Abstract 5998

# CBP-1018, a Bi-Ligand-Drug Conjugate treated in Patients with Advanced Solid Tumors: A Phase 1, Multi-Center, Open-Label, Dose-Escalation and Dose expansion Study

Type: Abstract

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**Background**

Prostate-specific membrane antigen (PSMA) is highly expressed on prostate cancer and folate receptor α (FRα) overexpressed in various malignant tissues which both related to tumor invasiveness. CBP-1018 is a first-in-class bi-ligand-drug conjugate targeting both PSMA and FRα with monomethyl auristatin E (MMAE) as payload.

**Methods**

This phase 1 study included both a dose-escalation and expansion stage. In the dose-escalation stage, an accelerated titration was conducted in single patient at 0.03mg/kg followed by an i3+3 design for dose levels (DLs) ≥ 0.06 mg/kg, Q2W (IV.) in a 4-week cycle. This stage mainly enrolled patients (pts) with metastatic castration resistant prostate cancer (mCRPC) which had experienced standard treatment failure or intolerance before. The primary objectives were to evaluate the safety and tolerability, determine dose limiting toxicity (DLT) and maximum tolerated dose (MTD). Additionally, pharmacokinetics (PK) and preliminary efficacy will also be evaluated.

**Results**

As of 27 April 2023, 20 pts (18 mCRPC, 1 bladder cancer and 1 ureteral carcinoma) were enrolled at 6 dose levels (DLs). No DLTs or drug-related deaths were observed. For 15 pts (75%) experienced treatment-related adverse events (TRAEs) ≥ grade 3, most common were neutrophil decrease (50%), WBC decrease (40%), hypokalemia (10%) and hypertriglyceridaemia (10%). Among 17 evaluable mCRPC pts, 5 SD and 7 Non-PD were observed with 9 pts delayed administration and 6 pts dropped for Covid-19. Prostate-specific antigen (PSA) 50% decrease was detected in 2 pts. The median PFS was 9.2 months (95%CI, 1.7-9.2) in mCRPC pts. For PK profile of CBP-1018 and free MMAE, $t_{1/2z}$ was ranged 0.54-1.15 h and 38.27-57.27 h, respectively, no accumulation of both substances after multiple doses.

**Conclusions**

CBP-1018 was well-tolerated at DLs of 0.03-0.14 mg/kg Q2W. Multiple SD and PSA decrease were observed at DLs of 0.08-0.14 mg/kg, conferred a promising preliminary antitumor activity in pts with mCRPC despite of Covid-19's impacts. MTD was not reached and dose-escalation to establish the RP2D is continuing.

**Clinical trial identification**

NCT04928612

**Editorial acknowledgement**

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