Title:
Preliminary pharmacokinetics (PK), safety and efficacy of two dosing regimens of CS1003 (anti-PD-1) in solid tumors: 200 mg every 3-week (Q3W) and 400 mg every 6-week (Q6W) dosing

Category: Investigational immunotherapy

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Background:
CS1003 is a novel humanized IgG4 anti-PD-1 monoclonal antibody. In Phase 1a dose-escalation, CS1003 showed a well-tolerated safety profile with no dose-limiting toxicity, and a wide therapeutic window at doses up to 10 mg/kg Q3W (maximum administrated dose, MAD) in patients (pts) with solid tumors. Two fixed-dose regimens were explored in the Phase Ib portion of this ongoing clinical trial in pts with selected solid tumors.

Methods:
Pts were enrolled in cohort A (200 mg Q3W) or cohort B (400 mg Q6W) to receive CS1003 intravenously. Safety, preliminary tumor activity (overall response per RECIST v1.1 by investigators) and PK were assessed.

Results:

As of 21 Mar 2020, 29 and 30 pts were enrolled in cohorts A and B, with a median treatment duration of 15.0 (range: 3.0-50.4) and 14.4 (range: 4.7-27.7) weeks, respectively. Following the first dose, the mean C_{max} value of CS1003 in cohort B was around doubling of that in cohort A (112 vs 44 μg/ml) but lower than that (189 μg/ml) at the MAD, demonstrating sufficient safety

margin. The mean C_{trough} value of cohorts A and B were 9.2 and 18.8 μg/ml, respectively, expecting a complete PD-1 receptor occupancy throughout the dosing intervals with both regimens. The steady-state PK data of cohort B will be updated. In cohorts A and B, 97% (28/29) and 93% (28/30) pts had treatment-emergent adverse events; 41% (12/29) and 47% (14/30) pts had all-grade treatment-related adverse events (TRAEs), respectively. The TRAE profiles were comparable in both cohorts overall with two Grade (G) ≥ 3 events (G3 dermatitis and G4 Type 1 diabetes mellitus in cohort B), and the rest were G1/2. Among the 29 efficacy-evaluable pts in cohort A, there were 3 complete response (2 confirmed), 3 partial response (PR, 2 confirmed) and 5 stable disease (SD). Among the 27 efficacy-evaluable pts in cohort B, there were 4 PR (1 confirmed) and 13 SD.

Conclusions:
The preliminary safety and efficacy profiles of CS1003 at 200 mg Q3W and 400 mg Q6W appear comparable. PK data are also supportive of selecting either regimen for future development while 400 mg Q6W offers greater dosing flexibility to pts and physicians.

Clinical trial identification: NCT03475251.