

## Evaluation of the 12-Gene Molecular Score and the 21-Gene Recurrence Score as Predictors of Response to Neo-adjuvant Chemotherapy in Estrogen Receptor-Positive, HER2-Negative Breast Cancer

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### Introduction

- Neo-adjuvant chemotherapy (NaCT) facilitates complete surgical resection in locally advanced breast cancer.
- While ER- tumors show substantial rates of pathological complete response (pCR), complete response to NaCT in ER+, HER2- breast tumors is limited (7-10%).
- Response biomarkers would enable patients with ER+, HER2- breast cancer to be selected for NaCT.

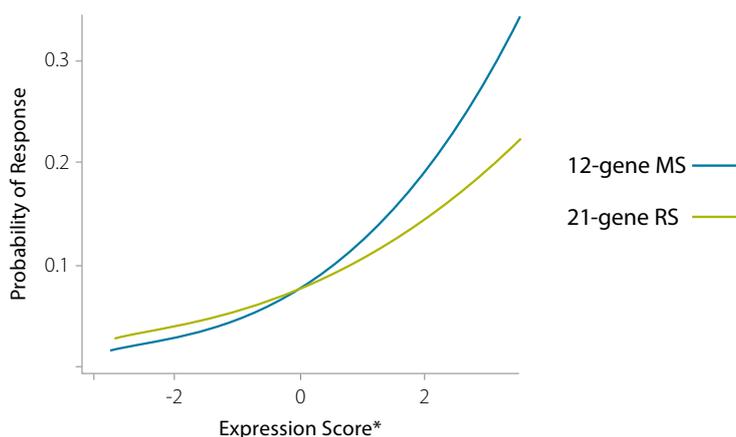
### Methods

To assess the comparative value of the 21-gene recurrence score (21-gene RS) and the 12-gene molecular score (12-gene MS) in predicting neo-adjuvant response, six public microarray expression data sets were used to approximate 12-gene MS and 21-gene RS for n=764 NaCT treated patient samples. This included n=59 pCR (8% response rate).

### Results

- The microarray approximated 12-gene MS and 21-gene RS were moderately well correlated ( $r = 0.71$ ) with correlation coefficients similar to those seen in qPCR data.
- Both the 12-gene MS and 21-gene RS scores were predictive of NaCT response with higher expression scores indicative of increased probability of response (12-gene MS  $p=9.4 \times 10^{-5}$ ; 21-gene RS  $p=0.0041$ ).

\*As both scores were aligned using z transformation, their ranges differ from those observed on clinical reports.



- When analyzed together in the same model, the 12-gene MS remained a significant predictor of response ( $p=0.0079$ ) while the 21-gene RS did not ( $p=0.79$ ), indicating that the 12-gene MS has additional predictive power not present in the 21-gene RS.

### Discussion

- The two commercial breast cancer prognostic scores were significant predictors of response to neo-adjuvant chemotherapy.
- In direct comparison, the 12-gene MS outperformed the 21-gene RS as a predictive marker for NaCT.
- Limitations of this study include the use of microarray-based expression data and the limited availability of clinical parameters.

### Bottom Line

- This in-silico study confirms the previous finding from the ABCSG34 study, that the EndoPredict 12-Gene Molecular Score is predictive for NaCT.
- The study also shows that EndoPredict does not only have superior prognostic power compared to Oncotype Dx (as shown in TransATAC<sup>1</sup>) but also superiority of the test as a predictive marker for NaCT response.

REFERENCES: 1. Buus et al.: *J Natl Cancer Inst*. 2016

