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Updated results of a phase Ib study of regorafenib (REG) plus pembrolizumab (PEMBRO) for first-line treatment of advanced hepatocellular carcinoma (HCC)

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Background

REG is a tyrosine kinase inhibitor with immunomodulatory activity and PEMBRO is an anti-PD-1 monoclonal antibody. Based on potential synergistic effects, we designed a phase Ib study of REG plus PEMBRO for first-line treatment of advanced HCC.

Methods

This is an ongoing, dose-finding study in patients (pts) who had no prior systemic therapy. In the first cohort, pts received REG 120 mg/day orally for 3 weeks on/1 week off plus PEMBRO 200 mg IV q 3 weeks. In later cohorts, the REG dose could be escalated (160 mg) or reduced (80 mg); the PEMBRO dose is fixed. The primary objective is safety and tolerability. Secondary objectives are to define the maximum tolerated dose (MTD) and recommended phase II dose and assess antitumor activity.

Results

By April 29, 2020, a total of 36 pts were treated with REG 120 mg. Median age was 66 years (range 29–81); 31%/69% of pts were BCLC stage B/C; 100% Child–Pugh A; ECOG status 0/1 was 72%/28%. Dose-limiting toxicities occurred in 4/18 evaluable pts: grade (Gr) 3 ALT/AST increased with Gr 2 bilirubin increased (n=2); Gr 3 rash (n=2). The REG MTD was 120 mg. Gr 3 or 4 treatment-emergent adverse events (TEAEs) occurred in 31/36 pts (86%); the most common are shown in the table below. Incidence of Gr 3 hand–foot skin reaction was 8%, Gr 3 maculopapular rash 6%, and Gr 3 rash 3%; there were no cases of Gr 4 rash. One Gr 5 TEAE was reported (not drug-related). TEAEs led to a REG dose reduction or interruption in 72% of pts and to a PEMBRO dose interruption in 53%. Median treatment duration (range) including pts ongoing was 2.5 months (0.2–15.9) for REG and 3.5 months (0.03–19.2) for PEMBRO. Of 32 evaluable pts, 9 (28%) had a partial response and 20 (63%) had stable disease (RECIST 1.1); disease control rate was 91%.

Conclusions

The combination of REG plus PEMBRO for first-line treatment of advanced HCC showed no unexpected safety signals and encouraging antitumor activity. Assessment of REG 80 mg plus PEMBRO is ongoing.Table: 990P

TEAEs (Gr 3/4 in ≥10% pts), n (%)	Gr 3	Gr 4
AST increased	7 (19)	0
ALT increased	5 (14)	2 (6)
Hypertension	5 (14)	0
Bilirubin increased	5 (14)	0
Lipase increased	4 (11)	1 (3)

MedDRA v22.0; CTCAE v4.03 grade.ALT, alanine aminotransferase; AST, aspartate aminotransferase; TEAE, treatment-emergent adverse event.

Clinical trial identification

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