**Background**

Soto, a specific, irreversible KRAS$^{G12C}$ inhibitor, has monotherapy clinical activity in KRAS p.G12C-mutated solid tumors, with an objective response rate of 7.1% for heavily pretreated CRC in the CodeBreaK 100 phase I trial. KRAS$^{G12C}$ blockade can lead to accumulation of activated EGFR. Combining Soto with an EGFR inhibitor may produce synergistic antitumor activity. The safety and efficacy of Soto with PMab, a monoclonal antibody specific to EGFR, in KRAS p.G12C-mutated CRC are being evaluated in this ongoing phase Ib study (NCT04185883).

**Methods**

This study includes a dose exploration phase to identify a safe/tolerable daily oral dose of Soto with PMab (6mg/kg IV Q2W) in patients (pts) with previously treated mCRC, and a dose expansion phase. Dose exploration is reported.

**Results**

As of 4/23/21, 8 pts (5 female, median age: 60.5 yrs [range: 31-79]) were enrolled in dose exploration with 960 mg QD Soto and 6mg/kg IV Q2W PMab. Median number of lines of therapy for metastatic disease was 3.5 (range 1-10); 5 pts had prior Soto. Median treatment (tx) duration was 4.4 months (range: 1.4, 8.8). No dose limiting toxicities (DLTs) were observed during the DLT evaluation period (first 28 days). Tx-related adverse events (TRAEs) of any grade related to Soto or PMab were reported for 4 and 8 pts, respectively. No grade 4 or fatal TRAEs occurred. Two pts had PMab TRAEs leading to dose modification of PMab (1–dermatitis acneiform, 1–dry skin, rash, hypokalemia, hypomagnesemia) and 1 pt had a Soto TRAE leading to dose modification of Soto (diarrhea). There was 1 confirmed partial response, 5 stable disease (SD), 1 progressive disease (PD), and 1 not evaluated but with clinical PD. Of pts with prior Soto, 4 had decrease in sum of target lesions; 4 had SD and 1 with PD developed new lesions despite a decrease in size of target lesions. Sotorasib exposures were similar to those observed in monotherapy study.

**Conclusions**

Combination of Soto (960 mg QD) and PMab (6mg/kg IV Q2W) was safe and tolerable with promising efficacy in heavily pretreated pts with KRAS p.G12C-mutated CRC. AEs are consistent with known AEs for Soto and PMab. Updated safety and efficacy data will be presented.

**Clinical trial identification**

NCT04185883.

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**Legal entity responsible for the study**

Amgen Inc.

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Disclosure

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