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## Breast

### 21-Gene Assay to Inform Chemotherapy Benefit in Node-Positive Breast Cancer

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*NEJM: 1 December, 2021, DOI: 10.1056/NEJMoa2108873*

#### BACKGROUND

The recurrence score based on the 21-gene breast-cancer assay has been clinically useful in predicting a chemotherapy benefit in hormone-receptor-positive, human epidermal growth factor receptor 2 (HER2)-negative, axillary lymph-node-negative breast cancer. In women with positive lymph-node disease, the role of the recurrence score with respect to predicting a benefit of adjuvant chemotherapy is unclear.

#### METHODS

In a prospective trial, we randomly assigned women with hormone-receptor-positive, HER2-negative breast cancer, one to three positive axillary lymph nodes, and a recurrence score of 25 or lower (scores range from 0.0 to 100, with higher scores indicating a worse prognosis) to endocrine therapy only or to chemotherapy plus endocrine (chemoendocrine) therapy. The primary objective was to determine the effect of chemotherapy on invasive disease-free survival and whether the effect was influenced by the recurrence score. Secondary end points included distant relapse-free survival.

#### RESULTS

A total of 5083 women (33.2% premenopausal and 66.8% postmenopausal) underwent randomisation, and 5018 participated in the trial. At the prespecified third interim analysis, the chemotherapy benefit with respect to increasing invasive disease-free survival differed according to menopausal status ( $P=0.008$  for the comparison of chemotherapy benefit in premenopausal and postmenopausal participants), and separate prespecified analyses were conducted. Among postmenopausal women, invasive disease-free survival at 5.0 years was 91.9% in the endocrine-only group and 91.3% in the chemoendocrine group, with no chemotherapy benefit (hazard ratio for invasive disease recurrence, new primary cancer [breast cancer or another type], or death, 1.02; 95% confidence interval [CI], 0.82 to 1.26;  $P=0.89$ ). Among premenopausal women, invasive disease-free survival at 5.0 years was 89.0% with endocrine-only therapy and 93.9% with chemoendocrine therapy (hazard ratio, 0.60; 95% CI, 0.43 to 0.83;  $P=0.002$ ), with a similar increase in distant relapse-free survival (hazard ratio, 0.58; 95% CI, 0.39 to 0.87;  $P=0.009$ ). The relative chemotherapy benefit did not increase as the recurrence score increased.

#### CONCLUSIONS

Among premenopausal women with one to three positive lymph nodes and a recurrence score of 25 or lower, those who received chemoendocrine therapy had longer invasive disease-free survival and distant relapse-free survival than those who received endocrine-only therapy, whereas postmenopausal women with similar characteristics did not benefit from adjuvant chemotherapy.