Title:

A Multi-Center, Open-Label, Dose-Expansion Phase Ib Study of CS1001, an Anti-Programmed Death-Ligand 1 (PD-L1) Human Monoclonal Antibody (mAb): Preliminary Results from CS1001 Monotherapy in Patients (pts) with High-Microsatellite Instability (MSI-H) or Mismatch Repair Deficient (dMMR) Tumors

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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 patients (pts). This Phase Ib study 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 monotherapy in pts with MSI-H/dMMR tumors.

Method:

Pts with MSI-H/dMMR unresectable or metastatic solid tumors who have failed from prior line (s) of treatment and have no satisfactory alternative treatment options were enrolled, receiving CS1001, 1200 mg fixed dose, once every 3 weeks, intravenous infusion. 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, 21 pts (12 [57.1%] were male), the median (range) age of 53 (25-71) years, were enrolled in the MSI-H/dMMR cohort. All had an ECOG performance status of 1. A total of 9 pts remained on treatment, and 12 pts discontinued CS1001 treatment, mostly due to disease progression. No discontinuation was caused by AEs. Eight (8) pts

had partial response (Objective Response Rate [ORR]: 38.1%), among which, 6 were confirmed. Four (4) pts had stable disease. The duration of response (DoR) ranged from 0.03+ to 8.6+ months, median DoR was not achieved. 18 pts had CS1001-related AEs with the most frequently reported being anaemia (5), aspartate aminotransferase increased (4), alanine aminotransferase increased (4) and white blood cell count decreased (4). One (1) pt had Grade (G) 3 CS1001-related AE (anaemia), no G4 or G5 CS1001-related AEs were reported. Serious AEs were reported in 2 pts and neither was CS1001-related. Immune-related AEs assessed by investigators occurred in 9 pts, with the most frequent events being platelet count decreased (2, G1), amylase increased (2, G1), and hyperthyroidism (2, G1).

Conclusion:

Promising anti-tumor activity and a tolerable safety profile in pts with MSI-H/dMMR solid tumors were observed. The ORR is similar to that has been reported for pembrolizumab (39.6%) [1]. The anti-tumor activity and safety results support further exploration and development of CS1001 in such pt population.

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Reference:

1. Marcus L, Lemery SJ, Keegan P, Pazdur R. FDA approval summary: pembrolizumab for the treatment of microsatellite instability-high solid tumors. Clin Cancer Res. 2019