Preliminary safety and efficacy results from phase Ib study of the anti-CTLA-4 monoclonal antibody (mAb) CS1002 in combination with anti-PD-1 mAb CS1003 in patients with advanced solid tumors

Sarwan Bishnoi[1], Rasha Cosman[2], Maggie Moore[3], Richard Eek[4], Andrew Mant[5], Robert Zielinski[6], Stephen L. Chan[7], Yiding Ma[8], Qianru Zhang[8], Thomas Yau[9], Morteza Aghmesheh[10], Archie N. Tse[8]

[1]Department of oncology, Ashford Cancer Centre Research, Adelaide, Australia; [2] Department of oncology, St Vincent's Hospital, Sydeny, Australia; [3] Department of Medical Oncology, The Alfred Hospital, Melbourne, Australia; [4] Department of medical oncology, Border Medical Oncology, Albury, Australia; [5] Medical Oncology Unit, Box Hill Hospital, Melbourne, Australia; [6] Discipline of Medicine,Orange Health Service, Orange, Australia; [7]Deparment of Clinical Oncology, The Chinese University of Hong Kong, Prince of Wales Hospital, Hongkong, China; [8]CStone Pharmaceuticals (Su Zhou) Co., Ltd, Suzhou, China; [9] Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Hongkong, China; [10] Department of Medical Oncology, Southern Medical Day Care Centre, Wollongong, Australia

Background

CS1002 is a humanized immunoglobulin G1 (IgG1) mAb directed against CTLA-4, and CS1003 is a humanized, recombinant IgG4 anti-PD-1 mAb. In dose-escalation phase Ia, CS1002 was well-tolerated with no dose-limiting toxicities (DLTs) in patients (pts) with solid tumors. Phase Ib includes dose-escalation (part 2) and dose-expansion (part 3) to assess the safety and antitumor activity of C1002 combined with CS1003 in selected tumors. Part 2 showed the combination was well-tolerated with no DLT and a maximum toxicity dose was not reached. Here we present the safety and efficacy of CS1002 and CS1003 in part 3.

Methods

In part 3, pts with anti-PD-(L)1 naïve pretreated MSI-H/dMMR tumors or anti-PD-(L)1 refractory melanoma were randomized and treated with CS1002 (Arm A: CS1002 0.3 mg/kg Q6W, continuous; Arm B: CS1002 1 mg/kg Q3W, up to 4 doses) and CS1003 200 mg fixed dose Q3W continuously. Safety and antitumor activity were assessed.

Results

As of 01 March 2021, 33 pts with MSI-H/dMMR tumors or melanoma (16 in A and 17 in B) were enrolled and treated with CS1002 and CS1003. Twenty-nine (87.9%) pts experienced adverse events (AEs) (A: 81.3% ; B: 94.1%), of whom 21 (63.6%) pts had treatment-related AEs (TRAEs) (A: 62.5%; B: 64.7%). The most common

TRAEs (⩾20%) were diarrhoea and fatigue (7 pts each, 21.2%). CTCAE Grade ⩾3

CS1002 and CS1003-related AEs occurred in 5 (15.2%) pts (2 in A and 3 in B). Serious AEs related to treatment were reported in 6 (18.2%) pts (3 each in A and B).

Two (6.1%) pts experienced AEs leading to discontinuation of CS1002 and CS1003. No death due to AEs was reported. Of the 9 and 7 evaluable pts with MSI-H/dMMR tumors in A and B, objective response rate (ORR) was 44.4% (4 pts achieved partial response, PR) and 57.1% (1 had complete response and 3 had PR), respectively. Among 4 evaluable pts with melanoma each in A and B, ORR was both 50% with 2 pts each achieving PR.

Conclusions

The combination of CS1002 and CS1003 demonstrated an acceptable safety profile and showed promising preliminary anti-tumor activity in pts with MSI-H/dMMR tumors and anti-PD-(L)1 refractory melanoma at two dose levels. One dose regimen will be chosen to support further exploration.

Clinical trial identification:
NCT03523819