(26%, median delay: 28 days), motivated by recent surgery in 26 cases (26%) and co-morbidities in 8 cases (8%). Median duration of BV treatment was 5.4 months. Treatment discontinuation was observed in 150 patients (40%): 106 (28%) had treatment-free interval, 44 (12%) had a maintenance therapy (16 with BV alone). Among those receiving irinotecan-based regimens, the incidence of any events (grade 3/4) was 48% (vs 85% in PCT; $p < 0.0001$): neutropenia (17 vs 37%; $p < 0.0001$) and diarrhea (11 vs 32%; $p < 0.0001$). In line with the known safety profile of BV (any grade), hypertension was observed in 21 vs 22% ($p = 0.58$), arterial/venous thrombosis (11 vs 19%; $p = 0.0009$), proteinuria (32 vs 27%; $p = 0.10$) and gastrointestinal perforation (0.3 vs 1.5%; $p = 0.097$).
ETNA is one of the first real-life, post-marketing cohort study conducted to compare results of real practice with those of the PCT. Primary data indicated that patients differed to those included in the PCT with regard to several aspects. Common BV-associated effects were similar to those observed in the PCT. The safety profile of FOLFIRI regimen seems more manageable than that of IFL regimen but the lower frequency of neutropenia and diarrhea could also be related to an under-reporting of these in real-life.

6071 POSTER

Radioembolization with 90Y-resin microspheres as a salvage treatment for refractory liver-dominant colorectal metastases: a matched-pair analysis

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Background: Despite advances in systemic chemotherapy and biological agents, liver metastases continue to present a life-limiting prognosis for colorectal cancer (CRC) patients. This prospective study assessed the safety and efficacy of radioembolization (RE) with ^{90}Y-resin microspheres as a salvage therapy in patients with progressive liver-dominant CRC metastases compared with matched historical controls who received best supportive care (BSC).
Materials and Methods: A matched-pair analysis for overall survival was conducted in patients who presented after multiple lines of systemic chemotherapy/biological agents with extensive (>20%) liver involvement and tumour progression as confirmed by imaging (CT/MRI), alkaline phosphatase (ALP), tumour markers (CEA) and/or clinical symptoms. Patients treated with RE were matched with historical controls by tumour load, synchronous/metachronous metastases, ALP and CEA >200 U/mL. Overall survival from the date of progression prior to salvage treatment was calculated using Kaplan-Meier analysis. The relationships between baseline covariates (including Karnofsky performance status, tumour load, number of lines chemotherapy) and overall survival were examined by multivariate Cox proportional hazard model (SAS, Carey, NC).
Results: 58 patients (29 RE; 29 BSC) were recruited with extensive liver tumour involvement: median (range) 30% (20−50%) and 25% (10−75%) respectively. Patients in both cohorts received a median of 3 (2−6) prior lines of chemotherapy. RE was a significant predictor of survival (Hazard Ratio = 4.8; 95%CI 2.4−9.5) and the only parameter found to be a significant contributor to the prognosis. Compared with BSC, patients receiving RE survived significantly longer (median: 8.3 vs. 3.5 months; $p < 0.001$). This benefit was clearly evident at 3 months (97% vs. 59% survival) and sustained through 12-months follow up (24% vs. 0% survival). Progression-free survival was 5.5 and 2.1 months with RE and BSC, respectively ($p < 0.001$). Adverse events following RE included thrombocytopenia and sepsis (3%), and abdominal pain (3%). Three possible cases of radiation-induced liver disease were medically managed and not considered life-threatening (median survival: 9.8 months; range: 9.0−16.6 months).
Conclusions: RE provides substantial clinical benefit as evidenced by significant increased liver disease stabilization and prolonged overall survival in patients for whom there are limited treatment options.

6072 POSTER

Bevacizumab related adverse events in patients affected by metastatic colorectal cancer: a meta-analysis

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Background: Bevacizumab, a recombinant humanized monoclonal antibody targeting the vascular endothelial growth factor, is widely used in patients with metastatic colorectal cancer. Bevacizumab suffers by several adverse events which may be different according to the diverse kind of treated tumours. We performed a systematic review and meta-analysis of published randomized clinical trials (RCTs) investigating bevacizumab in the treatment of patients affected by advanced colorectal cancer to better understand the overall risk of side effects.
Methods: PubMed, Medline, CancerLit, and Embase databases were searched for RCTs, comparing chemotherapy plus bevacizumab *versus* chemotherapy alone in metastatic colorectal cancer patients. Also abstracts presented at the main international meetings until April 2009 were analyzed. Odds ratios (ORs) and Number Needed to Harm (NNH) for main side effects were calculated with their 95% confidence intervals (CI) using fixed-effects model.
Results: Nine controlled trials encompassing 7,132 patients, were eligible for the present analysis. Patients receiving bevacizumab plus chemotherapy have a risk twice superior (OR 1.92 95% CI 1.51−2.44) of developing all-grade hypertension corresponding to a NNH 9 and seven times superior of developing grade 3−4 hypertension (OR 6.94 95% CI 5.07−9.52; NNH 11). Moreover, the risk of the other grade 3−4 toxicities were: bleedings (OR 1.83 95% CI 1.11−3.01 NNH 83), proteinuria (OR 4.20 95% CI 2.17−8.12 NNH 73), thromboembolic events (OR 1.19 95% CI 0.98−1.45 NNH 77), cardiac events (OR 1.72 95% CI 0.72−4.13 NNH 167), and oxaliplatin-related neuropathy events (OR 1.55 95% CI 1.29−1.87 NNH 17).
Conclusions: Patients affected by metastatic colorectal cancer and treated with chemotherapy plus bevacizumab have a significant increased risk of developing severe hypertension, proteinuria, and bleedings. Surprisingly, in our analysis, bevacizumab is not associated with higher onset of thromboembolism events, but it increases the oxaliplatin-related neurotoxicity.

6073 POSTER

Interim analysis of epidermal-growth factor receptor (EGFR) expression in a single-arm, phase II, first-line study (20060314) of panitumumab with FOLFIRI in the management of metastatic colorectal cancer (mCRC)

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Background: The fully human anti-EGFR monoclonal antibody panitumumab (Vectibix®) is an important monotherapy treatment option for chemotherapy-refractory patients (pts) with EGFR-expressing, *KRAS* wild-type mCRC. Preclinical data show sensitivity of EGFR inhibitors to be linked to EGFR expression as determined by immunohistochemistry (IHC). Thus, EGFR expression has historically been a defining criterion for treatment with an EGFR inhibitor. However, growing clinical evidence suggest that this marker correlates poorly with response, with objective responses observed in pts with no or all levels of EGFR expression.
Material and Methods: Pts with histologically confirmed mCRC receive panitumumab (6 mg/kg) and FOLFIRI every 2 weeks. This Amgen-sponsored study (20060314) is ongoing to evaluate the primary endpoint

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.

6075 POSTER

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.

6076 POSTER

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