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Biomarkers in breast cancer

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PREDICTING RISK FOR LATE METASTASIS: THE PAM50 RISK OF RECURRENCE (ROR) SCORE AFTER 5 YEARS OF ENDOCRINE THERAPY IN POSTMENOPAUSAL WOMEN WITH HR+ EARLY BREAST CANCER: A STUDY ON 1,478 PATIENTS FROM THE ABCSG-8 TRIAL

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Introduction: Despite great improvements in overall outcomes of endocrine-responsive breast cancer, the main challenge in improving long-term cure of these patients remains their inherent risk for late relapse. Particularly in patients with initially favorable molecular characteristics (e.g. luminal A), the annual relapse risk persists well beyond 5 years follow-up. Extending adjuvant therapy may be an option to reduce risk of late metastasis. It would be of great value to differentiate patients at high vs. low risk of late relapse for clinical decision making and patient counseling. The goal of this work is to evaluate the ability of the PAM50 signature to predict late metastasis in a large cohort of endocrine responsive breast cancer.

Methods/patients: NanoString has developed a PAM50-based breast cancer gene signature assay that is used to categorize a breast tumor specimen into intrinsic breast cancer subtypes and to provide a risk-of-recurrence (ROR) score. Using the nCounter DX Analysis System, this assay directly measures the mRNA expression levels of 58 different genes in a single hybridization. NanoString's assay has been optimized to be performed with FFPE tissue samples in local hospital pathology laboratories. This ROR score has been clinically validated in several studies, and has been suggested to predict late recurrences in a transATAC study. Out of 3,714 patients of ABCSG-8, 1,671 patients could be re-consented to this study, with 1,620 FFPE blocks available. Out of those, 1,478 (91.2%) passed the PAM50 analysis.

Results: PAM50 ROR provided significant additional prognostic information to clinical factors with respect to late distant-relapse-free survival (DRFS) (Chi-Square 15.3, $p < 0.0001$) and late RFS (Chi-Square 11.4, $p = 0.0007$) in multivariate models, with probabilities for DRFS after year 5 of 98.7% for low ROR patients vs. 91.5% for high ROR patients. This was true both for node-positive and node negative disease.

Discussion: PAM50 ROR can successfully be used to differentiate patients with respect to their risk for late metastasis, in addition to established clinicopathological risk factors. This ability to predict late metastasis may be used in the future to identify patients with endocrine-responsive breast cancer who need or alternatively who can be spared extended adjuvant therapy.

Disclosure: S. Ferree: employee of nano string J.W. Cowens: employee of nano string All other authors have declared no conflicts of interest.