5577 **Poster Session**

First-in-human, phase I study of CBP-1008, a bi-specific ligand drug conjugate, in patients with advanced solid tumors.

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Background: Folate receptor α (FRα) and vanilloid subfamily member 6 of transient receptor potential channels (TRPV6) are overexpressed in many solid tumors including ovarian cancer hence could be promising therapeutic targets. CBP-1008 is a first-in-class bi-specific ligand drug conjugate targeting FRα and TRPV6 carrying monomethyl auristatin E (MMAE) as payload. **Methods:** CBP-1008 was administered by intravenous infusion. Phase Ia study included a dose-escalation period initiated by accelerated titration (0.015, 0.03mg/kg d1,15; q28d) and then switched to 3+3 scheme (0.12, 0.15, 0.17, 0.18mg/kg d1,15; q28d) and a dose expansion period. Phase Ib clinical expansion study included 3 cohorts, platinum-resistant ovarian cancer (PROC), metastatic triple negative breast cancer (TNBC) and other solid tumors. The primary objective was to assess the safety and preliminary efficacy. **Results:** As of September 30, 2022, 178 patients received at least one dose of study drug were enrolled (phase Ia: n=35; phase Ib: n=143) and received median 3 prior regimens. Included tumor species were PROC (n=101), TNBC (n=25), ER+/Her2+ breast cancer (BC) (n=17), colorectal cancer (n=6), pancreatic cancer (n=12) and others (n=17). In phase Ia study, DLTs were observed in 3 patients (0.12, 0.15, 0.18mg/kg, n=1 each), including grade 4 hypophosphatemia, neutropenia, febrile neutropenia, and grade 3 hyperglycemia, alanine aminotransferase (ALT) elevation. MTD was not yet reached. Majority of adverse events were mild to moderate. Grade 3/4 treatment-emerging adverse events (TEAEs) occurred in ≥ 3% subjects were neutropenia (n=85), decreased leukocyte count (n=49), anaemia (n=10), AST elevation (n=7), ALT elevation (n=7). Drug-related death was observed in 1 patient. A total of 82 PROC patients at dose of 0.15mg/kg or above were evaluable for efficacy assessment. There were 21 patients achieved partial response (PR) and 30 patients achieved stable disease (SD). The objective response rate (ORR) and the disease control rate (DCR) were 25.6% and 62.2%, respectively. The median progression-free survival (mPFS) was 3.7 months (95% CI: 2.7-5.1). In 34 PROC patients with FRα expression ≥25% and ≤3 prior treatment regimens, ORR was 32.4% and mPFS was still 3.7 months (95% CI: 3.3-7.3). Given the small sample size, efficacy data of breast cancer and other solid tumors will be analyzed after recruiting more patients. **Conclusions:** The current result showed that CBP-1008 has manageable safety profile. Antitumor activity was observed in PROC patients at dose of 0.15mg/kg or above, especially in PROC patients with FRα expression ≥25% and ≤3 prior treatment regimens. Jifang Gong, Jian zhang and Ning Li contributed equally to this work. Xichun Hu , Lin Shen and Lingying Wu are the corresponding authors. Clinical trial information: NCT04740398. Research Sponsor: Coherent Biopharma (Suzhou) Co., Ltd.