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Panitumumab retreatment followed by regorafenib versus the reverse sequence in chemorefractory metastatic colorectal cancer patients with RAS and BRAF wild-type circulating tumor DNA (ctDNA): Final results of the randomized PARERE trial by GONO

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Background

PARERE (NCT04787341) is an open-label, multicenter, randomized phase II trial evaluating the role of anti-EGFR re-treatment (re-tx) in *RAS* and *BRAF* wild-type (wt) chemorefractory mCRC patients (pts) with *RAS* and *BRAF* wt circulating tumor DNA (ctDNA) at the time of study entry. Preliminary results on secondary endpoints showed higher objective response rate (ORR) and disease control rate (DCR) and longer progression-free survival (PFS) with panitumumab (pani) re-tx as compared to regorafenib (rego), with no unexpected safety findings.

Methods

Pts with *RAS* and *BRAF* wt mCRC who previously derived benefit from first-line anti-EGFR-containing regimens were screened for the absence of *RAS* and *BRAF* mutations in their ctDNA after ≥ 1 anti-EGFR-free line of tx. Eligible pts were randomized 1:1 to receive pani followed by rego after progression (arm A) *versus* (vs) the reverse sequence (arm B). The primary endpoint was overall survival (OS). Assuming a median OS of 9 months (mos) for arm A, 155 events were required to detect a HR of 0.69 in favor of arm B (two-sided log-rank test, type I error = 0.15, 80% power).

Results

Between December 2020 and December 2024, 428 pts underwent molecular screening and 213 with *RAS* and *BRAF* wt ctDNA were randomized (arm A/B = 106/107). At a median follow-up of 31.9 mos, 169 (79% arm A/B: 84/85) OS events were registered. No OS difference was observed between the two arms, with a median OS of 11.7 and 11.6 mos in arm B and A, respectively (HR: 1.13, 85% CI: 0.90-1.41, $p = 0.441$). Post-study tx were similarly administered (arm A/B = 51%/44%). In the subgroup analysis, shorter OS was observed in arm A among pts with an anti-EGFR-free interval ≤ 6 mos (p for interaction = 0.041). Higher ORR and DCR, and longer PFS with pani were confirmed, regardless of the tx sequence.

Conclusions

Anti-EGFR re-tx is an option in the continuum-of-care of chemorefractory mCRC pts with *RAS* and *BRAF* wt tumors, with no alterations of acquired resistance in their ctDNA. A clearly better tx sequence was not identified, except for the subgroup of pts with an anti-EGFR-free interval ≤ 6 mos where the rego-first sequence seems preferable.

Clinical trial identification

NCT04787341.

Legal entity responsible for the study

Gruppo Oncologico del Nord Ovest (GONO).

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Disclosure

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