The First-in-Human, Dose-Finding PROCLAIM-CX-072 Trial to Assess the Antitumor Activity and Tolerability of the Probody™ Therapeutic CX-072 in Combination With Ipilimumab or Vemurafenib in Solid Advanced Tumors

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BACKGROUND

Probody therapeutics are fully recombinant antibody prodrugs that remain relatively inactive systemically and in healthy tissue, However, significant life-threatening immune-related adverse events (irAEs) are known toxicities of PD-1/PD-L1–axis blocking antibodies, especially when used in a wide variety of combinations such as with ipilimumab.

Preclinical studies using a surrogate for CX-072 demonstrated that protease activation restores binding of CX-072 to PD-L1 in vitro and in situ. Studies of tumor samples from 200 patients with a variety of malignancies confirm Probody therapeutic activation in >90% of the samples, which corroborates the presence of tumor microenvironment proteases in the overwhelming majority of tumors necessary to ensure activation of the Probody therapeutic.

Given that CX-072 is activated by tumor-associated proteases, it is expected to be relatively inactive in peripheral tissue, necessary to ensure activation of the Probody therapeutic.

OBJECTIVE

The PROCLAIM-CX-072 trial (Clinicaltrials.gov identifier NCT03013491) is investigating safety, tolerability, and antitumor activity of multiple dose levels of CX-072 in combination with immunotherapy or alone in patients with solid tumors with tumor expression of PD-L1.

STUDY DESIGN

This first-in-man, open-label, dose-escalation phase 1/2 trial of CX-072 includes 12 dose-escalation groups of 4-6 patients each, 4 cohorts of 4 patients each for each of the 4 dose levels of CX-072 to confirm tumor lysis activity in PD-L1–positive tumors (Part A), and a dose-expansion phase (Part B) (Figure 2).

END POINTS

Primary End Points

Safety and tolerability of CX-072 alone or in combination with ipilimumab or vemurafenib

Secondary End Points

Response rate (objective response rate) of CX-072 alone and in combination with ipilimumab or vemurafenib

Specific Assessments

Imaging for tumor response assessment will be performed every 3 months for the first 12 months, then every 6 months thereafter. After the last dose of study medication, patients who have not experienced tumor progression or early discontinuation will have tumor assessments at 6-month intervals for a total of 2 years, then annually for another 3 years.

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References