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Prognostic value of baseline neutrophil/lymphocyte ratio in HER2-positive metastatic breast cancer: Exploratory analysis from the CLEOPATRA trial

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Background

The prognostic value of neutrophil/lymphocyte ratio (NLR) for HER2-positive metastatic breast cancer (MBC) is not well studied. This study aims to evaluate the prognostic role of baseline NLR in HER2-positive MBC patients treated with trastuzumab/pertuzumab.

Methods

The clinical data of 780 patients from CLEOPATRA were applied from VIVLI platform, and 248 HER2-postive MBC were collected from six local hospitals. Propensity score matching (PSM) and inverse probability of treatment weighting (IPTW) analyses were used to control bias. The associations between clinicopathological factors, NLR and progression-free survival (PFS) and overall survival (OS) were analyzed by univariate and multivariate analyses.

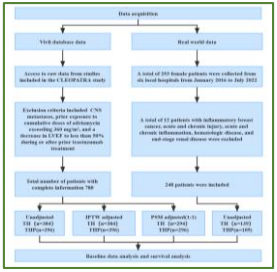

Fig1.The flowchart of our study.

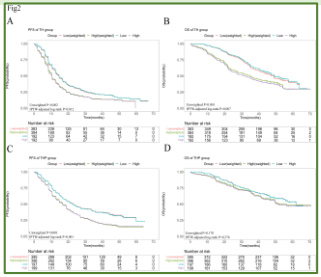

Fig2. The KM curves of (A) PFS and (B) OS before and after IPTW analyses according to the low or high NLR in TH group. The KM curves of (C) PFS and (D) OS before and after IPTW analyses according to the low or high NLR in THP group.
Abbreviations: KM, Kaplan-Meier; PFS, progression-free survival; OS, overall survival; IPTW, inverse probability of treatment weighting; TH group, trastuzumab plus docetaxel group; THP group, pertuzumab plus trastuzumab plus docetaxel.

Results

After PSM or IPTW adjustment, the subgroups were similar. Low baseline NLR was prognostic with better PFS and OS in the TH group in raw, PSM and IPTW models. Upon IPTW, low NLR, versus high NLR, was associated with improved PFS (HR 1.35, 95% CI 1.07-1.70, P = 0.012) and OS (HR 1.47, 95% CI 1.12-1.94, P = 0.006) in the TH group. In the THP group, low baseline NLR was also correlated with better PFS, but not for OS in the three models. After IPTW, patients with low NLR were associated with better PFS (HR 1.52, 95% CI 1.20-1.93, P = 0.001) comparing that with high NLR.

Multivariate analyses showed that low baseline NLR was a predictor for PFS and OS in TH group, and PFS in the THP group in the three models. In the real-world study, low baseline NLR was a predictor of better PFS among patients with trastuzumab plus docetaxel or trastuzumab plus pertuzumab plus docetaxel therapy (P = 0.025 and 0.009 respectively).

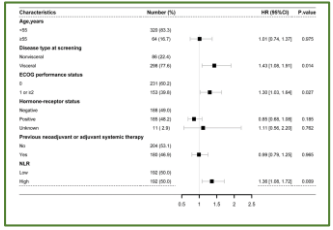

Fig3. Forest plots showed independent influences on PFS in the TH group by multivariate analysis.
Abbreviations: HR, hazard ratio; 95% CI, 95% confidence interval; NLR, neutrophil to lymphocyte ratio; PFS, progression-free survival; TH group, trastuzumab plus docetaxel group.

Conclusions

Low baseline NLR is associated with better survival outcome among HER2-positive MBC receiving docetaxel plus trastuzumab or docetaxel plus trastuzumab plus pertuzumab as first-line therapy. Re-analyses of prospective randomized studies are needed to verify the role of baseline NLR in HER2-positive MBC treated with trastuzumab/pertuzumab.

Clinical trial identification

Many studies have shown that higher neutrophil/lymphocyte ratio (NLR) was correlated with worse survival in triple-negative breast cancer (BC), but there were some controversies in HER2-positive metastatic BC (MBC). Our previous study with a total of 843 early HER2-positive BC proved that low baseline NLR was associated with better survival outcome in patients receiving trastuzumab therapy. This exploratory analysis of 780 HER2-positive MBC from CLEOPATRA trial shows that low baseline NLR is significantly associated with better progression-free survival (PFS) and overall survival (OS) among patients receiving docetaxel plus trastuzumab, and with PFS among those receiving docetaxel plus trastuzumab plus pertuzumab. Another cohort analysis of 248 HER2-positive MBC from six local hospitals also shows the similar results. These findings suggest that HER2-positive MBC with low high NLR might benefit less from treatment of docetaxel plus trastuzuma/pertuzumab, and need intensive treatment for those metastatic disease.

Legal entity responsible for the study

The authors

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Disclosure

All authors have declared no conflicts of interest