

## 2007 ASCO Breast Cancer Symposium – Abstract 27

### Association of individual genes with risk of relapse in operable breast cancer: Analysis of E2197

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**Introduction:** Identification of genes associated with outcome may lead to better understanding to the biologic factors contributing to relapse after standard chemotherapy (CT) or chemohormonal therapy (CHT), discovery of new targets for therapeutic intervention, and development of improved classifiers for predicting outcomes.

**Methods:** A sample of 776 of 2885 patients enrolled on E2197 who did (N=179) or did not have a recurrence after CT (if hormone receptor [HR]-neg) or CHT (if HR-pos) and had available tissue were evaluated by quantitative RT-PCR for a panel of 371 genes, including 21 genes included in the Oncotype DX™ Recurrence Score (RS). All patients had 0-3 positive nodes and received four 3-week cycles of doxorubicin (60 mg/m<sup>2</sup>) and cyclophosphamide 600 mg/m<sup>2</sup> (AC) or docetaxel 60 mg/m<sup>2</sup> (AT) plus hormonal therapy (if HR-pos). HR, Her2/neu (HER2) expression, and nuclear/histological grade were determined centrally. Cox proportional hazards models were used to identify individual genes and permutation analysis was used to control the number of false discoveries (Korn et al. J Stat Planning Inference 124: 379, 2004). The effect of adjustment for RS is shown for the HR-pos HER2-neg group.

**Results:** There was no significant difference in recurrence between the two treatment arms after a median followup of 76 months. The number of genes associated with a significant difference in relapse ( $P \leq 0.05$ ) are shown, with the maximum number of potential false discoveries shown in parenthesis. Genes that are highly associated ( $P \leq 0.01$ ) with recurrence are shown in the table and ranked in order of greatest to least significance.

**Conclusions:** Multiple genes were identified that were related to the residual risk after CT or CHT, and may therefore be prognostic and/or predictive. Many of the genes identified are associated with immune function. The biological implications of the specific genes identified will be discussed.

HR	HER2	Adjusted	No. Genes	Increased Recurrence	Decreased Recurrence
Pos	Neg	None	41 (4)	TOP2A, DEPDC1, NUSAP1, AURKB, KIFC1, GAPDH, BUB1B, BIRC5, TYMS, PLK1, PTTG1, CENPF	STK11, ZW10, ACTR2, RASSF1, GADD45B, NPC2, ID1, MMP2
Pos	Neg	RS	8 (2)	TOP2A, NUSAP1	ACTR2, CD247, ZW10, PIM2, SLC1A3, GBP1
Neg	Neg	None	18 (3)	GRB7	APOC1, EST2, PIM2, CD68, BIRC3
Neg	Pos	None	3 (2)	None	ESR1, TFF1
Pos	Pos	None	5 (2)	ERBB2, GRB7	MAPT, RPLPO, PGR