EndoPredict®
Breast Cancer Recurrence Test

The EndoPredict Score Predicts Response to Neoadjuvant Chemotherapy and Neoendocrine Therapy in Hormone Receptor-Positive, Human Epidermal Growth Factor Receptor 2-Negative Breast Cancer Patients from the ABCSG-34 Trial

Dubsky P. et al., European Journal of Cancer, published online June 2020

Introduction

- Neoadjuvant chemotherapy (NaCT) and neoadjuvant endocrine therapy (NET) can reduce pre-operative tumour burden in patients with ER-positive, HER2-negative early-stage breast cancer.

- Accurate identification of those patients who will benefit is critical to improve outcomes through personalized therapy selection while minimizing unnecessary treatment for those unlikely to respond.

Study Design

- The primary objective of this prospective translational study was to test the predictive value of the EndoPredict 12-Gene Molecular Score (MS) with regard to tumour response after NaCT or NET within the ABCSG-34 trial.

Methods

- The analysis included all women with hormone receptor-positive (HR+), HER2- tumours participating in ABCSG-34. Patients received either NaCT (8 cycles of anthracycline/taxane-based chemotherapy) or NET (6 months of letrozole) based on menopausal status, HR expression, grade, and Ki67.

- Diagnostic cores were tested using EndoPredict to produce the EP 12-Gene MS. EPclin could not be calculated in this setting.

- Primary endpoint: Residual Cancer Burden score (RCB0/I [good tumour response] vs RCBII/III [poor tumour response]) at surgery.

- The association of the EP risk groups (cutoff: 5) and RCB was evaluated.

Results

- 217 patients with HR+, HER2- tumours were included in the analysis (134 NaCT / 83 NET).

- Patients treated with NaCT were younger and had more aggressive disease characteristics than those treated with NET.

- Pathologic response to treatment (RCB 0-I): NaCT 24.6% vs NET 18.1%.

- EP risk classification dependent on therapy: NaCT: EP 12-Gene MS low risk (N=9), EP 12-Gene MS high risk (N=125)
  NET: EP 12-Gene MS low risk (N=44), EP 12-Gene MS high risk (N=39)

- Predictive Performance

NaCT:

◊ The EP 12-Gene MS was a significant predictor of response to NaCT (p=0.0001; AUC: 0.736).

◊ No patient with an EP low-risk score showed a good tumour response after NaCT (negative predictive value (NPV): 100%).

◊ Response was better among patients with EP high-risk disease, with 33 patients exhibiting RCB 0-I (positive predictive value (PPV): 26.4%).

NET:

◊ The EP 12-Gene MS was a significant predictor of response to NET (p=0.015; AUC: 0.726).

◊ More patients with EP low-risk disease (12/44) had a good tumour response (PPV: 27.3%) compared to those with EP high-risk disease (3/39; NPV: 92.3%).

Distribution of the EP 12-Gene MS based on tumor response (RCB) for patients treated with NaCT or NET. The horizontal line indicates the threshold between low and high risk.
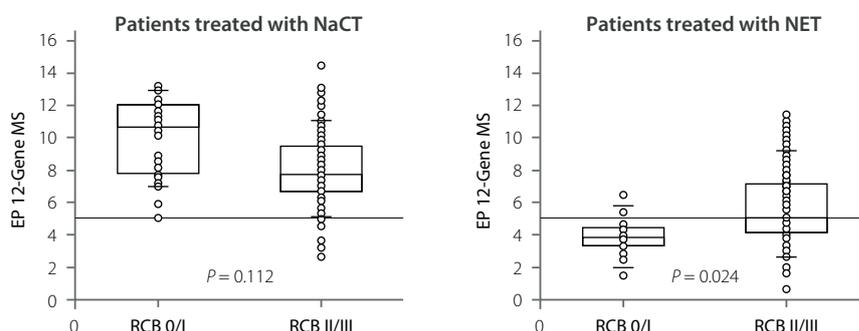
Conclusion

- The key clinical value of this study is the high negative predictive value of the 12-Gene MS, indicating that **patients with a low 12-Gene MS have a very low probability to achieve a good tumour response after NaCT** but a higher probability to respond to NET with six months of letrozole.
  - This is clinically relevant to surgical planning. Although clearly dependent on multiple factors, breast conservation is unlikely to be driven by NaCT in the low-risk MS group.

- Importantly, the study shows that a high 12-Gene MS was strongly associated with a poor tumour response (RCB II-III) to NET.
  - Adjuvant endocrine therapy remains an important therapy in these patients, but neoendocrine treatment is very unlikely to be beneficial in terms of tumour shrinkage.

Bottom Line

- **This prospective translational study shows that the 12-Gene MS predicted response to NaCT or NET for patients with HR-positive, HER2-negative early-stage breast cancer.**

- **The 12-Gene MS is able to identify patients with poor treatment response to neoadjuvant therapy:**

	EndoPredict Low Score	EndoPredict High Score	Predictive Performance EndoPredict Score (p-value)
Response to Neoadjuvant Chemotherapy	**0.0%**	**26.4%**	**p=0.0001**
Response to Endocrine Therapy	**27.3%**	**7.7%**	**P=0.015**

  - **Patients with a low-risk molecular score rarely responded with substantial tumour shrinkage after NaCT but had a higher probability to respond to NET with six months of letrozole.**

  - **Patients with a high-risk molecular score rarely responded to NET and had a higher probability to respond to NaCT.**

- **The 12-Gene MS can add valuable information to aid personalized treatment selection in neoadjuvant therapy.**