#5P; HER2DX risk-score in HER2-positive breast cancer following neoadjuvant and adjuvant anti-HER2-based treatment: an updated survival analysis

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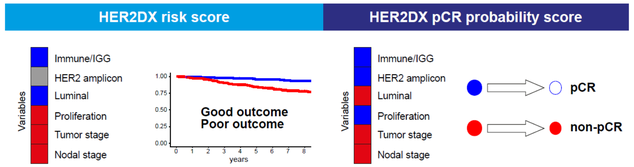
Background and objectives

- The risk-score of the HER2DX genomic test (HER2DX risk-score) (**Figure 1**) was first validated in an independent combined dataset of 268 patients (pts) with early-stage HER2 positive (HER2+) breast cancer treated with neoadjuvant (NA) and adjuvant anti-HER2-based treatment (EBioMedicine 2022).
- Here, we report an updated survival analysis with longer follow-up, with a special focus on the value of HER2DX risk-score beyond pathological complete response (pCR).

Figure 1. HER2DX components associated with risk-score and pCR-score.



Methods

- A dataset of 268 pts with early-stage HER2+ disease obtained from a combined cohort of 3 NA studies was used for an independent validation of the standardized HER2DX risk-score (**Figure 2**).
- The dataset was composed of 147 pts from Hospital Clinic, 84 pts from PAMELA trial and 37 pts from the Padova University cohort. All pts received NA/adjuvant chemotherapy (ChT) and 1-year of trastuzumab; 56% of pts received dual HER2 blockade; and 9% pts with residual disease (RD) received adjuvant T-DM1 (**Table 1**). pCR was achieved in 44% of the pts.
- The Kaplan-Meier method and stratified Cox models were used to estimate hazard ratios (HRs) to evaluate the association between HER2DX, event-free survival (EFS) and overall survival (OS) .

Figure 2. Clinical cohorts.

HER2DX validation cohort

- **HCB** (n = 147) (trastuzumab-based NA ChT)
- **PAMELA trial** (n = 84) (NA trastuzumab and lapatinib, adjuvant trastuzumab-ChT)
- **Padova** (n = 37) (trastuzumab-based NA ChT)

Results

- Median follow-up was 73.2 months (vs. 52.7 months in the prior report). HER2DX risk score as a continuous variable was significantly associated with EFS (HR=1.92, p=0.003) (**Fig. 3-4**) and OS (HR=2.23, p=0.009) (**Fig. 5**).
- According to the prespecified cut-off, the HER2DX low-risk group had longer EFS than high-risk (7-year 94.6% vs. 77.5%; HR=0.24, p=0.002) (**Fig. 3-4**). HER2DX risk-score was significantly (HR=1.90; p=0.003) associated with EFS independently of pCR status and hormone receptor status (**Fig. 3**).

Table 1. Baseline characteristics of patients.

Age	
Median (range) yr	56 (29 – 86)
cT – no. (%)	
T1	84 (31%)
T2-T3	184 (69%)
cN– no. (%)	
No	162 (60%)
N1-3	106 (40%)
Hormone receptor – no. (%)	
Positive	173 (65%)
Negative	90 (34%)
Unknown	5 (2%)
TILs – no. (%)	
<10	132 (49%)
10-50	85 (32%)
>50	10 (4%)
Unknown	41 (15%)
Neoadjuvant ChT backbone – no. (%)	
Anthracyclines – taxane	134 (50%)
Platinum – taxane	11 (4%)
Taxane	38 (14%)
No ChT	85 (32%)
Neoadjuvant anti-HER2– no. (%)	
Trastuzumab	268 (100%)
Pertuzumab	65 (24%)
Lapatinib	85 (32%)

Figure 3. EFS HR forest plots in the combined cohort (n=268).

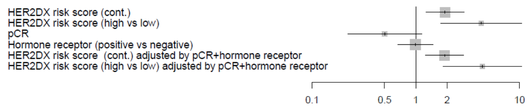


Figure 4. EFS in the combined cohort (n=268).

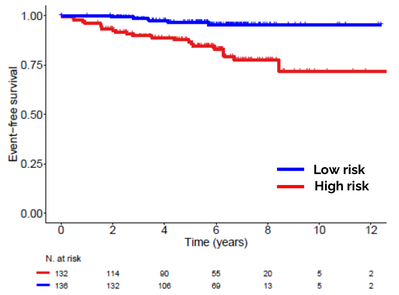
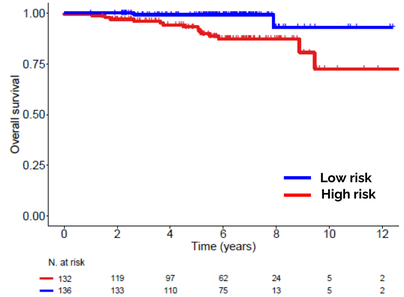


Figure 5. OS in the combined cohort (n=268).



- Within pts with a pCR (n=118), the HER2DX low-risk group had longer EFS than the high-risk (5-year 96.5% vs. 88.4%; HR=0.33, p=0.178) (**Figure 6**).
- Within pts with RD (n=150), the HER2DX low-risk group had longer EFS than the high-risk (5-year 95.6% vs. 85.3%; HR=0.20, p=0.004) (**Figure 7**), and it was significantly (HR=2.03; p=0.006) associated with EFS independently of hormone receptor status and adjuvant T-DM1 (**Figure 8**).

Figure 6. EFS in patients with pCR (n=118).

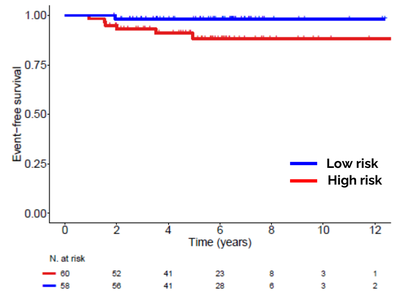


Figure 7. EFS in patients with RD (n=150).

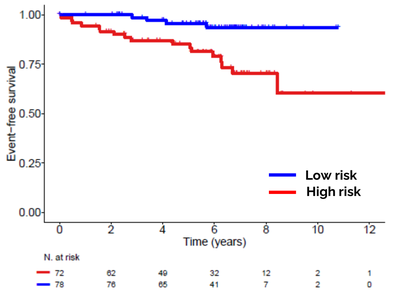
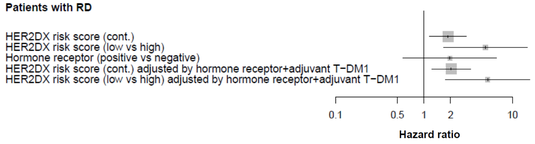


Figure 8. EFS HR forest plots in RD (n=150).



Conclusions

The HER2DX risk-score determined in baseline pre-treatment core-biopsies provides prognostic information beyond pCR status in patients with early-stage HER2+ breast cancer treated with neoadjuvant and adjuvant anti-HER2 treatment.

References and Acknowledgements

1. Prat et al. eBioMedicine. 2022.

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Conflicts of interest: OM has declared travel expenses and consulting fees from Roche and Reveal, and speaker fees from Eisai, Daiichi and Novartis.