Clinical outcomes associated with tislelizumab in patients with advanced hepatocellular carcinoma who have been previously treated with sorafenib or lenvatinib in RATIONALE-208

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Conclusions

Tislelizumab was investigated beyond the first-line setting, as effective second- and third-line treatment options are limited for patients with advanced HCC and there is an unmet medical need.

This analysis indicated that tislelizumab was clinically active and well tolerated in patients with advanced HCC who have received prior systemic treatment with SOR/LEN.

The results of this descriptive-only secondary analysis support the potential role of tislelizumab as a treatment option beyond the first-line setting for patients with advanced HCC.

Background

Tislelizumab is an anti-programmed cell death protein 1 (PD-1) monoclonal antibody with high affinity and specificity for PD-1, engineered to limit antibody-dependent cellular phagocytosis, a potential mechanism of resistance to anti-PD-1 therapy.[1–3]

Tislelizumab demonstrated clinical activity and was generally well tolerated in patients with previously treated advanced hepatocellular carcinoma (HCC) in the open-label, multicenter, Phase 2 RATIONALE-208 study (NCT03419897).[4]

After a median follow-up of 12.4 months, objective response rate (ORR) was 13.3%; median progression-free survival (PFS) was 2.7; median overall survival (OS) was 13.2 months.[4]

At the time of initiation of this study, only sorafenib (SOR) and lenvatinib (LEN) were recommended first-line treatments for patients with advanced HCC.[5–7]

Methods

- Here, we report the results of a descriptive-only secondary analysis of patients who were patients who had been previously treated with SOR/LEN and had received one or more doses of tislelizumab

Scan QR code to read full study methods

Results

Patient disposition

- As of February 2020 (data cutoff), 249 patients were enrolled and 235 patients had received prior treatment with SOR/LEN (**Table 1**)
- Median follow-up duration for patients previously treated with SOR/LEN was 12.5 months (range: 0.1–21.3) and 30 (12.8%) of 235 patients were still on-treatment at data cutoff

Efficacy

- Confirmed ORR by IRC in patients previously treated with SOR/LEN was 13.6% (95% CI: 9.5, 18.7), including two complete responses and 30 partial responses (**Table 2**)
- Disease control was achieved in 55.3% of patients and median DoR was not reached (**Table 2**)
- Best change in target lesion size from baseline is reported in **Figure 1**
- Median PFS by IRC was 2.7 months (**Figure 2**), and median OS was 13.5 months (**Figure 3**)

Table 1. Baseline demographics and disease characteristics

		All patients (n=235)
Age, years	Median (range)	62.0 (29–90)
Sex, n (%)	Male	206 (87.7)
Race, n (%)	Asian	112 (47.7)
	White	96 (40.9)
	Other	6 (2.6)
	Unknown	21 (8.9)
ECOG PS, n (%)	0	121 (51.5)
	1	114 (48.5)
Prior lines of anticancer therapy, n (%)	1	126 (53.6)
	≥ 2	109 (46.4)
BCLC staging at study entry, n (%)	B	24 (10.2)
	C	211 (89.8)
Child-Pugh score at study entry,* n (%)	A	234 (99.6)
Extrahepatic spread, n (%)	Present	187 (79.6)
Macrovascular invasion, n (%)	Present	42 (17.9)
HCC etiology†, n (%)	Hepatitis B	114 (48.5)
	Hepatitis C	36 (15.3)
	History of alcohol abuse	76 (32.3)
	NASH	42 (17.9)

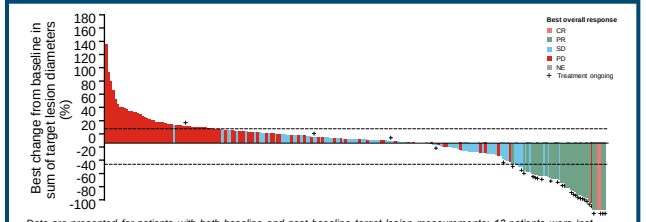
*One patient had Child-Pugh B at study entry, but this was not expected to affect the study results. †Some patients had multiple HCC etiologies. BCLC, Barcelona Clinic Liver Cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; HCC, hepatocellular carcinoma; NASH, non-alcoholic steatohepatitis

Table 2. Summary of antitumor activity by IRC

	All patients (n=235)
ORR (CR+PR), % (95% CI)	13.6 (9.5, 18.7)
Best overall response, n (%)	
CR	2 (0.9)
PR	30 (12.8)
SD*	98 (41.7)
PD	95 (40.4)
Not assessable†	10 (4.3)
DCR (CR+PR+SD), % (95% CI)	55.3 (48.7, 61.8)
Median DoR, months (95% CI)	NE (14.0, NE)

*Includes two patients assessed as non-CR/non-PD due to lack of measurable disease per IRC; †No or unevaluable post-baseline assessment. CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response; IRC, independent review committee; NE, not evaluable; ORR, overall response rate; PR, partial response

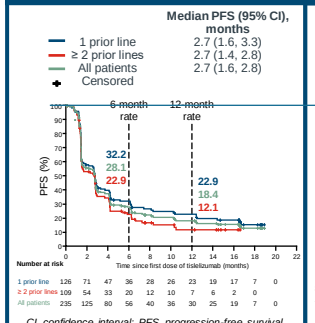
Figure 1. Best change in target lesion size from baseline by IRC



Data are presented for patients with both baseline and post-baseline target lesion measurements; 13 patients were 'not assessable' per IRC. Overall number of patients included: n=222

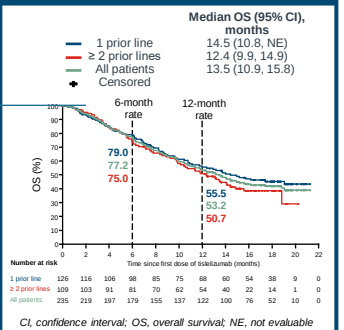
CR, complete response; IRC, independent review committee; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease

Figure 2. Kaplan-Meier curve for PFS by IRC



CI, confidence interval; PFS, progression-free survival

Figure 3. Kaplan-Meier curve for OS



CI, confidence interval; OS, overall survival; NE, not evaluable

Safety

- Tislelizumab was generally well tolerated in patients previously treated with SOR/LEN (**Table 3**; **Table 4**)

Table 3. Summary of AEs

Patients, n (%)	All patients (n=235)
Any TEAE	223 (94.9)
Grade ≥ 3 TEAE	116 (49.4)
Serious TEAEs	87 (37.0)
TEAE leading to discontinuation	26 (11.1)
TEAE leading to dose delay	72 (30.6)
TEAE leading to death*	24 (10.2)
TEAEs reported in ≥ 15% of patients	
AST increased	61 (26.0)
ALT increased	46 (19.6)
Blood bilirubin increased	43 (18.3)
Decreased appetite	39 (16.6)
Asthenia	39 (16.6)

**21 patients had disease progression reported as the primary cause of death. AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LEN, lenvatinib; SOR, sorafenib; TEAE, treatment-emergent AE*

Table 4. Immune-mediated AEs

Patients, n (%)	All patients (n=235)
Any immune-mediated TEAE	50 (21.3)
Grade ≥ 3 TEAE	12 (5.1)
Immune-mediated TEAEs reported in ≥ 2% of patients (any grade)	
Hypothyroidism	16 (6.8)
Hyperthyroidism	6 (2.6)
Hepatic-related immune-mediated TEAEs reported in ≥ 1% of patients (any grade)	
AST increased	4 (1.7)
ALT increased	3 (1.3)
Hepatitis	3 (1.3)

Data are listed in order of decreasing frequency. AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TEAE, treatment-emergent AE

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