objective response rate and secondary endpoints, including disease control rate, time to response and progression-free survival. This abstract will review the correlation between EGFR expression and response rate (⩾17 weeks evaluation) in pts with *KRAS* wild-type or mutant tumours.
Results: Recruitment completed 18 June 08 with 154 pts enrolled. At interim analysis (15 Oct 08), *KRAS* evaluable samples for 92% of pts and EGFR evaluable samples for 84% of pts are available. Of the 85 pts with KRAS wild-type (wt) tumours, and the 57 pts with KRAS mutant (mt) tumours 78%/54% are male; median age is 64 years (range 21−84)/66 years (range 37−80) and 95%/93% of pts had ECOG PS 0−1, respectively. A higher proportion of responders in the wt subset have no EGFR staining versus non-responders (28% vs 5%; Table) with no notable difference seen for pts in the mt subset (13% vs 12%). In the wt subset incidence of moderate and strong maximum staining intensity is lower for responders than non-responders.

	KRAS wt (n = 84)		KRAS mt (n = 56)		All pts (n = 152)	
	Responder (N = 40)	Non-responder (n = 44)	Responder (n = 16)	Non-responder (n = 40)	Responder (n = 63)	Non-responder (n = 89)
Pts with EGFR data	36 (90)	43 (98)	15 (94)	33 (83)	52 (83)	77 (87)
3+ (strong)	3 (8)	11 (26)	2 (13)	1 (3)	5 (10)	12 (16)
2+ (moderate)	6 (17)	14 (33)	7 (47)	11 (33)	13 (25)	26 (34)
1+ (weak)	17 (47)	16 (37)	4 (27)	17 (52)	22 (42)	33 (43)
0	10 (28)	2 (5)	2 (13)	4 (12)	12 (23)	6 (8)

Conclusions: Within the parameters of this small data set, this analysis suggests that EGFR expression unlike *KRAS* status may not be essential for determining response to treatment.

6074 POSTER

Bevacizumab (bev) combined with chemotherapy as 2nd-line treatment for metastatic colorectal cancer (mCRC): results from the phase II BEVACOLOR study

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Background: Bev is approved for treatment of patients (pts) with mCRC in combination with fluoropyrimidine-based chemotherapy. This study assessed efficacy and safety of bev plus chemotherapy regimens commonly used as 2nd-line treatment for mCRC.
Materials and Methods: Prospective, open-label, single-arm, multicentre phase II trial (EUDRACT 2005–000800−14). Pts with mCRC who had progressed or relapsed after 1st-line treatment (oxaliplatin- or irinotecan-based) received bev 2.5 mg/kg/week plus FOLFOX, FOLFIRI, XELIRI, or irinotecan until disease progression. Primary endpoint: disease-control rate (DCR). Secondary endpoints: progression-free survival (PFS), overall survival (OS) measured from 2nd-line treatment and safety. The trial was funded by Roche France.

Table: Response rates, PFS and OS by 2nd-line chemotherapy regimen

Outcome	Bev in combination with:				
	FOLFIRI (n = 30)	FOLFOX (n = 14)	Irinotecan (n = 8)	XELIRI (n = 1)	All (n = 53)
Overall response rate, n (%)	11 (37)	4 (29)	2 (25)	0	17 (32)
Disease control rate, n (%)	27 (90)	11 (79)	7 (88)	1 (100)	46 (87)
Progressive disease, n (%)	2 (7)	2 (14)	1 (13)	0	5 (9)
Median PFS, months (95% CI)	7.8 (6.0−8.7)	5.3 (3.9−6.0)	8.4 (5.9−9.4)	2.6 (NA)	6.5 (5.8−7.8)
Median OS, months (95% CI)	21.7 (17.3−26.4)	13.9 (9.6−27.8)	24.1 (9.7−NR)	14.5 (NA)	19.3 (14.2−25.1)

2 pts were not evaluable. NA=not applicable; NR=not reached.

Results: 53 pts (66% male, median age 62 years, ECOG PS 0−2) received 2nd-line bev plus FOLFIRI (57%), FOLFOX (26%), irinotecan (15%), or XELIRI (2%). DCR was 87% (95% CI 77−97%) and ORR was 32% (95% CI 19−46%). Median PFS and OS were 6.5 (95% CI 5.8−7.8) and 19.3 months (95% CI 14.2−25.1), respectively. The table below provides DCR, PFS and OS by chemotherapy regimen. Median OS for pts receiving 2 lines of chemotherapy was 9.7 months (95% CI 7.8−13.6), and for those receiving 3, 4 and >4 lines was 20.1 (14.2−24.2), 18.7 (13.6−25.7) and 30.9 months (27.8−NR), respectively. Grade 3/4 adverse events included neutropenia (21%), diarrhoea (15%) and asthenia (9%). Grade 3/4 targeted toxicities (known to occur with bev) were reported in 6 pts (11%): hypertension (n = 2), haemorrhage (n = 1) and embolism (n = 3). Serious adverse events (SAE) were reported in 13 pts. One SAE was considered to be related to bev. No toxic deaths were observed.
Conclusions: Bev plus standard 2nd-line chemotherapy is highly active in pts with mCRC and has an acceptable safety profile.

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A triple combination of Imatinib, Bevacizumab and Cetuximab plus modified FOLFOX-6 in advanced untreated colorectal cancer

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Background: Imatinib inhibits PDGFR interfering with pericytes, the structural support to newly formed tumor blood vessels. It may thus synergize with bevacizumab. Microenvironment and tumor targeted agents along with chemotherapy could be a promising add-on approach.
Methods: Cetuximab 500 mg/m^2, Bevacizumab 5 mg/kg and modified FOLFOX-6 were given i.v. on day 1 and repeated every 2 weeks. Imatinib 400 mg/day per os was given continuously. Due to the cost and potential toxicity of the combination, the endpoint for this phase II study was very ambitious: at least 25% of complete response (medically or surgically achieved), lasting a minimum of 12 months in advanced untreated colorectal cancer patients with clearly unresectable disease.
Results: Of 26 patients (16 with 1 site of disease), 17 completed the first 4 months of treatment according to the protocol, while 9 had to discontinue one biologic drug due to side effects (5 cetuximab, 3 imatinib and 1 bevacizumab). Grade 3−4 toxicity: diarrhea 12%, neutropenia 24%, skin rash 24%, hypersensitivity reactions 16%, asthenia 8%, neuro 8%. All patients were evaluable for response. Eleven responses (1 CR and 10 PR), 13 SD and 2 PD were observed, corresponding to 42% RR (95% CI = 23−61). The minimum follow up is 12 months; median PFS is 10 months. One patient among responders underwent radiofrequency ablation and 17 patients underwent surgery: 8 R-0, 3 R-1, 5 R-2 and 1exploratory laparotomy. Major post surgical complications occurred in 5/17 patients. No evidence of macroscopic disease after the entire treatment plan was obtained in 13/26 patients: 12 surgical and 1 medical CR. 7/13 were disease free at 6 months, but only 3 were still disease free at 12 months. ERCC1, ERCC2/XDP, GSTP1, TS, EGF, COX2, CYCLIN D, FCgR polymorphisms and K-RAS mutations were evaluated on all 26 patients, but no correlations were found with clinical outcome.
Conclusions: The triple combination of biologics with modified FOLFOX-6 is feasible and tolerable as initial aggressive treatment. However, the primary endpoint of the study was not met. In fact the activity (42% RR) was not outstanding. Moreover, the high resectability rate (69%) must be interpreted in the light of the short duration of the surgically induced CR.

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BOXER: A multicentre phase II trial of capecitabine and oxaliplatin plus bevacizumab as neoadjuvant treatment for patients with liver-only metastases from colorectal cancer unsuitable for upfront resection

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Background: Capecitabine/oxaliplatin+bevacizumab (CAPOX+Bev) is a standard treatment option for metastatic colorectal cancer (CRC). Complete resection of liver metastases (mets) appears to improve long-term survival. Increasingly, patients (pts) with synchronous liver mets are being treated with neoadjuvant therapy. Additionally, neoadjuvant therapy may allow some pts with initially unresectable liver mets to be adequately downsized to achieve resection.
Method: This prospective single arm phase II study assessed response rate (RR) to CAPOX+Bev in pts considered unsuitable for upfront resection of liver-only mets. Eligible pts had unresectable liver-only mets (synchronous: N = 24 or metachronous: N = 4) according to pre-specified