EndoPredict®
Breast Cancer Recurrence Test

Comparison of the Performance of 6 Prognostic Signatures for Estrogen Receptor – Positive Breast Cancer

A Secondary Analysis of a Randomized Clinical Trial

Sestak I. et al., JAMA Oncology Published online February 15, 2018. doi:10.1001/jamaoncol.2017.5524

Study Background

Differentiating low risk patients who can be safely treated with endocrine therapy alone from higher risk patients who may benefit from chemotherapy is a priority for breast cancer management. Multigene expression profiles have been commercially available for over a decade and have significantly increased clinicians' ability to predict breast cancer patients' risk of disease recurrence. However, little is known about their comparative performance for prediction and risk stratification of overall and late distant recurrence.

Study Aim

To compare the performance of prognostic signatures for breast cancer distant recurrence (DR) in years 0-10 and in years 5-10 using the TransATAC sample cohort.

The study evaluates six different prognostic algorithms. Two of them included clinicopathological information only without a molecular component (Clinical Treatment Score [CTS]) or immunohistochemistry data [IHC4]), the other four are gene expression signatures. As both CTS and IHC4 were developed in TransATAC, they cannot be directly compared with the gene expression signatures.

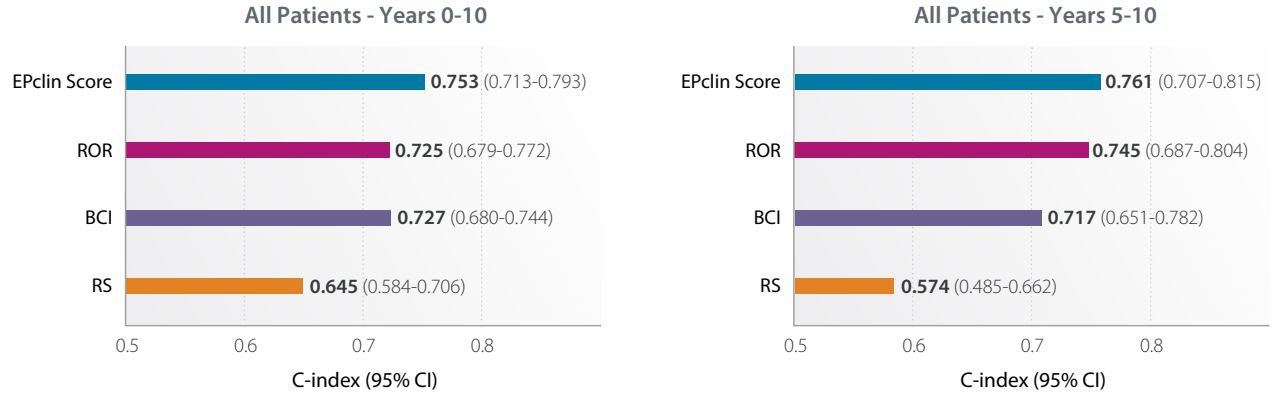
*This summary focuses on the results of the four commercially available prognostic gene expression signatures: EndoPredict (EPclin Score), Breast Cancer Index (BCI), Oncotype DX (RS) and Prosigna (ROR).**

Clinical Cohort Description

Cohort	Treatment	Primary Endpoint	Number of Women	Median Follow-up
• Primary breast cancer • ER+, HER2- • Node negative or node positive (1-3 positive LN) • Postmenopausal	• 5 years endocrine therapy only (tamoxifen or anastrozole) • None of the women received chemotherapy	• Distant Recurrence (DR)	• 774 – N0: 591 (76%) – N1-3 LN: 183 (24%)	• 10 years

Prognostic Accuracy of Gene Expression Signatures

Prognostic Ability to Detect Distant Recurrence



Adapted from eTable 2 in the Supplement.

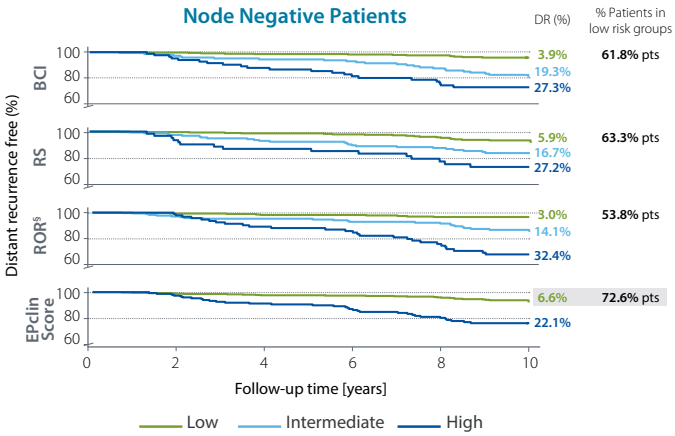
The C-index is a standard statistic for prognostic power that is used to compare prognostic accuracy of different tests. The greater the C-Index, the better is the prognostic power of a test.

EndoPredict was the most prognostic signature for distant recurrence in all patients, including node negative and node positive disease, in years **0-10** and in years **5-10**.

** Breast Cancer Index, Oncotype DX and Prosigna are trademarks of their respective owners.*

Accuracy to Identify Low Risk Patients in Years 0-10

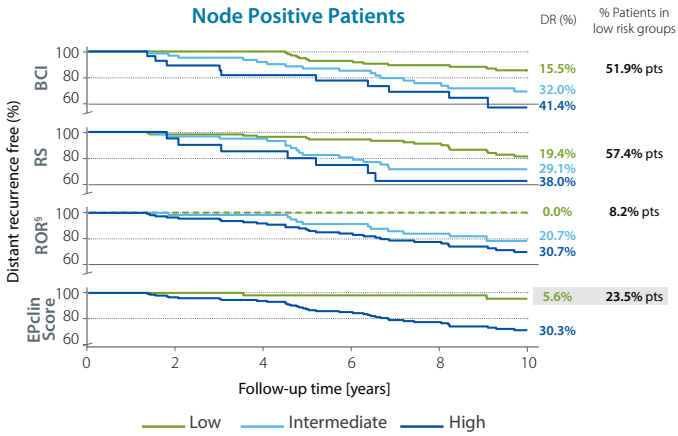
Node Negative Patients



In node negative patients, all signatures identified patients with low risk of distant recurrence (<10%) in years 0-10.

Compared to all other signatures, EndoPredict identified more node negative patients as low risk who might safely avoid chemotherapy.

Node Positive Patients



In node positive patients, EndoPredict was one of the two signatures that identified patients with "true" low risk of distant recurrence (<10%).

Compared to Prosigna, EndoPredict identified more node positive patients as low risk who might safely avoid chemotherapy (23.5% for EPclin Score compared to 8.2% for ROR).

Risk of Distant Recurrence in Years 5-10

Node Negative Patients

		10-y Risk	% Patients in low risk groups
BCI	Low	2.6%	63.6%
	Intermediate	14.4%	
	High	15.9%	
RS	Low	4.8%	65.6%
	Intermediate	9.6%	
	High	16.1%	
ROR§	Low	1.4%	54.6%
	Intermediate	10.0%	
	High	23.2%	
EPclin Score	Low	4.3%	73.5%
	High	14.6%	

Compared to all other signatures, EndoPredict identified more node negative patients as low risk for whom an extended endocrine therapy might not be justified.

Node Positive Patients

		10-y Risk	% Patients in low risk groups
BCI	Low	9.5%	54.6%
	Intermediate	14.3%	
	High	36.5%	
RS	Low	17.9%	61.0%
	Intermediate	19.5%	
	High	27.5%	
ROR§	Low	0.0%	9.7%
	Intermediate	13.0%	
	High	25.0%	
EPclin Score	Low	3.3%	26.0%
	High	23.6%	

Compared to Prosigna, EndoPredict identified more node positive patients for whom an extended endocrine therapy might not be justified (26% of patients in the low risk group for EndoPredict compared to 9.7% for Prosigna).

§ Prosigna cutoff values were trained in TransATAC and therefore were optimized for these patients' cohort.

Conclusions:

In the adjuvant setting, the need for chemotherapy or extended endocrine therapy (for late recurrence) are important clinical questions. Available prognostic signatures are good predictors for distant recurrence in the first 5 years after diagnosis. Signatures showed different prognostic performance in their ability to predict distant recurrence between 5 and 10 years where these tests may be valuable for decision making with regards to extended endocrine treatment. The combination of clinical and molecular information enhanced prognostic performance, particularly for prediction of late recurrence and for women with node positive disease.

Compared to other prognostic signatures:

- EndoPredict was the best prognostic signature in predicting distant recurrence in years 0-10 and in years 5-10 in all patients, including node negative and node positive disease.
- EndoPredict identified the largest group of women with breast cancer, both in node negative and node positive disease, at low risk* of distant recurrence who might safely avoid chemotherapy.
- EndoPredict identified the largest group of women with breast cancer, both in node negative and node positive disease, at low risk of late distant recurrence for whom an extended endocrine therapy might not be justified.

**Low risk: <10% chance of distant recurrence in 10 years.*

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