First-in-human/phase I trial of HS-20089, a B7-H4 ADC, in patients with advanced solid tumors


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Background

B7-H4, a transmembrane glycoprotein in the B7 superfamily, has limited expression in normal tissues but is highly expressed in various cancers. HS-20089 is a novel B7-H4 directed antibody-drug conjugate (ADC) with a drug to antibody ratio of 6. We conducted a first-in-human phase I trial to evaluate the dose-limiting toxicity (DLT), safety, tolerability, pharmacokinetics, and efficacy of HS-20089 in patients (pts) with advanced solid tumors refractory to standard therapy.

Methods

Eligible pts were enrolled in sequentially escalating dose cohorts (0.7 to 7.2 mg/kg) of HS-20089 administered intravenously every 3 weeks. The accelerated titration combined with Bayesian optimal interval (BOIN) was used as the dose escalation schedule in this phase I dose escalation trial.

Results

As of Apr. 11th, 2023, 44 pts with advanced solid tumors (41 breast cancers, 2 ovarian cancers, and 1 endometrial cancer) received HS-20089 treatment. Three DLTs were observed in 2 pts (both in 7.2 mg/kg). The most common treatment-emergent adverse events (≥20%) were leukopenia, neutropenia, nausea, anemia, thrombocytopenia, vomiting, fatigue, increased alanine aminotransferase, anorexia, increased aspartate aminotransferase and hyponatremia. No interstitial lung disease and infusion reaction were reported. Of 33 response-evaluable pts, 8 partial responses (PRs) were observed in pts treated with HS-20089 (response rate: 24.2%), including 3 confirmed PRs and 5 PRs awaiting confirmation. The disease control rate was 63.6%. In the subset of 16 triple-negative breast cancer (TNBC) pts, 6 PRs were observed (response rate: 37.5%), including 2 confirmed PRs and 4 PRs awaiting confirmation. At potential target therapeutic dose (4.8 and 5.8 mg/kg), 5 PRs of 12 pts were observed (response rate: 41.7%) in TNBC. The patient achieving PR with the longest treatment duration of 403 days remains on treatment in 0.7 mg/kg cohort.

Conclusions

Based on data from the ongoing study, HS-20089 was well tolerated and showed antitumor activities in advanced solid tumors, with encouraging clinical efficacy in TNBC.

Clinical trial identification

NCT05263479.

Legal entity responsible for the study

Hansoh Pharmaceutical Group Co. Ltd.

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Hansoh Pharmaceutical Group Co. Ltd.
Disclosure
H. Wei, C. Li, L. Yang, Q. Huang, Z. Cao, Q. Wu: Financial Interests, Institutional, Full or part-time Employment, Medical staff: Hansoh Pharmaceutical Group Co, Ltd. All other authors have declared no conflicts of interest.

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