662 PHASE I/II STUDY OF IPILIMUMAB PLUS NIVOLUMAB COMBINED WITH SACITUZUMAB GOVITECAN IN PATIENTS WITH METASTATIC CISPLATIN-INELIGIBLE UROTHELIAL CARCINOMA

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Background Sacituzumab govitecan (SG) demonstrated an ORR of 27% and median OS of 10.5 months (Mo) in metastatic urothelial carcinoma (mUC) patients (pts) progressing after platinum chemotherapy and PD1/L1 inhibitor. The combination of SG and pembrolizumab is safe and active following platinum chemotherapy. Ipilimumab (IPI) 3mg/kg plus Nivolumab (NIVO) 1mg/kg (I3+N1) has shown promising activity in post-platinum mUC pts. Given the potential synergism between immunogenic cell death induced by SG and IPI-NIVO, we hypothesized that the combination of SG and IPI-NIVO would be safe and active as a frontline treatment for cisplatin ineligible mUC.

Methods 3+ 3 design was used for the phase I dose escalation of SG at 8 mg/kg and 10 mg/kg dose levels. I3+N1 was given IV every 3 weeks x 4 cycles followed by NIVO 360 mg IV day 1 every 3 weeks. SG was given IV at days 1,8 every 3 weeks The primary endpoint was safety and recommended phase 2 dose (RP2D) based on dose limiting toxicity (DLTs) observed in cycle 1; key secondary endpoints include ORR, DOR, PFS and OS. Key inclusion criteria were ECOG-PS 0–1, cisplatin-ineligibility, treatment naïve, no prior PD1/L1 inhibitor except >3 months earlier for localized disease.

Results The study has completed phase I dose escalation after enrolling a total of 9 patients (8 men, 1-woman, median age: 74 years). Six patients were enrolled at SG 8 mg/kg with 1 DLT, and 3 patients at 10 mg/kg with 2 DLTs. DLTs included grade 3 skin rash (n=2) and grade 3 pneumonitis (n=1). The RP2D of SG was determined to be 8 mg/kg with I3+N1. The most common treatment-related adverse events (TRAE) included anemia (66.6%) neutropenia (66.6%), pruritus (66.6%), fatigue (66.6%), and diarrhea (66.6%). 2 patients developed grade 2 infusion reactions to SG. Other grade $\geq$ 3 TRAE included neutropenia (55.5%), anemia (33.3%), arthralgia (11.1%), and elevated amylase/lipase (11.1%). Of the 9 patients, 6 patients were considered evaluable for response of whom 4 had partial response (ORR 66.6%). With the median follow-up time of 18.8 Mo (95% CI 14.8-NR), the median DOR was 10.7 Mo (range 4.6–12.0); mPFS was 8.78 Mo (95% CI 3.8-NR) and mOS was NR.

Conclusions The RP2D of SG was identified as 8mg/kg in combination with I3+N1 as first-line therapy for cisplatin-ineligible mUC. Early signals of promising activity were observed in a small cohort of evaluable pts. The Phase 2 trial is ongoing coupled with exploratory biomarker analyses. NCT04863885

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