Association Between the 21-Gene Recurrence Score (RS) and Benefit from Adjuvant Paclitaxel in Node-positive, ER-positive Breast Cancer Patients (pts): Results from NSABP B-28

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Background: RS predicts outcome in node- and node+, ER+ pts treated with adjuvant endocrine therapy. RS also predicts benefit from adjuvant chemotherapy, with high RS pts receiving most of the benefit. We evaluated the association between RS and paclitaxel benefit in node+, ER+ pts from the NSABP B-28 trial.

Methods: B-28 compared four cycles of doxorubicin/cyclophosphamide (AC) vs. AC followed by paclitaxel X 4 (AC→T). Pts ≥50 yrs and those<50 yrs with ER+ and/or PR+ tumors also received 5 yrs of tamoxifen concurrently with chemotherapy. Between 8/95 and 5/98 3060 pts were accrued. The present study includes 1065 pts, ER+ by central tissue microarray IHC assay, tamoxifen treated and assessed by RS. Median follow-up time was 11.2 yrs.

Results: Of the 1065 pts, 386 (36%) had low RS (<18); 364 (34%) intermediate RS (18-30); and 315 (30%) high RS (≥31). RS was a significant predictor of LRR, DFS event, distant recurrence (DR) and death in univariate analyses both in pts treated with AC as well as in those treated with AC→T (Table). Pts with low RS had similar outcomes at 10 yrs when treated with AC→T vs. AC (LRR: 3.1% vs. 3.4%, HR= 1.19; DFS event: 23.9% vs. 24.5%, HR=1.01; DR: 19.1% vs. 19.2%, HR=0.95; Death 11.5% vs. 8.5%, HR=1.28 respectively.) The majority of paclitaxel benefit was observed in pts with intermediate RS (LRR: HR=0.75, DFS event: HR=0.84, DR: HR=0.88, death: HR=0.74) or high RS (LRR: HR=0.80, DFS event: HR=0.81, DR: HR=0.86, death: HR=0.86). Interaction tests between RS and paclitaxel benefit were not statistically significant (LRR: p=0.75, DFS event: p=0.65, DR: p=0.93, death: p=0.30).

Table: 10-year Cumulative Incidence of LRR, DFS Event, Distant Recurrence and Death According to the 21-Gene RS and Treatment Group

Category	RS Low (n=386)	RS Intermediate (n=364)	RS High (n=315)	Log-rank p
LRR				
AC	3.4 (1.4-7.0)	8.3 (4.8-13.2)	13.2 (8.3- 19.1)	0.004
AC→T	3.1 (1.3-6.3)	6.2 (3.3-10.4)	11.4 (7-17.0)	0.037
	HR=1.19	HR=0.75	HR=0.80	
DFS Event				
AC	24.5 (18.8, 31.5)	46.6 (39.5, 54.4)	54.7 (47, 62.8)	<0.001
AC→T	23.9 (18.5, 31.2)	39.6 (32.8, 47.1)	49.5 (42, 57.5)	<0.001
	HR=1.01	HR=0.84	HR=0.81	
Distant Recurrence				
AC	19.2 (14, 25.8)	37.5 (30.6, 45.2)	46.8 (39, 55.3)	<0.001
AC→T	19.1 (14.1, 25.5)	32.7 (26.3, 40.2)	41.8 (34.5, 49.9)	<0.001
	HR=0.95	HR=0.88	HR=0.86	
Death				
AC	8.5 (5.2, 13.7)	30.1 (23.8, 37.5)	39.3 (32, 47.7)	<0.001
AC→T	11.5 (7.7, 6.9)	20.7 (15.9, 28)	34.7 (27.8, 42.7)	<0.001
	HR=1.28	HR=0.74	HR=0.86	

Conclusions: RS significantly predicts risk for LRR, DFS event, distant recurrence and death in node-positive, ER-positive pts treated with AC or AC→T adjuvant chemotherapy. Pts with low RS have similar outcomes whether treated with AC or with AC→T and most of paclitaxel benefit is evident in pts with intermediate/high RS. Although there was no significant interaction between RS and paclitaxel benefit, these results support previous findings of lack of chemotherapy benefit in pts with low RS.