A Phase 1 Open-Label, Dose Escalation and Expansion Trial to Investigate the Safety, Pharmacokinetics and Pharmacodynamics of CB307, a Trispecific Humabody® T-cell Enhancer, in Patients with PSMA+ Advanced and/or Metastatic Solid Tumors (POTENTIA)

CT206

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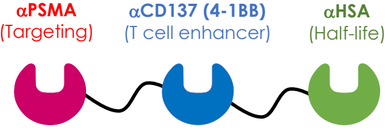
Introduction

Background and Mechanism of Action

- Prostate-specific membrane antigen (PSMA, FOLH)
  - PSMA is a clinically validated target for imaging and emerging therapeutics in metastatic castration resistant prostate cancer (mCRPC)[1, 2]
  - PSMA is also expressed in a variety of solid tumors [3]
- CD137 or 4-1BB (*TNFRSF9*)
  - CD137 is a co-stimulatory receptor expressed on activated, antigen experienced T cells and NK cells
  - Clinical studies of agonistic antibodies targeting CD137 were hampered due to either lack of efficacy or severe liver toxicity[4]
  - CD137 targeting T cell enhancers have shown a better cytokine release syndrome (CRS) profile in recent clinical studies[5, 6]
  - Preclinical models suggest that CD137 targeting T cell enhancers promote anti-tumor memory response

Figure 1. CB307 is a half-life extended PSMA x CD137 molecule designed to enhance T cell activation in a PSMA+ tumors



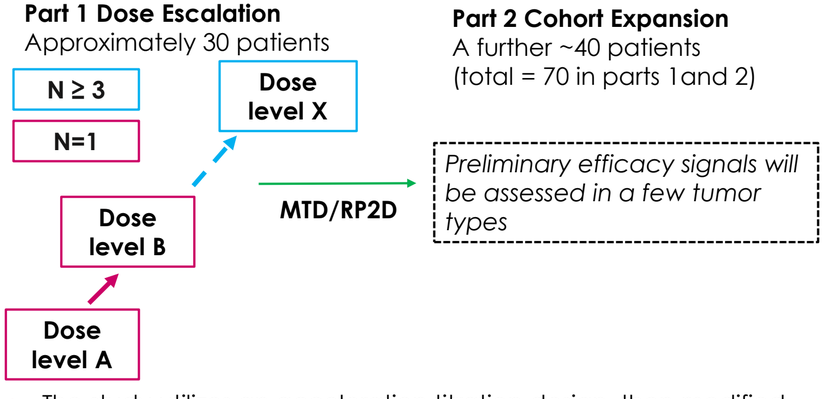
- CB307 is a trispecific Humabody® V_H T cell enhancer that binds to CD137, PSMA and human serum albumin (HSA) to increase the activity of tumor-specific T cells
- Molecular weight of CB307 is less than 50kDa

POTENTIA Clinical Study Design

Advantages of CB307 in immuno-oncology

- Better biodistribution and tumor penetration than mAb due to small molecular size and albumin binding[7]
- Conditional T cell activation through CD137 only in a PSMA+ tumor microenvironment
- Diverse T cell generation against multiple tumor antigens and generation of memory T cells for longer response
- Minimal risk of CRS

Figure 2. POTENTIA Clinical Study Design



- The study utilizes an acceleration titration design, then modified continuous reassessment method to guide the dose escalation
- The study is currently enrolling patients in the dose escalation part
- No treatment related SAE or DLT has been reported
- No patient discontinued the study treatment due to adverse events

Eligibility Criteria

Figure 3. Key Inclusion Criteria

- Patients who are not amenable to standard of care with ECOG PS 0-1, Age ≥ 18
- PSMA positive advanced or metastatic solid tumor assessed by IHC or PSMA-PET
- RECIST measurable disease or elevated serum PSA (prostate only)
- Adequate organ function and recovered from previous treatment

Figure 4. Key Exclusion Criteria

- Central nervous system or leptomeningeal metastasis
- Discontinuation from previous immune-checkpoint inhibitors due to intolerable toxicity
- Patients with active infection
- Patients with autoimmune disease or regular immunosuppressant use

The trial registration identifier: NCT04839991

Please also visit # 2877 at poster section 37 for pre-clinical CB307 study data

References

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