A Combined Phase I/II Study of a Novel Bicycle Tumor-targeted Immune Cell Agonist® BT7480 in Patients with Nectin-4 Associated Advanced Malignancies

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ABSTRACT

BACKGROUND

• BT7480 is a novel, first-in-class, Nectin-4/CD137 Bicycle tumor-targeted immune cell agonist® (Bicycle TICA®) that activates CD137 through CD137 and Nectin-4 co-ligation
• Nectin-4 is overexpressed in urothelial, pancreatic, breast, ovarian, esophageal, head and neck, gastric and lung cancers1-4, among others
• Nectin-4 and CD137 are co-expressed in a variety of human tumors5-8
• BT7480 is designed to have rapid tumor penetration and a short terminal half-life
• BT7480 exhibited a favorable preclinical profile including an early activation of myeloid cells that preceded the activation of cytotoxic cells. A) MC38-Nectin-4 tumor bearing mice (huCD137-C57Bl/6) were treated with vehicle or 5 mg/kg BT7480 iv at 0h and 24h. Tumors were harvested at 24, 48, 96, or 144h as indicated, and processed for transcriptional analysis by NanoString. The cytotoxic cell score (left y-axis) and G1L, G1L7, and CD24 mRNA counts (right y-axis) were overlaid over the course of the study (days post dosing). B) Macrophage cell score in response to BT7480 or a non-binding control (NB-BCY) in MC38-Nectin-4 bearing mice. C) In the cancer immunity cycle, BT7480 likely acts to both initiate as well as sustain the anti-tumor immune response.

ENROLLMENT CRITERIA

• Solid tumors associated with Nectin-4 expression (including urothelial, NSCLC, ovarian, breast, gastric, HNSCC, or esophageal)
• Fresh or archival tumor tissue
• Acceptable hematologic and organ function
• Exclusion criteria include uncontrolled brain metastasis, uncontrolled hypertension, autoimmune disease, or prior CD137 targeted therapy

OBJECTIVES

Primary Phase 1
• Safety and tolerability of BT7480 as monotherapy and in combination or in patients with renal insufficiency
• Clinical activity of BT7480 as monotherapy and in combination

Secondary Phase 2
• Clinical activity of BT7480 as monotherapy and in combination in patients with renal insufficiency
• Safety and tolerability of BT7480 as monotherapy and in combination
• Assess additional measures of antitumor efficacy
• PK parameters of BT7480 as monotherapy and in combination or in patients with renal insufficiency
• Incidence of anti-drug antibody development
• CD137 target engagement in peripheral blood

STUDY DESIGN

• Monotherapy dose escalation is ongoing
• Open-label dose escalation, dose confirmation, and dose expansion study of BT7480 given as a single agent or in combination with a checkpoint inhibitor
• Up to 200 patients are expected to be enrolled in approximately 20 sites globally
• Study initiated in BT7480 monotherapy dose escalation with accelerated single-subject cohort followed by 3+3 design
• Following monotherapy RP2D, study parts include:
  - Phase 1: optional combination dose escalation
  - Phase 1 optional dose confirmation in patients with renal insufficiency
  - Phase 1 and Phase 2 BT7480 monotherapy and optional combination dose expansions
  - BT7480 is administered as an intravenous infusion QW in a 28-day cycle
  - Tumor response assessed per RECIST every 8 weeks

REFERENCES

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