257P Multi-gene prognostic signatures and prediction of pathological complete response of ER-Positive HER2-negative breast cancer patients to neo-adjuvant chemotherapy

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Background: Determining which early stage breast cancer patients should receive chemotherapy is an important clinical and economic issue. Chemotherapy has many adverse side effects, impacting on quality of life, along with significant economic consequences. Biomarkers that can predict patient response to chemotherapy can help avoid ineffective overtreatment. The aim of this work is to assess if the OncoMasTR (OM) signature can predict pathological complete response (pCR) to neo-adjuvant chemotherapy, and to compare its predictive value with EndoPredict (EP) and Oncotype DX (RS).

Methods: Gene expression datasets derived from breast cancer patients that had pre-treatment biopsies, received neo-adjuvant chemotherapy and an assessment of pCR were obtained from GEO (GSE16716, GSE20271, GSE25066, GSE32646, GSE34138, GSE41998, GSE22226). Patients with ER-positive, HER2-negative disease and pCR data were selected. OM, EP and RS numeric risk scores were approximated by applying the gene coefficients to the corresponding mean probe expression values. Association with pCR was estimated using logistic regression.

Results: A total of 813 patients with 66 pCR events were included in the analysis. OM, EP and RS prognostic scores were moderately well correlated according to the Pearson's correlation coefficient: OM vs EP (min=0.44; mean=0.67; max=0.81), OM vs RS (min=0.34; mean=0.62; max=0.79), and RS vs EP (min=0.55; mean=0.79; max=0.89). Significant predictors of pCR with p-values of 0.0001 for all three signatures. Odds ratios for a 1 standard deviation increase in risk score, adjusted for cohort, were similar in magnitude and not significantly different: OM 1.66 (1.29 to 2.16), EP 1.76 (1.37 to 2.27), RS 1.84 (1.44 to 2.35).

Conclusions: In this in silico analysis, OM, EP and RS prognostic scores were significantly predictive of pCR to neo-adjuvant chemotherapy in ER-positive, HER2-negative breast cancer. Optimal stratification for neo-adjuvant chemotherapy offers the opportunity for personalised care, improved therapy response rates, and reduced ineffective treatment and costs.

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