Title:
A Multi-Center, Open-Label, and Dose-Expansion Phase Ib Study of CS1001, an Anti-Programmed Death-Ligand 1 (PD-L1) Human Monoclonal Antibody (mAb): Preliminary Results from CS1001 in Combination with Oxaliplatin and Capecitabine (XELOX) in Patients (pts) with Unresectable, Locally Advanced or Metastatic Gastric and Gastro-Esophageal Junction Carcinoma (GC/GEJ)

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Background:
CS1001 is the 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 Phase Ib study of CS1001 was conducted to evaluate the preliminary anti-tumor activity and safety of CS1001 in pts with multiple types of solid tumors or lymphomas. Here we present preliminary results from CS1001 in combination with XELOX in pts with unresectable, locally advanced or metastatic GC/GEJ.

Method:
Pts with unresectable, locally advanced or metastatic GC/GEJ who have not received systemic treatment for advanced or metastatic disease were enrolled, receiving CS1001 1200 mg fixed dose, intravenous (IV) infusion, in combination with XELOX regimen (oxaliplatin 130 mg/m^2, IV, Day 1 and capecitabine 1000 g/m^2/time, twice a day orally, Days 1-14), once every 3 weeks (Q3W). Adverse events (AEs) were monitored throughout the study and graded per NCI CTCAE v4.03. Efficacy was assessed per RECIST v1.1.

Results:
As of 01 Jul 2019, 29 pts (23 [79.3%] were male), the median (range) age of 60.0 (40-73) years, were enrolled in the GC/GEJ cohort. 17 pts entering the study with an ECOG performance status of 1. 15 pts remained on treatment. A total of 14 pts discontinued CS1001, mostly due to disease progression and AEs. 18 pts had partial response (Objective Response Rate: 62.1%), among which, 15 were confirmed. Six (6) pts had stable disease. The diseae control rate was 82.8%. The median duration of response was 6.2 months. All pts had treatment-emergent AEs, among which, 28 pts had CS1001-related AEs with the most frequently reported ones being platelet count decreased, white blood cell count decreased, and anaemia (14 pts each). 11 pts had ≥ Grade (G) 3 CS1001-related AEs. Two (2) G4 CS1001-related AEs were reported: platelet count decreased and blood alkaline phosphatase increased (1 pt each). Serious AEs (SAEs) were reported in 9 pts and 5 had CS1001-related SAEs (platelet count decreased: 2 pts; blood creatinine increased, pneumonia, and chest discomfort: 1 pt each). Immune-related AEs assessed by investigators occurred in 18 pts with the most frequent events being rash (5, ≤G2) and amylase increased (4, ≤G2). AEs that led to CS1001 discontinuation occurred in 3 pts, which included G3 hepatic function abnormal, G3 hypothyroidism, and G2 pneumonia: all were considered as CS1001-related by the investigators.

Conclusion:
The combination regimen of CS1001 and XELOX showed promising anti-tumor activity with a tolerable safety profile. The preliminary safety and efficacy profile of CS1001 support further exploration and development of CS1001 in such pt population. The efficacy and safety of CS1001 in combination with XELOX in patients with unresectable, locally advanced or metastatic GC/GEJ is further investigated in an ongoing Phase III trial (GEMSTONE-303, NCT03802591).

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