Long-term outcome data using EndoPredict as risk stratification and chemotherapy decision biomarker in hormone receptor positive, HER2-negative early breast cancer

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5-year prospective data in a real-world patient cohort

Study population

- 368 HR+, HER2-, N0-3
- Patients prospectively enrolled in a clinical routine setting 2012 – 2015
- Demographic, clinical and pathological data assessed at baseline
- All tumour samples tested with EndoPredict

Analysis

- Treatment compliance, local recurrence, distant metastases and survival were evaluated
- Statistical analysis by Kaplan-Meier and Cox proportional hazards regression model

Patient characteristics

- Median age 60
- 33% pre-menopausal
- 35% pT2, 3% pT3
- 65% Grade 2, 16% Grade 3
- 24% 1-3 positive lymph nodes
- 65% EPclin low-risk

Klein et al., SABCS 2022
Significantly prognostic in a prospective real-world patient cohort

Classification by EPclin Risk Score

EPclin high-risk: 35% (n=130)
EPclin low-risk: 65% (n=238)

67% of EPclin high-risk patients received chemotherapy

DMFS by EPclin Risk Class

- Median follow-up 8.2 years
- 5-year DMFS:
  - EPclin low 96.6%
  - EPclin high 85.5%
  - HR 2.21, p=0.005

EndoPredict is significantly prognostic with excellent 5y outcome of EPclin low-risk patients in this prospective real-world patient cohort

Klein et al., SABCS 2022
Excellent 5-year outcome of EPclin low-risk patients

**DFS by EPclin Risk Class**

![Graph showing DFS by EPclin Risk Class]

**Tumor related DMFS by EPclin Risk Class**

![Graph showing Tumor related DMFS by EPclin Risk Class]

Numbers at risk:

<table>
<thead>
<tr>
<th>Risk Class</th>
<th>Low Numbers</th>
<th>High Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>238 234 231 223 217 214 209 187 110 51</td>
<td>130 126 123 116 109 99 95 85 63 22</td>
</tr>
<tr>
<td>High</td>
<td>6</td>
<td>2</td>
</tr>
</tbody>
</table>

Hazard ratio: 2.08 (95%-CI: 1.26 - 3.44) p=0.004

Hazard ratio: 4.55 (95%-CI: 2 - 11.41) p<0.001

Klein et al., SABCS 2022
Prospective confirmation of chemotherapy benefit prediction

DFS in EPclin high risk patients by CTx treatment

EndoPredict predicts chemotherapy benefit

- 130 pts (35%) classified as EPclin high-risk
- 67% received chemotherapy
- 5-year DFS
  - EPclin high with CTx 89.1% (95% CI: 0.827-0.961)
  - EPclin high no CTx 68.9% (95% CI: 0.562-0.845)
  HR 0.46, p=0.036

Patients categorized as EPclin high-risk significantly benefitted from adjuvant chemotherapy

Klein et al., SABCS 2022
Prospective confirmation of pre- and postmenopausal validation studies

Premenopausal patients

Postmenopausal patients

EndoPredict accurately identifies patients who may safely avoid chemotherapy, regardless of menopausal status.

*Including death by any cause

Klein et al., SABCS 2022
Prospective confirmation of superiority compared to Ki67 classification

Classification of Ki67 low/high by EPclin

Discordant classification

- 19% of luminal A (ki67 low) classified as EPclin high
- 33% of luminal B (ki67 high) classified as EPclin low

EPclin-based risk stratification was significantly associated with improved DFS of EPclin low-risk patients compared to EPclin high-risk patients in both Ki67 subtypes

- Ki67 high: HR 3.77 (95% CI 1.19-18.93; p=0.022)
- Ki67 low: HR 4 (95% CI 1.25-12.04; p=0.021)

EndoPredict showed better classification accuracy in comparison to Ki67 subtypes, resulting in a more precise estimation of prognosis
Prospective outcome data in clinical routine

Long-term prognostic in prospective real-world patient cohort
- Excellent 5y outcome of EPclin low-risk patients

Prospective confirmation of chemotherapy benefit prediction
- Patients categorized as EPclin high-risk significantly benefitted from adjuvant chemotherapy

Prospective confirmation of pre- and postmenopausal validation studies
- Accurately identifies patients who may safely avoid chemotherapy, regardless of menopausal status

Prospective confirmation of improved classification over conventional factors
- Better classification accuracy in comparison to Ki67 subtypes

Klein et al., SABCS 2022
Retrospective evaluation of outcomes in a real-world, prospective cohort using EndoPredict: Results from the Charité registry

Wolfgang D. Schmitt¹, Paul Jank², Inga Hoffmann¹, Berit M. Pfitzner³, Lauren Lenz⁴, Wyatt Clegg⁴, Elke Keil⁵, Sarah Ratzel⁴, Elizabeth Cogan⁴, Jens Blohmer⁶, Pauline Wimberger⁷, Ralf Kronenwett⁸, David Horst¹, Carsten Denkert²

5-year data from real-world prospective patient cohort

Study population
- 842 HR+, HER2-, N0-3
- Patients prospectively tested in a clinical routine setting 2011 – 2016
- All patients received EndoPredict test results before decision making on systemic treatment

Analysis
- Treatment and recurrence history obtained from patient surveys
- Patient demographics, clinical characteristics, and EndoPredict results retrieved from patient records
- Recurrence estimates calculated by Cox proportional hazards models and Kaplan-Meier estimates

Patient characteristics
- Median age 54
- 35% pT2, 4% pT3
- 39% Grade 2, 6% Grade 3
- 36.5% 1-3 positive lymph nodes
- 49.5% EPclin low-risk
- 44% treated with chemotherapy

Schmitt et al., SABCS 2022
EndoPredict is a significant predictor of distant recurrence in clinical practice

Cox proportional hazards model by chemotherapy treatment

<table>
<thead>
<tr>
<th></th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No chemotherapy</td>
<td>4.34 (1.75, 9.58)</td>
<td>0.0024</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>0.92 (0.36, 2.25)</td>
<td>0.87</td>
</tr>
</tbody>
</table>

Continuous EPclin score is a significant predictor of 5-year distant recurrence in patients not treated with chemotherapy

Schmitt et al., SABCS 2022
Low-risk is low-risk – independent from nodal status

EPclin low-risk, endocrine therapy only

- **EPclin low-risk 5-year distant recurrence**
  - All patients: 1.6%, (95% CI 0.7% - 3.4%)
  - Exploratory subgroup analysis:
    - Node negative 1.3% (95% CI 0.5% - 3.5%)
    - Node positive 2.4% (95% CI 0.6%-9.2%)

Patients with EPclin low-risk scores had a low risk of 5-year distant recurrence even in the absence of chemotherapy treatment, independent from nodal status

Schmitt et al., SABCS 2022
Chemotherapy vs. no chemotherapy in EPclin high-risk patients

EPclin high-risk, +/- chemotherapy

- The concordance between EPclin Risk Class and chemotherapy status was 0.89
  - 5.5% of EPclin low-risk and 81.6% of EPclin high-risk patients received treatment with chemotherapy

**EPclin high-risk 5-year distant recurrence**

- DRFI with chemotherapy: 3.6% (95% CI 2.1%-6.3%)
- DRFI without chemotherapy: 6.8% (95% CI 2.6%-17.4%)

Patients with high EPclin risk may have worse prognosis without chemotherapy, but they may benefit the most from chemotherapy

Schmitt et al., SABCS 2022
Another prospective real-world confirmation of EndoPredict validation data

Significant predictor

• EPclin was a significant predictor for patient-reported outcomes in the absence of chemotherapy treatment

Low-risk is low-risk

• Patients with EPclin low-risk scores had a low risk of 5-year distant recurrence without chemotherapy, independent from nodal status

Chemotherapy benefit

• Patients with EPclin high-risk scores may benefit the most from chemotherapy

Schmitt et al., SABCS 2022