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Prediction of Distant Recurrence by EndoPredict in Patients with Estrogen Receptor-Positive, HER2-Negative Breast Cancer who Received Adjuvant Endocrine Therapy plus Chemotherapy (ET+C) or Endocrine Therapy Alone (ET)

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Background

- EndoPredict (EPclin) is a prognostic test validated for early breast cancer patients with oestrogen receptor positive, HER2-negative disease to help make decisions between 5 years of endocrine therapy alone or with chemotherapy[1,2,3].
- TAILORx reported that women with ER-positive, node-negative disease did not derive any chemotherapy benefit if they had mid-range Oncotype risk score (>11 and <25)[4].
- It is an important clinical question to investigate who benefits from chemotherapy in women with ER-positive, HER2-negative disease.

Objective

To investigate in a non-randomised setting whether EPclin can predict chemotherapy benefit in pre- and postmenopausal women with ER-positive, HER2-disease who have received five years of endocrine therapy alone (ET) or in combination with chemotherapy (ET+C)

Methods

- A total of 3746 women with ER-positive, HER2-negative disease were included in this analysis.
- 2630 patients received 5 years of ET alone (ABCSG-6/8, TransATAC) and 1116 patients received ET+C (GEICAM 2003-02/9906).
- The primary objective was to evaluate the 10-year DRFI rates as a continuous function of EPclin separately for patients in ET+C and ET.
- Secondary objectives included assessing prognostic ability of EPclin between ET+C and ET for specific follow-up periods (years 0-10, 0-5 and 5-10).
- The primary endpoint was DRFI and the secondary endpoint was breast cancer free interval (BCFI).
- Cox proportional hazard models used to estimate 10-year DRFI/BCFI rates and to assess the prognostic information provided by EPclin.

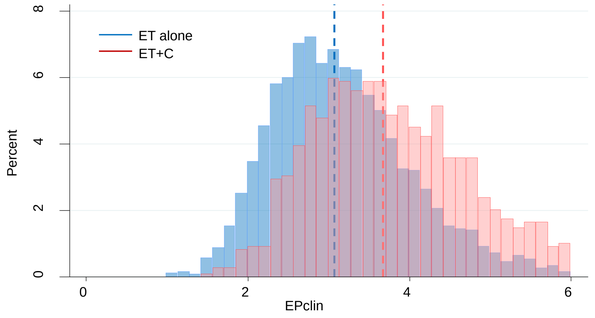
Results

- Baseline demographics for the two cohorts are shown in Table 1.
- Median follow-up for those on ET alone was 9.6 years (IQR 6.0-10.0) vs. 9.2 years (7.5-10.0) for ET+C.
- Significant larger EPclin scores for those on ET+C compared to ET alone (Figure 1).

Table 1: Baseline characteristics according to treatment received (ET vs. ET+C).

	ET only (N=2630)	ET+C (N=1116)
Age (years), median (IQR)	63.7 (58.0-70.7)	51.0 (44.0-59.0)
Postmenopausal	2630 (100.0%)	544 (48.8%)
Tumour stage		
T1a/b	422 (16.1%)	84 (7.5%)
T1c	1333 (50.7%)	508 (45.5%)
T2	829 (31.5%)	487 (43.6%)
T3	43 (1.6%)	37 (3.3%)
Nodal status		
Negative	1846 (70.2%)	616 (55.2%)
Tumour grade		
Well	615 (23.4%)	131 (11.7%)
Intermediate	1683 (64.0%)	605 (54.2%)
Poor	212 (8.1%)	322 (28.9%)
DRFI (0-10 years)	279 (10.6%)	146 (13.1%)
BCFI (0-10 years)	398 (15.1%)	171 (15.3%)
DRFI (5-10 years)	120/2202 (5.5%)	53/1008 (5.3%)
BCFI (5-10 years)	182/2155 (8.5%)	66/997 (6.6%)

Figure 1: Baseline EPclin scores (ET vs. ET+C). Vertical lines = median.



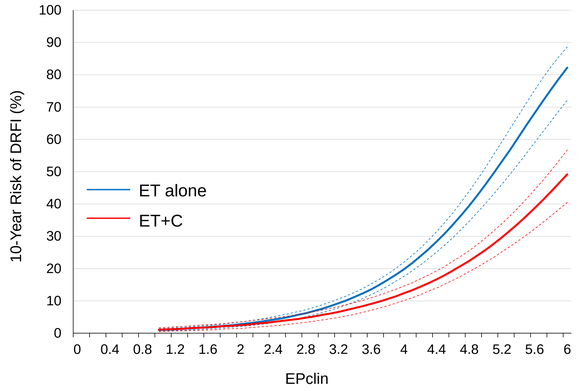
10-year risks according to ET alone vs. ET+C

Table 2: 10-year DRFI risks (95% CI) according to EPclin score (ET vs. ET+C).

EPclin	1	2	3	4	5	6
ET alone	1.0% (0.6-1.4)	2.8% (2.1-3.5)	7.6% (6.4-8.8)	19.8% (17.6-22.0)	46.1% (40.2-51.4)	82.2% (72.1-88.6)
ET+C	1.1% (0.5-1.7)	2.5% (1.5-3.5)	5.7% (4.1-7.2)	12.4% (10.1-14.6)	25.8% (22.0-29.5)	49.2% (40.5-56.7)

- Significant different 10-year risks between ET alone vs. ET+C studies with increasing EPclin (Table 2, Figure 2).
- Interaction between EPclin and treatment was significant (P=0.02).
- Similar results found for BCFI as endpoint (P-interaction=0.025).

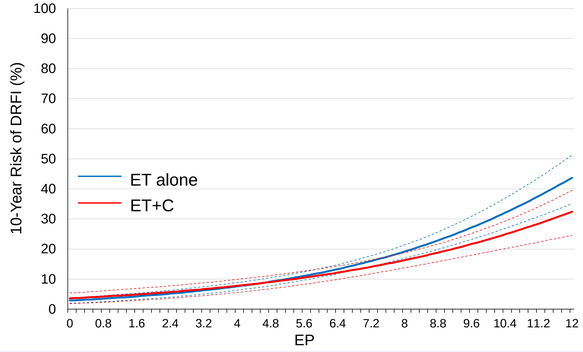
Figure 2: 10-year risks according to EPclin scores for ET vs. ET+C.



- No significant differences in 10-year risks were observed between ET alone vs. ET+C with increasing molecular EP score (Figure 3).

→No significant interaction between treatment and EP molecular (P=0.17).

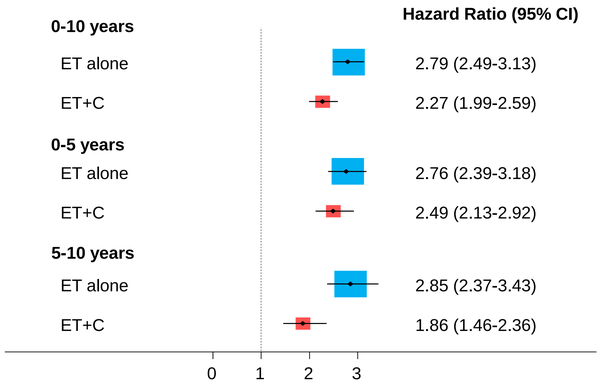
Figure 3: 10-year risks according to EP (molecular) scores for ET vs. ET+C.



Hazard Ratios for ET alone vs. ET+C

- EPclin highly prognostic in all time periods for those on ET alone and ET+C (Figure 4).
- Similar HRs observed when adjusted for clinic-pathological variables.

Figure 4: Univariate hazard ratios according to different time periods (ET vs. ET+C).



Conclusions

- Patients with a high EPclin score on ET+C had a significantly lower 10-year DR risk than those on ET alone.
- No differences in 10-year DR risks were observed between ET alone and ET+C for low EPclin scores (<3.3 low risk cut-off).
- Significant test for interaction was observed
  → potential benefit of adding chemotherapy to those with high EPclin scores.
- Results are derived from a non-randomised, retrospective analysis.
  → Results can give insight into the value of EPclin for the prediction of chemotherapy benefit for women with ER-positive, HER2-negative breast cancer.

References

1 Dubsky *et al.*, 2012; 2 Buus *et al.*, 2017; 3 Martin *et al.*, 2014; 4 Sparano *et al.*, 2018