PS2-08-01: A predictive gene signature for benefit from dose-dense adjuvant chemotherapy in patients with high-risk early breast cancer: results from the PANTHER phase III trial

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Conclusions

We developed a gene signature which **selects patients** with breast cancer (BC) for **dose-dense** adjuvant chemotherapy (DD-ACT) instead of 3-weekly standard dose (SD-ACT) regardless of any clinicopathologic factor.

We aim to **validate** the gene signature in independent patient cohorts.

Introduction

- DD-ACT improves outcomes compared to SD-ACT [1, 2].
- The PANTHER trial (n=2003) enrolled patients with N+ or high-risk N- BC that received sequential (F)EC and docetaxel, tailored DD-ACT (tDD-ACT) versus SD-ACT (Figure 1 and Table 1).

Methods and Materials

- RNA was extracted from FFPE surgical biospecimens.
- RNA sequencing data from 481 patients were retained for analysis.
- Multivariable Cox proportional hazards models were adjusted for BC subtype, tumor size, nodal status, and grade (median follow-up was 10 years).

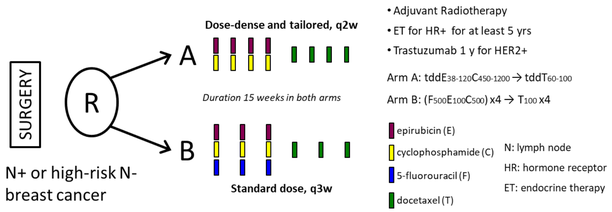


Figure 1. Study design of phase 3 PANTHER trial (NCT00798070).

Results

- The **dd-Sensitive signature** was an independent **predictor of benefit** from tDD-ACT ($p_{interaction}$ = 0.018) compared to SD-ACT independent of clinicopathologic factors.
- Patients in the **dd-Sensitive+** subgroup (n=159, **33%** of the cohort) derived **greater benefit** (**Δ=13%**) from tDD-ACT compared to SD-ACT for the primary endpoint of breast-cancer recurrence-free survival (Figure 2 and 3), whereas patients in the **dd-Sensitive-** subgroup received the same benefit from both tDD and SD dosing (Figure 2 and 4).

Table 1. Patient characteristics by treatment group.

Variable	N	SD-ACT N = 242[1]	tDD-ACT N = 239[1]	p-value[2]
Age (years)	481	50 (44, 57)	52 (44, 58)	0.3
Menopausal status	481			0.3
Premenopausal		136 (56%)	126 (53%)	
Postmenopausal (0,5-5 years)		42 (17%)	38 (16%)	
Postmenopausal (> 5 years)		56 (23%)	71 (30%)	
Uncertain		8 (3.3%)	4 (1.7%)	
Clinical subtype	481			0.7
ER+/HER2-		157 (65%)	154 (64%)	
HER2+		49 (20%)	44 (18%)	
TNBC		36 (15%)	41 (17%)	
Tumor size	481			0.6
≤ 2 cm		96 (40%)	100 (42%)	
> 2 cm		146 (60%)	139 (58%)	
Lymph nodes	481			0.2
N0		10 (4.1%)	16 (6.7%)	
N1-3		147 (61%)	151 (63%)	
N4-9		65 (27%)	48 (20%)	
N10+		20 (8.3%)	24 (10%)	
Histological grade	479			0.3
I		14 (5.8%)	18 (7.6%)	
II		106 (44%)	89 (38%)	
III		122 (50%)	130 (55%)	
Unknown		0	2	
dd-Sensitive biomarker	481			0.053
dd-Sensitive+		70 (29%)	89 (37%)	
dd-Sensitive-		172 (71%)	150 (63%)	

[1] Median (Q1, Q3); n (%)
[2] Wilcoxon rank sum test; Pearson's Chi-squared test

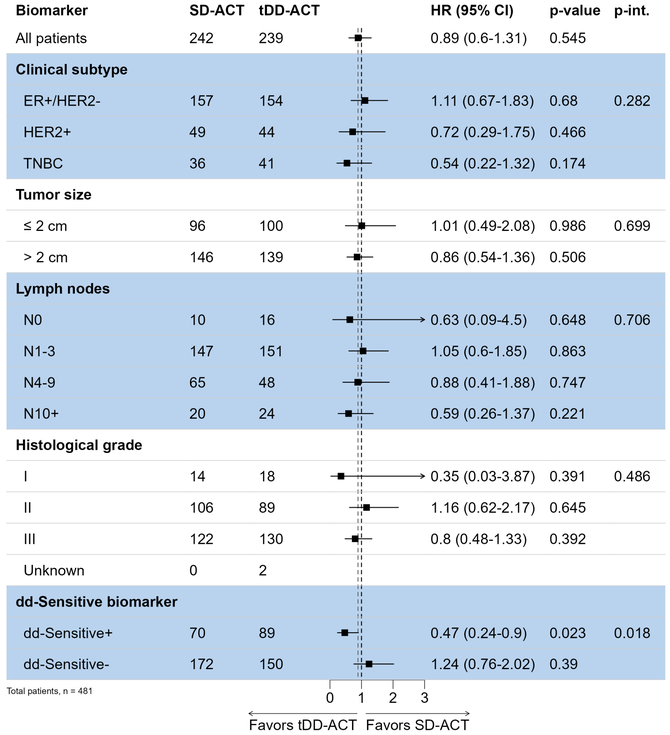


Figure 2. Subgroup analysis of breast cancer recurrence-free survival.

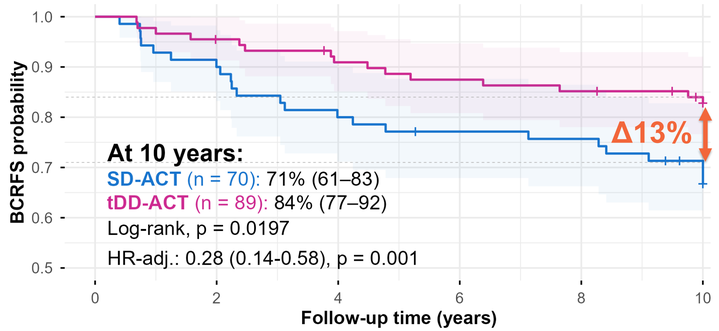


Figure 3. Kaplan-Meier plot for BCRFS probability at 10 years for the **dd-Sensitive+** (n=159, **33%**) subgroup.

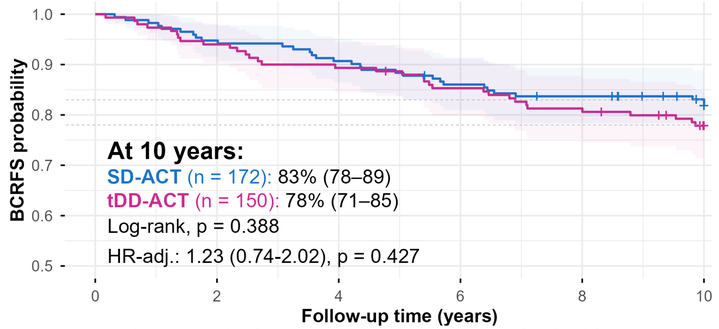


Figure 4. Kaplan-Meier plot for BCRFS probability at 10 years for the **dd-Sensitive-** (n=322, **67%**) subgroup.



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References

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2. Matikas A, Möbus V, Greil R, *et al.*, J Clin Oncol., 2024

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