A Phase Ia/Ib trial of the anti-programmed death-ligand 1 (PD-L1) human monoclonal antibody (mAb), CS1001, in patients (pts) with advanced solid tumors or lymphomas

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Objective
CS1001 is a first full-length, fully human anti-PD-L1 mAb developed by the OMT transgenic rat platform, which mirrors natural IgG4 human antibody with expected pharmacokinetics (PK) profiles, and may potentially reduce the risk of immunogenicity and toxicity in pts. This first-in-human Phase Ia/Ib study of CS1001 was conducted to evaluate the safety, tolerability, PK profile, and anti-tumor activity of CS1001 in pts with advanced solid tumors or lymphomas.

Methods
Pts with advanced solid tumors or lymphomas were enrolled in the dose escalation Phase Ia, receiving CS1001, Q3W, IV, at escalating doses from 3, to 10, 20, 40 mg/kg and 1200 mg fixed dose. Dose escalation followed a 3+3 dose escalation scheme. Dose-limiting toxicity (DLT) was evaluated within 3 weeks after the initial dose. Pts with various tumor types were enrolled in the dose expansion Phase Ib to assess anti-tumor activity and safety, including GC, cholangiocarcinoma,
NSCLC, HCC, etc. Safety was assessed by monitoring the frequency and severity of adverse events (AEs) per NCI CTCAE v4.03, tumor response was assessed per RECIST v1.1 (solid tumors) or Lugano 2014 (lymphomas).

Results

As of 30 Nov 2018, 29 pts, median age of 53 (23-75) years, were enrolled in Phase Ia, 3 mg/kg (N = 3); 10 mg/kg (4); 20 mg/kg (3); 40 mg/kg (3) and 1200 mg fixed dose (16). 20 pts discontinued treatment, mostly due to disease progression (14). 2 pts discontinued treatment due to AEs (Grade [G] 4 hepatic function abnormal and G3 pulmonary tuberculosis, neither of which were related to CS1001). Median treatment duration was 126 (21-408+) days. No DLTs were observed. The most frequent TRAEs included anaemia (48.3%) and proteinuria (44.8%). SAEs were reported in 6 pts and they were not related to CS1001. irAEs occurred in 7 pts. Among the 29 pts, 7 (24%) pts had PR, mDoR was not reached. In Phase Ib, 162 pts were enrolled as of 15 Mar 2019.

Conclusions

CS1001 is well tolerated without DLT across the dose levels investigated. Evidence of anti-tumor activities was observed. Currently, 1200 mg fixed dose Q3W is being explored in various tumor types in Phase Ib, safety and efficacy results of selected Phase Ib expansion arms will be reported at the conference presentation.

Clinical trial identification

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