3576 General Poster Session (Board #14H), Sat, 8:00 AM-12:00 PM

Efficacy of chemotherapy plus cetuximab according to metastatic site in *KRAS* wild-type metastatic colorectal cancer (mCRC): Analysis of CRYSTAL and OPUS studies. *Presenting Author: C. Kohne, Onkologie Klinikum Oldenburg, Oldenburg, Germany*

Background: In the CRYSTAL and OPUS studies, adding cetuximab to first-line chemotherapy (CT) improved clinical benefit in patients (pts) with *KRAS* wild-type (wt) mCRC. R0 resection of colorectal liver metastases is a potentially curative option in this setting. In a descriptive analysis of these trials the benefit of treatment according to metastatic site (liver-limited disease [LLD] and non-LLD) was investigated. **Methods:** Treatment arms were compared according to metastatic site for response rates (RR), R0 resection rates (R0R), progression-free (PFS) and overall survival (OS) times. **Results:** In CRYSTAL, R0 resection was significantly enhanced with CT + cetuximab vs CT alone (5.1 vs 2.0%, odds ratio 2.65, p=0.027). The proportion of pts with LLD was comparable in each study and treatment arm (21-30%). In both LLD and non-LLD pts, adding cetuximab to CT improved outcome across efficacy endpoints (Table). The highest RORs were seen in pts with LLD in the CT + cetuximab groups of both studies, with 2.3-fold (CRYSTAL) and 3.7-fold (OPUS) increases in rates vs CT alone. PFS was significantly higher in the CT + cetuximab arm in LLD pts in CRYSTAL (p=0.035) and in non-LLD pts in CRYSTAL (p=0.012) and OPUS (p=0.023). In non-LLD pts, adding cetuximab to CT significantly increased OS in CRYSTAL (p=0.013), prolonging median OS by 5.1 months, and prolonged OS by 3.4 months in OPUS. **Conclusions:** Adding cetuximab to first-line CT improved clinical outcome in mCRC pts with both LLD and non-LLD. In pts with non-LLD treated with FOLFIRI + cetuximab, the OS benefit exceeded 5 months.

Efficacy according to treatment arm for patients with *KRAS* wt tumors grouped by metastatic site.

	All patients		LLD		Non-LLD	
	CT	CT + cetuximab	CT	CT + cetuximab	CT	CT + cetuximab
CRYSTAL, n	350	316	72	68	278	248
RR, %	39.7	57.3	44.4	70.6	38.5	53.6
R0R, %	2.0	5.1	5.6	13.2	1.1	2.8
Median PFS	8.4	9.9	9.2	11.8	8.1	9.5
Median OS	20.0	23.5	27.7	27.8	17.4	22.5
OPUS, n	97	82	23	25	74	57
RR, %	34.0	57.3	39.1	76.0	32.4	49.1
R0R, %	3.1	7.3	4.3	16.0	2.7	3.5
Median* PFS	7.2	8.3	7.9	11.9	6.0	7.6
Median* OS	18.5	22.8	23.9	26.3	16.4	19.8

* Medians are in months.

3577 General Poster Session (Board #15A), Sat, 8:00 AM-12:00 PM

A multicenter, multinational retrospective analysis of mitomycin C (MMC) in refractory metastatic colorectal cancer (mCRC). *Presenting Author: R. Ferrarotto, Hospital Sírio Libanês, São Paulo, Brazil*

Background: A considerable number of mCRC patients (pts) who progress on standard treatment with 5-fluorouracil (5FU), oxaliplatin, irinotecan and monoclonal antibodies still have good performance and desire further treatment. MMC has been widely used in this situation, and despite good tolerability, there is no agreement on its role. **Methods:** In order to assess the activity of MMC in the refractory mCRC setting, we retrospectively evaluated 109 heavily pre-treated pts who received MMC as single agent or in combination for mCRC at three different institutions. **Results:** Of the 109 pts, 30 (27.5%) were treated at M. D. Anderson Cancer Center (USA); 55 (50.5%) at Hospital Sírio Libanês (Brazil) and 24 (22%) at Instituto do Câncer de São Paulo (Brazil). Median age was 54 years old, 57% were male and 94% were performance status ECOG 0 or 1 at diagnosis. MMC was used in second-line in 11%, third-line in 37.6% and fourth-line or beyond in 51.4% of pts. Median TTF on the regimen prior to MMC therapy was 3.7 months. 42% received MMC as single agent while 58% received MMC combinations, mainly with fluoropyrimidines (49%). Severe toxicity was rare (1.8%), with dose reductions in 6.4% of pts. Clinical benefit with MMC, defined as improved symptoms by clinician assessment, was 12%. By response criteria, no radigraphic responses were seen. Median survival was only 4.6 months (95% CI of 4.1 to 5.5). **Conclusions:** This retrospective data represents the largest reported series of refractory mCRC patients treated with MMC. There were no patients with radiographic response and the low clinical benefit rate is not consistent with an active regimen. The median survival of 4.6 months is similar to the median survival expected for best supportive care in the refractory setting (4.5 months). This lack of activity strongly suggests that mitomycin should not be used in refractory mCRC.

3578 General Poster Session (Board #15B), Sat, 8:00 AM-12:00 PM

Phase II trial of chemotherapy with high-dose FOLFIRI plus bevacizumab in the front-line treatment of patients with metastatic colorectal cancer (mCRC) and genotype UGT1A1*1/ UGT1A1*1 or UGT1A1*1/ UGT1A1*28 (FFCD 0504 trial): Final results. *Presenting Author: E. Mitry, Institut Curie, St. Cloud, France*

Background: The combination of high-dose irinotecan (260mg/m²) with LV5FU2 (FOLFIRI HD regimen) is feasible with an acceptable safety profile and promising efficacy data (Ducreux et al. Oncology 2008;74:17-24). The aim of this phase II study was to evaluate the combination of FOLFIRI HD plus bevacizumab (B) in patients (pts) selected on the UGT1A1 polymorphism, which could be predictive of the irinotecan toxicity and efficacy. **Methods:** Pts with UGT1A1 *1/*1 (group 1) or *1/*28 (group 2) genotypes and previously untreated mCRC were treated with bevacizumab 5 mg/kg D1, irinotecan 260 mg/m² D1, LV 400 mg/m² D1, 5FU 400 mg/m² IV bolus D1 and 5FU 2400 mg/m² 46h infusion D1-2 every 2 weeks. Using Bryant & Day design with objective response rate (ORR) (independent review, H0 ≤ 40%; H1 ≥ 60%) and toxicity (gr 4 neutropenia or febrile neutropenia or gr 3-4 diarrhea; H0 ≥ 20%; H1≤ 5%) as primary endpoints; a total of 108 pts, 54 in each group, was required (alpha 5% and power 80%) with a planned interim analysis after the inclusion of 17 pts by group. The trial will be stopped at interim analysis if ≤ 7 pts had an OR and/or ≥ 3 pts had a severe toxicity. All analyses were performed in ITT. **Results:** At the time of interim analysis, done when the 17th pt of group 1 had a 6-months follow-up, 86 pts were included (group 1: 40 pts, group 2: 46 pts). Results of primary endpoints at the interim analysis are presented in the table. According to interim analysis rules, the trial was closed to inclusion for unacceptable toxicity. **Conclusions:** The trial was stopped after interim analysis because of unacceptable toxicity according to trial's criteria, even if toxicity was manageable and most of the patients continued the treatment after dose adaptation. Defined toxicity criteria to stop the trial at interim analysis may have been too strict and not clinically adapted. There is however no clear benefit of the FOLFIRI HD - B combination in terms of efficacy.

	Group 1	Group 2
N	17	17
ORR (%)	52.9	58.8
Toxicity (%)	41.2	18.8

3579 General Poster Session (Board #15C), Sat, 8:00 AM-12:00 PM

Bevacizumab plus capecitabine as maintenance treatment after initial treatment with bevacizumab plus XELOX in previously untreated metastatic colorectal cancer: Updated findings from a randomized, multicenter phase III trial. *Presenting Author: S. Yalcin, Hacettepe University Hospitals, Ankara, Turkey*

Background: Colorectal cancer is one of the most frequent malignancies second to breast cancer in women and third to lung cancer and prostate cancer in men. The aim of this study in first-line metastatic colorectal cancer (mCRC) was to achieve a better progression-free survival (PFS) with less risk of toxicity by administrating bevacizumab (BEV) + capecitabine + oxaliplatin (XELOX) for 6 cycles, stop oxaliplatin and go with maintenance therapy (BEV + capecitabine) until progression. **Methods:** BEV (7.5 mg/kg) + XELOX (capecitabine 1000 mg/m² bid d1–14 + oxaliplatin 130 mg/m² d1 q3w) were administered until progression (Arm A) or 6 cycles of BEV + XELOX followed by BEV + capecitabine were administered until progression (Arm B). PFS was the primary endpoint; secondary endpoints included overall survival (OS), objective response rate (ORR), and safety. A sample size of 118 patients (pts) was calculated to achieve 80% power to detect an increase of 1.5 months in median PFS between Arm A (9.5 months) and Arm B (11.0 months) with a standard deviation of 3.9 months and a significance level of 0.05 using a 10% drop-out rate. **Results:** A total of 121 pts were randomized. No significant differences were found in demographic characteristics between the two arms. Median treatment period was 8.3 (range 0.7–13.4) and 6.8 (range 0.7–12.4) months in Arms A and B, respectively. Interim analysis showed no statistically significant difference in median PFS and ORR between arms (Table). Tolerability was acceptable in both arms with grade 3/4 diarrhoea in 7.7% vs. 6.2%, weakness in 15.2% vs. 8.4%, hand-foot syndrome in 6.3% vs. 9.4% and neuropathy in 2.8% vs. 4.6% of pts in Arms A and B, respectively. **Conclusions:** BEV + capecitabine as maintenance therapy following induction BEV + XELOX is noninferior to continuous BEV + XELOX until progression. These interim findings suggest that maintenance therapy with BEV + capecitabine is an appropriate option following induction BEV + XELOX in pts with mCRC. Updated data will be presented.

Efficacy	Arm A (n=61)	Arm B (n=61)
Median PFS, months	8.3	9.9
ORR, %	57.4	69.2