colorectal cancer (mCRC) patients. However, with the use of all the three active cytotoxics upfront, some concerns may arise about the activity of second-line treatments for these patients. In this retrospective analysis, we evaluated the outcome of second-line treatments in patients treated with first-line FOLFOXIRI enrolled in two consecutive phase II and in one phase III studies.

Material and Methods: Overall, a total of 196 initially unresectable mCRC patients were treated with first-line FOLFOXIRI administered for a maximum of 12 cycles. Among the 185 patients so far progressed, 136 (74%) received a second-line treatment and were evaluable for response. Thirty-nine patients (26%) did not receive second line treatments mainly because of deterioration of performance status (PS) or liver function, refusal or death.

Results: Patients' characteristics at the time of second-line treatment included: M/F = 88/48 patients, median age 63 yrs (range 27–76), ECOG PS $\geqslant$ 1 = 52 patients (38%).

Three (2.2%) complete and 28 (20.6%) partial responses were observed for an overall RR of 22.8%; 35.3% of patients obtained a stable disease while 41.9% progressed.

The table reports the regimens used in second-line and the RR obtained.

	Number of patients	RR (%)
Overall	136	22.8
FOLFOXIRI	32	37.5
FOLFIRI	35	31.4
FOLFOX	14	28.6
Mitomycin plus 5-Fluorouracil/Capecitabine	19	5.3
Infusional 5-Fluorouracil/Capecitabine	14	14.3
Cetuximab-containing regimens	7	0
Bevacizumab-containing regimens	3	0
Other regimens (Irinotecan alone, Irinotecan-Oxaliplatin, Irinotecan-Gemcitabine, Raltitrexed, Oxaliplatin plus Raltitrexed or Mytomicin)	12	8.3

After a median follow up of 48 months from the start of salvage treatment, the median PFS and OS were 5.93 and 13.2 months, respectively.

At an explorative analysis, patients treated with second-line FOLFOXIRI, FOLFIRI or FOLFOX had a higher RR (33.3% vs 7.3%, p = 0.0003), PFS (6.9 vs 3.5 months, p = 0.001) and OS (15.2 vs 9.2 months, p = 0.004) compared to patients treated with other regimens.

Conclusions: First-line FOLFOXIRI does not impair the possibility to obtain objective responses and to delay tumour progression with second-line treatments containing the same agents used upfront.

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Final results from PRECEPT: efficacy and safety of second-line treatment with panitumumab and FOLFIRI in patients with metastatic colorectal cancer (mCRC)

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Background: Panitumumab (pmab) is a fully human antibody against the epidermal growth factor receptor (EGFR), a therapeutic target in patients (pts) with mCRC. Response to anti-EGFR therapies can be predicted by mutation status of *KRAS* in tumors. This prospective analysis evaluated the effect of tumor *KRAS* status on efficacy of second-line pmab+FOLFIRI.

Methods: Pts with unresectable, measurable mCRC (ECOG status 0/1) were enrolled in this phase 2, open-label, single-arm study after failure of first-line treatment with oxaliplatin-based chemotherapy+bevacizumab (ClinicalTrials.gov ID: NCT00411450; sponsor: Amgen). Pts received pmab 6 mg/kg + FOLFIRI Q2W until disease progression or intolerability. Tumor assessments were performed at weeks 8, 16, 24, 32, and Q12W thereafter. *KRAS* status was determined by real-time PCR on DNA extracted from fixed tumor sections. Efficacy endpoints included objective response (per investigator), progression-free survival (PFS), and overall survival (OS). Safety endpoints included incidence of adverse events (AEs). Endpoints were evaluated by tumor *KRAS* status.

Results: 109 pts enrolled in the study and received $\geqslant$1 dose of pmab; 59% had tumors with wild-type (WT) *KRAS*, 41% had tumors with mutated (MT) *KRAS*. Efficacy outcomes (excluding 2 pts missing information at baseline) are shown (Table). Hazard ratios (95% CL) by *KRAS* status were 0.8 (0.5, 1.1) for PFS and 0.6 (0.4, 0.9) for OS. Pmab-related AEs were reported in 93% of pts; 94 pts (82%) had grade $\geqslant$3 AEs (related and unrelated). The most common AEs (WT/MT KRAS) were diarrhea (81%/62%), nausea (53%/58%), fatigue (55%/47%), rash (50%/56%), and acneiform dermatitis (41%/36%). The most common serious AEs were dehydration (10% of all pts), pyrexia (5%), and deep vein thrombosis (3%).

Conclusions: Numerical differences in PFS and OS in favor of pts with WT *KRAS* were observed. Pmab had a safety profile consistent with other pmab+FOLFIRI trials in pts of the same study population.

Best Objective Response[a], n (%)	WT *KRAS* (N = 64)	MT *KRAS* (N = 43)
Complete response[b]	2 (3)	1 (2)
Partial response[b]	13 (20)	6 (14)
Stable disease	26 (41)	18 (42)
Disease progression	13 (20)	11 (26)
Unable to evaluate/not done	10 (16)	7 (17)
Objective response rate, n responders	15	7
Response rate, % (95% CL)	23 (13, 34)	16 (5, 27)
PFS, n events	54	43
Median weeks (95% CL)	26 (19, 33)	19 (12, 25)
OS, n deaths	34	36
Median weeks (95% CL)	50 (39, 76)	31 (23, 47)

[a]Primary analysis set (N = 107); [b]Confirmed at next assessment.

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Efficacy and safety of bevacizumab-based combination regimens in patients with metastatic colorectal cancer: final results from a randomised phase II study of bevacizumab + FOLFIRI vs. bevacizumab + XELIRI (FNCLCC ACCORD 13/0503 study)

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Background: The combination of bevacizumab (bev) and chemotherapy improves overall survival and/or progression-free survival (PFS) compared with chemotherapy alone in patients (pts) with metastatic colorectal cancer (mCRC). This randomised non-comparative phase II trial evaluated the efficacy and safety of bev in combination with either XELIRI or FOLFIRI as first-line therapy for mCRC.

Materials and Methods: Pts were eligible for inclusion in this study if they had histologically proven measurable mCRC, were 18–75 years of age, and had an Eastern Cooperative Oncology Group performance status of 0–2. Pts were treated with either 8 cycles of XELIRI (irinotecan 200 mg/m^2 on Day 1 and capecitabine 1000 mg/m^2 bid on Days 1–14) + bev 7.5 mg/kg on Day 1, every 3 weeks or 12 cycles of FOLFIRI (irinotecan 200 mg/m^2 on Day 1 + 5-fluorouracil [5-FU] 400 mg/m^2 + folinic acid 400 mg/m^2 on Day 1 followed by 5-FU 2400 mg/m^2 via 46-h infusion) + bev 5 mg/kg on Day 1, every 2 weeks. Bev was continued until disease progression. Pts $\geqslant$65 years of age received a lower daily dose of capecitabine (800 mg/m^2 bid). The primary endpoint was crude PFS at 6 months.

Table. Efficacy and tolerability of bev + XELIRI and bev + FOLFIRI in pts with mCRC

Outcome	Bev + XELIRI (n = 72)	Bev + FOLFIRI (n = 73)
Efficacy, % (95% CI)		
Objective response rate[a]	58 (47–70)	58 (46–69)
Crude 6-month PFS	79 (70–88)	84 (75–92)
Safety, %		
$\geqslant$1 grade 3/4 AE (grade 4)	58 (8)	59 (12)
Grade 3/4 neutropenia (grade 4)	17 (3)	26 (4)
Grade 3/4 diarrhoea (grade 4)	12 (1)	5 (0)
Grade 3/4 cardiovascular (grade 4)	13 (3)	11 (1)

[a]Evaluated by Response Evaluation Criteria in Solid Tumours. AE, adverse event; CI, confidence interval; PFS, progression-free survival.