

ASSOCIATION OF NEUTROPHIL-TO-LYMPHOCYTE RATIO AND PLATELET-TO-LYMPHOCYTE RATIO WITH CLINICAL OUTCOMES TO TISLELIZUMAB MONOTHERAPY IN PATIENTS WITH PREVIOUSLY TREATED ADVANCED HEPATOCELLULAR CARCINOMA

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Background Tislelizumab, an anti-PD-1 monoclonal antibody, demonstrated clinical activity and was well-tolerated in patients with previously treated advanced hepatocellular carcinoma (HCC) in the Phase 2 RATIONALE-208 study (NCT03419897). We explored whether baseline neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) or their post-treatment change correlated with clinical efficacy of tislelizumab treatment.

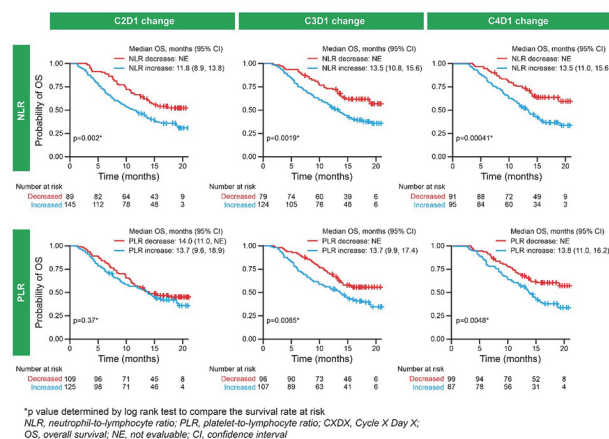
Methods Eligible patients (>18 years) who had received ≥1 prior line of systemic therapy for advanced HCC were administered open-label tislelizumab (200 mg) intravenously every 3 weeks until no further clinical benefit was observed. NLR and PLR were assessed using peripheral blood samples collected at baseline, Cycle 2 Day 1 (C2D1), C3D1, and C4D1. Survival analysis (progression free survival [PFS] and overall survival [OS]) was conducted by Kaplan-Meier method and survival rate at risk was compared by log rank test. Logistic regression was used to analyze association of post-treatment change of NLR or PLR with objective response rate (ORR). In the baseline analysis, median NLR or PLR in this study was used as a cut-off. All statistical analysis results are post-hoc exploratory and thereby p values are descriptive.

Results Overall, 249 patients were enrolled, of which 249, 234, 203, and 186 patients had evaluable NLR and PLR data at baseline, C2D1, C3D1, and C4D1, respectively. Analysis of NLR at baseline, using median NLR (3.2) as cut-off, demonstrated higher OS (p=0.0024) and PFS (p=0.071) in NLR-low versus NLR-high groups (median OS [mOS]:17.4 versus 9.9 months; median PFS [mPFS]: 2.8 versus 1.5 months). Analysis of PLR at baseline, using median PLR (141.4) as cut-off, showed higher OS (p=0.0085) and PFS (p<0.0001) in PLR-low versus PLR-high groups (mOS: 16.2 versus 10.8 months; mPFS: 2.8 versus 1.4 months). In post-treatment analysis, patients with decreased NLR or PLR at C2D1, C3D1 or C4D1 had higher ORR (table 1) and longer OS (figure 1) compared with patients with increased NLR or PLR at each timepoint.

Abstract 362 Table 1 Post-treatment decreases in NLR or PLR were associated with response to tislelizumab monotherapy

NLR	C2D1 change		C3D1 change		C4D1 change	
	Decreased (N=89)	Increased (N=145)	Decreased (N=79)	Increased (N=124)	Decreased (N=91)	Increased (N=95)
ORR (95% CI), p value*	22% 0.31 (0.14, 0.67) 0.0031	8%	27% 0.28 (0.12, 0.61) 0.0015	9%	26% 0.22 (0.09, 0.55) 0.0011	7%
PLR	Decreased (N=109)	Increased (N=125)	Decreased (N=96)	Increased (N=107)	Decreased (N=99)	Increased (N=87)
	ORR (95% CI), p value*	19% 0.47 (0.22, 1.02) 0.0556	10%	25% 0.24 (0.10, 0.57) 0.0012	8%	27% 0.13 (0.04, 0.38) 0.0002

*Determined by logistic regression
NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; CXDX, Cycle X Day X; ORR, objective response rate; OR, odds ratio; CI, confidence interval



Abstract 362 Figure 1 Post-treatment decreases in NLR or PLR were associated with improved OS following tislelizumab monotherapy

Conclusions In patients with previously treated advanced HCC that received tislelizumab monotherapy, lower baseline NLR or PLR was associated with longer OS and PFS, and post-treatment decreases of NLR or PLR were associated with higher ORR and longer OS. These observations support NLR and PLR as potential prognostic biomarkers in patients with advanced HCC treated with tislelizumab and will be further investigated in an on-going Phase 3 study (NCT03412773).

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Trial Registration NCT03419897

Ethics Approval This study was conducted according to the ethical principles of the Declaration of Helsinki, Good Clinical Practice guidelines, the principles of informed consent and the requirements of the public registration of clinical trials. Written informed consent was obtained from each patient prior to screening. The protocol was approved by the institutional ethics committee and was monitored by the investigators and study sponsor.

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