TPS2691 Poster Session

Phase 2 trial of TU2218, TGFβ-RI, and VEGF-R2 dual inhibitor in combination with pembrolizumab in patients with biliary tract cancer and head and neck cancer.

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Background: TU2218 is a low molecular weight dual kinase inhibitor highly specific to TGFβR1 and VEGFR2 and has a potential to be an efficacious therapy against cancer growth. In vitro and in vivo nonclinical studies have shown that TU2218 reduced the growth and migration/invasion of tumor cells and increased antitumor effects in combination with anti-PD-1/anti PD-L1 antibodies. To investigate safety and tolerability of TU2218 Phase 1a trial was conducted with 6 dose level escalation (30mg/day → 60mg/day → 105mg/day → 150mg/day → 195mg/day → 270mg/day) of TU2218 alone, and it was confirmed that TU2218 was safe and tolerated in all dose levels. And to explore the synergistic effect of TU2218 in combination with Pembrolizumab and to decide RP2D Phase 1b trial was conducted with 3 dose level escalation (105mg/day → 150mg/day → 195mg/day) of TU2218 in combination with Pembrolizumab in patients with advanced solid tumors. The RP2D of TU2218 was established as 195mg/day in combination with Pembrolizumab, the total 19 patients received the treatment and most frequently observed TRAE was pruritus and proteinuria, and three Grade 3 TRAEs (Pruritus, Rash Maculo-Popular, Malaise) were observed. The MTD was not identified during dose escalation period. The ORR of overall dose levels demonstrated 19%, and DCR was about 63%. In particular, 80% DCR was observed in TU2218 195mg/day in combination with Pembrolizumab. The trial was expanded to the specific cancer types, Biliary Tract Cancer and Head and Neck Cancer using the established RP2D for Phase 2 trial. **Methods:** Locally advanced unresectable or metastatic biliary tract cancer (BTC) patient whose tumor has progressed on/after first line standard anticancer therapy and anti-PD-(L)1 agent-naïve metastatic or with unresectable, recurrent head and neck squamous cell carcinoma (HNSCC) patient whose tumor express PD - L1 (CPS ≥1) as determined by an FDA-approved test or recurrent or metastatic HNSCC with disease progression on or after platinum-containing chemotherapy are eligible for this non-randomized, open-label multicenter trial. All patients are administered with TU2218 195mg/day (97.5mg BID) on a 2 weeks-on/1 week-off in combination with Pembrolizumab 200mg IV Q3 weeks and will be evaluated by investigator-assessed objective response rate (ORR) defined as the proportion of patients with a best overall response of complete response (CR) or partial response (PR) according to RECIST version 1.1. If 2 or less patients out of 22 evaluable BTC patients are observed with CR/PR and 3 or less patients out of 22 evaluable HNSCC patients are observed with CR/PR, this suggests futility and the cohort may be stopped. Up to 40 BTC patients and up to 36 HNSCC patients are planned to be enrolled and a dropout rate of up to 10% is expected. As of this abstract submission date, 14 BTC patients and 8 HNSCC patients have been enrolled. Clinical trial information: NCT05784688. Research Sponsor: TiumBio., Co., Ltd.; Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc.