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

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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 appeared to be well-tolerated in patients (pts) with solid tumors. Phase Ib comprised dose-escalation (part 2) and dose-expansion (part 3) to assess the safety and anti-tumor activity of C1002 in combination with CS1003 in selected tumors. The preliminary safety and efficacy results of part 2 and part 3 were reported at ESMO 2021. Here we present the updated results of part 3.

Methods

Dose expansion of part 3 is designed as below:

<table>
<tr><th>Arm</th><th>Patients</th><th>CS1002</th><th>CS1003</th><th>Assessment</th></tr>
<tr><td>A</td><td rowspan="2">Patients with anti-PD-(L)1-naïve, pretreated MSI-H/dMMR tumors or anti-PD-(L)1-refractory melanoma</td><td>0.3 mg/kg Q6W i.v.</td><td rowspan="4">200 mg, Q3W i.v.</td><td rowspan="4">Tumor assessment was performed per RECIST V1.1 by investigators, Q9W in the first year and Q12W thereafter.

AEs were graded according to NCI-CTCAE V4.03.</td></tr>
<tr><td>B</td><td>1 mg/kg Q3W i.v. , up to 4 doses</td></tr>
<tr><td>C</td><td rowspan="2">Patients with anti-PD-(L)1-refractory hepatocellular carcinoma</td><td>0.3 mg/kg Q6W i.v.</td></tr>
<tr><td>D</td><td>3 mg/kg Q9W i.v.</td></tr>
<tr><td colspan="5">QnW= once every n weeks; i.v.= intravenous; RECIST= Response Evaluation Criteria In Solid Tumors; NCI-CTCAE= National Cancer Institute Common Terminology Criteria for Adverse Event.</td></tr>
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Results

As of 6 Aug 2021, 42 pts (arm A: 21; arm B: 21) with MSI-H/dMMR tumors or melanoma (MEL) and 12 pts (arm C: 6; arm D: 6) with hepatocellular carcinoma (HCC) were enrolled and treated with CS1002 and CS1003. Of the 13 evaluable pts with MSI-H/dMMR tumor in arm A, and 14 in arm B, objective response rate (ORR) was 46.2% (1 patient had complete response [CR]; 5 pts had partial response[PR]) and 57.1% (1 CR, 7 PR), respectively. Among 6 evaluable pts with MEL in each of Arms A and B, ORR was 33.3% (2 PR) and 50.0% (1 CR, 2 PR), respectively. Of the 9 evaluable pts with HCC, ORR was 11% (1 PR). 48 (88.9%) pts had adverse events (AEs), of whom 36 (66.7%) pts had treatment-related AEs (TRAEs) (arm A: 61.9%; arm B: 76.2%; arm C: 50.0%; arm D: 66.7%). The most common TRAE (≥20%) was fatigue (25.9%). CTCAE Grade ≥3 TRAEs occurred in 9 (16.7%) pts (arm A: 4; arm B: arm 4; arm C: 0; arm D: 1). Serious TRAEs occurred in 7 (13.0%) pts (arm A: 3; arm B: 3; arm C: 0; arm D: 1). 5 (9.3%) pts had AEs leading to discontinuation of CS1002 and CS1003.

Conclusions

The combination of CS1002 and CS1003 demonstrated a promising anti-tumor activity and favorable safety profile in pts with MSI-H/dMMR tumors, anti-PD-(L)1-refractory MEL and anti-PD-(L)1-refractory HCC at two dose levels of CS1002.

Clinical trial identification:

NCT03523819