Results: A total of 102 out of 735 mCRC patients (13,9%) were analyzed. Median age was 57.3 year and 55% were male. The outcomes were as follows: ORR 12%, DCR 39%, and mPFS 4.0 months (CI95% 3.29-5.03). Of note, 28 patients (27%) had a mPFS $>$ 6 months with rechallenge (range from 6.57 to 14.2 months) and constituted the best-responders group. Data of prognostic characteristics and molecular alterations are available for 19 of these patients. The prognostic subgroup classification was as follows: 9 patients (47.4%) PPC, 5 patients (26.3%) GPC, and 5 (26.3%) BPC. Most frequent molecular alterations were: APC (68.4%), TP53 (63%), RAS (47.4%), and PIK3CA (21%). Concomitant APC and TP53 mutations were detected in 47.4% of patients. No associations between prognostic characteristics and molecular alterations were observed.

Conclusions: This study suggests that rechallenge with oxaliplatin can achieve a clinically meaningful mPFS $>$ 6 months in 27% of patients. No enrichment in GPC and BPC was observed. APC, TP53 and RAS detected in this best-responders group are the major tumour genes which are frequently mutated in mCRC. A more extensive molecular analysis should be carried out to better characterise the patients who benefit the most from this treatment strategy.

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PD-13 Plasma RAS dynamics and efficacy of anti-EGFR rechallenge in patients with RAS/BRAF wild-type metastatic colorectal cancer: REMARRY and PURSUIT trials

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Background: Assessment of plasma RAS (pRAS) mutations in circulating-tumor DNA at 'just before' rechallenge with anti-EGFR monoclonal antibody (EGFR mAb) may predict efficacy for the rechallenge therapy in patients with RAS/BRAF V600E wild-type metastatic colorectal cancer (mCRC). However, the clinical impact of pRAS status at progression on prior EGFR mAb for the rechallenge therapy is unknown. The REMARRY trial is a prospective longitudinal study to investigate the pRAS dynamics, and PURSUIT trial is a phase II trial to investigate the efficacy of EGFR mAb rechallenge in patients with pRAS wild-type just before rechallenge therapy.

Methods: Eligibility criteria of REMARRY included RAS/BRAF V600E wild-type mCRC; ECOG PS 0-1; CR or PR during prior EGFR mAb; and progressed $\leq$ 2 months from the last administration of EGFR mAb. pRAS status by the BEAMing method (OncoBEAM RAS CRC Kit) was prospectively monitored at timepoints of progression on EGFR mAb and each subsequent therapy. Among participants of the REMARRY, patients who satisfied the following eligibility criteria were enrolled in PURSUIT; pRAS wild-type within 28 days prior to enrollment in PURSUIT; being refractory or intolerant to fluoropyrimidine, oxaliplatin, and irinotecan; and $\geq$ 4 months of EGFR mAb-free interval. Study treatment was rechallenge with panitumumab 6 mg/kg + irinotecan 150 mg/m2q2wks. Primary endpoint of PURSUIT was a confirmed objective response rate (ORR) according to RECIST v1.1. Biomarker analysis was performed for blood samples after disease progression on prior EGFR mAb, immediately prior to PURSUIT, and after disease progression in PURSUIT using plasma next generation sequencing (Guardant360). Plasma RAS, BRAF V600E, and EGFR extracellular domain mutations were defined as acquired resistances for EGFR mAb.

Results: Between May 2019 and May 2021, 183 patients were enrolled in REMARRY from 27 institutions, and 50 patients were enrolled in PURSUIT; median age, 68 years; left-sided primary, 44 patients; and prior EGFR mAb, 1st/2nd/$\geq$3rd lines in 28/6/16 patients. Confirmed ORR and disease control rate were 14% (90% CI, 7.8%—23.9%) and 80% (95% CI, 67.0%—88.8%), respectively. In addition, 4 patients showed an unconfirmed PR. Median progression-free survival (PFS) was 3.6 months (95% CI, 3.0—4.7 months). Among 31 patients with biomarker results after disease progression on prior EGFR mAb, ORR occurred in 5 of 21 patients (23.8%) with pRAS/BRAF/EGFR wild-type, whereas no responses occurred in patients whose tumors harbored any pRAS/BRAF/EGFR mutations (0/10) (p=0.092). Median PFS was 4.2 months and 2.8 months in patients without vs with pRAS/BRAF/EGFR mutations, respectively (p=0.06). In terms of pRAS/BRAF/EGFRstatus immediately prior to PURSUIT, 4 of 22 patients with wild-type responded to the study treatment (ORR, 18.2%), while one patient harboring pKRAS/EGFR co-mutations in 9 patients with any mutations also responded (ORR, 11.1%) (p=0.63). No trend in PFS was observed between the groups; median, 3.1 month and 3.3 months in patients with wild-type and those with any mutations (p=0.62).

Conclusions: Plasma RAS/BRAF/EGFR mutational status after progression on prior EGFR mAb may identify patients with RAS/BRAF V600E wild-type mCRC who could benefit from rechallenge with EGFR mAb.

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PD-14 Resectability, conversion, and resection rates with survival according to RAS and BRAF mutations in a prospective metastatic colorectal cancer study (liver-limited subgroup in the RAXO study)

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Background: RAS and BRAF mutations are associated with worse outcomes for patients with colorectal cancer (CRC) liver metastases, but little is known about their effects on resectability, conversion, and resection rates.