Clinical outcomes in patients (pts) with previously treated advanced hepatocellular carcinoma (HCC) experiencing hepatitis B virus (HBV) DNA increases during tislelizumab (TIS) treatment in RATIONALE-208

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Background

The effect of checkpoint inhibitor therapy on HBV infection is uncertain. TIS, an anti-PD-1 antibody, was clinically active and well tolerated in pts with previously treated advanced HCC in the Phase 2 RATIONALE-208 study (NCT03419897). Objective response rate by independent committee review (IRC) in pts with a history of HBV infection was consistent with the overall population (12.5% vs 13.3%, respectively). We explored whether TIS treatment was associated with increased HBV DNA and the clinical significance of HBV DNA elevations.

Methods

Pts with ≥ 1 prior systemic therapy for advanced HCC received TIS 200 mg IV Q3W. Pts with inactive, chronic, or active HBV were eligible if HBV DNA levels were < 500 IU/mL at screening (pts with detectable hepatitis B surface antigen [HBsAg] or detectable HBV DNA were required to be managed per treatment guidelines). HBV DNA testing was conducted every 4 cycles if HBV DNA was detectable at screening, or when clinically indicated.

Results

Among 249 enrolled pts, 128 had a history of HBV infection. Of these pts, 114 were HBsAg positive at baseline (BL), 36 had detectable HBV DNA at BL, and 32 had detectable HBV DNA and HBsAg at BL. Clinically significant increases in HBV DNA levels from BL were reported in 7 pts, with no pattern relative to the time of TIS initiation (**Table**). All 7 pts were HBsAg positive at BL and had been receiving antiviral treatment for ≥ 3 months before the first dose of TIS. Six out of the 7 pts had increases in alanine transaminase (ALT) from BL during the study (**Table**), 4 of whom had ≥ 3-fold increases in ALT which were observed concurrently or soon after HBV DNA increases. IRC-assessed best overall response (BOR) was partial response (PR) for 1 pt with increased HBV DNA and progressive disease for the remaining 6.

HBV-related treatment-emergent adverse events (TEAEs) were reported in 6 of the 7 pts (2 pts had a Grade 3 TEAE of hepatitis B; 2 pts had a Grade 2 TEAE of HBV reactivation; 2 pts had a TEAE of increased HBV DNA, with one Grade 1 and one Grade 3 event). All HBV-related TEAEs were non-serious and did not result in discontinuation of TIS.

Conclusions

Clinically significant increases in HBV DNA from BL were reported in a small number of pts, which does not suggest that TIS is associated with increased HBV DNA. Tumor responses in these pts were consistent with the overall population and HBV-related TEAEs were manageable and did not require discontinuation of TIS, demonstrating that HBV DNA increases did not impact treatment. The effects of TIS in pts with HBV infection will be further investigated in an ongoing Phase 3 trial (NCT03412773).

Table

Pt	1	2	3	4	5	6†	7
Peak increase from BL							
HBV DNA, IU/mL	708*	10390*	1090*	12900	2528*	99200*	5130*
ALT, U/L	181	182	27	-48	190	256	44.9
Time from 1st dose of TIS to HBV DNA increase, days	35	189	41	34	112	223	336

*HBV DNA was undetectable at BL

†BOR: PR