3000 **Oral Abstract Session**

A phase Ia/Ib study of CBP-1008, a bispecific 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 hence could be promising therapeutic targets. CBP-1008 is a first-in-class bi-specific ligand drug targeting FRα and TRPV6 carrying monomethyl auristatin E (MMAE) as payload. Here we report the first-in-human, multicenter, phase Ia/Ib study designed to explore the safety, pharmacokinetics and efficacy of CBP-1008 in advanced solid tumors. **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 (OC), metastatic triple negative breast cancer (TNBC) and other solid tumors. The primary objective was to assess the safety and preliminary efficacy. **Results:** As of January 13, 2022, 106 patients received at least one dose of study drug were enrolled (phase Ia: n = 30; phase Ib: n = 76) and received median 3 prior regimens. Included tumor species were OC (n = 52), TNBC (n = 20), ER+/Her2+ breast cancer (BC) (n = 16), lung cancer (n = 3), pancreatic cancer (n = 2) and others (n = 13). 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). MTD was not yet reached. Majority of adverse events were mild to moderate. The most common grade 3/4 treatment-emerging adverse events (TEAEs) were neutropenia (37.7%), AST elevation (6.6%), ALT elevation (5.7%), hyperglycemia (2.8%), hypohemoglobinemia (2.8%) and nausea (1.9%). Drug-related death was not observed. A total of 69 patients at dose of 0.15mg/kg or above were evaluable for efficacy assessment. There were 11 patients achieved partial response (PR) (OC n = 8, ER+/Her2+ BC n = 2, TNBC n = 1) and 30 patients achieved stable disease (SD). In 32 advanced platinum-resistant OC patients with FRα and/or TRPV6-positive expression, 6 PR and 16 SD were observed. Moreover, 6/18 PR (33.3%) and 8/18 SD (44.4%) were observed in enriched OC patients who showed high score of FRα/TRPV6 receptor. **Conclusions:** The preliminary results showed that CBP-1008 has manageable safety profile. Antitumor activity was observed in patients with FRα/TRPV6 receptor expression, especially in platinum-resistant OC cohort with high score of the two receptors. Clinical trial information: NCT04740398. Research Sponsor: Coherent Biopharma (Suzhou) Co., Ltd.