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A phase Ib study of the PD-1 antagonist CS1003 plus lenvatinib (LEN) in Chinese patients (pts) with the first-line (1L) unresectable hepatocellular carcinoma (uHCC)

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Background

CS1003 is a novel humanized IgG4 anti-PD-1 monoclonal antibody. LEN, a multi-kinase inhibitor of VEGFR 1-3, FGFR 1-4, PDGFRα, RET, and KIT, is approved for the treatment of 1L uHCC in multiple countries. Here we report the preliminary efficacy and safety from a phase Ib trial of CS1003 + LEN in 1L uHCC.

Methods

In this open-label phase Ib study, pts with 1L uHCC, BCLC stage B or C, Child-Pugh class A, and ECOG PS ≤ 1 received 200 mg CS1003 intravenously once every 3 weeks and LEN orally (body weight ≥ 60 kg: 12 mg/day; < 60 kg: 8 mg/day) daily. Dose-limiting toxicity (DLT) was monitored during the first cycle in Part 1. Additional pts were enrolled in Part 2 for efficacy expansion. The primary endpoint was objective response rate (ORR) assessed by investigators per RECIST v1.1. Secondary endpoints included safety and other efficacy parameters.

Results

As of 21 Mar 2020, no DLTs were reported in Part 1. A total of 19 pts were treated (Part 1, n=8; Part 2, n=11) and 17 remained on study treatment. The median treatment duration of CS1003/LEN was 15.0 (range: 0.7-27.4) weeks. Among the 16 efficacy-evaluable pts, ORR was 37.5% with 6 pts achieving partial response (3 confirmed); duration of response (DoR) ranged from 0.03+ to 4.17+ months, and median DoR was not reached. Tumor shrinkage was observed in 6 of the 7 pts with stable disease. Treatment-related adverse events (TRAEs) occurred in 16 pts (84.2%). The most common TRAEs were hypothyroidism (n=5), platelet count decreased (n=5) and protein urine present (n=5). CTCAE Grade (G) ≥3 TRAEs occurred in 3 pts (15.8%). One pt had a G3 bilirubin conjugated increased that was attributed to both CS1003 and LEN. The other two pts had a G3 diarrhoea and a G3 hypophosphataemia, respectively, that were only related to LEN. No new safety signals were identified.

Conclusions

The CS1003 + LEN combination shows promising antitumor activity and an acceptable safety profile in Chinese pts with 1L uHCC. A multi-regional, double-blinded, randomized phase III trial of LEN with or without CS1003 in 1L uHCC is underway.

Clinical trial identification

NCT03809767.

Legal entity responsible for the study

CStone Pharmaceuticals (Su Zhou) Co., Ltd.

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Disclosure

J. Ni, Q. Qi, Y. Ma, Z. Qin: Full/Part-time employment: CStone Pharmaceuticals (Su Zhou) Co., Ltd. A. Tse: Shareholder/Stockholder/Stock options, Full/Part-time employment: CStone Pharmaceuticals (Su Zhou) Co., Ltd. All other authors have declared no conflicts of interest.