Preliminary safety, pharmacokinetics (PK), and efficacy results from a phase I study of CS1003, an anti-programmed death-1 (PD-1) monoclonal antibody (mAb) in Chinese patients (pts) with advanced solid tumors or lymphoma

Type: Abstract

Category: Immunotherapy of cancer

Authors: Lin. Shen[1], Yanqiao. Zhang[2], Ye. Guo[3], Jifang. Gong[1], Zhigang. Ma[2], Wei. Peng[3], Xiaolu. Tao[4], Kezhen. Liu[5], Yuan. Wang[5], Qinzhou. Qi[5], Jing. Ni[5];

1. Gastrointestinal Oncology, Beijing Cancer Hospital, Beijing, China,
2. Gastroenterology, Harbin Medical University Cancer Hospital, Harbin, China,
3. Oncology, Shanghai East Hospital, Tongji University, School of Medicine, Shanghai, China,
4. Translational Medicine and Early Development, CStone Pharmaceuticals (Su Zhou) Co., Ltd., Shanghai, China,
5. Clinical Development and Regulatory Affairs, CStone Pharmaceuticals (Su Zhou) Co., Ltd., Shanghai, China

Background

CS1003 is a humanized IgG4 anti-PD-1 mAb which also cross-reacts with mouse PD-1 and allows the evaluation of CS1003-based therapies in syngeneic mouse tumor models. A first-in-human (FIH) study of CS1003 was conducted in Australia (NCT03475251). Here we report the preliminary results from a bridging study of CS1003 in China.

Methods

A 3+3 dose-escalation design was undertaken in this phase I, open-label study. Safety and tolerability were assessed by monitoring adverse events (AEs). Tumor assessments were performed per RECIST v1.1 or IPCG criteria.

Results

As of 21 Mar 2019, a total of 12 pts (median age 52.5 [22-68] years) were treated with CS1003 intravenously once every 3 weeks (Q3W) at fixed doses of 60 mg (N = 7) and 200 mg (N = 5). 8 pts remain on study treatment. No dose-limiting toxicities were observed. The most frequent ($n \geq 2$) treatment-related AEs (TRAEs) were bilirubin conjugated increased, blood bilirubin increased, asthenia, anaemia, hyperthyroidism, hypothyroidism, and rash. One serious TRAE (Grade [G] 4 white blood cell count increased) was observed; it was also reported as an immune-related AE (irAE). Other reported irAEs included G1 or 2 asthenia, hyperthyroidism, hypothyroidism, and rash ($n \geq 2$). No other $G \geq 3$ TRAEs were identified. PK data were available in 7 pts as of data cutoff, the exposure of CS1003 increased proportionally with dose, and the concentration-time profiles exhibit general PK properties of an IgG4 mAb. Among the 9 evaluable pts, 1 pt with esophageal carcinoma achieved a confirmed partial response (PR) and 1 pt with uterine leiomyosarcoma achieved a PR which was confirmed after the cutoff date (both remain on study treatment); 3 pts had stable disease.

Conclusions

CS1003 appears well tolerated in Chinese pts with a PK profile similar to that observed in the FIH study conducted in Australia. The preliminary safety and efficacy

data support continued investigation of CS1003. A phase Ib study is ongoing to further evaluate the safety and efficacy of CS1003 at 200 mg Q3W in selected tumor types in Chinese pts.

Clinical trial identification
NCT03809767