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Sotorasib (soto), panitumumab (pani) and FOLFIRI in the first-line (1L) setting for KRAS G12C–mutated metastatic colorectal cancer (mCRC): Safety and efficacy analysis from the phase Ib CodeBreaK 101 study

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Background

In the phase 1b CodeBreaK 101 (NCT04185883) study, the addition of soto plus pani to FOLFIRI demonstrated an acceptable safety profile and a promising response rate of 60% for patients (pts) with previously treated *KRAS* G12C–mutated mCRC. Here, we evaluate the safety and efficacy of soto, pani, and FOLFIRI in treatment (Tx)-naïve pts with *KRAS* G12C–mutated mCRC.

Methods

Pts with *KRAS* G12C–mutated mCRC who had not received any prior systemic Tx for metastatic disease were enrolled at 17 global sites (between Jul 2021 and Mar 2024) and received the recommended phase 2 dose of soto (960 mg, oral, daily), pani (6 mg/kg, intravenous [IV], once every 2 weeks [Q2W]), and FOLFIRI (IV Q2W). Primary endpoint was safety and tolerability. Secondary endpoints included objective response rate, disease control rate, and median time to response.

Results

Forty pts were enrolled and treated (58% male; median age: 60 years). Tx-related adverse events (TRAEs) of any grade occurred in 100% of pts, and grade ≥ 3 TRAEs occurred in 53% of pts; no fatal event was reported. The most common grade ≥ 3 TRAEs included neutropenia (23%), dermatitis acneiform (18%), and diarrhea (10%). 30 pts had confirmed partial responses, with an overall response rate of 75%. Treatment with soto, pani, and FOLFIRI resulted in a disease control rate of 93% and median time to response of 1.5 months.Table: 505O

Response by investigator assessment*	Soto + pani and FOLFIRI (N=40)
Objective response rate, confirmed (95% CI)	30 (75.0) (58.8, 87.3)
Partial response	30 (75.0)
Stable disease	7 (17.5)
Progressive disease	1 (2.5)
Not evaluable	1 (2.5)
Not done	1 (2.5)
Disease control rate (95% CI)	37 (92.5) (76.1, 98.4)
Median time to response, months (range)	1.5 (1.2, 6.9)

*Data are presented as n (%) unless indicated otherwise.

Conclusions

This study provides the first data set on the use of a $KRAS^{G12C}$ inhibitor in 1L mCRC. The combination of soto, pani, and FOLFIRI

demonstrated a tolerable safety profile and promising response rates in pts with Tx-naïve *KRAS* G12C–mutated mCRC. CodeBreaK 301 (NCT06252649), a phase 3 study, is currently enrolling to evaluate this combination in 1L mCRC against standard of care.

Clinical trial identification

NCT04185883.

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Disclosure

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