technical criteria or potentially resectable liver-only mets diagnosed synchronously with the primary tumour (N = 17). Resectability was reassessed after every 4 cycles of CAPOX+Bev. Bev was discontinued a minimum 8 weeks prior to surgery. Secondary objectives included complete resection rate, safety and feasibility of the regimen, PFS and OS.
Results: 46/47 pts recruited to the study commenced treatment. 1 pt was ineligible (evaluated for safety only). Based on current best response (table) CAPOX+Bev resulted in an overall response rate of 78% [95%CI 63−89%].

Response (RECIST)	Number = 45	%
CR	3	7
PR	32	71
SD	7	16
PD	3	7

With a median follow-up of 10.2 months, median PFS is 11.5 months.
28/45 pts had unresectable disease at entry. 1/28 has achieved CR; 9/28 have been converted to resectable (4 awaiting surgery); 3/28 are awaiting final assessment regarding resectability.
17/45 pts had potentially resectable synchronous liver mets at entry. 2/17 achieved CR; 10/17 have proceeded to surgery; 3/17 remain resectable and are continuing CAPOX+Bev or awaiting surgery.
15/45 pts have undergone liver resection. With surgery performed a median of 10.9 weeks (range 8.7−24) after Bev, no grade 3/4 perioperative complications have been reported. One grade 2 post-op anastamotic leak has been reported-2%. Specific grade 3/4 Bev-related toxicities were: venous thromboembolism-6.5%, hypertension-2%, duodenal perforation-2%.
Conclusion: In pts with initially unresectable or a synchronous diagnosis of liver-only CRC mets, CAPOX+Bev is associated with a high RR (78%). At least 9/28 (32%) of unresectable pts have been downstaged to potentially resectable. In our study, surgery was safe and feasible as early as 8.7 weeks post Bev. Updated results to be presented.
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6077 POSTER

A meta-analysis of the CRYSTAL and OPUS studies combining cetuximab with chemotherapy (CT) as 1st-line treatment for patients (pts) with metastatic colorectal cancer (mCRC): Results according to KRAS and BRAF mutation status

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Background: The CRYSTAL and OPUS studies demonstrated that adding cetuximab to CT (FOLFIRI or FOLFOX4, respectively) as 1st-line treatment for mCRC significantly reduced the risk of disease progression and increased the chance of response, compared with CT alone, in pts with KRAS wild-type (wt) tumors. The objective of the current meta-analysis was to evaluate progression-free survival (PFS) and overall response rate (ORR) in combined CRYSTAL and OPUS pt populations, according to KRAS and BRAF mutation status.
Materials and Methods: The meta-analysis was performed on pooled raw data from the two randomized controlled studies for the primary clinical efficacy endpoints: PFS (CRYSTAL) and ORR (OPUS). Primary definitions were employed, as provided by the individual study protocols. In both studies, the primary analysis of PFS and ORR was based on an independent radiology review committee assessment. Hazard ratios (HRs) for the treatment effect on PFS were obtained by applying a Cox proportional hazards model to pooled raw data adjusted for study and stratified by ECOG performance status, the common stratification factor in both studies. Odds ratios (ORs) for the treatment effect on ORR were obtained by performing a logistic regression on pooled raw data using the same adjustment. Mutations in KRAS (codons 12/13) and BRAF (codon 600) were detected by mutation-specific qPCR.
Results: The meta-analysis of 482 pts with KRAS wt tumors demonstrated that addition of cetuximab to CT provided a significant benefit for the primary study endpoints PFS and ORR. Overall, the addition of cetuximab to CT in pts with KRAS wt tumors significantly reduced the risk of disease progression by 36% (HR 0.64; 95% CI: 0.50−0.83). Furthermore, the likelihood of achieving a response was >2-fold higher among pts with KRAS wt tumors who received cetuximab plus CT, compared with those who received CT alone (OR 2.09; 95% CI: 1.44−3.02). In the adjusted Cox proportional hazards model and the adjusted logistic regression model, tests on heterogeneity did not indicate a difference in the treatment effect across studies. Data on the impact of BRAF mutation status on cetuximab activity will be presented at the meeting.
Conclusions: The meta-analysis results strengthen the findings obtained from the CRYSTAL and OPUS pt populations with KRAS wt tumors. Adding cetuximab to CT significantly reduces the risk of disease progression and increases the chance of response in the 1st-line treatment of mCRC.

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Cetuximab plus FOLFIRI in 1st-line treatment of metastatic colorectal cancer: Quality of life (QoL) analysis of patients (pts) with KRAS wild-type (wt) tumours in the CRYSTAL trial

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Background: The phase III CRYSTAL study previously showed that adding cetuximab to FOLFIRI as 1st-line treatment for mCRC significantly improves overall response rate and progression-free survival, and extends overall survival by nearly 4 months compared with FOLFIRI alone in pts with KRAS wt tumors. This analysis assessed the impact of treatment on QoL, a secondary endpoint in the CRYSTAL study, in pts with KRAS wt tumors.
Methods: Pts were randomized 1:1 to cetuximab qw (400 mg/m^2 initial dose then 250 mg/m^2/wk) + FOLFIRI q2w (irinotecan 180 mg/m^2, folinic acid 400 mg/m^2, 5-FU bolus 400 mg/m^2, 5-FU infusion 2400 mg/m^2 over 46 h) (n = 599) or FOLFIRI alone (n = 599). QoL was assessed with the EORTC QLQ-C30 (v3.0) questionnaire at baseline, every 8 weeks, and at final tumor assessment. The analysis focused on Global Health Status (GHS) and Social Functioning (SF) scales. A pattern-mixture model that included the drop-out pattern was employed. Analysis of QoL data was performed for the subset of pts with KRAS wt tumors (cetuximab + FOLFIRI, n = 161; FOLFIRI, n = 169).
Results: Pt populations were generally comparable in the two arms, except for fewer pts who had received prior adjuvant chemotherapy (19% vs 24%) and more females (46% vs 37%) in the FOLFIRI arm compared with the cetuximab + FOLFIRI arm. Questionnaire completion rates were similar in the two arms. There were no significant differences between treatment arms in the best and worst scores for the GHS and SF scales. Pts reported less nausea and vomiting in the cetuximab + FOLFIRI arm (p = 0.055), while dyspnoea (p = 0.046) and change from baseline score in physical functioning scale (p = 0.017) were better in the FOLFIRI arm. No between-group difference was observed in the time taken for a 20% decrease in QoL on the GHS (p = 0.46) or SF (p = 0.43) scales. Pattern-mixture analyses showed no significant differences between the two arms for changes from baseline on the GHS (p = 0.63) or SF (p = 0.81) scales. For both treatment arms, a decrease in SF score was seen at week 32 with a subsequent increase at later visits. The proportion of pts maintaining or improving their QoL was consistent across treatment arms over all timepoints.
Conclusions: The addition of cetuximab to chemotherapy did not affect outcomes on either the GHS or SF scales in pts with KRAS wt tumors, despite the skin reactions related to cetuximab treatment that might be expected to contribute to deterioration in social functioning.