



Prognostic value of the immune infiltration score in early breast cancer patients receiving dual HER2 blockade with trastuzumab and pertuzumab: an exploratory analysis of a randomized clinical trial

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Significance

Immune infiltration score provides prognostic sights in early breast cancer patients receiving dual HER2 blockade with trastuzumab and pertuzumab.

BACKGROUND

Although the survival benefit of dual epidermal growth factor receptor 2 (HER2) blockade with trastuzumab and pertuzumab was definitely demonstrated in HER2-amplified early breast cancer, sufficient biomarkers are urgently required to explain the heterogeneous response to dual HER-2 blockade therapy. The prognostic significance of immune infiltration in TRYPHAENA trial was investigated to tailor treatment in current analysis.

METHODS

Among the 225 HER2-amplified early breast cancer patients randomly assigned to trastuzumab/pertuzumab concurrently or sequentially with standard chemotherapy as neoadjuvant therapy in TRYPHAENA trial, 162 patients with available gene expression profile and complete follow-up data were enrolled. The normalized gene expression matrix (GSE109710) based on the NanoString nCounter array was downloaded from Gene Expression Omnibus database and further used to estimate the immune infiltration score (IIS) for each patient by the Immune Cell Abundance Identifier tool. A cut-off of IIS to stratify patients was determined by the R-based survminer package. Multivariable Cox proportional event-free survival (EFS) hazard ratios were preformed.

RESULTS

Among the 162 women included in the analysis (median [range] age, 49.0 [27-81] years), the pathologic complete response (pCR) rate was 50.0% (21/42) in patients with a high IIS (>0.628) and 66.7% (80/120) in patients with a low IIS (≤ 0.628).
At a median follow-up of 4.7 years, the multivariable-adjusted hazard ratio for EFS was 2.933 (95%CI, 1.223-7.033) for the high IIS and 0.356 (95%CI, 0.127- 0.999) in patients who achieved pCR, respectively.

Table 1. Comparison of patient characteristics.

Characteristics	High (n=42)	Low (n=120)	p-value
Age,y			
≥50	18(42.9%)	57(47.5%)	0.604
<50	24(57.1%)	63(52.5%)	
Histology grade			
G1	3(7.1%)	3(2.5%)	0.584
G2	16(38.1%)	48(40.0%)	
G3	16(38.1%)	46(38.3%)	
Unknown	7(16.7%)	23(19.2%)	
Hormone receptor status			
positive	17(40.5%)	65(54.2%)	0.127
negative	25(59.5%)	55(45.8%)	
Clinical stage			
II	21(50.0%)	65(54.2%)	0.606
III	21(50.0%)	54(45.0%)	
pCR			
yes	21(50.0%)	80(66.7%)	0.055
no	21(50.0%)	40(33.3%)	

Table 2. Cox regression for EFS.

Variable	Univariate analysis		Multivariable analysis	
	hazard ratio (95%CI)	P	hazard ratio (95%CI)	P
Age (≥50 vs <50 y)	1.628(0.747-3.545)	0.220	1.779(0.760-4.165)	0.184
Histology grade (G3 vs G1/G2)	0.855(0.563-1.300)	0.464	1.019(0.633-1.641)	0.938
HR (positive vs negative)	0.918(0.426-1.982)	0.828	0.920(0.369-2.296)	0.859
Clinical stage (III vs II)	2.207(0.975-4.995)	0.058	1.278(0.820-1.991)	0.279
pCR (yes vs no)	0.408(0.187-0.889)	0.024	0.356(0.127-0.999)	0.050
IIS (high vs low)	2.812(1.300-6.084)	0.009	2.933(1.223-7.033)	0.016

CONCLUSIONS

Our analysis demonstrates an independent prognostic value of IIS in patients receiving trastuzumab/pertuzumab-based neoadjuvant chemotherapy.

REFERENCES

1. Ignatiadis M, Van den Eynden G, Roberto S, et al. Tumor-Infiltrating Lymphocytes in Patients Receiving Trastuzumab/ Pertuzumab-Based Chemotherapy: A TRYPHAENA Substudy. *J Natl Cancer Inst.* 2019;111(1):69–77. doi:10.1093/jnci/djy076

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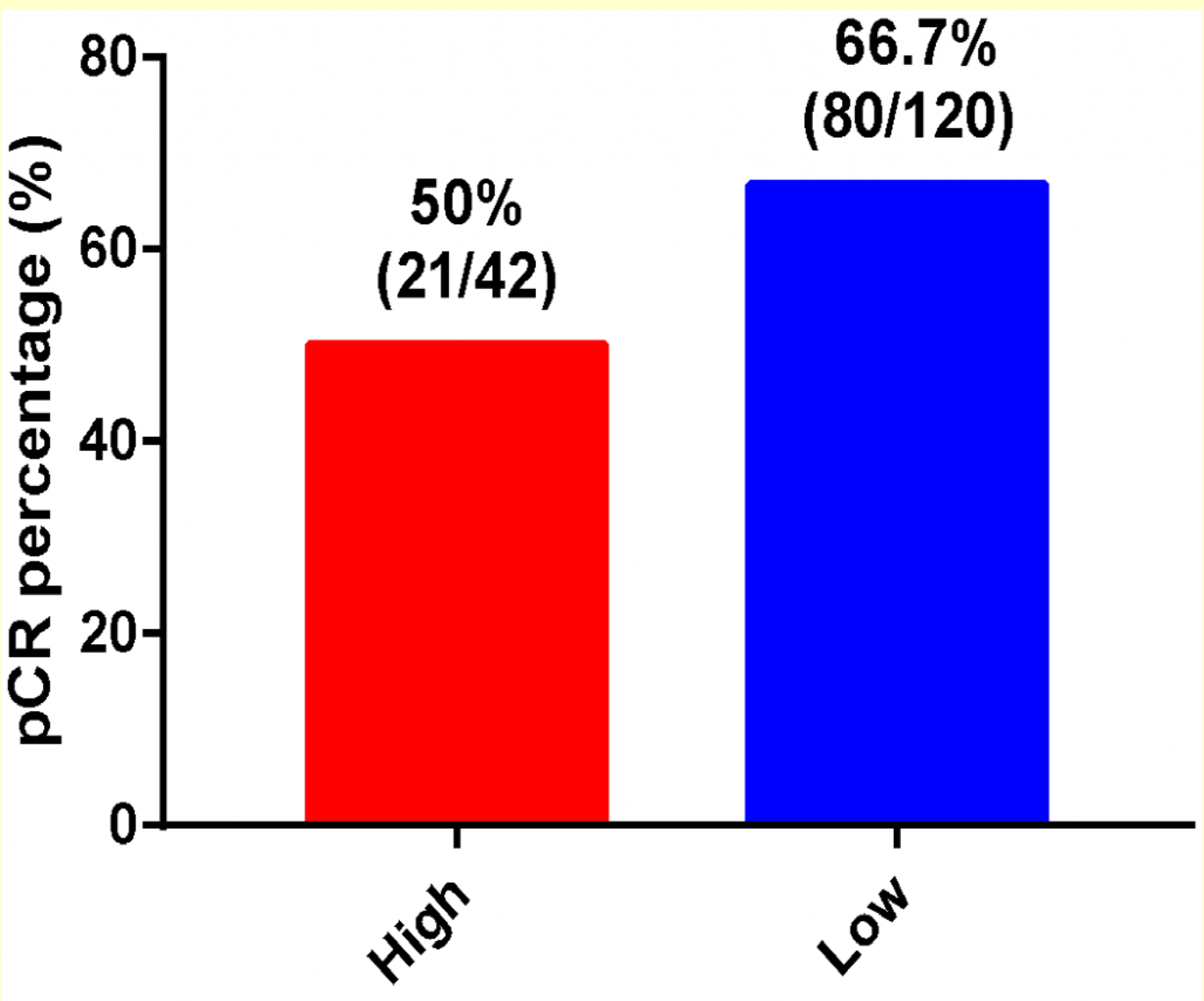


Figure 1. The pCR rate in high and low IIS group

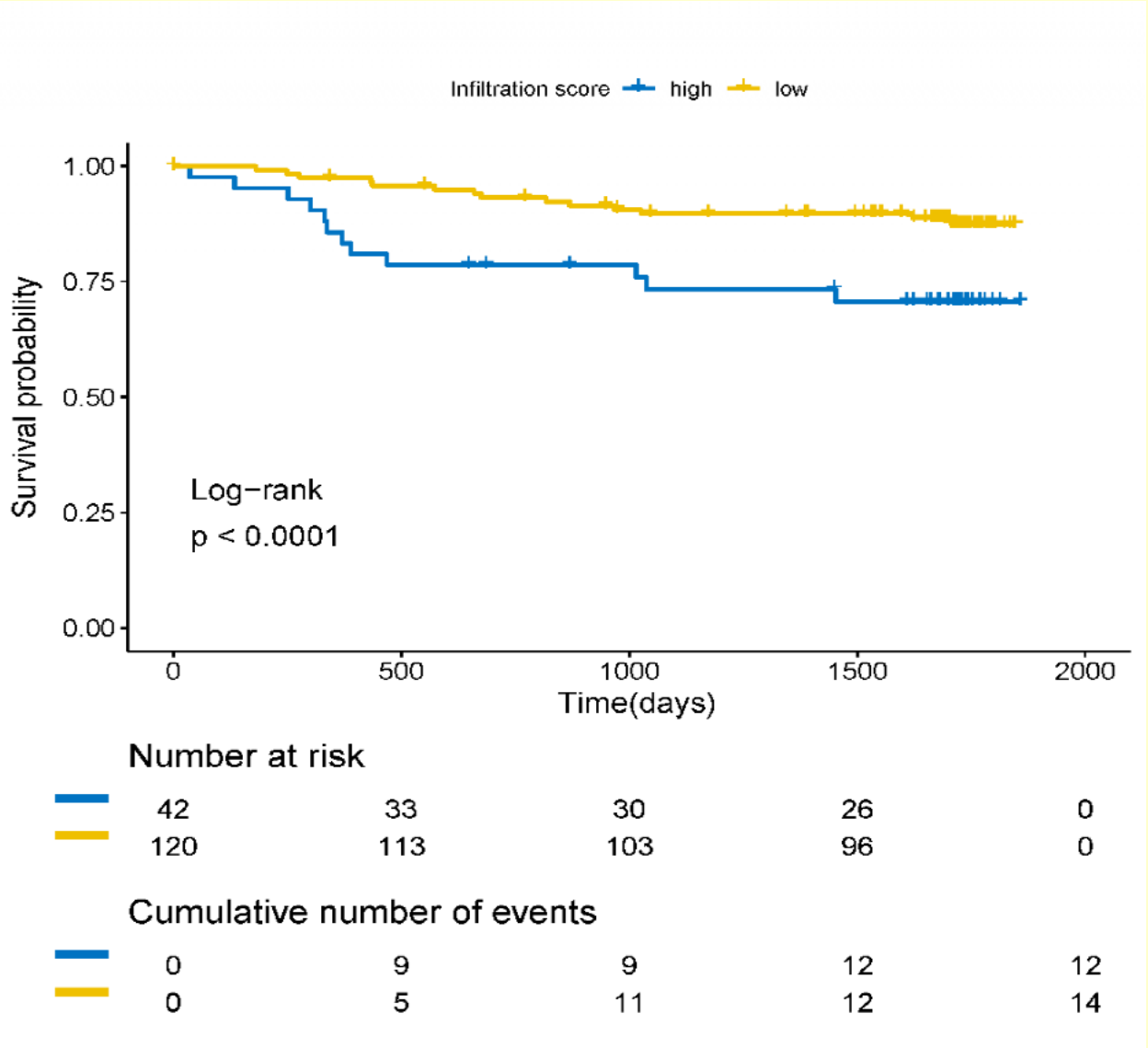


Figure 2. Survival analysis of high vs. low IIS