TPS4201 Poster Session

A multiregional, randomized, controlled, open-label, phase 3 study of the anti-claudin18.2 (CLDN18.2) antibody-drug conjugate (ADC) arcotatug tavatecan (IBI343) in gastric or gastroesophageal junction adenocarcinoma (G/GEJA): Trial in progress.

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Background: CLDN18.2 has been a validated therapeutic target for G/GEJA. As a next-generation ADC, arcotatug tavatecan (IBI343) composed of anti-CLDN18.2 monoclonal antibody conjugated to exatecan (topoisomerase I inhibitor) with unique IgG1 Fc silencing to attenuate antibody-dependent cellular cytotoxicity and complement-dependent cytotoxicity. Previous phase 1 studies of IBI343 observed manageable safety profiles with encouraging efficacy in G/GEJA, pancreatic ductal adenocarcinoma and biliary tract cancer (2024 ASCO Annual Meeting [3037], ESMO GI 2024 [396MO], ESMO Asia 2024 [132MO]). Here, we present the trial in progress of a phase 3 study (G-HOPE-001, NCT06238843) evaluating efficacy and safety of IBI343 monotherapy versus treatment of investigator's choice in previously treated patients (pts) with CLDN18.2-positive G/GEJA. **Methods:** This multiregional, randomized, controlled, open-label, phase 3 study planned to enroll 450 pts. Main inclusion criteria are: 1) locally advanced unresectable or metastatic G/GEJA; 2) positive CLDN18.2, defined as immunohistochemical (IHC) membrane staining intensity $\geq$ 2+ in $\geq$ 75% of tumor cells as measured by the VENTANA CLDN18 (43-14A) Assay; 3) radiologically evaluable disease, measurable and/or non-measurable disease per RECIST v1.1; 4) received and progressed on 2-4 prior regimens of systemic therapy which must include a fluoropyrimidine, platinum, and a taxane or irinotecan. Main exclusion criteria are: 1) positive HER-2, defined as IHC 3+ or IHC 2+/ in situ hybridization+; 2) history of treatment with topoisomerase inhibitor-based ADCs. Pts are randomized in a 1:1 ratio to receive IBI343 6mg/kg Q3W in the experimental arm or to receive treatment of investigator's choice including irinotecan, paclitaxel, or trifluridine/tipiracil in the control arm. Stratification factors include region (Asian country/region other than Japan vs. European Union and United States vs. Japan), primary site of the tumor (stomach vs. gastroesophageal junction) and history of prior gastrectomy (yes vs. no). The primary endpoints are progression-free survival (PFS) per RECIST v1.1 and overall survival (OS). The secondary endpoints include objective response rate (ORR), disease control rate (DCR), duration of response (DoR) and time to response (TTR) per RECIST v1.1, quality of life (QoL), safety, pharmacokinetics (PK) and immunogenicity. The trial is currently enrolling pts in China and Japan. Clinical trial information: NCT06238843. Research Sponsor: Innovent Biologics (Suzhou) Co., Ltd.