TPS4202 **Poster Session**

Telisotuzumab adizutecan (ABBV-400; Temab-A) in combination with fluorouracil, leucovorin, and budigalimab in locally advanced/metastatic gastric, gastro-esophageal junction, or esophageal adenocarcinoma (a/m GEA).

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Background: The *MET* proto-oncogene and its receptor tyrosine kinase gene product (c-Met protein) are involved in normal cellular functions such as cell proliferation and differentiation but can be abnormally activated and upregulated in cancer to promote tumor growth. *MET* gene amplification and increased c-Met protein expression are associated with poor survival outcomes in gastric cancer. The antibody-drug conjugate Temab-A (ABBV-400) is composed of the c-Met–directed antibody telisotuzumab conjugated to a potent topoisomerase 1 inhibitor. A phase 1 study (NCT05029882) investigating Temab-A monotherapy demonstrated manageable safety and encouraging efficacy in patients with previously treated, advanced GEA, with an objective response rate of 29% (12/42) and clinical benefit rate of 71% (30/42) (Strickler et al. *Ann Oncol*. 2024;35:1439P). This study evaluates Temab-A in combination with fluorouracil (5-FU), leucovorin/folinic acid (LV), and budigalimab (budi; a PD-1–blocking antibody). **Methods:** This multicenter,phase 2, open-label, randomized study (NCT06628310) will enroll ~180 adult patients with HER2-negative a/m GEA who have not received prior systemic therapy in the a/m setting, have not received a prior PD-(L)1 inhibitor, have Eastern Cooperative Oncology Group performance status 0–1, and have measurable disease per RECIST v1.1. Primary objectives of the study are to evaluate safety and tolerability, evaluate efficacy as measured by progression-free survival and objective response, and select the recommended phase 3 dose of Temab-A in combination with 5-FU, LV, and budi. Secondary objectives include assessment of dose-limiting toxicities (DLTs) in the dose-escalation stage, evaluation of pharmacokinetics, and further evaluation of efficacy measures (duration of response, disease control, and overall survival). The study consists of 2 stages: dose escalation and dose optimization. During BOIN-directed dose escalation, ~18 patients receive escalating doses of Temab-A administered once every 4 weeks (Q4W) in combination with fixed doses of 5-FU (2400 mg/m^2 Q2W), LV (400 mg/m^2 Q2W), and budi (500 mg Q4W). DLTs are assessed during the first 28-day cycle. During dose optimization, ~162 patients are randomized 1:1:1 to 1 of 2 selected doses of Temab-A in combination with 5-FU, LV, and budi or a control arm of FOLFOX + budi. Randomization is stratified by PD-L1 expression and primary tumor location. Treatment is administered until disease progression, intolerable toxicity, or other discontinuation criteria are met. Either archived formalin-fixed paraffin-embedded tissue or a fresh biopsy is required for biomarker research that will include evaluation of c-Met protein expression and *MET* genomic alterations. Clinical trial information: NCT06628310. Research Sponsor: AbbVie, Inc.; n/a.