Title:

Preliminary safety, pharmacokinetics (PK) and pharmacodynamics (PD) from a Phase I study of CS1002, an anti-cytotoxic T-lymphocyte antigen-4 (CTLA-4) monoclonal antibody (mAb) in patients (pts) with advanced solid tumors

Type: Abstract

Authors: Dusan KOTASEK[1]; Morteza AGHMESHEH[2]; Amy PRAWIRA[3]; Rasha COSMA[3], Ning LI[4]; Wenyi SUN[4], Ruijie GU[4]; Yiru WANG[4]; Ying PAN[4], Archie N. TSE[4], Xiaolu TAO[4]

1. Ashford Cancer Centre Research, Adelaide, Australia and University of Adelaide;
2. Southern Medical Day Care Centre, Wollongong, Australia
3. St Vincent's Hospital, Darlinghurst, NSW, Australia
4. CStone Pharmaceuticals (Su Zhou) Co., Ltd, Suzhou, China

Keywords:
CS1002, CTLA-4, Phase 1, immunotherapy

Background
CS1002 is a human immunoglobulin G1 (IgG1) mAb directed against CTLA-4.

Methods
A Phase I, open-label, multi-center study was conducted to evaluate the safety, tolerability, PK, and anti-tumor activity of CS1002 in pts with advanced solid tumors in Australia. A modified 3+3 dose escalation design was undertaken. Tumor assessments were performed per RECIST V1.1. Absolute lymphocyte count (ALC) was measured at baseline, pre-dose at Day 1 of all treatment cycles and Week 13, Days 8 and 15 of Cycle 1.

Results
As of 08 Feb 2019, a total of 13 Caucasian pts (median age, 58 [48–75] yrs) were treated with CS1002, iv, Q3W, across 3 escalating doses (1 mg/kg, N=6; 3 mg/kg, N=3 and 10 mg/kg, N=4). Baseline ECOG scores were 0 (7) or 1 (6), all pts were of Stage IV disease and had at least 1 regimen of anti-cancer treatment (median, 3 [1-6]). No DLT was observed, and MTD was not reached.
All 13 pts had AEs, of whom 3 pts reported treatment-related AEs: fatigue (2, Grade [G] 1 or 2) and diarrhea (2, G1 or 3). SAEs were reported in 3 pts and they were not related to CS1002. irAEs occurred in 2 pts. No death or permanent discontinuation due to AEs were reported. A total of 11 pts discontinued the study, mostly due to disease progression (7). Two pts were still on treatment.
PK results (N=13) showed that AUC_{tau} and C_{max} values increased dose-proportionally in the dose range of 1-10 mg/kg. The terminal elimination half-life ($t_{1/2}$) ranged from 12 to 15 days across 3 dose levels. No significant drug accumulation was observed (accumulation index <1.6) after repeat dosing of CS1002. Increase of ALC within 2 doses of the drug administration was consistently observed across all 3 dosing cohorts, showing a similar trend as reported for ipilimumab.
Among 12 efficacy evaluable pts, 2 had stable disease and 7 had progressive disease, the remaining 3 pts were considered as non-responders.

Conclusions

CS1002 at 1, 3 and 10 mg/kg appears to be well tolerated. The preliminary safety and PK/PD profile support continued exploration and development of CS1002 in combination with other immune-oncology agents. The enrollment is completed at the time of drafting, and updated results will be presented.

Clinical trial identification:

NCT03523819