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 Cisplatin and 5-Fluorouracil (CF) Chemotherapy in Patients (pts) with Esophageal Squamous Cell Carcinoma (ESCC)

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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 cisplatin and 5-fluorouracil (CF) chemotherapy as 1L treatment in pts with unresectable locally advanced, recurrent or distant metastatic ESCC.

Method:

Pts with histologically confirmed unresectable, recurrent or distantly metastatic, locally advanced ESCC who have not received systemic treatment were enrolled, receiving CS1001 1200 mg fixed dose intravenous (IV) infusion and CF regimen (cisplatin, 80 mg/m^2, IV, Day 1 and 5-fluorouracil, 800 mg/m^2/day, continuous IV, Days 1-5), both once every 3 weeks (Q3W) a cycle. 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, 23 pts (18 [78.3%] were male), the median (range) age of 61.0 (45-73) years, were enrolled in the ESCC 1L cohort. 18 pts entering the study with an ECOG performance status of 1. 17 pts remained on treatment. A total of 6 pts discontinued CS1001, mostly due to AEs. Among the 18 efficacy-evaluable pts, 14 pts had partial response (Objective Response Rate: 77.8%), among which, 12 were confirmed. Two (2) pts had stable disease. The duration of response (DoR) ranged from 0.03+ to 8.4+ months, median DoR was not achieved. All (23) pts had treatment-emergent AEs, among which, 20 pts developed CS1001-related AEs. The most frequent CS1001-related AEs included anaemia (10), blood corticotrophin increased (9), neutrophil count decreased (6), and amylase increased (6). 13 pts had ≥ Grade (G) 3 CS1001-related AEs, with the most frequently reported ones being anaemia (5) and white blood cell count decreased (3). No G5 CS1001-related AEs were reported. Serious AEs (SAEs) were reported in 11 pts and 6 of them experienced CS1001-related SAEs. Immune-related AEs assessed by investigators occurred in 16 pts, with the most frequent events being amylase increased (6, ≤G3), blood corticotrophin increased (5, G1), and hypothyroidism (4, ≤G2). AEs that led to CS1001 discontinuation occurred in 3 pts, of which, hyponatraemia (G4) was considered as CS1001-related by the investigators. There was 1 AE led to death reported: multiple organ dysfunction syndrome, which was not considered as CS1001-related by the investigators.

Conclusion:
The combination regimen of CS1001 and CF 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.

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