#12P; HER2DX in HER2-positive Inflammatory Breast Cancer: a correlative analysis from a phase II clinical trial

Filipa Lynce[1,2], Fara Braso-Maristany[3], Adrienne Waks[1,2], Patricia Villagrasa[4], Guillermo Villacampa[4,5], Esther Sanfeliu[6], Harold Burstein[1,2], Patricia Galván[3], Laia Paré[4], Leilani M. Anderson[1], Charles M.Perou[7], Joel S. Parker[8], Ana Vivancos[8], Molly K. DiLullo[1], Sonia Pernas[9]; Eric P. Winer[10], Beth Overmoyer[1], Elizabeth Mittendorf[1], Aleix Prat[3,4], Sara M. Tolaney[1,2]

Affiliations: [1]Dana-Farber Cancer Institute, Boston, USA; [2]Harvard Medical School, Boston, USA, USA; [3]IDIBAPS, Barcelona, Spain, [3]Reveal Genomics, Barcelona, Spain; [5]Vall d 'Hebron Institute of Oncology (VHIO), Barcelona, Spain; [6]Pathology Dept. Hospital Clinic, Barcelona, Spain; [7]Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC; [8]Life Edit Therapeutics, Morrisville, NC, USA; [9]Catalan Institute of Oncology, Barcelona, Spain; [10]Yale Cancer Center, New Haven, CT, USA; 10Brigham and Women's Hospital, Boston, MA, USA; USA

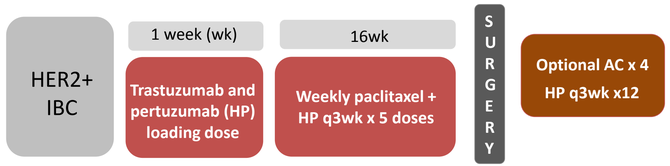
BACKGROUND

- HER2DX is a 27-gene assay for early-stage HER2+ breast cancer (BC) based on clinical data and the expression of 4 signatures (immune, proliferation, luminal, and HER2).
- Inflammatory Breast Cancer (IBC) is an aggressive form of breast cancer and usually associated with poor clinical outcomes.
- Here we evaluated the utility of HER2DX in HER2 positive (HER2+) IBC for the first time.

METHODS

Standardized HER2DX was evaluated centrally on baseline pre-treatment tumors from a phase II clinical trial (**Fig. 1**), in which patients (pts) with HER2+ IBC were treated with neoadjuvant paclitaxel, trastuzumab and pertuzumab (THP) x 16 weeks (*Pernas et al. Ther Adv Med Oncol 2022*). The primary aim of this correlative analysis was to evaluate the pCR rates (ypT0/isN0) according to HER2DX pCR-score pre-defined cutoffs (i.e., low, medium, and high). Secondary objectives included comparison of the HER2DX scores and signatures in IBC vs. stage II-III HER2+ non-IBC treated with neoadjuvant THPx12 weeks on the DAPHNe trial (NCT03716180). Descriptive statistics were used. Means between two groups were compared using a Student's t-test.

Figure 1 – Design of phase II trial in IBC (NCT01796197)



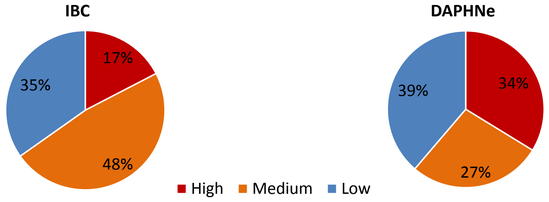
RESULTS

- This study enrolled 23 pts with HER2+ IBC. The pCR rate was 43.5% (10/23).
- HER2DX was evaluated in all pts (n=23) (**Table 1**). In IBC, the pCR rates in HER2DX pCR-high, pCR-med and pCR-low groups were 75.0% (3/4; 95% CI 19.4-99.4), 45.5% (5/11; 16.7-76.7) and 25.0% (2/8; 3.2-65.1), respectively (**Fig. 2, 3**). HER2DX high-risk in IBC represented 95.7% (**Fig. 4**).
- Compared to non-IBC, IBC had a lower % of HER2DX pCR-high disease, higher % of HER2DX pCR-medium, and similar % of HER2DX pCR-low disease (**Fig. 2**).
- Among the 4 HER2DX signatures, the HER2 amplicon was expressed at lower values in IBC vs. non-IBC (p=0.004), despite a similar % of HER2 3+ disease.

Table 1 – Patients baseline characteristics in IBC and non-IBC trials

Study	IBC	Non-IBC (DAPHNe)
N	23	80
HER2 IHC 3+ - n. (%)	19/21 (90.5%)	68/78 (87.2%)
Clinical tumor T4 stage - n. (%)	23 (100%)	0 (0%)
Clinical nodal+ status - n. (%)	21 (91.3%)	28 (35%)
Hormone receptor positive - n. (%)	12 (52.2%)	56 (70.0%)
pCR rate - n. (%)	10 (43.5%)	48 (60.0%)

Figure 2 – pCR-score groups distribution in IBC (N=23) and DAPHNe (N=80) trials



Correspondence to: Filipa Lynce, MD **Contact:** filipa_lynce@dfci.Harvard.edu **Twitter:** @FilipaLynce
Presenter's disclosures (A.W.): AstraZeneca (Advisory board), Macrogenics, Merck and Genentech (Research funding to institution)

RESULTS

Figure 3 – pCR rates according to pCR-score groups in IBC (N=23)

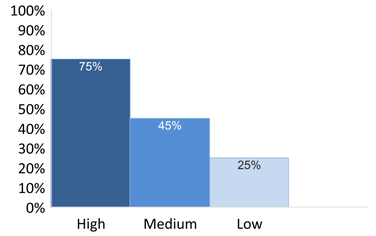
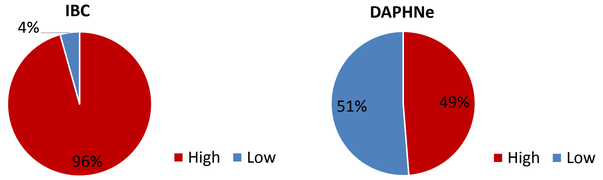


Figure 4 – HER2DX risk-score groups distribution in IBC (N=23) and DAPHNe (N=80) trials



CONCLUSION

HER2DX pCR-high designation may be less frequent in HER2+ IBC compared to HER2+ non-IBC. Lower mRNA expression of HER2 amplicon genes, and higher tumor burden at diagnosis, might explain the differences observed in the distribution of HER2DX scores and signatures between HER2+ IBC and non-IBC.

This trial was funded by Genentech and the HER2DX assay was funded by Reveal Genomics.