TPS3635 Poster Session

Telisotuzumab adizutecan (ABBV-400; Temab-A) monotherapy vs trifluridine/tipiracil plus bevacizumab in patients with refractory metastatic colorectal cancer with increased c-Met protein expression: An open-label, randomized, phase 3 trial.

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Background: c-Met protein expression is increased in several solid tumors, including colorectal cancer (CRC). Temab-A is a c-Met–directed antibody-drug conjugate consisting of the antibody telisotuzumab conjugated to a potent topoisomerase 1 inhibitor payload. Preliminary data from the ongoing first-in-human study of Temab-A (NCT05029882) indicate a tolerable safety profile and promising antitumor activity in patients with third-line or later metastatic (m)CRC (Sharma et al. *JCO* 2023;41:3015). Herein, we describe a phase 3 study comparing Temab-A monotherapy with the standard of care (trifluridine/tipiracil plus bevacizumab) in patients with refractory mCRC with c-Met expression of 3+ in ≥10% of tumor cells by immunohistochemistry (IHC). **Methods:** This is an open-label, randomized, controlled, global phase 3 study(NCT06614192). Patient eligibility includes age ≥18 years, confirmed c-Met expression of 3+ in ≥10% of tumor cells, metastatic adenocarcinoma of the colon/rectum, measurable disease per RECIST v1.1, ECOG performance status 0–1, prior treatment with a fluoropyrimidine (eg, 5-FU or capecitabine), oxaliplatin, irinotecan, and an anti-VEGF antibody (unless locally not approved) or an anti-EGFR antibody if indicated, and appropriate targeted therapy or immunotherapy if targetable mutations present (eg, *BRAF* V600E or *HER2*) or MSI-H/dMMR. Prior treatment with regorafenib and/or fruquintinib is permitted, but no prior treatment with trifluridine/tipiracil Study-specific c-Met protein expression IHC cutoff is defined as 3+ intensity in ≥10% of tumor cells. The study consists of 2 stages. In stage 1, at least 60 patients will be randomized 1:1 to receive 2 different doses of intravenous (IV) Temab-A. In stage 2, 400 patients will be randomly assigned 1:1 to receive either the optimized dose of IV Temab-A or oral trifluridine/tipiracil plus IV bevacizumab. In stage 1, primary objectives are to determine the recommended phase 3 dose and to evaluate the efficacy, as measured by objective response (OR), and safety of Temab-A; secondary objectives are to assess progression-free survival (PFS), overall survival (OS), duration of response (DOR), disease control rate (DCR), and pharmacokinetics. In stage 2, the primary objectives are to demonstrate the superiority of Temab-A over trifluridine/tipiracil plus bevacizumab in terms of OR and OS; secondary objectives are to evaluate PFS, DOR, DCR, and safety of Temab-A treatment, and its impact on patient-reported outcomes. Response will be assessed by blinded independent central review per RECIST v1.1. Safety evaluations include adverse event monitoring, vital sign measurements, ECG variables, and clinical laboratory testing. Enrollment began in December 2024. Clinical trial information: NCT06614192. Research Sponsor: AbbVie Inc.; n/a.