#8P; First decision impact study of HER2DX in patients with HER2-positive early breast cancer

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Background and objectives

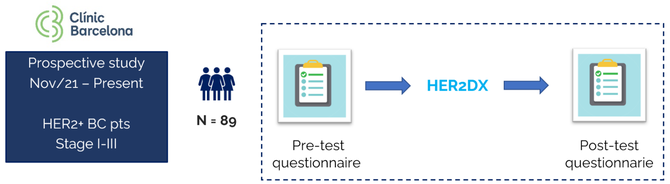
- HER2DX is a genomic test based on the expression of 27 genes tracking 4 signatures (luminal, proliferative, immune and HER2 amplicon) (**Figure 1**) that provides prognostic (HER2DX risk score) and predictive information (HER2DX pathologic complete response [pCR] score) in HER2 positive (HER2+) early breast cancer (BC). Here, we report the initial results of the first ongoing decision impact study of HER2DX at Hospital Clinic of Barcelona.

Figure 1. HER2DX components.

Methods

- This is an ongoing observational, prospective, pilot, unicentric study, since Nov/2021 (**Figure 2**), to analyze the impact of HER2DX in clinical practice in early-stage HER2+ BC. Any medical oncologist of the Breast Unit could order the test (11 oncologist participated). A survey was completed by the treating physician before and after receiving the result of HER2DX.
- The main objective was to assess the % of change in the therapeutic plan after obtaining the HER2DX report.
- Secondary objectives included 1) assess changes in the physician's confidence before and after the test in a scale from 1 to 5 (1 being the lowest confidence a 5 the maximum) and 2) analyze the association of the HER2DX pCR-score with the pathological response after neoadjuvant therapy (NAT).
- Descriptive statistics were used.

Figure 2. Study design.



Principal objective: % of change in the intention of the treatment plan

Results

- 89 patients (pts) have been recruited until 2nd of Feb/2023. Median age was 53 years (range 30-79) and 52% of pts were postmenopausal. Most pts had T1-2 tumors (87%), negative nodes (64%), grade 2 (56%) or 3 (41%), ductal histology (87%), hormone receptor positive (65%), median Ki67 of 35% (range 4-90%) and median tumor-infiltrating lymphocytes of 10% (range 0-90%) (**Table 1**).
- 78% of pts received NAT and 22% were treated with upfront surgery.

Table 1. Baseline characteristics of patients.

	All (N = 89)	HER2DX High risk (n = 44)	HER2DX Low risk (n = 45)	p
Histology– no. (%)				0.636
Ductal	77 (87%)	37 (84%)	40 (89%)	
Lobulillar	4 (4%)	3 (7%)	1 (2%)	
Apocrine	4 (4%)	1 (2%)	3 (7%)	
Micropapilar	3 (3%)	2 (5%)	1 (2%)	
Neuroendocrine	1 (1%)	1 (2%)	0	
Menopausal status – no. (%)				0.083
Premenopausal	42 (47%)	25 (57%)	17 (38%)	
Postmenopausal	46 (52%)	18 (41%)	28 (62%)	
Unknown	1 (1%)	1 (2%)		
cT – no.(%)				0.004
T1	42 (6%)	13 (30%)	29 (64%)	
T2	35 (40%)	20 (45%)	15 (33%)	
T3	9 (10%)	8 (18%)	1 (2%)	
T4	3 (3%)	3 87%)	0	
cN– no. (%)				< 0.001
N0	57 (64%)	14 (32%)	43 (96%)	
N1	27 (30%)	25 (57%)	2 (4%)	
N2	2 (2%)	2 (5%)	0	
N3	3 (3%)	3 (7%)	0	
Hormone receptor – no.(%)				0.602
Positive	58 (65%)	30 (68%)	28 (62%)	
Negative	29 (33%)	13 (30%)	16 (36%)	
Unknown	2 (2%)	1 (2%)	1 (2%)	
Ki67				0.627
Median (range)	35 (4 - 90)	35 (4 - 90)	33 (8 - 75)	
TILs				0.034
Median (range)	10 (0 - 90)	5 (0 - 60)	15 (0 - 90)	
Grade– no. (%)				0.870
G1	3 (4%)	1 (3%)	2 (5%)	
G2	45 (56%)	23 (58%)	22 (54%)	
G3	33 (41%)	16 (40%)	17 (42%)	

Results

- A change in the treatment plan before and after the HER2DX result (**Figure 3**) was observed in 49 of 87 (56%) cases (**Figure 4**).
- De-escalation of therapy was observed in 59% of pts (less intense chemotherapy [ChT] in 57% of them) and escalation in 41% of pts (more intense ChT in 65% of them).
- The confidence in the decision improved in 67% of cases.
- Among 56 evaluable pts treated with NAT, HER2DX pCR score was significantly associated with pCR (81% in pCR-medium/high and 32% in pCR-low; odds ratio= 9.3, p= 0.001) (**Figure 5**), independently of type of therapy (**Figure 6**).

Figure 3. Example of HER2DX results report.

Figure 5. pCR according to HER2DX pCR score group.

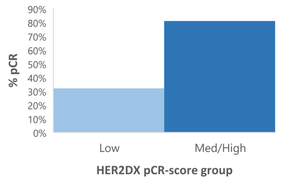


Figure 4. Decision change.

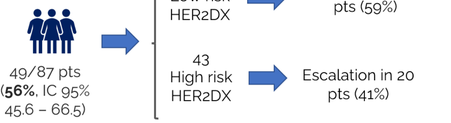


Figure 6. Neoadjuvant treatment by pCR score group.

	pCR score Med/High (n = 37)	pCR score Low (n = 19)	p
Dual HER2 blockade – no. (%)	34 (92%)	17 (89%)	0.557
Multi-agent ChT – no. (%)	27 (73%)	12 (63%)	0.323

Conclusions

In this first pilot and prospective study, HER2DX impacted clinical care in early-stage HER2+ breast cancer.

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.