

Recent studies have shown that patients with *KRAS* p.G13D mutations treated with Cmax have longer overall survival (OS) and progression-free survival (PFS) than patients with other *KRAS* mutations. Cmax 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 Cmax in CRC patients with the *KRAS* p.G13D mutation.

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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:** FOLFIRI 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-Fluorouracil 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 doses 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.

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**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<sup>2</sup> d1, d8) followed by capecitabine (1000 mg/m<sup>2</sup> b.i.d d1–14) and oxaliplatin (100 mg/m<sup>2</sup> d1) on a 21-day cycle.

**Results:** A total of 38 patients were treated. At 800 mg/m<sup>2</sup>, two of six patients experienced dose-limiting toxicities (diarrhea and thrombocytopenia). Therefore, the clinically recommended dose was defined as 600 mg/m<sup>2</sup> gemcitabine (d1, d8) followed by 1000 mg/m<sup>2</sup> capecitabine (b.i.d d1–14) and 100 mg/m<sup>2</sup> 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.

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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 1<sup>st</sup> line, 23 in 2<sup>nd</sup> line and 10 in 3<sup>rd</sup> 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.