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Arcotatug tavatecan (IBI343/TAK-921) versus treatment of physician's choice (TPC) in previously treated, advanced gastric or gastroesophageal junction adenocarcinoma (G/GEJA): First interim analysis of the randomized, open-label, phase 3, G-HOPE-001 study

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Background

Arcotatug tavatecan is a novel CLDN18.2-targeted ADC comprising an Fc-silenced antibody designed to reduce on target, off-tumor toxicity and conjugated to an exatecan-derived TOPO I inhibitor payload for selective delivery to tumor cells. Here, we report the prespecified first interim analysis (IA1) of the G-HOPE-001 study.

Methods

Patients (pts) with unresectable or metastatic G/GEJA, CLDN18.2 IHC $\geq 2+$ in $\geq 75\%$ of tumor cells who had progressed on 2-4 prior regimens were randomized 1:1 to arcotatug tavatecan 6mg/kg Q3W or TPC (irinotecan, paclitaxel or trifluridine/tipiracil) until progression or unacceptable toxicity. Stratification factors were regions, primary tumor site and prior gastrectomy. Primary endpoints were IRRC-assessed PFS per RECIST v1.1 and OS. The prespecified IA1 included the PFS final analysis and an OS futility analysis, with a data cutoff of February 13, 2026.

Results

In IA1, 408 pts from China and Japan (male: 62.0%, median age: 58.0, ECOG PS 1: 71.6%, primary tumor at stomach: 81.6%, primary tumor resection: 43.6%) were randomized to arcotatug tavatecan (N=203) and TPC (N=205) arms. IRRC-assessed median PFS was 5.5 months vs 2.9 months (HR: 0.47 [95% CI: 0.34-0.65], p-value <0.0001). With 34.8% of events, median OS was 9.9 months vs 7.4 months (HR: 0.63 [95% CI: 0.45-0.89]). IRRC-assessed ORR was 23.6% in arcotatug tavatecan and 5.3% in TPC. Grade ≥ 3 (G3+) TEAEs occurred in 45.8% pts with arcotatug tavatecan vs 57.9% pts with TPC. Common gastrointestinal TEAEs ($\geq 10\%$) with arcotatug tavatecan vs TPC were nausea (38.9% vs 40.6%), vomiting (22.2% vs 28.4%) and diarrhea (12.8% vs 34.5%). Interstitial lung disease was not observed. TRAEs leading to treatment discontinuation occurred in 1.0% of pts in each arm. No TRAE led to death.

Conclusions

Arcotatug tavatecan demonstrated a statistically significant and clinically meaningful improvement in PFS with a manageable safety profile versus TPC for CLDN18.2+ G/GEJA in the 3L+ setting. OS results will be evaluated at the prespecified IA2.

Clinical trial identification

NCT06238843.

Legal entity responsible for the study

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Disclosure

All authors have declared no conflicts of interest.

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