TPS4618 Poster Session

A phase 2, open-label, randomized study of livmoniplimab in combination with budigalimab versus chemotherapy in patients with metastatic urothelial carcinoma.

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Background: Urothelial carcinoma (UC) has a high mortality rate in patients (pts) with metastatic disease. While immune checkpoint inhibitors (CPI), including programmed cell death protein 1 (PD-1) inhibitors combined with chemotherapy (CTx) or enfortumab vedotin (EV), have been approved for first-line treatment of metastatic (m)UC, many pts have de novo or develop acquired resistance. For pts without response to frontline treatment or whose disease has progressed on prior CPI combinations, optimal treatment is unclear and new therapies are urgently needed. Glycoprotein A repetitions predominant (GARP) is a membrane-bound receptor that complexes with latent transforming growth factor (TGF)-β1; the release of active TGF-β1 from this complex suppresses antitumor responses. Livmoniplimab (livmo), an antibody targeting the GARP:TGF-β1 complex, prevents release of active TGF-β1, thereby promoting antitumor activity. A first-in-human phase 1 study (NCT03821935) demonstrated that combining livmo and the anti–PD-1 mAb budigalimab (budi) resulted in a manageable safety profile and promising antitumor activity in pts with PD-1–refractory advanced UC (J Clin Oncol 2024;42[suppl 4]: abs 617). Herein, we describe the phase 2 study that is evaluating livmo + budi vs CTx in pts with mUC (NCT06632951). **Methods:** This multicenter, open-label, randomized study is enrolling pts aged ≥18 years who have mUC, measurable disease per RECIST v1.1, ECOG PS 0–1, and have experienced disease progression on anti–PD-1 or anti–PD-1 ligand 1 therapy. Platinum (Pt)-eligible pts must have received a Pt-containing regimen; pts who can receive EV must have experienced disease progression on/after receiving EV treatment. Primary objectives are to identify the recommended phase 3 livmo dose in combination with budi and evaluate overall survival. Secondary objectives include evaluating progression-free survival, best overall response of complete or partial response, duration of response, and assessment of safety and tolerability, pharmacokinetics, and immunogenicity of the combination. Pts will be randomized 1:1:1 to 3 arms: 1) livmo dose 1 Q3W + budi Q3W; 2) livmo dose 2 Q3W + budi Q3W; or 3) investigator's choice of CTx (paclitaxel, docetaxel, or gemcitabine). Pts will be stratified by ECOG PS (0 vs 1) and first-line therapy (pembrolizumab + EV vs CTx). Treatment for pts in Arms 1 and 2 will continue until a maximum of 35 cycles. For pts in Arm 3, treatment will continue for the duration that is consistent with local guidelines/practice for this pt population. No crossover between arms will be permitted. For all pts, treatment is discontinued at disease progression or if other protocol-defined discontinuation criteria are met. In total, approximately 150 pts (50 pts/arm) are planned for enrollment globally. Clinical trial information: NCT06632951. Research Sponsor: AbbVie, Inc.; n/a