EndoPredict®

Breast Cancer Prognostic Test

eurobio SCIENTIFIC

CLINICAL SUMMARY

Prediction of distant recurrence using EndoPredict among women with ER+, HER2- node-positive and node-negative breast cancer treated with endocrine therapy only

Filipits M. et al.: Clin Cancer Res. 2019; 25:3865-3872

Introduction

- For women with ER-positive (ER+), HER2-negative (HER2-), node negative/positive (N0/+) breast cancer there is a long-term risk of recurrence even 5 to 20 years after diagnosis. This leads to a treatment decision five years after diagnosis of whether or not to continue endocrine therapy.
- A previous evaluation of EndoPredict Breast Cancer Prognostic Test (EPclin) in the combined ABCSG-6/8 cohorts (median follow-up 5.3 years) showed that EPclin predicted both early (0-5 years) and late (5-10 years) distant recurrence.

Study design and methods

- The study assessed the ability of EPclin to predict early (0-10 years) and late (5-15 years) distant recurrence of breast cancer in women enrolled in the randomized phase III ABCSG-6 and -8 trials using a longer follow-up of up to 15 years.
- All patients received maximum five years of adjuvant endocrine therapy only (tamoxifen or tamoxifen + anastrozole).
- Primary endpoint, distant recurrence-free rate (DRFR), was assessed 10 and 15 years after diagnosis for the overall cohort, by nodal status, and for patients who were DR-free at year 5.
- Prognostic power was assessed for EPclin alone and in comparison with clinical factors as well as CTS5 (Clinical Treatment Score post-5 years: developed to identify prognostic factors for late relapse. CTS5 combines nodal status, tumor size, tumor grade and age).

Results

- The analysis included 1,702 postmenopausal women with early stage ER+, HER2- breast cancer (N0: 68.5%; N+: 31.5%) with maximum follow-up 16.6 years (median 9.6 years which is 4.3 years more than the previous analysis).
- 1,386 women were distant recurrence-free at 5 years and were assessed for late metastasis.

Overall cohort

- **In both the univariate and multivariate analyses, EPclin score was a significant predictor of distant recurrence (entire follow-up period and late metastasis after 5 years).**
- Estimated 0-10 years DRFR was 95.5% EPclin low risk vs 80.3% EPclin high risk (Fig. 1a, Tab. 1).
- Estimated 5-15 years late DRFR in patients who were recurrence–free after 5 years was 95.7% EPclin low risk vs. 84.1% EPclin high risk (Fig. 1b, Tab. 1).
- Relationship between the EPclin score and 5-15 years risk of distant recurrence was shown as a function of EPclin score (Fig. 2).

Kaplan-Meier curves of estimated DRFR

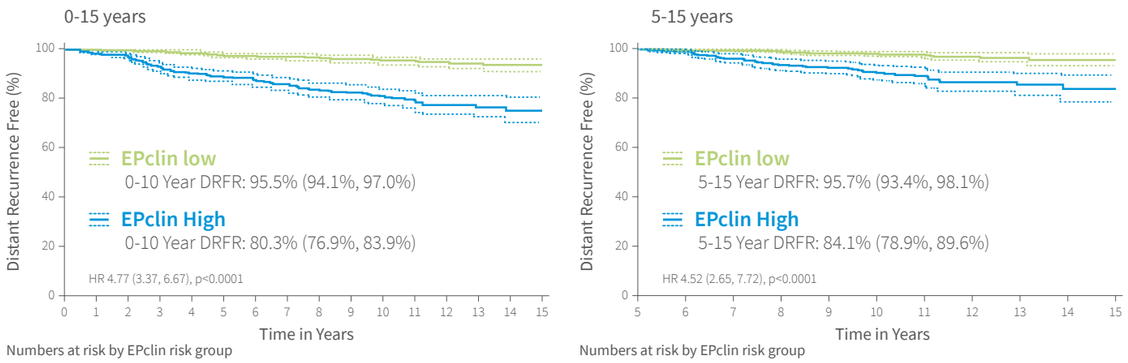

Fig. 1: Kaplan-Meier curves of estimated DRFR for patients with newly diagnosed disease in a) all patients and b) those patients who were distant recurrence-free at 5 years.

Risk of late recurrence 5 to 15 years after diagnosis

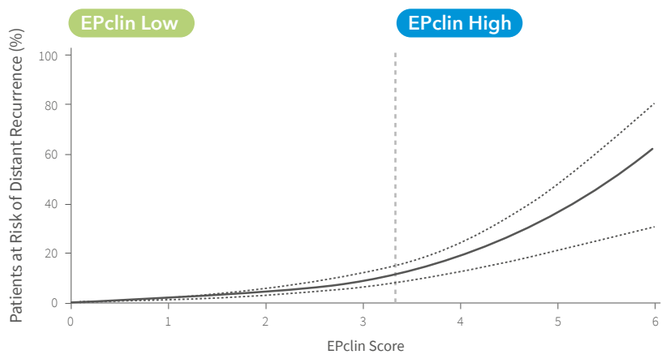

Fig. 2: Risk of late recurrence 5 to 15 years after diagnosis. The distant recurrence risk curve (solid black line) and 95% confidence intervals (dashed black lines) are shown as a function of EPclin score. The cut-off between low- and high-risk EPclin scores is denoted by the blue dashed line.

Node negative / node positive

- **In the multivariable analysis EPclin score remained a significant predictor of distant recurrence for the whole time period and for late metastasis after 5 years regardless of nodal status.**
- Among women with node-negative disease, the risk of 0-10 years and 5-15 years distant recurrence was significantly reduced among those with low EPclin scores (Tab. 1).
- Similar results were observed for all patients with positive disease and for women with 1-3 positive nodes (Tab. 1).

	Low-risk EPclin score		High-risk EPclin score	
Patient group	**0-10 year DRFR**	**95% CI**	**0-10 Year DRFR**	**95% CI**
All patients	95.5%	94.1%, 97.0%	80.3%	76.9%, 83.9%
Node-negative	95.5%	94.0%, 97.1%	87.0%	82.6%, 91.7%
Node-positive	95.6%	92.2%, 99.1%	75.8%	71.0%, 80.9%
1-3 positive nodes	95.6%	92.2%, 99.1%	80.9%	75.9%, 86.1%
Patient group	**0-15 year DRFR**	**95% CI**	**0-15 Year DRFR**	**95% CI**
All patients	93.4%	90.9%, 95.9%	74.6%	69.6%, 80.0%
Node-negative	94.5%	92.7%, 96.4%	78.5%	69.2%, 89.2%
Node-positive	85.4%	71.8%, 100%	71.5%	65.7%, 77.8%
1-3 positive nodes	84.7%	70.3%, 100%	75.1%	68.3%, 82.6%
Patient group	**5-10 year DRFR[a]**	**95% CI**	**5-10 Year DRFR[a]**	**95% CI**
All patients	97.9%	96.8%, 99.0%	90.6%	87.6%, 93.6%
Node-negative	97.9%	96.7%, 99.1%	94.1%	90.5%, 97.8%
Node-positive	98.3%	95.9%, 100%	88.0%	83.8%, 92.5%
1-3 positive nodes	98.2%	95.8%, 100%	90.5%	86.2%, 94.9%
Patient group	**5-15 year DRFR[a]**	**95% CI**	**5-15 Year DRFR[a]**	**95% CI**
All patients	95.7%	93.4%, 98.1%	84.1%	78.9%, 89.6%
Node-negative	96.9%	95.2%, 98.5%	84.9%	75.1%, 96.0%
Node-positive	87.8%	74.0%, 100%	83.0%	77.1%, 89.4%
1-3 positive nodes	87.0%	72.4%, 100%	84.0%	77.1%, 91.6%

Tab. 1: DRFR for different time periods according to nodal status.

CI; Confidence interval; DRFR, Distant recurrence-free rate
[a]DRFR for patients who were distant recurrence free after 5 years.

EPclin versus CTS5 score

- In the full cohort, EPclin score significantly added prognostic information to the CTS5 score ($p<0.001$). Conversely, CTS5 score did not significantly add prognostic information to the EPclin score ($p=0.0622$).
- This was also observed for the subset of patients with N0 and N+ disease.

Conclusions

- EPclin was highly predictive of both early and late DR in both N0 and N+ women.
- EPclin significantly added prognostic information to the clinical late metastasis nomogram CTS5.
- **This data demonstrates the prognostic value of EPclin in predicting early and late distant recurrence, which may aid in identifying patients having a) most likely no additional benefit from adjuvant chemotherapy and b) those who can safely discontinue endocrine therapy at five years.**

Bottom line

This re-analysis of two clinical validation studies of EndoPredict (ABCSG6 and ABCSG8) with a longer follow-up of up to 16.6 years (median 9.6 years) confirmed that EndoPredict was highly predictive of both early and late distant recurrence (DR) in both node-negative and node-positive women. Together with the recently published study that showed the ability of EndoPredict to predict chemotherapy benefit *(Sestak et al., 2019)* this study provides the basis for two critical treatment decisions at diagnosis and five years after diagnosis, which is whether or not to give chemotherapy and whether to forgo extended endocrine therapy.

Eurobio Scientific GmbH
Nattermannallee 1, Building S19
50829 Köln
Germany

info-INT@eurobio-scientific.de
www.eurobio-scientific.de

ENDO_MD_CS_FILIPITS_15Y_09_24_EN