

Title:

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

Category: Hepatocellular carcinoma (HCC)

Background:

CS1003 is a novel humanized IgG4 anti-PD-1 monoclonal antibody. LEN, a multi-kinase inhibitor of VEGFR 1-3, FGFR 1-4, PDGFR α , 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 1b trial of CS1003 + LEN in 1L uHCC.

Methods:

In this open-label Phase 1b study, pts with 1L uHCC, BCLC stage B or C, Child-Pugh class A, and ECOG PS \leq 1 received 200 mg CS1003 intravenously once every 3 weeks and LEN orally (body weight \geq 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) \geq 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 3 trial of LEN with or without CS1003 in 1L uHCC is underway.

Clinical trial information: NCT03809767.