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Abstract CT010: Phase I dose-escalation and expansion study of JS107, a claudin 18.2 (CLDN18.2)-targeting antibody-drug conjugate (ADC), as monotherapy or in combination for patients (pts) with advanced solid tumors

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Abstract

Background:

JS107 is a monomethyl auristatin E conjugated, CLDN18.2 specific ADC. JS107 exhibited potent anti-tumor activities in preclinical studies with a tolerable safety profile. Here we report the safety and efficacy results of JS107 monotherapy or in combination for pts with advanced solid tumors from the first-in-human phase 1 trial (NCT05502393).

Methods:

In Part A of the study, pts with advanced solid tumors refractory to standard therapies were treated with JS107 at 0.15-3.5 mg/kg Q3W during dose escalation and CLDN18.2+ pts were treated with JS107 at 2.0 and 3.0 mg/kg Q3W during dose expansion. In Part B of the study, pts with CLDN18.2+, HER2-negative, previously untreated, advanced gastric or gastroesophageal junction cancer (GC/GEJ) were treated with JS107 combined with toripalimab (240 mg Q3W) and XELOX (capecitabine and oxaliplatin), in dose escalation (JS107 at 2.0-3.0 mg/kg Q3W) and expansion (JS107 at 2.0 mg/kg Q3W) phases. The primary endpoint was safety. Secondary endpoints included efficacy and pharmacokinetics (PK).

Results:

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As of January 7, 2025, 63 pts were enrolled in Part A (22 in dose escalation and 41 in dose expansion) and 27 enrolled in Part B (9 in dose escalation and 18 in dose expansion). The

maximum tolerated dose was not reached for JS107 monotherapy and was 2.5 mg/kg for combination treatment. Grade 3 and above treatment-related adverse events (TRAEs) occurred in 47.6% pts in Part A and 40.7% pts in Part B. The most frequent grade 3 and above TRAE was neutropenia (22.2%) in Part A and thrombocytopenia (18.5%) in Part B. Among pts with CLDN18.2-high (defined as ≥20% of tumor cells with ≥2+ staining intensity) GC/GEJ who received JS107 monotherapy at 2.0-3.0 mg/kg (n=24), the objective response rate (ORR) was 34.8% (8/23, 95%CI 16.4-57.3) and median progression-free survival was 4.11 months (95%CI 3.15-9.63). Among efficacy evaluable pts with CLDN18.2-high GC/GEJ in Part B (n=14), the ORR was 78.6% (11/14, 95%CI 49.2-95.3). A positive association between CLDN18.2 expression level and efficacy was observed in Part A and Part B. PK analysis showed a dose-dependent ADC and total antibody exposure at doses of 0.15-3.5 mg/kg. JS107 elimination half-life was 4.41-6.96 days at doses of 2.0-3.5 mg/kg, with no obvious accumulation observed after multiple dosing.

Conclusions:

JS107 monotherapy or in combination with toripalimab and XELOX showed promising efficacy in pts with CLDN18.2-high advanced GC/GEJ with a manageable safety profile. The clinical benefit of CLDN18.2 ADC combination treatment was thus demonstrated for the first time. Further clinical development of JS107 in CLDN18.2+ advanced solid tumors is warranted.

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