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HER2DX genomic test in HER2-positive/hormone receptor-positive (HER2+/HR+) breast cancer (BC) treated with neoadjuvant trastuzumab (T) and pertuzumab (P): A correlative analysis from the PerELISA trial

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Background

HER2DX is a prognostic and predictive assay in early-stage HER2+ BC based on clinical data and the expression of 4 gene signatures (immune, proliferation, luminal differentiation and HER2 amplicon), including ERBB2 levels. Here, we evaluated the ability of HER2DX to predict efficacy of a de-escalated, chemotherapy (CT)-free neoadjuvant regimen in HER2+/HR+ BC.

Methods

HER2DX was evaluated on pre-treatment FFPE tumor samples from the PerELISA phase II study for postmenopausal patients (pts) with operable HR+/HER2+ BC. Pts received 2-week (wk) letrozole (L), and then underwent re-biopsy for Ki67 evaluation. Patients with endocrine therapy sensitive tumors (EST) (i.e., >20% Ki67 relative reduction at wk 2) continued L and 5 cycles of trastuzumab T+P. Primary aim was to test the ability of HER2DX risk-score, HER2DX pCR score and HER2DX ERBB2 score (as continuous variables and group categories) to predict pathological complete response (pCR) in patients with EST. Logistic regression and receiver-operator curve (ROC) analysis assessed associations of HER2DX scores with 1) pCR and 2) EST.

Results

HER2DX was evaluated in 55 pts (86%) enrolled in PerELISA and 40 pts (73%) had EST. The pCR rate in pts with EST was 22.5% (9/40). In this group, HER2DX pCR score, but not HER2DX risk-score, was significantly associated with pCR (p=0.012; Area under ROC [AUC]=0.80). The pCR rate in low, medium, and high HER2DX pCR score groups was 8.0% (2/25), 43.0% (6/14) and 100.0% (1/1), respectively. HER2DX ERBB2 score was significantly associated with pCR (p=0.004; AUC=0.88) and independently of HER2 levels (2+ vs 3+). The pCR rate in low, medium, and high HER2DX ERBB2 score groups was 0.0% (0/12), 8.3% (1/12) and 50.0% (8/16), respectively. HER2DX pCR score was also significantly associated with Ki-67 response following 2-wk L (p=0.004; AUC=0.77). The rate of EST in low, medium, and high HER2DX pCR score groups was 89.3% (25/28), 66.7% (14/21) and 16.7% (1/6), respectively.

Conclusions

HER2DX predicts endocrine sensitivity and pCR following neoadjuvant T+P+letrozole in pts with early-stage HER2+/HR+ BC. HER2DX could help tailor systemic therapy in this context.

Legal entity responsible for the study

The authors.

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Disclosure

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