Tislelizumab monotherapy for patients with previously treated advanced hepatocellular carcinoma: RATIONALE-208 Chinese subpopulation

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Zhenggang Ren*,[1] Zhiwei Li,[2] Tao Zhang,[3] Weijia Fang,[4] Sheng Hu,[5] Hongming Pan,[6] Chia-Jui Yen,[7] Jinlin Hou,[8] Yajin Chen,[9] Guo-Liang Shao,[10] Chiun Hsu,[11] Bai Yuxian,[12] Zhiqiang Meng,[13] Ming-Mo Hou,[14] Congying Xie,[15] Yong Liu,[16] John Wu,[17] Bai Li,[18] Sandra Chica-Duque,[19] Ann-Lii Cheng[20]

[1]Liver Cancer Institute, Zhongshan Hospital, Fudan University, Shanghai, China; [2]Division of Hepatobiliary and Pancreatic Surgery, The First Affiliated Hospital, Zhejiang University, Hangzhou, China; [3]Abdominal Oncology Department, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; [4]Department of Medical Oncology, The First Affiliated Hospital, Zhejiang University, Hangzhou, China; [5]Department of Internal Medicine Oncology, Hubei Cancer Hospital, Wuhan, China; [6]Department of Medical Oncology, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Zhejiang, China; [7]Clinical Medicine Research Center, National Cheng Kung University Hospital, Tainan, Taiwan; [8]Southern Medical University, Hepatology Unit, Nanfang Hospital, Guangzhou, China; [9]Department of Hepatobiliary Surgery, Sun Yat-Sen University, Guangzhou, China; [10]Department of Radiology, Zhejiang Cancer Hospital, Hangzhou, China; [11]Department of Oncology, National Taiwan University Hospital, Taipei, Taiwan; [12]Department of Medical Oncology, Harbin Medical University Cancer Hospital, Harbin, China; [13]Department of Integrative Oncology, Shanghai Cancer Hospital, Fudan University, Shanghai, China; [14]Division of Hematology and Oncology, Chang Gung Memorial Hospital and Chang Gung University, Taoyuan, Taiwan; [15]Radiation and Medical Oncology Department, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China; [16]Xuzhou Central Hospital, Xuzhou, China; [17]BeiGene (Ridgefield Park) Co., Ltd., Ridgefield Park, NJ, USA; [18]BeiGene (Beijing) Co., Ltd., Beijing, China; [19]BeiGene (San Mateo) Co., Ltd., San Mateo, CA, USA; [20]Department of Oncology, National Taiwan University Cancer Center and National Taiwan University Hospital, Taipei, Taiwan. *Presenting author

Conclusions

Tislelizumab demonstrated durable antitumor activity in Chinese patients with previously treated advanced HCC.

IRC-assessed ORR was 12.3% and 12.9% in the Chinese and overall populations, respectively, indicating responses in the Chinese population did not differ from the overall population. Median DoR was not reached in either population.

The safety and tolerability of tislelizumab was similar in Chinese and overall populations, and in line with the established profile of the PD-1/PD-L1 inhibitor class.[1,2]

Further insights into the use of tislelizumab in first-line HCC are anticipated from the ongoing, global, randomized Phase 3 RATIONALE-301 study (NCT03412773).[3]

Background

Tislelizumab, a monoclonal antibody with high binding affinity to the PD-1 receptor, was specifically engineered to minimize Fcγ receptor binding on macrophages.[4,5]

The global, single-arm Phase 2 RATIONALE-208 study (NCT03419897) investigated the efficacy, safety and tolerability of tislelizumab monotherapy in patients who had received at least one prior line of systemic therapy for advanced hepatocellular carcinoma (HCC).[6]

In the primary analysis, tislelizumab demonstrated encouraging and durable clinical activity and was well tolerated in the overall study population (N=249; data cutoff: Feb 27, 2020).[6]

Given that over 50% of HCC cases worldwide occur in China,[7] this analysis explored whether the clinical activity of tislelizumab in the RATIONALE-208 study varied between the overall population and the subpopulation enrolled in Mainland/Taiwan China.

Methods

- The study design for the RATIONALE-208 study has been reported previously[6] (scan QR code to read full study methods):

Results

Patient disposition

- 249 patients were enrolled in the study and received tislelizumab, of whom 122 were enrolled in Mainland/Taiwan China (hereafter referred to as the Chinese population) (**Table 1**)
- The main difference in baseline characteristics between the populations was HCC etiology; most patients (89.3%) in the Chinese population had HCC caused by hepatitis B only, compared with half of patients (49.4%) in the overall population (**Table 1**)
- At the data cutoff date (Jun 30, 2021) the median follow-up was 12.9 and 12.7 months in the Chinese and overall populations, respectively

Efficacy

- Independent review committee-assessed antitumor activity was not impacted by region (**Table 2**)
- Among responding patients, responses were ongoing in 0/15 patients (0.0%) and 8/32 patients (25.0%) in the Chinese and overall populations, respectively, at the time of data cutoff (**Figure 1**)
- Overall survival and progression-free survival were similar in the Chinese and overall populations (**Figures 2 and 3**)

Safety and tolerability

- Median duration of tislelizumab exposures were 2.8 (range: 0.7–35.2) months and 4.1 (range: 0.5–36.6) months for the Chinese and overall populations, respectively
- Tislelizumab was generally well tolerated in both the Chinese and overall populations (**Table 3**)

Table 1. Baseline demographics and disease characteristics

		Chinese population (n=122)	Overall population (N=249)
Median age, years (range)		55.0 (28–75)	62.0 (28–90)
Sex, n (%)	Male	109 (89.3)	217 (87.1)
ECOG PS, n (%)	0	66 (54.1)	129 (51.8)
	1	56 (45.9)	120 (48.2)
BCLC staging, n (%)	B	9 (7.4)	24 (9.6)
	C	113 (92.6)	225 (90.4)
Child-Pugh, n (%)	A	121 (99.2)*	248 (99.6)*
Extrahepatic spread, n (%)		106 (86.9)	200 (80.3)
Macrovascular invasion, n (%)		15 (12.3)	46 (18.5)
Prior lines of systemic therapy, n (%)	1 line	72 (59.0)†	138 (55.4)†
	≥ 2 lines	50 (41.0)	111 (44.6)
HCC etiology, n (%)	Hepatitis B only	109 (89.3)	123 (49.4)
	Hepatitis C only	4 (3.3)	31 (12.4)
	Hepatitis B and C	0 (0)	5 (2.0)
	Non-viral	9 (7.4)	90 (36.1)
Prior anti-cancer systemic therapy, n (%)	SOR and LEN naïve‡	14 (11.5)	14 (5.6)
	SOR and/or LEN treated	108 (88.5)	235 (94.4)

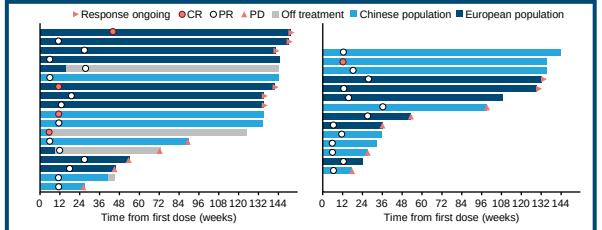
One patient had Child-Pugh classification B at study entry; †One patient received prior sorafenib treatment as adjuvant therapy and no subsequent systemic therapies; ‡All patients received oxaliplatin-based therapy as first-line therapy. Prior treatment with immune checkpoint inhibitors was not permitted. BCLC, Barcelona Clinic Liver Cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; HCC, hepatocellular carcinoma; LEN, lenvatinib; SOR sorafenib. Data cutoff: Jun 30, 2021

Table 2. Summary of antitumor activity by IRC

	Chinese population (n=122)	Overall population (N=249)
ORR (CR + PR), % (95% CI)	12.3 (7.1, 19.5)	12.9 (9.0, 17.7)
Best overall response, n (%)		
CR	3 (2.5)	5 (2.0)
PR	12 (9.8)	27 (10.8)
SD*	37 (30.3)	100 (40.2)
PD	64 (52.5)	107 (43.0)
Not assessable†	6 (4.9)	10 (4.0)
DCR (CR + PR + SD), % (95% CI)	42.6 (33.7, 51.9)	53.0 (46.6, 59.3)
Median DoR, months (95% CI)	NR (5.0, NE)	NR (14.6, NE)

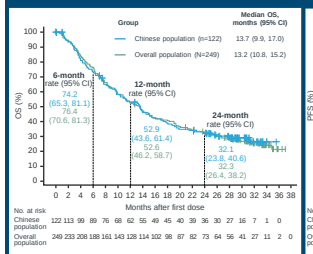
Includes two patients assessed as non-CR/non-PD due to a lack of measurable disease per IRC; †No post-baseline assessment or an unevaluable post-baseline assessment. CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response; IRC, independent review committee; NE, not estimable; NR, not reached; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease. Data cutoff: Jun 30, 2021

Figure 1. Duration of response (IRC-assessed)



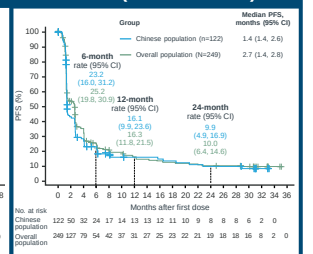
All responders included; each bar represents an individual patient (n=15 [Chinese population]; n=32 [overall population]). Treatment period is plotted only up to the time of the last tumor assessment for patients who were still on treatment. IRC, independent review committee; CR, complete response; PD, progressive disease; PR, partial response. Data cutoff: Jun 30, 2021

Figure 2. Kaplan-Meier plot of OS



CI, confidence interval; OS, overall survival. Data cutoff: Jun 30, 2021

Figure 3. Kaplan-Meier plot of PFS (IRC-assessed)



CI, confidence interval; IRC, independent review committee; PFS, progression-free survival. Data cutoff: Jun 30, 2021

Table 3. Summary of adverse event incidence

Patients, n (%)	Chinese population (n=122)		Overall population (N=249)	
	Treatment-emergent	Treatment-related	Treatment-emergent	Treatment-related
Any	112 (91.8)	81 (66.4)	236 (94.8)	158 (63.5)
Grade ≥ 3	52 (42.6)	23 (18.9)	123 (49.4)	38 (15.3)
Serious	44 (36.1)	13 (10.7)	93 (37.3)	18 (7.2)
Leading to death	9 (7.4)	0 (0)	26 (10.4)*	0 (0)
Leading to dose delay†	35 (28.7)	25 (20.5)	79 (31.7)	46 (18.5)
Leading to treatment discontinuation	12 (9.8)	6 (4.9)	28 (11.2)	13 (5.2)
Immune-mediated	28 (23.0)	28 (23.0)	55 (22.1)	55 (22.1)
Grade ≥ 3	6 (4.9)	6 (4.9)	11 (4.4)	11 (4.4)

23 patients had disease progression reported as the primary cause of death; †Included patients who were held for dosing after last dose administration, and eventually leading to decision of dose discontinuation. Data cutoff: Jun 30, 2021

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Disclosures

All authors have submitted their disclosures to the WCGI online Declaration of Interests platform.

*Author contact details: ren.zhenggang@zs-hospital.sh.cn (Zhenggang Ren)