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Association Between the 21-Gene Recurrence Score Assay (RS) and Risk of Loco-Regional Failure in Node-Negative, ER-Positive Breast Cancer: Results from NSABP B-14 and NSABP B-20.

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Background: RS has been validated to quantify risk of distant recurrence in tamoxifen-treated patients with N-, ER+ breast cancer. In this report we investigate the association between RS and risk for loco-regional recurrence in N-, ER+ breast cancer patients treated in two NSABP protocols (NSABP B-14 and NSABP B-20).

Subjects and Methods: Details on patient eligibility, methods of RNA extraction, the RT-PCR methodology used and the genes included in the RS have been previously published in detail (Paik, NEJM 2004). The primary endpoint for this analysis was time to first local or regional recurrence (LRR). Occurrence of distant metastasis, 2nd primary cancer and death before LRR were censored in the analysis. For the correlation between RS and LRR in tamoxifen-treated patients, such patients from B-14 and B-20 were combined in one group. The correlation between RS and LRR was also evaluated in the placebo-treated patients from NSABP B-14 and in the tamoxifen plus chemotherapy treated patients from NSABP B-20.

Results: The present analyses include a total of 895 tamoxifen-treated patients (668 from B-14 and 227 from B-20), 355 placebo-treated patients (from B-14) and 424 chemotherapy and tamoxifen-treated patients (from B-20). LRR in tamoxifen-treated patients was significantly associated with RS (see Table, $p=3.1E-6$). There were also similar associations in placebo-treated patients from B-14 ($p=0.022$) and in tamoxifen plus chemotherapy-treated patients from B-20 ($p=0.028$).

Treatment	RS Group	10-year Event Rate (KM)	95% CI	Log-Rank P-value	Event/Total
Placebo	Low Risk	10.8%	(5.8%,15.8%)	0.022	19/171
	Intermediate Risk	20.0%	(9.9%,30.0%)		15/85
	High Risk	18.4%	(9.5%,27.4%)		19/99
Tamoxifen	Low Risk	4.3%	(2.3%,6.3%)	<0.00001	24/473
	Intermediate Risk	7.2%	(3.4%,11.0%)		16/194
	High Risk	15.8%	(10.4%,21.2%)		33/228
Chemo+TAM	Low Risk	1.6%	(0%,3.5%)	0.028	4/218
	Intermediate Risk	2.7%	(0%,6.4%)		2/89
	High Risk	7.8%	(2.6%,13.0%)		8/117

In multivariate analysis, RS was a significant predictor of LRR in tamoxifen-treated

patients independent of age, clinical tumor size and tumor grade.

Conclusion: Similar to the association between RS and risk for distant recurrence, the present analyses demonstrate that such an association also exists between RS and risk for LRR. This information may have clinical implications relative to loco-regional therapy decisions and follow up requirements for patients with node-negative, ER-positive breast cancer.