Recent studies have shown that patients with *KRAS* p.G13D mutations treated with Cmab have longer overall survival (OS) and progression-free survival (PFS) than patients with other *KRAS* mutations. Cmab might also have therapeutic benefits in CRC patients with the *KRAS* p.G13D mutation (Bando H, Gastrointestinal Cancers Symposium, 2011). Survival estimates in patients with the p.G13D mutation not treated with anti-epidermal growth factor receptor (EGFR) antibodies from another cohort were necessary, because only the National Cancer Institute of Canada (NCIC) CO.17 study, which suggested that CRC patients with the *KRAS* p.G13D mutation have a worse prognosis than those with other *KRAS* mutations, provides survival data as reference.

Methods: From 2008 to 2010, we selected 47 consecutive patients with the *KRAS* mutant mCRC that had been refractory to 5-fluorouracil (5-FU), oxaliplatin, and irinotecan; these patients had never received anti-EGFR antibodies. We retrospectively assessed the OS according to the *KRAS* mutational status (p.G13D versus other mutations). The relationship between the *KRAS* mutational status and OS were evaluated using the log-rank test.

Results: Among these patients, 12 and 35 had the *KRAS* p.G13D and other *KRAS* mutations, respectively. The baseline characteristics of each subset were not remarkably different. OS was not remarkably different between the p.G13D and other mutations (hazard ratio, 1.10; p = 0.79). In addition, OS curves divided by the major genotypes were not different in G12D (n = 15), G12S (n = 8), G12V (n = 7), and G13D.

Conclusions: It suggested there was no remarkable difference of survival between CRC patients with the p.G13D and other *KRAS* mutations after the failure of 5-FU, oxaliplatin, and irinotecan. These results were different from those of the NCIC CO.17 study. Our results may serve as reference data for further clinical trials on the therapeutic effect of Cmab in CRC patients with the *KRAS* p.G13D mutation.

6110 POSTER

Combination Chemotherapy With Capecitabine (C), Irinotecan (I) Oxaliplatin (O) and Bevacizumab (B) (XELOXIRIA) as First Line Treatment of Metastatic Colorectal Cancer (MCRC) − Preliminary Results of a Phase I-II Trial

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Background: FOLFOXIRI has been shown to be superior to FOLFIRI with respect to response rate and survival in patients (pts) with metastatic colorectal cancer (mCRC). Capecitabine has the advantage over 5-Flourouracil of the convenience of oral administration and possibly lower toxicity.

Materials and Methods: We conducted a prospective phase I-II study in pts with mCRC to determine the Maximum Tolerable Dose (MTD) and the efficacy of fixed dosed of Capecitabine (C), Oxaliplatin (O) and Bevacizumab (B) in combination of escalating doses of Irinotecan (I). The planned treatment in the first 3 pts was: I 150 mg/sqm over 90 min on day 1, O 130 mg/sqm over 2-h on day 1, C 2,000 mg/sqm/day from day 1 to 14, and Bevacizumab 7.5 mg/kg over 30 min on day 1. Cycles repeated every 3 weeks. I dose was increased to 200 mg/sqm or C dose was decrease to 1300 mg/sqm/day in subsequent groups of 3 pts on the basis of the observed dose limiting toxicities (DLT). We report here the result of the first 30 patients.

Results: Pts characteristic are: sex (M/F) = 18/12, PS (0/1/2) = 3/22/5, age (median/range) = 51/24−73 years, sites of disease (single/multiple) = 10/20. The DLT was G3−4 diarrhea that was observed in 2 out of 3 pts receiving I at 200 mg/sqm, The I recommended dose was 150 mg/sqm which continued as phase II trial. Grade 3−4 toxicities were: nausea and vomiting 21.4%, diarrhea 41.4%, neutropenia 20.6%, thrombocytopenia 3.4%, febrile neutropenia 14.3%, fatigue 17.9%, acute hypersensitivity reaction 3.4%. Response evaluation was done according to ITT analysis. 6 Pts were not assessable for response because of 2 or less cycles of chemotherapy (3 consent withdrawal, 2 grade 4 toxicity, one toxic death). One CR, and 12 PR were observed for an overall response rate of 43% (95% CI: 26−60%). Nine had SD and 2 progressed. Relative dose intensity for C was 0.78; for O was 0.91 and for I was 0.91. At a median follow-up of 12 months median progression free survival (PFS) was 18.3 months and median overall survival was not reached.

Conclusion: These results demonstrate that this combination is toxic at the recommended dose, with diarrhea being the dose limiting toxicity. Recruitment continues with reduction in C dose to 800 mg. This combination has significant antitumour activity in advanced CRC and encouraging PFS.

6111 POSTER

Combining Capecitabine, Oxaliplatin and Gemcitabine (XELOXGEM) for Colorectal Carcinoma Patients Pretreated With Irinotecan − a Multicenter Phase I/II Trial

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Background: Capecitabine plus oxaliplatin (XELOX) is an effective second-line regimen for advanced colorectal carcinoma (CRC) patients pretreated with irinotecan. Previous studies have shown supra-additive anti-tumour activity of gemcitabine (GEM) when administered with oxaliplatin. We investigated the dose, toxicity, and efficacy of a second-line XELOXGEM regimen in CRC patients pretreated with irinotecan.

Patients and Methods: Patients with metastatic or recurrent CRC who failed after a first-line irinotecan-containing regimen received escalating doses of gemcitabine (600, 800, 1000 mg/m^2 d1, d8) followed by capecitabine (1000 mg/m^2 b.i.d d1−14) and oxaliplatin (100 mg/m^2 d1) on a 21-day cycle.

Results: A total of 38 patients were treated. At 800 mg/m^2, two of six patients experienced dose-limiting toxicities (diarrhea and thrombocytopenia). Therefore, the clinically recommended dose was defined as 600 mg/m^2 gemcitabine (d1, d8) followed by 1000 mg/m^2 capecitabine (b.i.d d1−14) and 100 mg/m^2 oxaliplatin (d1). The most common grade 3/4 toxicities were neutropenia (32%), thrombocytopenia (13%), anemia (11%) and peripheral neuropathy (11%). Ten (26.3%) and 23 (60.5%) patients experienced partial response and stable disease, respectively. The median progression-free survival and overall survival were 5.4 months (95% CI 3.8–6.9 months) and 17.7 months (95% CI 8.4–26.9 months), respectively.

Conclusions: The XELOXGEM triplet combination is an active and safe second-line regimen for advanced CRC patients pretreated with irinotecan.

6112 POSTER

Health-related Quality of Life at 12 Months in Patients With Metastatic Colorectal Cancer (mCRC) Initiating a Treatment With Bevacizumab (Bv) Plus Chemotherapy (CT) − Results From the CONCERT French Non Interventional Study

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Background: Chemotherapy and targeted treatments can impact Health-Related Quality of Life (HRQoL) in cancer patients (pts). HRQoL is an increasingly important endpoint measured in clinical trials in mCRC pts who are now living longer, to assess treatment outcomes and improve mCRC care.

Patients and Methods: This prospective, multicenter, non-interventional cohort study assessed pts with mCRC initiating a treatment with Bv plus CT (all lines) in daily medical practice in France and followed-up for 36 months. Changes in HRQoL, a secondary efficacy endpoint of CONCERT, were assessed using the QLQ-C30 questionnaire at baseline, 6 and 12 months of follow-up.

Results: Of the 765 evaluable patients included in the cohort, 435 (60%) were men, median age 66 years (25−88), ECOG score of 0 or 1 (90%). HRQoL was assessed in 133 pts (17%) who completed the questionnaire at M1 and M12 (100 in 1st line, 23 in 2nd line and 10 in 3rd line), their profile was comparable to the whole population. Mean Global health QoL at 12-months from baseline was −1.6 points. Mean score differences for functional and symptom scale scores between baseline and 12 months are shown in the table.

Conclusion: Compliance to HRQoL questionnaires was low in a real life setting. Use of bevacizumab and chemotherapy treatments in clinical practice routine seems to be associated with no clinically significant changes and no deterioration in HRQoL scores in patients with mCRC.

	1st line (n = 100)		Total (n = 133)
	Baseline	Score variation	Score variation
Functional scale			
Social functioning	80.4±23.8	−7.9±29.1	−6.3±28.9
Role functioning	77.8±28.0	−5.6±31.6	−4.7±29.4
Physical functioning	84.9±16.5	−4.2±18.1	−3.8±18.5
Cognitive functioning	86.5±19.8	−1±22.5	−0.8±20.4
Emotional functioning	74.9±22.2	+1±26.5	+1.5±25.5
Symptom scale			
Insomnia	26.5±32.6	−6.1±30.3	−4.8±30.3
Constipation	20.3±29.5	−2.4±37.7	−3.4±34.8
Appetite loss	18.6±26.3	0±34.4	−2.3±33.3
Pain	16.7±2.5	−1.3±30.9	−0.6±31.1
Fatigue	31.2±25.1	2±25.9	+1.3±25.7
Diarrhea	16.5±24.5	2±29.7	+2.3±30.0
Nausea and vomiting	9.1±20.8	2.4±26.3	+3±23.8
Dyspnea	13.1±22.9	3.1±24.1	+4.6±23.8
Financial difficulties	8.2±20.9	0.7±20.3	+0.5±20.7
Global health status/QoL	**66±20.4**	**−2.5±25.6**	**−1.6±24.6**

6113 POSTER

Efficacy and Safety at 12 Months of 1st Line Bevacizumab (Bv) Plus Chemotherapy (CT) in Elderly Patients (Pt) With Metastatic Colorectal Cancer (mCRC) in Daily Clinical Practice − the CONCERT French Observational Cohort Study

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Background: There are limited data on treatment outcomes in the growing population of elderly patients with mCRC. Elderly patients are often underrepresented in randomized oncology clinical trials. We investigated the efficacy and safety of 1st line Bv combined with various CT in elderly patients subgroups (⩾70 yrs and ⩾75 yrs) with mCRC in the CONCERT cohort study.
Patients and Methods: This prospective, multicenter, non-interventional study assessed pts with mCRC initiating a treatment with Bv and CT (all lines) in daily medical practice in France followed-up for 36 months. We analyzed patients' demographics, treatment patterns, safety, progression free survival (PFS), overall survival (OS) in three subgroups: <70 yrs, ⩾70 yrs and ⩾75 yrs.
Results: Of the 515 patients treated in 1st line in the CONCERT study, 328 pts were ⩾70 yrs (including 91 pts ⩾75 yrs). At baseline, 14.3% of pts in the ⩾75 yrs group had poor ECOG PS (⩾2) vs. 7.4% in the ⩾70 yrs; 70.3% pts ⩾75 yrs vs. 52.1% in the <70 yrs group. Co-morbidities were reported in 69.0% of pts ⩾70 yrs; 70.3% pts ⩾75 yrs vs. 52.1% in the <70 yrs group. Median PFS (months) was 11.4, 95% CI [10.0; 12.3] <70 yrs group; 10.0, 95% CI [8.9; 11.8] ⩾70 yrs group and 9.5, 95% CI [7.9; 11.3]) ⩾75 yrs group. Median OS was not reached in the 3 subgroups. The incidence of Bv-related adverse events (AEs) was 56.3% in the ⩾75 yrs group, 53.9% in the ⩾70 yrs group and 52.8% in the <70 yrs group.
Incidence of main Bv-targeted AEs per age group is shown in the table.

	<70 yrs (n = 299)	⩾70 yrs (n = 178)	⩾75 yrs (n = 87)
Related AEs	52.8%	53.9%	56.3%
Grade 3/4 AEs	8.7%	11.2%	11.5%
Targeted AEs (all grades)	51.2%	52.2%	56.3%
Bleeding	25.1%	19.7%	20.7%
Proteinuria	15.1%	16.9%	21.8%
Hypertension	13.4%	16.9%	20.7%
Neutropenia	9.7%	12.4%	13.8%
Venous thromboembolic events	3.3%	6.2%	9.2%
Wound healing disorder	3.3%	2.8%	3.4%
Fistula	2.3%	2.8%	2.3%

Hypertension, proteinuria, venous thromboembolic events and neutropenia were more common in older than in younger patients. No treatment-related death was reported across all age groups at 12 months.
Conclusion: Results of this prospective cohort study suggest that the efficacy of 1st line treatment with Bv and CT is independent of age and is tolerable in elderly patients with mCRC.

6114 POSTER

Clinical Outcomes of Bevacizumab (BV) + XELOX Combination for the First-line Treatment of Patients (pts) With Advanced Cancer of the Colon or Rectum (ACRC) − Preliminary Results of the OBELIX Study

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Background: BV, an anti-vascular endothelial growth factor antibody, when combined with other chemotherapeutic drugs, prolongs OS and PFS in ACRC patients. Several phase IV and observational studies provide information on the clinical outcome of the BV-treated pts in large cohorts. We conducted a multicentric, open-label, single arm, non-comparative study to confirm these results in a general Italian population of patients with ACRC.
Materials and Methods: Previously untreated pts with histologically confirmed ACRC receiving XELOX (Capecitabine 1000 mg/m^2 bid for 14 days + Oxaliplatin 130 mg/m^2 d1, q3w) for 8 courses + BV (7.5 mg/kg, d1, q3w) until disease progression, death, or unacceptable toxicities were enrolled. The primary end-point was progression free survival (PFS). Secondary were safety, RR, OS, percentage of R0 resectability and QoL of patients.
Results: 205 assessable patients were enrolled between Feb 2008 and Nov 2009 (male 56%; median age 64 yrs range 34−80). All of pts resulted with an ECOG PS 0−1. 104 pts (51%) had metastases confined in 1 site (41% liver only, 10% lung only). Pts received 7 courses of XELOX (range 1−13) and 8 courses of BV (range 1−34). Median PFS was 10.26 months (95% CI 8.79–11.21) and median OS reached 21.31 months (95% CI 19.93–not reached); best ORR was 43% with a clinical benefit of 73% and a median duration of response.of 9.8 months (range 7.9–10.8). 26 pts (13%) underwent liver surgery of whom 12% had a R0/R1 resection. 102 pts (49.8%) experienced a G3−4 adverse events.
Conclusion: OBELIX study shows efficacy data of Bevacizumab administered in first line ACRC in the Italian clinical practice consistent with those observed in prospective randomized clinical trials and other large observational studies.

6115 POSTER

Modelling Tumour Kinetics Including Early Response, Tumour Nadir and Progression During First-line Chemotherapy of Metastatic Colorectal Cancer (mCRC)

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Background: Recently, Piesseveaux et al. (Ann. Oncol 2009 20(8): 1375–1382) proposed to use a relative early decrease of tumour size of 20% in first-line therapy for mCRC as a predictor for clinically relevant outcomes (TTP and OS). This method is based on heuristics and not on theoretical considerations. In the present investigation, we deloped a model with the ability to predict individual tumour size kinetics.
Material and Methods: Based on the data of two randomized trials, the FIRE-1 (n = 479) and the CIOX (n = 185) study, we developed a mathematical model which allowed to formulate non-linear U-shaped individual relationships between time and tumour size. This model provides a simple method to capture tumour load at baseline and its decrease to evaluate their impact on TTP and OS by Cox proportional hazard regression. This formal approach allows deriving prediction rules and helps to define a practical way to apply them to patients: how to schedule early