The systemic inflammatory response identifies patients with adverse clinical outcome from immunotherapy in hepatocellular carcinoma.

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Introduction

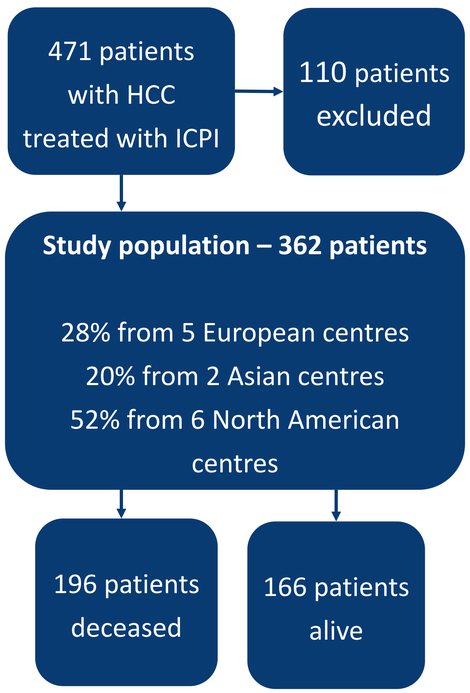
- Inflammation plays a crucial role in the HCC pathogenesis and prognosis
- Systemic inflammation has been linked to hyper-progressive disease following immunotherapy in HCC[1]
- Inflammation-based biomarkers include **neutrophil to lymphocyte ratio** (NLR)[2] , **platelet to lymphocyte ratio** (PLR)[2] and **prognostic nutritional index** (PNI) (calculated by albumin (g/l) x absolute lymphocyte count[3])

Aim

To investigate the prognostic value of inflammation-based biomarkers (**NLR, PLR and PNI**) on survival and response to ICPIs in patients with HCC

Methods

- Multi-centre retrospective registry of patients receiving immune checkpoint inhibitors (ICPIs) across 3 continents between 2015-2018
- Patient demographics, treatment, staging variables and complete blood count results were collected
- Patients were classified in poor risk categories **if NLR≥5, PLR≥300 or PNI<45**
- Each biomarker was correlated with **objective response rates** (ORR) by RECIST v.1.1 criteria. Kaplan Meier and log rank tests were used to assess inflammatory markers in relationship with **progression free** (PFS) and **overall survival** (OS)
- This was followed by multivariable analysis using Cox regression models.



Results

Baseline characteristics	n=472 (%)
Gender	
Male	284 (78.5)
Female	78 (21.5)
Age	
<65	180 (49.7)
≥ 65	182 (50.3)
Aetiology	
HBV	81 (22.4)
HCV	121 (33.4)
Alcohol induced	81 (22.4)
NASH	43 (11.9)
Other	36 (9.94)
Cirrhosis	
Present	259 (71.5)
Absent	103 (28.5)
Portal vein thrombosis	
Present	247 (68.2)
Absent	115 (31.5)
Child-Pugh Class	
A	272 (75.1)
B	90 (24.9)

Table 1 – clinicopathological features

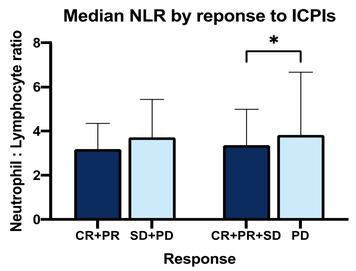


Figure 1 NLR is significantly higher in patients who are refractory to ICPI therapy

Median OS was 8.6 months, and median PFS was 3.5 months

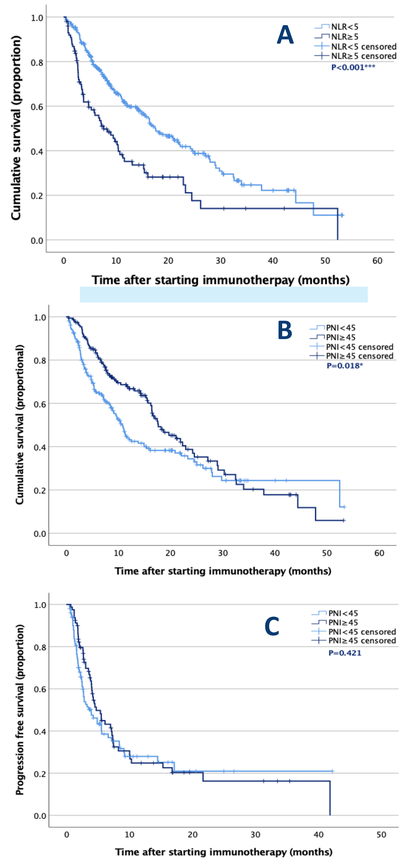


Figure 2 Kaplan Meier curves comparing inflammatory markers with overall and progression free survival.
A - NLR≥5 is associated with worse overall survival
B - PNI<45 is associated with worse overall survival
C - NLR≥5 is associated with worse progression free survival

- Systemic inflammation was associated with **worse ORR**, as measured by **NLR≥5** (12% vs 22%, p=0.034)
- A significantly **shorter OS** was also observed for patients with **NLR≥5** (5.1 vs 9.5 months, p<0.001) and **PNI<45** (7.2 vs 10.5 months, p=0.018)
- **NLR** (p<0.001) remaining an independent **predictor of OS** following multivariable analysis as well as **Child-Pugh class** (p=0.004) and **portal vein thrombosis** (p=0.010).
- **Shorter PFS** was also observed in patients with **NLR≥5** (2.1 vs 3.7 months, p=0.036) and **portal vein thrombosis** (2.7 vs 3.7, p=0.030)
- **NLR5** and **portal vein thrombosis** remain independent prognostic factors for PFS after multivariable analysis (p<0.05).

Conclusion

Systemic inflammation measured by the NLR and PNI is associated with **worse response and survival** in HCC patients receiving ICPI therapy independent of common clinicopathologic characteristics. Therapeutic targeting of the systemic inflammatory response may augment responsiveness to ICPI.

References:

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