The Systemic Inflammatory Response Identifies Patients with Adverse Clinical Outcome from Immunotherapy in Hepatocellular Carcinoma

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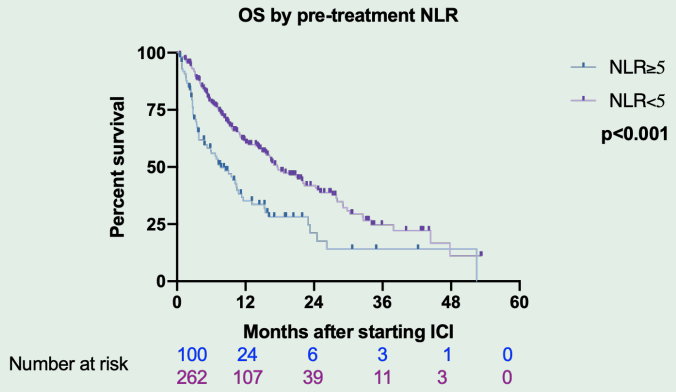
BACKGROUND

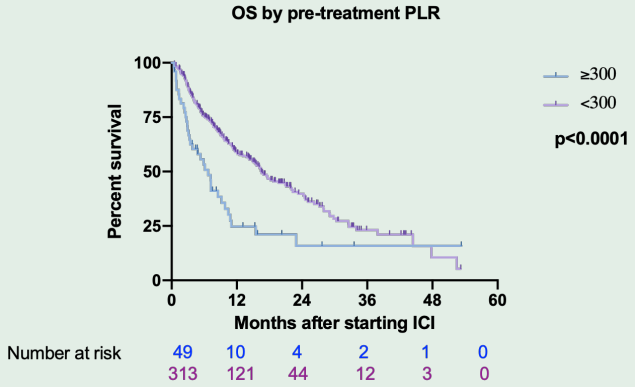
Systemic **inflammation** is a hallmark of cancer, and it has a pivotal role in **HCC** development and progression. The role of systemic inflammation in influencing outcomes of patients treated with immunotherapy for HCC has not been fully elucidated.

METHODS

We conducted a retrospective study including 362 patients receiving immune-checkpoint inhibitors (ICIs) across 3 continents, evaluating the influence on **overall survival (OS)**, **progression free survival (PFS)** and **radiologic responses (ORR)** of the following inflammatory markers:

- Neutrophiles to lymphocytes ratio (NLR);
- Platelet to lymphocytes ratio (PLR);
- Prognostic nutritional index (PNI).





RESULTS

In our **362 patients** treated with immunotherapy, median OS and PFS were **9 and 3.5 months** respectively. Amongst tested inflammatory biomarkers, patients with **NLR ≥ 5 had shorter OS (7.7 vs 17.6 months, p < 0.0001), PFS (2.1 vs 3.8 months, p = 0.025) and lower ORR (12% vs 22%, p = 0.034),** similarly, patients with **PLR ≥ 300 reported shorter OS (6.4 vs 16.5 months, p < 0.0001) and PFS (1.8 vs 3.7 months, p = 0.0006) (Figure 1).** NLR emerged as independent prognostic factors for OS in univariate and multivariate analysis (HR 1.95, 95%CI 1.45-2.64, p < 0.001; HR 1.73, 95%CI 1.23-2.42, p = 0.002) and PLR remained an independent prognostic factor for both OS and PFS in multivariate analysis (HR 1.60, 95%CI 1.6-2.40, p = 0.020; HR 1.99, 95%CI 1.11-3.49, p = 0.021) **(Table 1).** Patients with **PNI < 45, reported shorter mOS** (10.8 vs 17.7 months, HR 1.60, 95%CI 1.23-2.18, p=0.018) and not significantly shorter mPFS (2.5 vs 4 months, HR 1.28, 95% CI 0.91-1.65 p=0.17); PNI was not confirmed to be prognostic in the multivariate model (HR 0.99, 95%CI 0.71-1.37, p=0.940).

CONCLUSIONS

Systemic inflammation measured by **NLR** and **PLR** is an independent negative prognostic factor in HCC patients undergoing ICIs therapy.