Sotorasib in combination with panitumumab in refractory KRAS G12C-mutated colorectal cancer: Safety and efficacy for phase Ib full expansion cohort

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Background

Sotorasib (Soto), a KRASG12C inhibitor, showed modest clinical activity as monotherapy in heavily pretreated patients (pts) with KRAS G12C-mutated colorectal cancer (CRC) in the CodeBreaK 100 phase II study, with a 9.7% objective response rate (ORR). Early data from the CodeBreaK 101 phase Ib dose exploration (n=8) and expansion (n=18) cohorts showed promising antitumor activity for the combination of Soto and panitumumab (Pmab), an EGFR antibody, in chemorefractory KRAS G12C-mutated metastatic CRC (mCRC). Here, we report results from the fully enrolled dose expansion cohort of 40 pts with refractory mCRC.

Methods

CodeBreaK 101 (NCT04185883) subprotocol H includes dose exploration and expansion in multiple cohorts. Key eligibility criteria for the refractory mCRC cohort included progression on or after prior fluoropyrimidine, oxaliplatin, irinotecan and an anti-angiogenic agent. Primary endpoint is safety. Secondary endpoints include antitumor activity, progression-free survival (PFS), overall survival (OS), and pharmacokinetics (PK).

Results

As of March 25, 2022, 40 pts (75% female, median age 57.5 years) were enrolled and received oral Soto 960 mg daily and Pmab 6 mg/kg IV every 2 weeks. Median prior lines of therapy was 2. Treatment-related adverse events (TRAEs) of any grade occurred in 37 (92.5%) pts. Grade 3 TRAEs occurred in 9 (22.5%) pts; related to Soto and Pmab in 6 (15%) and 8 (20%) pts, respectively. No TRAEs were Grade >3 or resulted in treatment discontinuation. Safety findings were consistent with known profiles of Soto and Pmab. Confirmed ORR was 30% (95% CI: 16.6, 46.5). Disease control rate was 90% (95% CI: 76.3, 97.2). Tumor shrinkage of any magnitude was observed in 35 (87.5%) pts. Soto PK exposures were consistent to those observed in monotherapy studies.

Conclusions

This dataset provides further evidence of safety and tolerability for the combination of Soto and Pmab in heavily pretreated pts with KRAS G12C-mutated mCRC, with 3-fold higher response than previously observed with Soto monotherapy, supporting further development of this combination. Longer follow up data with duration of response, PFS, and OS will be presented.

Clinical trial identification

NCT04185883.

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