Prediction of recurrence with the Onco*type* DX recurrence score in node-positive, HR-positive, breast cancer patients treated with adjuvant chemotherapy: Results from PACS01 trial.

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Background: The Recurrence Score (RS) predicts outcome in node- and node+, ER+ pts treated with endocrine therapy and predicts chemotherapy benefit. We studied the prognostic impact of RS in node+, HR+ pts treated with adjuvant chemotherapy plus endocrine therapy in PACS01 **Methods:** PACS01 compared FECX6 with FECX3+ docetaxel X3(FEC-D) in 1999 pts. After a protocol amendment, HR-positive pts received 5 yrs of tam after chemo. The current study includes 530 pts from the PACS01 parent trial who were central IHC HR+ with sufficient tissue for Onco*type*DX. The primary objective was to estimate the association between RS and distant recurrence free interval (DRFI). Secondary endpoints included disease free survival (DFS) and overall survival (OS). Median follow-up time was 7.7 yrs **Results:** Of the 530 pts, 209 (39.4%) had low RS; 159 (30.0%) intermediate RS; and 162 (30.6%) high RS. 74.2% were treated with tam. In the primary analysis, RS was a significant predictor of DRFI (HR= 4.1 for a 50 point difference, *P*<0.001), DFS (HR=3.3, *P*<0.001) and OS (HR=5.0, *P*<0.001). In multivariate analyses, RS provided independent prognostic information beyond clinicopathologic factors including treatment, age, tumor size & grade, number of + nodes, surgery type and Ki-67 status (*P*<0.001). RS was a significant predictor of DRFI, DFS, and OS in both treatment arms (*P*<0.001). There was no statistically significant interaction between RS and treatment arm in predicting distant recurrence (*P*=0.79). **Conclusions:** The 21-gene RS maintains significant prognostic impact in HR+, node+ pts who have received FEC or FEC-D adjuvant chemotherapy. These findings emphasize the need to target pts with high residual risk for recurrence with additional therapies to overcome unfavorable biology, potential endocrine and/or chemotherapy resistance.

End point (95%CI)	**RS low n=209**	**RS intermediate n=159**	**RS high n=162**	**Log-rank p-value**
DRFI %	93.7 (89.4-96.3)	87.3 (81.0-91.6)	69.3 (61.5-75.8)	p<0.001
DFS %	90.8 (86.0-94.1)	84.9 (78.3-89.6)	64.6 (56.7-71.4)	p<0.001

End point (95%CI)	RS low n=209	RS intermediate n=159	RS high n=162	Log-rank p-value
OS %	99.0 (96.2-99.8)	95.6 (90.9-97.9)	85.6 (79.1-90.2)	p<0.001

Kaplan-Meier estimates of 5-yr DRFI, DFS, and OS.