TPS8655 Poster Session

Phase 1b/2 study evaluating telisotuzumab adizutecan (ABBV-400; Temab-A) in combination with budigalimab in patients (pts) with advanced non-squamous (NSQ) non-small cell lung cancer (NSCLC) with no prior treatment for advanced disease and no actionable genomic alterations.

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Background: c-Met (MET) protein expression is frequently increased in NSCLC and is associated with poor prognosis. 24% of pts with NSQ *EGFR* wildtype (WT) NSCLC exhibit increased c-Met protein expression, ie, ≥25% 3+ via IHC. Addition of programmed cell death (ligand) 1 (PD-[L]1) inhibitors to chemotherapy (CT) has improved treatment of NSCLC regardless of PD-(L)1 expression. However, more-effective therapies are needed, particularly for pts with no known actionable genomic alterations. Temab-A is an antibody-drug conjugate comprising the c-Met protein–targeting antibody telisotuzumab and the potent topoisomerase 1 inhibitor adizutecan payload attached via a stable cleavable linker. In an ongoing phase 1 study (NCT05029882), Temab-A monotherapy demonstrated manageable safety and promising efficacy in pts with advanced/metastatic (a/m) NSQ *EGFR* WT NSCLC in second line and later, with an objective response rate (ORR) of 48% (23/48) across all c-Met expression levels and clinical benefit rate of 85% (41/48) (De Miguel et al. *Ann Oncol*. 2024;35:S805-S806). Herein, we describe a study evaluating Temab-A in combination with the PD-1 inhibitor budigalimab. **Methods:** This multicenter, global,open-label, phase 1b/2, randomized (in part 2) study (NCT06772623) will enroll ~172 pts (≥18 yr) with a/m NSQ NSCLC. Eligible pts have ECOG 0 or 1, measurable disease per RECIST v1.1, and documented *EGFR* WT and PD-L1 status. Primary objectives are to evaluate safety and tolerability, assess efficacy as measured by ORR by blinded independent central review, and select the recommended phase 3 dose of Temab-A combined with budigalimab. Secondary objectives include assessment of efficacy outcomes (PFS, DOR, OS, and disease control rate), characterization of PK and immunogenicity, and evaluation of PD and potential predictive biomarkers. The study has 2 parts: a safety dose-escalation part 1 and a dose-optimization part 2. Part 1 enrolls ~12 pts who have received ≤1 prior systemic therapy for a/m NSCLC, including platinum-based CT, an immune checkpoint inhibitor, or targeted therapy. Pts receive escalating doses of Temab-A IV Q3W guided by BOIN design in combination with a fixed dose of budigalimab IV Q3W. Dose-limiting toxicities are evaluated during cycle 1. Part 2 enrolls ~160 pts who have not received prior systemic therapy for a/m NSCLC. Pts are randomized 1:1:1:1 to Temab-A at 1 of 2 doses determined in part 1 + budigalimab, to budigalimab + CT, or to SOC (pembrolizumab + CT) arms. Randomization is stratified by PD-L1 expression and history of brain metastases. Treatment continues until disease progression, intolerable toxicity, or other discontinuation criteria are met. The first dosing of the first patient enrolled is planned in March 2025. Clinical trial information: NCT06772623. Research Sponsor: AbbVie Inc.; n/a