A phase Ia study of a novel anti-HER2 antibody–drug conjugate GQ1001 in patients with previously treated HER2 positive advanced solid tumors

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Background

A novel anti-human epidermal growth factor receptor 2 (HER2) antibody–drug conjugate (ADC) GQ1001 was assessed in patients with previously treated HER2 positive advanced solid tumors in a global multi-center phase Ia dose escalation trial.

Aim

Primary: • To identify the dose-limiting toxicity of GQ1001 for dose expansion.
Secondary: • To assess safety and tolerability of GQ1001. • To assess the characteristics of pharmacokinetics (PK) after single or multiple doses of GQ1001. • To assess the GQ1001 associated immunogenicity (e.g. antiGQ1001 antibody/HAHA). • To evaluate the preliminary anti-tumor activity of GQ1001 by evaluation of objective response rate (ORR), disease control rate (DCR), duration of response (DoR), and progression-free survival.

Method

In this phase Ia trial, a modified 3 + 3 study design was adopted during dose escalation phase. Eligible patients with HER2+ tumors were enrolled, and GQ1001 monotherapy was administered intravenously every 3 weeks. The starting dose was 1.2 mg/kg, followed by 2.4, 3.6, 4.8, 6.0, 7.2 and 8.4 mg/kg. Extra patients were enrolled into 6.0, 7.2, and 8.4 mg/kg cohorts as dose expansion phase.

Results

A total of 32 patients were enrolled, predominantly in breast (9), gastric or gastro-esophageal junction (9) and salivary gland cancer (4). Median number of prior-line of therapies was 3 (0–11) and 37.5% patients received ≥ 2 lines of anti-HER2 therapies. No DLT was observed during dose escalation. MTD was not reached and dose recommended for dose expansion (DRDE) was determined as 8.4 mg/kg. Grade ≥ 3 treatment-related adverse events rate was 28.1% (9/32) and platelet count decreased (4/32, 12.5%) was the most common one. No drug-related death was observed. Objective response rate and disease control rate of 15 evaluable patients in 7.2 mg/kg and 8.4 mg/kg cohorts were 40.0% (6/15) and 60.0% (9/15). Pharmacokinetics analysis showed low exposure and accumulation of free DM1 in circulation..

Conclusion

GQ1001 is well tolerated and shows promising efficacy in previously treated HER2-positive advanced solid tumors. DRDE was determined as 8.4 mg/kg for following trials.

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