Impact of risk factors on overall survival (OS) in patients (pts) with unresectable hepatocellular carcinoma (HCC) treated with first-line (1L) tislelizumab (TIS)

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Background: TIS is a monoclonal antibody with high affinity and specificity for programmed cell death protein 1. In the phase 3 RATIONALE-301 trial (NCT03412773), TIS demonstrated non-inferior OS versus sorafenib (SOR) as 1L monotherapy for unresectable HCC (median [m] OS 15.9 [TIS] vs 14.1 [SOR] months [mo]; hazard ratio [HR] 0.85), with a favorable safety profile. Certain biomarkers are potential prognostic factors and may impact OS in 1L treatment of unresectable HCC; this exploratory analysis examined the effect of albumin-bilirubin (ALBI) grade, platelet count, platelet-lymphocyte ratio (PLR), and neutrophil-lymphocyte ratio (NLR) as predictors of OS in RATIONALE-301.

Methods: Systemic therapy-naïve adults with histologically confirmed HCC (Barcelona Clinic Liver Cancer Stage C or Stage B that was not amenable to or progressed after loco-regional therapy; Child-Pugh A), with ≥1 measurable lesion per RECIST v1.1, and an ECOG performance status ≤1 were randomized 1:1 to receive TIS (200 mg IV Q3W) or SOR (400 mg orally BID) until disease progression, intolerable toxicity, or withdrawal. The primary endpoint was OS.

Results: Overall, 674 pts were randomized (TIS n=342; SOR n=332). At data cutoff (July 11, 2022), minimum study follow-up was 33 mo. Demographic and baseline characteristics for biomarkers were generally balanced across arms. Numerically longer (≥2 mo) mOS was observed in biomarker subgroups ALBI grade 1 vs 2 and NLR ≤3 vs >3 with TIS or SOR, and PLR ≤141 vs >141 with TIS (**Table**). Both platelet count threshold subgroups were accompanied by a smaller difference (<2 mo) in mOS between biomarker cutoffs, which may indicate limited prognostic value for this biomarker. TIS also

demonstrated numerically longer OS versus SOR in the same subgroup categories: ALBI grade 1, PLR ≤141, and NLR ≤3.

Conclusions: This analysis suggests that ALBI grade, PLR, and NLR could have prognostic value for OS, irrespective of treatment. TIS demonstrated numerically improved mOS compared with SOR for PLR ≤141 and NLR ≤3, suggesting higher benefit for pts with a more favorable balance between systemic inflammation and immunity.

			Median OS (mo) (95% CI)	
	No. events/ No. pts	**HR for death (95% CI)**	**TIS**	**SOR**
ALBI grade				
≥2	156/180	0.84 (0.61, 1.16)	9.5 (7.2, 10.8)	9.1 (6.2, 13.1)
1	340/482	0.85 (0.69, 1.06)	19.9 (15.9, 24.2)	16.9 (13.7, 19.8)
Platelet count				
>150K	281/378	0.84 (0.66, 1.06)	14.9 (11.0, 19.8)	13.5 (11.6, 18.4)
≤150K	215/284	0.83 (0.63, 1.08)	16.6 (13.5, 22.7)	14.2 (11.6, 19.0)
PLR				
>141*	204/264	0.90 (0.68, 1.19)	10.5 (7.7, 16.5)	13.1 (8.9, 16.0)
≤141	292/398	0.79 (0.63, 1.00)	19.4 (15.2, 24.0)	14.5 (13.1, 19.2)
NLR				
>3	198/249	0.98 (0.74, 1.30)	9.8 (7.4, 12.9)	13.1 (8.7, 14.3)
≤3	298/413	0.74 (0.59, 0.93)	20.9 (15.9, 25.3)	15.2 (13.2, 19.2)

No., number. Intent-to-treat analysis set.
*Threshold used in RATIONALE-208