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Role of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte-ratio (PLR) in unresectable hepatocellular carcinoma (uHCC): Subgroup analysis of patients treated with camrelizumab (cam) + rivoceranib (rivo) in the CARES-310 trial.

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Background: CARES-310 (NCT03764293) evaluated the combination of the PD-1 inhibitor, cam, and the VEGFR-2 tyrosine kinase inhibitor, rivo, compared to sorafenib (sor) for the treatment of 543 patients (pts) with uHCC. Cam + rivo significantly improved mOS (22.1 months [mo] [95% CI 19.1-27.2] vs 15.2 mo [13.0-18.5] HR 0.62 [95% CI 0.49-0.80]; one-sided $p < 0.0001$) and mPFS (5.6 mo [95% CI 5.5-6.3] vs 3.7 mo [2.8-3.7]; HR 0.54 [95% CI 0.44-0.67]; one-sided $p < 0.0001$) compared to sor. The most common (≥20%) grade ≥3 treatment-related adverse events (TRAEs) for cam + rivo were hypertension (37.5%) and increased AST (16.5%) vs palmar-plantar erythrodysesthesia syndrome (15.2%) for sor. An elevated level of inflammation, including NLR and PLR, have been associated with poor survival outcomes in pts with HCC (Lin S, et al. *Trans Cancer Res*. 2021). Here, we present a subgroup analysis of the CARES-310 trial evaluating the impact of baseline (BL) NLR and PLR status on pt outcomes. **Methods:** The subgroup of pts treated with cam+rivo and BL NLR < 5 or ≥5 and PLR < 300 or ≥300 were evaluated for mOS, mPFS, overall response rate (ORR), disease control rate (DCR), and safety. **Results:** Of 272 pts treated with cam+rivo, 64.3% of pts had extrahepatic spread, median AFP was 84.1 ng/mL, 86.8% were Child-Pugh (CP) class A5, 13.2% were CP class A6, 73.5% were ALBI grade 1, 26.5% were ALBI grade 2. Additionally, 249 pts had NLR < 5, 10 pts had NLR ≥5, 252 pts had PLR < 300, and 7 pts had PLR ≥300. Pts with BL NLR < 5 and PLR < 300 demonstrated improved outcomes in mOS, mPFS, ORR, and DCR vs pts with BL NLR ≥5 and PLR ≥300 (Table). Rates of any grade TRAEs and grade ≥ 3 TRAEs were comparable between pts with BL NLR < 5 and ≥5 and PLR < 300 and ≥300 (Table). **Conclusions:** These results suggest that NLR and PLR may serve as a prognostic marker in patients with uHCC, but larger studies are needed to validate these findings. Clinical trial information: NCT03764293. Research Sponsor: Elevar Therapeutics; Jiangsu Hengrui Pharmaceuticals.

	NLR < 5 (n = 249)	NLR ≥5 (n = 10)	PLR < 300 (n = 252)	PLR ≥300 (n = 7)
mOS, mo (95% CI)	22.1 (20.3, 27.2)	9.9 (3.4, 14.3)	22.1 (19.1, 27.2)	NR (5.0, NR)
One-side P value[a] for OS	p = 0.0001		p = 0.112	
mPFS, mo (95% CI)	5.6 (5.5, 7.4)	4.4 (1.1, 7.4)	5.6 (5.5, 7.4)	3.1 (1.1, NR)
One-side P value[a] for PFS	p = 0.0592		p = 0.0126	
ORR[b],%	25.2	20.0	25.6	0
DCR[c], %	78.7	70.0	79.4	42.9
Any grade TRAE, n (%)	244 (98.0)	8 (80.0)	246 (97.6)	6 (85.7)
Grade ≥3 TRAEs, n (%)	248 (99.6)	9 (90.0)	251 (99.6)	6 (85.7)
irAEs, n (%)	141 (56.6)	2 (20.0)	139 (55.2)	4 (57.1)

[a]P value is calculated based on log-rank test;
[b]ORR defined as CR+PR per RECIST v1.1;
[c]DCR defined as CR, PR, and SD per RECIST v1.1.
Note: data not available for 13 pts. irAE, immune-related adverse event; NR, not reported.