New TAILORx data guides adjuvant therapy in younger breast cancer patients

June 3 2019

New information about adjuvant therapy to prevent recurrence of breast cancer in women 50 years of age or younger, or premenopausal, emerged today from the landmark Trial Assigning IndividuaLized Options for Treatment (Rx), or TAILORx. An analysis of a pre-specified secondary endpoint in this largest-ever breast cancer treatment trial found that an assessment of a woman's recurrence risk based on classic clinical features—tumor size and histologic grade, adds prognostic information that is complementary to the 21-gene Recurrence Score (RS) test. Integration of the RS with clinical risk may help identify more young women who may be spared chemotherapy than originally reported. It may also help identify young women who stand to benefit from more effective anti-estrogen therapy. The analysis was published today in the *New England Journal of Medicine* and presented at the 2019 meeting of the American Society of Clinical Oncology in Chicago.

The new findings complement the original, definitive TAILORx conclusion reported last year, that 70 percent of women with the most common type of breast cancer; that is, hormone receptor (HR)-positive, HER2-negative, axillary lymph node-negative breast cancer, can forego chemotherapy when guided by the RS. The trial was supported by the National Cancer Institute, part of the National Institutes of Health, and designed and led by the ECOG-ACRIN Cancer Research Group.

"Last year's TAILORx results gave clinicians high-quality data to inform personalized treatment recommendations for women," said lead author Joseph A. Sparano, M.D., associate director for clinical research at the

Albert Einstein Cancer Center and Montefiore Health System in New York City and vice chair of the ECOG-ACRIN Cancer Research Group. "With this new analysis, it is clear that women ages 50 or younger with a Recurrence Score result between 16 and 20 and at low risk, clinically, do not need chemotherapy. Furthermore, the integration of the Recurrence Score with clinical risk information could identify premenopausal women with higher clinical risk who may benefit from ovarian function suppression and more aggressive anti-estrogen therapy."

The objective of the pre-specified secondary analysis was to evaluate whether clinical risk provides additional prognostic or predictive information to the RS results. Of 9,427 women in TAILORx with a RS and clinical risk information, 70 percent were determined to be low clinical risk (LCR: tumor ?3 cm and low grade, ?2 cm and intermediate grade, or ?1 cm and high grade) and 30 percent were identified as high clinical risk (HCR: not meeting low clinical risk criteria). While clinical risk provided additional prognostic information across all RS groups, disease free survival and distant recurrence free interval rates were similar with and without chemotherapy in the entire RS 11-25 group irrespective of clinical risk.

For the overall population, clinical risk alone was not predictive of chemotherapy benefit. This was also true for the two-thirds of women who were over the age of 50. For the remaining women aged 50 or younger, there was trend favoring chemotherapy irrespective of clinical risk, though not significant. This finding is consistent with the treatment interaction originally reported, between age/menopausal status, RS, and chemotherapy benefit.

Researchers studied the association between age at diagnosis and chemotherapy benefit in the group of younger women (age 50 or less) in TAILORx with a RS of 16-25. This group was of particular interest because they were part (14 percent) of the 30 percent of women in the

original TAILORx findings for whom it was suggested that chemotherapy may be considered. Researchers sought to determine whether integration of RS and clinical information would help define this group. They found there was no benefit from chemotherapy for younger women (age 50 or less) with a RS of 16-20 and at low risk, clinically.

Researchers then explored the association between age at diagnosis and chemotherapy benefit in this group same, to determine if integration of RS and clinical risk could help identify premenopausal women who might stand to benefit from more effective anti-estrogen therapy. In the original TAILORx report, researchers noted that it was unclear if the modest chemotherapy benefit seen in this group was due to a cytotoxic effect in eradicating micrometastatic disease, a castration effect in inducing early menopause, or both. Integration of RS and clinical risk found a benefit for women aged 46-50 years who were premenopausal but not postmenopausal, and a trend toward chemotherapy in women aged 41-45 years, but no benefit in women aged 40 years or under who are less likely to develop premature menopause from chemotherapy. In addition, there was no consistent effect favoring chemotherapy in older women. Taken together, these findings suggest that the chemotherapy benefit observed for the RS 16-25 group may be due to a castration effect associated with cytotoxic therapy.

Based on evidence from several prior studies, the 21-gene expression assay (Oncotype DX Breast Recurrence Score) is widely used to provide prognostic information about the risk of breast cancer recurrence within 10 years, and to predict which patients are most likely to derive a large benefit from chemotherapy. The test is performed on a tumor biopsy sample. Women with a low score (0-10) typically receive only hormone therapy and those with a high score (26-100) receive hormone therapy and chemotherapy.

Provided by ECOG-ACRIN Cancer Research Group