoc analyses...The presentation of additional analyses from important data sets will remain a fundamental component of evidence synthesis," according to the commentary.

The reporting of findings beyond prespecified and primary objectives is important, and "judicious use of these data should continue to inform clinical practice," they wrote.

Kurt Samson is a contributing writer.