Impact of Risk Factors on Overall Survival in Patients With Unresectable Hepatocellular Carcinoma Treated With First-line Tislelizumab

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Abstract No: 4083 presented at ASCO 2023, Chicago, USA

Conclusions

Risk factors may impact overall survival (OS) in first-line (1L) treatment for patients with unresectable hepatocellular carcinoma (HCC). This exploratory analysis from RATIONALE-301 suggests that albumin-bilirubin (ALBI) grade could have prognostic value for OS, irrespective of treatment.

For patients with a more favorable balance between systemic inflammation and immunity, tislelizumab demonstrated numerically improved median OS compared with sorafenib for platelet-lymphocyte ratio (PLR) ≤141, and neutrophil-lymphocyte ratio (NLR) ≤3. For patients with PLR >141 or NLR >3 median OS was longer on sorafenib.

Background

HCC is one of the leading causes of cancer-related death worldwide.[1] Most patients present with advanced disease and therefore have a poor prognosis.[2] Certain HCC biomarkers may be prognostic factors, with a potential clinical role in the 1L treatment of unresectable HCC.[1]

Tislelizumab is a humanized monoclonal antibody with high affinity and binding specificity for programmed cell death protein 1, which was specifically engineered to minimize Fcγ receptor binding on macrophages.[2-4]

In the phase 3 RATIONALE-301 trial (NCT03412773), tislelizumab demonstrated noninferior OS versus sorafenib as 1L monotherapy for unresectable HCC (median OS 15.9 vs 14.1 months, respectively; hazard ratio 0.85), with a favorable safety profile.[5]

This exploratory analysis examined the effects of ALBI grade, platelet count, PLR, and NLR as predictors of OS in RATIONALE-301.

Methods

- The study design has been previously described[2,5]
- Systemic therapy-naïve adults with histologically confirmed, unresectable HCC were randomized (1:1) to receive tislelizumab 200 mg intravenously every 3 weeks or sorafenib 400 mg orally twice a day until disease progression, intolerable toxicity, or withdrawal of consent
- The primary endpoint was OS; key secondary endpoints included objective response rate, progression-free survival, and duration of response by blinded independent review committee, per RECIST v1.1; safety was also investigated
- This exploratory analysis examined OS in subgroups of patients defined by ALBI grade (≥2 vs 1), platelet count (>150K vs ≤150K), PLR (>141 vs ≤141), and NLR (>3 vs ≤3) as predictors of OS

Results

Baseline Characteristics

- At data cutoff (July 11, 2022), minimum study follow-up was 33 months
- Demographics and baseline characteristics for biomarkers were generally balanced across arms (**Table 1**)

Prognostic Biomarkers Analysis

- Tislelizumab demonstrated numerically longer (≥3 months) median OS versus sorafenib in the biomarker subgroup categories ALBI grade 1 (**Figure 1**), NLR ≤3 (**Figure 2**), and PLR ≤141 (**Figure 3**). The biomarker subgroups NLR >3 and PLR >141 demonstrated numerically shorter median OS for tislelizumab versus sorafenib
- A limited difference in median OS was observed between the higher and lower platelet count threshold subgroups (<2 months), which may indicate a restricted prognostic value for this biomarker (**Figure 4**)

Prognostic Biomarkers Analysis (Ctd.)

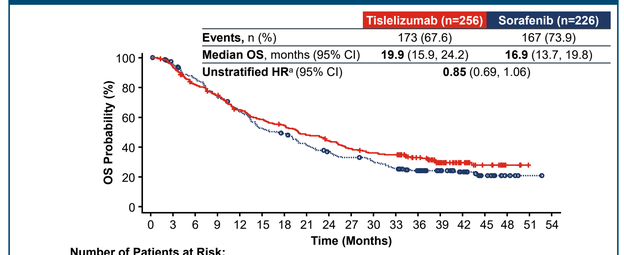
- The analysis suggests that ALBI grade could have prognostic value for OS, irrespective of treatment
- OS by potential risk factors in the intent-to-treat (ITT) analysis set is shown in **Figure 4**

Table 1. Baseline Characteristics (ITT Analysis Set)

	TIS (n=342)	SOR (n=332)	Total (N=674)
Age, years, mean (SD)	60.2 (12.5)	59.3 (12.7)	59.8 (12.6)
Male sex, n (%)	289 (84.5)	281 (84.6)	570 (84.6)
ECOG PS 1, n (%)	159 (46.5)	151 (45.5)	310 (46.0)
BCLC Stage, n (%)			
Stage B	70 (20.5)	80 (24.1)	150 (22.3)
Stage C	272 (79.5)	252 (75.9)	524 (77.7)
Hepatitis etiology, n (%)			
HBV	203 (59.4)	206 (62.0)	409 (60.7)
HCV	46 (13.5)	39 (11.7)	85 (12.6)
Uninfected	82 (24.0)	80 (24.1)	162 (24.0)
Child-Pugh class, n (%)			
5	263 (76.9)	248 (74.7)	511 (75.8)
6	77 (22.5)	84 (25.3)	161 (23.9)
ALBI grade[a], n (%)			180 (26.7)
≥2	82 (24.0)	98 (29.5)	482 (71.5)
1	256 (74.9)	226 (68.1)	
Platelet count[a], n (%)			
>150K	189 (55.3)	189 (56.9)	378 (56.1)
≤150K	149 (43.6)	135 (40.7)	284 (42.1)
PLR[a], n (%)			
>141	131 (38.3)	133 (40.1)	264 (39.2)
≤141	207 (60.5)	191 (57.5)	398 (59.1)
NLR[a], n (%)			
>3	129 (37.7)	120 (36.1)	249 (36.9)
≤3	209 (61.1)	204 (61.4)	413 (61.3)

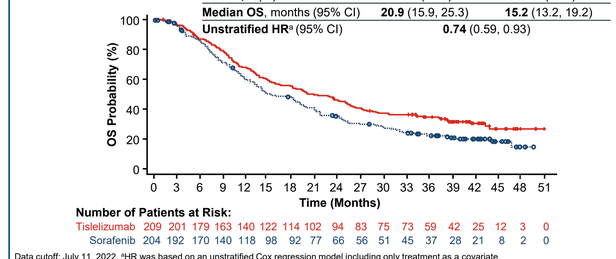
[a]Missing, n (%): TIS: 4 (1.2); SOR: 8 (2.4); Total: 12 (1.8). **Abbreviations**: ALBI, albumin-bilirubin; BCLC, Barcelona Clinic Liver Cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; HBV/HCV, hepatitis B/C virus; ITT, intent-to-treat; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio; SD, standard deviation; SOR, sorafenib; TIS, tislelizumab.

Figure 1. OS (ITT Analysis Set; ALBI Grade 1)



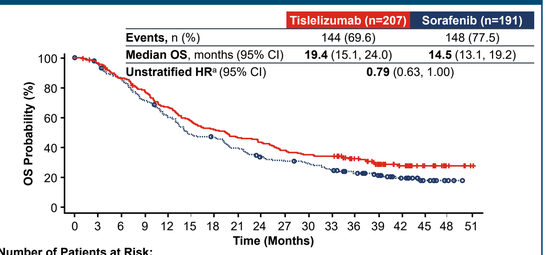
Data cutoff: July 11, 2022. [a]HR was based on an unstratified Cox regression model including only treatment as a covariate.
Abbreviations: ALBI, albumin-bilirubin; CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; OS, overall survival.

Figure 2. OS (ITT Analysis Set; NLR ≤3)



Data cutoff: July 11, 2022. [a]HR was based on an unstratified Cox regression model including only treatment as a covariate.
Abbreviations: CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; NLR, neutrophil-lymphocyte ratio; OS, overall survival.

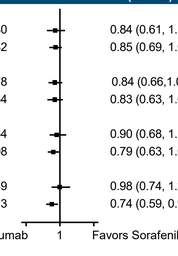
Figure 3. OS (ITT Analysis Set; PLR ≤141)



Data cutoff: July 11, 2022. [a]HR was based on an unstratified Cox regression model including only treatment as a covariate.
Abbreviations: CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; OS, overall survival; PLR, platelet-lymphocyte ratio.

Figure 4. Forest Plot of OS by Potential Risk Factors (ITT Analysis Set)

Subgroup	No. of Events/ No. of Patients	Hazard Ratio for Death (95% CI)	Median OS, mo (95% CI) Tislelizumab	Median OS, mo (95% CI) Sorafenib
Albumin-bilirubin 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 (13.47, 22.7)	14.2 (11.6, 19.0)
Platelet-lymphocyte ratio				
>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)
Neutrophil-lymphocyte ratio				
>3	198/249	0.98 (0.74, 1.23)	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)



Hazard ratio and its 95% CI were estimated from unstratified Cox regression model including treatment as covariate.
Abbreviations: CI: confidence interval; ITT, intent-to-treat; No., number; OS; overall survival.

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Acknowledgments

This study was sponsored by BeiGene, Ltd. Medical writing support, under the direction of the authors, was provided by Adeline Lum Nde, PhD, of Ashfield MedComms, an Inizio company, and was funded by BeiGene, Ltd. Editorial support was provided by Elizabeth Hermans, PhD, of BeiGene, Ltd.

Disclosures

Disclosure information is available online with the abstract details.

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