

30th Annual San Antonio Breast Cancer Symposium — Abstract #10

[10] Prognostic and predictive value of the 21-gene recurrence score assay in postmenopausal, node-positive, ER-positive breast cancer (S8814,INT0100)

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Objectives: The 21-gene Recurrence Score assay (RS) is prognostic for women with node-negative, ER-positive breast cancer (BC) treated with tamoxifen (T) alone and a high RS predicts a large, additional chemotherapy benefit. There are no data in a node-positive population with a T-alone control. The 2 primary objectives of this analysis were to determine if the RS 1) provides prognostic data for DFS in the T-alone control arm and 2) predicts a group that does not benefit from chemotherapy followed by T, despite positive nodes.

Patients and Methods: The phase III trial S8814 for postmenopausal women with node-positive, ER-positive BC showed CAF added DFS and OS benefit to T at 10 years, especially if T followed CAF (CAF-T). Optional specimen banking yielded tumor blocks or unstained slides for RT-PCR analyses of the 21 genes for the RS by Genomic Health, Inc. Analyses for DFS and OS were conducted by the SWOG Statistical Center using the T and CAF-T arms of S8814.

Results: 45% of S8814 participants provided specimens, with RNA sufficient for RT-PCR on 367 patients (T, 148; CAF-T, 219). The RS risk distribution was 40% low (<18), 28% intermediate (18-30), and 32% high (31). The RS was prognostic for DFS in the T-alone arm ($p=0.006$), with similar effects in the 1-3 and 4+ nodal subsets and for OS. There was no apparent DFS or OS benefit to CAF-T vs T in the low RS group, whereas there was a large CAF benefit in the high RS subset. Ten-year Kaplan-Meier DFS estimates (95% CI) and p-values for stratified logrank tests for T vs CAF-T in the 3 RS groups were (1) Low: 60% (40%-76%) vs. 64% (50%-75%), $p=0.97$; (2) Intermediate: 49% (32%-63%) vs. 63% (48%-74%), $p=0.48$; and (3) High: 43% (28%-57%) vs. 55% (40%-67%), $p=0.03$. In a time-dependent Cox model (employed due to non-proportional hazards), continuous RS score was prognostic in T alone in the first 5 years ($p<0.001$), but not subsequently ($p=0.80$), adjusting for nodes. For prediction of CAF benefit, the RS by treatment interaction was significant in the first 5 years for DFS ($p=0.029$), but not after 5 years ($p=0.58$), with nodal status strongly prognostic for both time periods. Results were similar for OS. Although the effects of RS on hazard rates were concentrated during the first 5 years, cumulative effects on DFS and OS were still observed at 10 years.

Conclusions: The RS is prognostic for T-treated patients with positive nodes. It is predictive of added CAF benefit in those patients whose tumors have a high RS. A low RS may define a group of women with positive nodes who do not appear to benefit from anthracycline-based adjuvant chemotherapy.