Preliminary Results of the First-In-Human, Dose-Finding PROCLAIM-CX-072 Trial Evaluating the PD-L1 Probody Therapeutic CX-072 in Combination With Ipilimumab in Patients With Advanced Solid Tumors

Ruth Fuller1, Rachel E. Samson2, Elisabeth de Vries3, Patricia Loefvass3, Henrik-Tobias Akerlas3, Nalayika Udo4, Jazzy Wymant5, Mary Josephine Fiddler6, Valentine Bort7, Javier Garcia-Cortes8, Rachel Humphrey,9 Mathias Will,9 Karen A. Audisio,10 Anthony El-Khoury,10 William Miele9 and the PROCLAIM Study Group

1 Cleveland Clinics Florida, Weston, FL, USA; 2 University of Melbourne, Melbourne, Victoria, Australia; 3 Copenhagen University Hospital, Copenhagen, Denmark; 4 European Institute of Oncology, Milan, Italy; 5 University of British Columbia, Vancouver, BC, Canada; 6 Massachusetts General Hospital, Boston, MA, USA; 7 Hospital Clinic, Barcelona, Spain; 8 VA Boston, Boston, MA, USA; 9 CytomX Therapeutics, Inc., Newton, MA, USA; 10 Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA

BACKGROUND

PD-L1 blockade strategies have shown clinical activity in multiple tumor types, with the overall rate of immune-related adverse events (irAEs) ranging from 15% to 60% across studies.2–6 PROBODY is a recombinant antibody prodrug technology designed to deliver fully recombinant antibodies to the cell membrane, with the potential to improve both efficacy and safety compared with native antibodies.3 The PROCLAIM-CX-072 trial is the first to evaluate this technology in combination with ipilimumab in patients with advanced solid tumors. Here, we report preliminary results of the dose-finding study and an ongoing open-label phase II study.

METHODS

Study Design

The PROCLAIM-CX-072 trial was a single-arm, open-label, multi-center, phase I/II study of CX-072 in combination with ipilimumab. The primary objectives were to determine the dose of CX-072 in combination with ipilimumab that is safe for further evaluation and to evaluate the antitumor activity of this combination therapy. Patients received 1 dose of ipilimumab (3 mg/kg) followed by 3 cycles of CX-072 (0.3, 1, 3, or 10 mg/kg) on days 1, 8, and 15 of a 28-day cycle. The treatment cycle could be repeated every 28 days if there was no disease progression or unacceptable toxicity. Patients were grouped according to the most severe grade experienced for a particular AE. AEs were coded using MedDRA v19.1. TRAE, treatment-related (to any study drug) adverse event. TEAE, treatment-emergent adverse event.

RESULTS

Patients

As of August 3, 2018, a total of 20 patients were enrolled; the MTD was not reached, and 6 patients (30%) were still receiving treatment. Among evaluable patients (n = 14) who had ≥1 postbaseline tumor assessment, best tumor response was overall stable disease, with 3 patients (21%) having a partial response. All responses are ongoing, with a maximum duration of response of 7.4 months.

Safety

The MTD has not been reached. No new or unexpected toxicities were observed, and there were no serious adverse events of any grade. The most common treatment-emergent adverse events (TEAEs) and TRAEs are listed in Table 4. Among evaluable patients (n = 14), 1 patient with grade 3 hyponatremia and grade 3 pneumonitis treated at 3 mg/kg + 3 mg/kg had a grade 3 pneumonitis on day 9 of cycle 1, which was felt to be related to therapy and caused discontinuation of treatment. There were no deaths during the study.

Duration of Treatment

The median duration of treatment was 3 cycles (12 weeks) for 14 patients. Among evaluable patients (n = 14), the median duration of treatment was 8 months (range: 2.5–11 months) for patients who discontinued because of progressive disease; no patients discontinued because of irAEs.

Objective Response

Among evaluable patients (n = 14), the objective response rate was 13.6% (95% CI: 1.1–41.3%) with CX-072 1 mg/kg + ipilimumab 3 mg/kg and 42.9% (95% CI: 19.2–64.6%) with CX-072 3 mg/kg + ipilimumab 3 mg/kg. All responses are ongoing, with a maximum duration of response of 7.4 months.

Objective Response Rate

The objective response rate with CX-072 1 mg/kg + ipilimumab 3 mg/kg was 33.3% (95% CI: 1.1–74.8%) for patients with grade 1–2 irAEs and 0% (95% CI: 0.0–50.0%) for patients with grade 3–4 irAEs. The objective response rate with CX-072 3 mg/kg + ipilimumab 3 mg/kg was 100% (95% CI: 60.0–100.0%) for patients with grade 1–2 irAEs and 33.3% (95% CI: 0.0–66.7%) for patients with grade 3–4 irAEs. All responses are ongoing, with a maximum duration of response of 7.4 months.

Tumor Regression

Among evaluable patients (n = 14), with CX-072 1 mg/kg + ipilimumab 3 mg/kg, median percentage change from baseline of target lesions was 23% (95% CI: 11.0–37.3%) at 7 weeks after the last dose of study medication. Among evaluable patients (n = 14), with CX-072 3 mg/kg + ipilimumab 3 mg/kg, median percentage change from baseline of target lesions was 38% (95% CI: 14.3–54.1%) at 9 weeks after the last dose of study medication.

Antibodies targeting the programmed cell death 1/programmed cell death ligand 1 (PD-1/PD-L1) pathway will be evaluated every 3 months for disease progression 12 months, then every 12 weeks thereafter. Any irAEs will be closely monitored every 14 days.

Study Design

• The MTD has not been reached
• No new or unexpected toxicities were observed
• There were no serious adverse events of any grade
• The most common treatment-emergent adverse events (TEAEs) and TRAEs are listed in Table 4
• Among evaluable patients (n = 14), the objective response rate was 13.6% (95% CI: 1.1–41.3%) with CX-072 1 mg/kg + ipilimumab 3 mg/kg and 42.9% (95% CI: 19.2–64.6%) with CX-072 3 mg/kg + ipilimumab 3 mg/kg.

CONCLUSIONS

The PROCLAIM-CX-072 trial is the first to evaluate this technology in combination with ipilimumab in patients with advanced solid tumors. Here, we report preliminary results of the dose-finding study and an ongoing open-label phase II study. The MTD has not been reached. No new or unexpected toxicities were observed, and there were no serious adverse events of any grade. The most common treatment-emergent adverse events (TEAEs) and TRAEs are listed in Table 4. All responses are ongoing, with a maximum duration of response of 7.4 months. This technology has the potential to improve both efficacy and safety compared with native antibodies by delivering fully recombinant antibodies to the cell membrane.

REFERENCES


Disclosure: Full disclosure form the authors is available online at: http://www.proclaim trial.com/disclosures

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