The 41-gene classifier TRAR predicts response of HER2 positive breast cancer patients in the NeoALTTO study

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BACKGROUND
Dual HER2-inhibition combined with neoadjuvant chemotherapy allows increased pathological complete response (pCR) rate. However, with the addition of new agents, there is a growing need to select patients to minimise overtreatment. Herein, we evaluated the 41-gene classifier TRAR to predict pCR to anti-HER2 therapies in the NeoALTTO trial.

PATIENTS AND METHODS
Gene expression data were obtained using RNA from 226 pretreatment tumour biopsies. Logistic regression analysis and the area under the receiver operating characteristic (ROC) curve (AUC) were used to evaluate TRAR predictive and discriminatory capabilities.

RESULTS
TRAR levels were associated with pCR (odds ratio, OR: 0.25, 95% confidence interval, CI: 0.15-0.42). The ROC analysis showed AUC values of 0.73 (95% CI: 0.67-0.80) overall; 0.70 (0.59-0.81) and 0.71 (0.62-0.80) for positive and negative oestrogen receptor cases and 0.74 (0.60-0.88), 0.76 (0.65-0.87) and 0.71 (0.59-0.83) for trastuzumab, lapatinib and combined treatment arms, respectively. TRAR provided reliable predictive information beyond established clinicopathological variables (OR: 0.26, 95% CI: 0.14-0.47). Furthermore, addition of TRAR to these variables provided greater predictive capability than the addition of PAM50: AUC 0.78 (0.72-0.84) versus 0.74 (0.67-0.81), p = 0.04.

CONCLUSION
TRAR represents a promising tool to refine the ability to identify patients sensitive to anti-HER2 (including trastuzumab-only)-based therapy and eligible for de-escalated treatment strategies.

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