EndoPredict®

Breast Cancer Prognostic Test

Clinical summary

Clinical validation of EndoPredict in premenopausal women with ER-positive, HER2-negative primary breast cancer

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Introduction

Myriad Genetics EndoPredict Breast Cancer Prognostic Test is validated to predict distant recurrence and response to chemotherapy in both pre- and postmenopausal women with ER+, HER2- breast cancer, with the majority of data available in the postmenopausal setting. To further confirm utility in younger patients, this study specifically evaluated the performance of EndoPredict in premenopausal women.

Study design

- ER+, HER2- primary breast tumor (pN0-1, ≤pT3) samples were obtained from the Bank of Cyprus Oncology Centre, Cyprus and the Nottingham University Hospitals NHS Trust, UK.
- Samples were collected from unselected cohorts of patients who were premenopausal at the time of diagnosis and were systemically treated with adjuvant endocrine therapy alone.
- Primary objective: To evaluate the association between the EPclin Risk Score and 10-year distant recurrence (DR).

Methods

- Samples were retrospectively tested with EndoPredict to produce the 12 Gene Molecular Score (EP) and, in combination with pathologic tumor size and nodal status, the EPclin Risk Score (EPclin).
- Association of EP and EPclin with 10-year distant recurrence-free survival (DRFS) was evaluated using Cox proportional hazards models stratified by cohort.
- 10-year DRFS was estimated for EP and EPclin high- and low-risk by Kaplan-Meier analysis. Subset analyses were performed by nodal status and treatment with ovarian function suppression (OFS).

Results

- 385 patients with a median follow-up of 9.7 years were included in the analysis.
- Median age at diagnosis 46.5 years; 62% grade 2, 15% grade 3, 16% N+.

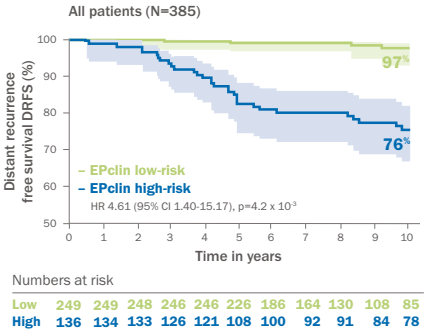
Association with distant recurrence:

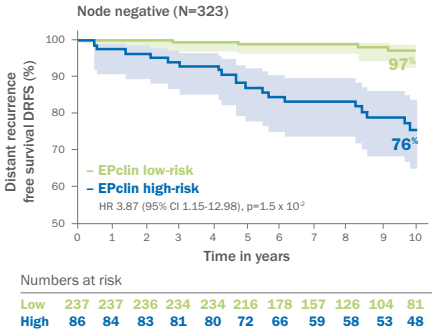
- In the univariate cox proportional hazards analysis, both EPclin (HR 3.6, $p<0.001$) and EP (HR 1.3, $p<0.001$) were strongly associated with increased risk of distant recurrence.
- This was true for women with node-negative (EPclin: HR 2.61, 95% CI 1.53-4.46; $p=4.8 \times 10^{-4}$) or node-positive disease (EPclin: HR 6.29, 95% CI 2.63-15.06; $p=3.9 \times 10^{-5}$).
- In the multivariate cox proportional hazards analysis, EPclin was the only factor significantly associated with the risk of distant recurrence within 10 years (HR 2.91, $p<0.001$), independent of age, tumor grade, Ki67, ER expression, and PR expression.

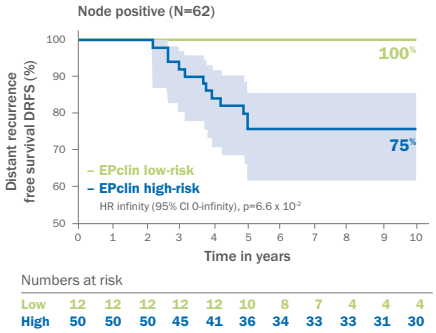
Distant recurrence-free survival:

- 65% of all patients were classified as EPclin low risk.
- The EPclin low-risk group had a significantly lower rate of distant recurrence at 10 years (3%, 95% CI 1-7%) compared to the high-risk group (24%, 95% CI 18-33%), both without chemotherapy ($p=4.2 \times 10^{-3}$).

- Similar DRFS results were observed for the EP 12-Gene Molecular Score: low-risk (0%) vs high-risk (16%) ($p=9.8 \times 10^{-5}$).
- Evaluation of DRFS by nodal status also demonstrated EPclin is strongly associated with the risk of distant recurrence within 10 years regardless of nodal status with a very low risk of 10-year distant recurrence in EPclin low-risk patients (3%, 95% CI 1-7% in N0 and 0% in N+, respectively). 73% of patients with node negative disease and 19% of patients with node positive disease were EPclin low risk.

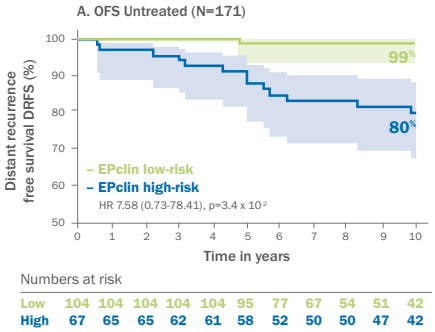


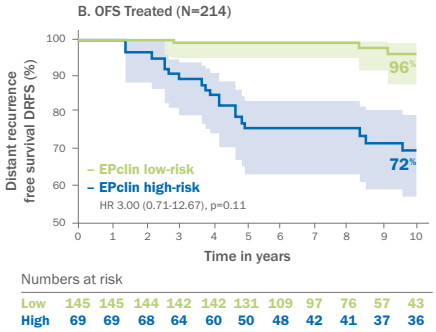




Association with OFS:

Exploratory subgroup analyses were performed in patients who had (n=214) or had not (n=171) received OFS.
Patients with low-risk EPclin scores in both subgroups had a good 10-year DRFS of 96% (with OFS) and 99% (without OFS), respectively.





Conclusion

- In this study, with a median follow-up time of 9.7 years, the EPclin and EP molecular scores were prognostic of 10-year distant recurrence in premenopausal women who received adjuvant endocrine therapy alone.
- EndoPredict identified 65% of premenopausal patients with a 10-year distant recurrence risk of <4% who could safely avoid adjuvant chemotherapy. 73% of patients with node negative disease and 19% with node positive disease were identified as low risk by EPclin.
- There seems to be no detectable difference between 10-year DRFS in patients with low-risk EPclin scores who received OFS treatment and those who did not, with less than 5% distant recurrence after 10 years in both groups.
- These results support the use of EndoPredict for all women with early-stage ER+, HER2- localized BC, regardless of menopausal status.

Bottom line

- **EndoPredict is validated for both post- and premenopausal patients.**
- **This data, consistent with previous work in populations of primarily postmenopausal women, indicates that menopausal status does not impact the performance and utility of the EndoPredict test.**
- **EPclin low-risk premenopausal patients had a similar 10-year DRFS with or without OFS in an exploratory subgroup analysis.**
- **EPclin low-risk breast cancer may be treated with endocrine therapy only and safely forgo adjuvant chemotherapy, regardless of menopausal and nodal status.**
- **The results highlight the importance of testing premenopausal women with ER+, HER2- breast cancer with EndoPredict.**

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