TPS2694: An Open-Label, Non-randomized, Multi-center Phase I Study Evaluating the Safety, Tolerability, Pharmacokinetics and Preliminary Efficacy of Bi-Ligand-Drug Conjugate CBP-1018 in Patients with Advanced Solid Tumor

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Reference

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Background

- Folate receptor 1 (FOLR1) and prostate specific membrane antigen (PSMA) are overexpressed on tumor and angiogenic endothelial cells in solid tumors, including prostate cancer, renal cell cancer and lung cancer. [1-2] Both have proven to be feasible targets for anti-cancer drug development. [3-4]
- CBP-1018 is a first-in-class bi-ligand drug conjugate targeting both FOLR1 and PSMA, with a tubulin inhibitor payload, monomethyl auristatin E (MMAE).

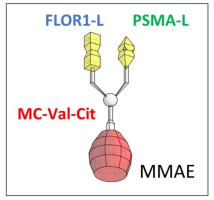

Figure 1. Structure of CBP-1018

- CBP-1018 has shown potent anti-tumor activity and acceptable safety profile in preclinical studies. We herein introduce the first-in-human study of CBP-1018 (NCT04928612).

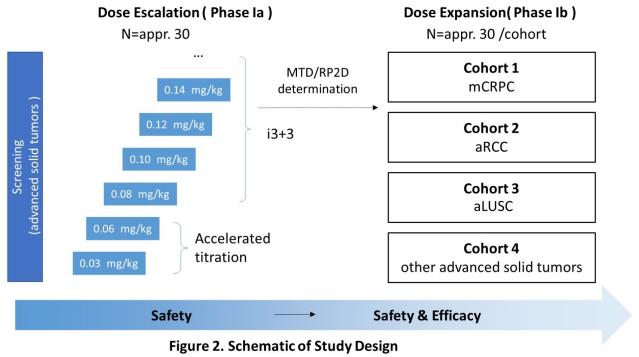

Figure 2. Schematic of Study Design

Study design

- This study is a phase Ia/Ib, multicenter, open-label study enrolling patients with advanced solid tumor relapsed after previous standard therapies.
- This study includes 2 parts: Ia (Dose Escalation) and Ib (Dose Expansion).
  - **Part A (Dose Escalation)** : CBP-1018 is administrated iv Q2W (4 weeks/cycle), with accelerated titration at lower doses (0.03 mg/kg and 0.06 mg/kg) and an i3+3 design at following doses (0.08 mg/kg, 0.10 mg/kg, 0.12 mg/kg and 0.14mg/kg, etc.).
  - **Part B (Dose Expansion)**: to further evaluate the efficacy and safety profile of CBP-1018 in 4 tumor-specific cohorts.

Cohort 1 (metastatic castration resistant prostate cancer, mCRPC), subjects with mCRPC have documented failure of prior standard of care (SoC).

Cohort 2 (advanced renal cell cancer, aRCC), subjects with advanced RCC have documented failure of prior SoC.

Cohort 3 (advanced lung squamous cell cancer, aLSCC), subjects with advanced LSCC have documented failure of prior SoC.

Cohort 4 (other advanced solid tumors), subjects with other advanced solid tumors have documented failure of prior SoC.

Primary Objectives

- Part A: The primary objective is to assess CBP-1018 safety, tolerability, dose limiting toxicity, maximum tolerated dose, and recommended phase 2 dose (RP2D).
- Part B: Objective response rate (ORR).

Secondary Objectives

- Secondary objectives include Preliminary efficacy parameters (objective response rate, duration of response and progression-free survival), pharmacokinetics, immunogenicity and biomarkers.

Key Inclusion Criteria

- Eastern Cooperative Oncology Group (ECOG) performance status 0-1.
- Life expectancy of ≥ 3 months, in the opinion of the Investigator.
- Pathologically documented, advanced solid tumors including metastatic castration resistant prostate cancer (mCRPC), advanced renal cell cancer (RCC), advanced lung squamous cell cancer (LSCC), etc.
- Subjects must have received prior standard therapy appropriate for their tumor type and stage of disease, or in the opinion of the Investigator, would be unlikely to tolerate or derive clinically meaningful benefit from appropriate standard of care therapy.
- At least one non-irradiated measurable lesion per RECIST 1.1 or bone lesion per PCWG3 (only for mCRPC), optional for low dose level (≤ 0.08 mg/kg) of Part A.
- Available archived or fresh tumor tissue samples, optional for low dose level (≤ 0.08 mg/kg) of Part A.
- Adequate bone marrow and organ function.

Key Exclusion Criteria

- Known prior or suspected hypersensitivity to study drugs or any component in their formulations.
- Concurrent malignancy within 5 years.
- Active central nervous system (CNS) metastases.
- Major surgery, systemic anticancer therapy or participation in other therapeutic studies within 4 weeks.
- Radiotherapy administrated within 21 days prior to the first dose of CBP-1018, or localized palliative radiotherapy administered within 7 days.
- Any toxicities attributed to prior anti-cancer therapy, other than alopecia and fatigue, that have not resolved to Grade 1 (NCI CTCAE 5.0) or baseline.
- Poorly controlled concurrent diseases.
- History of cardiovascular events within 12 months of enrollment.
- History of clinically significant lung diseases.
- Active bleeding disorder or other history of grade ≥ 3 hemorrhage within 4 weeks.
- History of deep vein thrombosis or pulmonary embolism within 6 months.
- Known history of testing positive for human immunodeficiency virus (HIV) or known acquired immunodeficiency syndrome (AIDS).
- Positive Hepatitis B Surface Antigen (HepBsAg) (indicative of chronic Hepatitis B), positive Hepatitis total core antibody with negative HepBsAg (suggestive of occult hepatitis B) or detectable Hepatitis C virus Ribonucleic acid (RNA) by PCR.
- Live-virus vaccination within 30 days prior to the first dose of CBP-1018. Seasonal influenza vaccines that do not contain live virus are allowed.
- Current or anticipated need for treatment with strong cytochrome P450 3A4 (CYP3A4) inhibitors or inducers.
- History or current evidence of any other condition, in the opinion of the Investigator.