IrCs was not however confirmed: ITT analysis showed 179/335 (53.4%) pts progression-free at 12 wks with Ir, 159/337 (47.2%) with IrCs, Δ −6.3%, with the 95% CI crossing the prespecified efficacy boundary (−13.8%, +1.3%). OS was not impaired (HR 1.07 [95% CI 0.90, 1.28]).
**Conclusions:** IrCs was associated with less diarrhoea as assessed by lopermide use, but severe diarrhoea was uncommon in both arms. However, we failed to prove non-inferiority of IrCs compared with Ir, so cannot recommend it as a standard treatment option for aCRC based on the PICCOLO trial data.
Sponsor − University of Leeds. Status − Closed to recruitment.

**6098** POSTER

**CRAFT Trial-Result From Multicenter Phase II Study of Modified FOLFOX7 (Combination Chemotherapy of Infusional 5-FU/l-Leucovorin and Intermittent Oxaliplatin) With Bevacizumab in the First-line Therapy of Colorectal Cancer**

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**Background:** A combination of LV+FU with oxaliplatin (FOLFOX) has been established as a standard first-line therapy for metastatic colorectal cancer (mCRC).
Therefore, prior clinical trial showed that additional bevacizumab (monoclonal antibody for vascular endothelial growth factor) to FOLFOX improved survival in patients(pts) with mCRC (NO16966 study, Saltz et al JCO2008). OPTIMOX1 study suggested that stop and go strategy for oxaliplatin reduced peripheral sensory neuropathy. However OPTIMOX study was not included Bevacizumab. Thus we conducted to confirm stop and go strategy of Bevacizumab containing FOLFOX in this trial.
**Materials and Methods:** Eligibility criteria included ECOG PS: 0−1, No Peripheral neuropathy (<Grade 1). Patients received mFOLFOX7 (oxaliplatin 85 mg/m$^2$, LV200 mg/m$^2$, 5FU 2400 mg/m$^2$ + bevacizumab 5 mg/kg q2 weeks for 8 cycles, maintenance without oxaliplatin for 8 cycles, and reintroduction mFOLFOX7 + bevacizumab for 8 cycles until progression. Primary endpoint was Progression Free Survival (PFS).
**Results:** Between March 2009 and June 2010, 52pts were enrolled. Baseline characteristics were median age of 64 years (range, 36−74); PS 0/1 (43/9 pts);male/female(32/20 pts), colon/rectum (25/27pts) and metastatic lesion liver/lung/lymph nodes (34/21/12 pts). A total of 48 pts were evaluated as Par Protocol Set population. 32pts moved from initial FOLFOX7 to maintenance mLV5FU2. 25pts moved to mFOLFOX7 reintroduction. Median PFS was 12.3months (95% CI, 8.6–18.2) and Median TTF was 9.9 months (95% CI, 5.3–11.4). Best overall response rate was 45%. Median mLV5FU2 courses were 7.2 cycles (range 2−8). Oxaliplatin reintroduction rate was 52%. The causes of reintroduction failure were disease progression (4 pts), successfully-liver resection (1pt), withdrawal consent (1pt), peripheral sensory neuropathy Grade 2 (1pt). Main grade 3/4 toxicity were: neutropenia (3pts), peripheral neuropathy (2pts), hypertension (2pts).
**Conclusions:** This study met its primary endpoint PFS. It was longer than NO16966. mFOLFOX7 without FU bolus and intermittent oxaliplatin indicated to reduce incidence of severe neutropenia and peripheral sensory neuropathy. The results suggested that our treatment strategy was well tolerate and effective for first line therapy in mCRC, and maintenance duration for 8 cycles, was reasonable.

**6099** POSTER

**The Value of Thymidine Kinase 1 (TK1) and Thymidine Phosphorylase (TP) Expression as Predictive Factors With the Treatment Efficacy of TAS-102, a Novel Antitumour Agent, in Patients (pts) With Metastatic Colorectal Cancer (mCRC)**

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**Background:** TAS-102 is a novel oral nucleoside antitumour agent, consisting of trifluorothymidine (FTD) and thymidine phosphorylase inhibitor which prevents degradation of FTD. We will report promising results at the congress that TAS-102 (A) significantly improved overall survival (OS) compared with placebo (P) (A, n = 112; P, n = 57; median OS, 9.0 vs. 6.6 months; HR, 0.56; p = 0.001). FTD has 2 mechanisms of action: it inhibits thymidylate synthase (TS) and is incorporated into DNA molecule after phosphorylation by TK1, leading to antitumour effects that differ from TS inhibitors such as fluoropyrimidine. Therefore, TK1 and TP seem to play key roles in eliciting the potent antitumour effects of TAS-102 in cancer pts. In this clinical study we have investigated whether TK1 and TP expression levels could be useful predictive factors.
**Material and Methods:** Patients with mCRC who had refractory or intolerable to standard chemotherapy regimens, including fluoropyrimidine, irinotecan and oxaliplatin; had ECOG PS of 0 to 2; and had adequate organ functions were randomly assigned to TAS-102 and placebo, in a ratio of 2:1. TAS-102 or placebo was orally administered twice daily at a dose of 70 mg/m$^2$/day from d 1 to 5 and from d 8 to 12 every 4 weeks. The H-scores for the cytoplasmic expression of TK1 and TP were blindly scored from immunohistochemical staining. The study primary endpoint was OS, and the correlation between TK1, TP expression and efficacy was analyzed.
**Results:** The expression data of TK1 and TP before treatment were available for 150 and 149 of pts treated, respectively. The median H-score for TK1 expression was 115.00 vs. 115.00 (mean; A/P, 116.06/113.53) and 115.00 of two pooled groups, and the median H-score for TP expression was 12.50 vs. 15.00 (mean; A/P, 21.58/27.35). Table 1 shows multivariate analysis by Cox proportional hazard model, which included interactions between treatment and TK1 (>115 vs. ⩽115), TP (>15 vs. ⩽15) categorized according to median pooled groups.
**Conclusions:** TAS-102 treatment significantly improved OS in pts with mCRC. TK1 and TP expression levels were not correlated with OS in pts treated TAS-102. Additional analyses will be reported at the congress.

Table 1

| Variable | OS (N = 149) | | |
|---|---|---|---|
| | HR | 95% CI | *p* |
| Treatment (A/P) | 0.61 | 0.41 to 0.91 | 0.015 |
| PS (1 or 2/0) | 1.58 | 1.07 to 2.33 | 0.022 |
| TP (>15/⩽15) | 1.17 | 0.79 to 1.74 | 0.433 |
| TK1 (>115/⩽115) | 1.20 | 0.81 to 1.78 | 0.367 |
| Treatment × TP | 0.89 | 0.60 to 1.32 | 0.566 |
| Treatment × TK1 | 0.90 | 0.61 to 1.34 | 0.610 |

**6100** POSTER

**Prolonged Survival of Patients With Metastatic Colorectal Cancer Who Underwent First-line Oxaliplatin Based Chemotherapy With the Introduction of Molecular Targeting Agents and Curative Surgery**

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**Background:** Recently, two types of molecular targeting agents were introduced for treatment of metastatic colorectal cancer (MCRC). However, it remains controversial whether these agents are associated with improved overall survival (OS) in oxaliplatin based chemotherapy.