## P-339 Real-world data (RWD) of the use of trifluridine/tipiracil hydrochloride (TFT) in patients with metastatic colorectal cancer: The Greater Manchester experience

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**Background:** Trifluridine/tipiracil hydrochloride has shown to improve progression-free survival (PFS) and overall survival (OS) in patients with metastatic colorectal cancer (mCRC). Exploratory analysis suggested that patients with good prognostic characteristics GPC (18 months since first diagnosis) carry better prognosis vs. poor prognostic characteristics (PPC). We report the Greater Manchester experience of the use of TFT.

**Methods:** All consecutive patients who received TFT between August 2016 and August 2019 were included. Data were collected from electronic records. Univariate survival analysis was performed with Kaplan-Meier curve and log-rank test. Cox regression was used for multivariable analysis.

**Results:** All consecutive pts (n=188) were included; median follow up was 7.1 months. Median age was 66 IQR (59-72); 60% were male; 22% had right; 43% had left; 35% had rectal cancers. RAS mutation was identified in 29.8%. Twenty-nine (16%) received bevacizumab and 23.4% received anti-EGFR treatment. Seventy-eight (41%) had $\leq$ 3 sites of metastases; 134 (74%), 120 (66%) and 70 (40%) had liver, lung and peritoneal metastasis respectively; 123 (65.4%) had $\leq$18months since diagnosis of first metastasis, 64 patients (34%) had GPC while 122 (64.9%) had PPC. Median time from stage IV diagnosis to starting treatment was 23.9 months IQR (14.9-38.5). Thirty-six (19%) had HB $<$ 0.001. Patients with GPC had better OS of 12.9 months (95% CI 10.11-15.77) compared to 7.45 months in patients with PPC (95% CI 10.1 to 15.7), p$<$ 0.001. Patients with liver metastasis had a shorter median PFS 2.7 months and OS 7.5 months (95% CI 6.3-8.8) when compared with patients with no liver metastasis with PFS 4.3 months (95% CI: 2.5 to 2.9), p=0.002 and OS of 12 months (95% CI: 9.3-14.7), p=0.001. Patients who were in the GPC group and had no liver metastasis had an improved median OS of 13.9 months when compared with the rest of patients in whom median OS was 7.8 (95% CI 7.2 to 20.7), p=0.002. Multivariable analysis showed that GPC was an independent prognostic factors for OS (HR 0.582; 95% CI 0.3-0.8; p=0.005). Grade 3 neutropenia was an independent prognostic factor for PFS (HR 0.55; 95% CI 0.39-0.79; p=0.001) and OS (HR0.4; 95% CI 0.2-0.6; P$<$ 0.001).

**Conclusion:** Our RWD on TFT was associated with a better OS than expected. This RWD study was able to validate GPC, GPC with no liver metastases and grade $\geq$ 3 neutropenia as subgroups benefiting the most from TFT.

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## P-340 Regorafenib dose-strategy in patients with metastatic colorectal cancer who progressed on standard treatment: A retrospective study

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**Background:** Regorafenib is recommended in patients with metastatic colorectal cancer (mCRC) after failure of at least two lines of treatment regardless of the RAS and BRAF mutation status. It significantly increased progression-free survival and overall survival in two phase III studies (CONCUR and CORRECT). The side effects such as fatigue and hand-foot skin reaction (HFSR) has limited its use with a standard dose, especially in fragile patients. However, the maximum effect of therapy can be achieved only with regard to the profile of adverse events, correct time points of starting, interruption and effectiveness control.

**Methods:** 25 patients with documented mCRC that was and progressing to 2 or more lines of standard therapy, were enrolled in this retrospective study. We assessed: age, sex, ECOG performance status, primary site of disease, primary tumor status, number and site metastasis, number of previous treatment, initial dose of regorafenib, duration of treatment, safety profile, progression-free survival and overall survival. The primary endpoints were the proportion of patients who were able to continue two cycles of or more of regorafenib and the correlation with the initial dose (80mg, 120mg, 160mg), as well as the safety of different schedules with or without de-escalating the dose. The secondary endpoint was overall survival in each group.

**Results:** Between January 2016 and March 2020, 25 patients were enrolled in this retrospective study. Starting dose in this study was different: 120mg - 76%, 160mg – 8%, 80mg - 16%. However, de-escalation was shown in 75% in the 120 mg group and 25% in 160mg group. In patients who received 120 mg with dose reduction, 76.5% were able to receive more than two cycles of regorafenib vs 17.6% in the 80 mg fixed-dose group and 5.9% in the 160 mg group. The most common grade 3-4 adverse events were hand-foot skin reaction (three patients in 120mg de-escalating dose group [12%]) and fatigue (1 patient [4%]). The median overall survival was 4 months in the 120mg de-escalating dose group vs 2 months in 80 mg fixed-dose group (CI 0-5.24; p= 0.044).

**Conclusion:** The dose-reduction dosing strategy according to AEs represents an alternative approach for optimising regorafenib with better safety profile and comparable activity.

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## P-341 Capecitabine/mitomycin versus 5-fluorouracil/mitomycin in combination with simultaneous integrated boost-intensity modulated radiation therapy for anal cancer

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**Background:** Within the past decade, several studies have tested capecitabin as a substitute for 5-FU in the treatment of localised squamous cell carcinoma of the anal canal (SCCAC) and reported similar clinical response rates, making capecitabin an acceptable and more convenient alternative to infusional 5-FU. However, the differences in efficacy between capecitabine and 5-FU in CRT with simultaneous integrated boost-intensity modulated radiation therapy (SIB-IMRT) for locally SCCAC are not documented. We performed this retrospective study to compare the response of capecitabine and 5-FU in survival and toxicity terms in patients with locally SCCAC treated with concurrent SIB-IMRT.

**Methods:** This retrospective, observational, cohort study included patients with locally SCCAC T2-4, any N, M0 or any T, N1-3, M0 treated with mitomycin C (10mg/m$^2$) and infusional 5-FU (750 mg/m$^2$; group 1) or capecitabine (825 mg/m$^2$; group2) associated with SIB-IMRT between July 2009 and April 2018 in the Institut Sainte Catherine. Ninety-six patients were included in group 1 between July 2009 and July 2017 and fifty-six patients were included in group 2 between October 2012 and April 2018. Individual data, survival, and toxicity were collected from electronic medical records. The primary endpoints were disease-free survival (DFS) and acute toxicities.

**Results:** The two groups are statistically (CI 95%, Chi-squared test or Fisher's exact test when appropriate) comparable in terms of sex (79 women (82%) of 96 group 1 patients versus 48 women (86%) of 56 group 2 patients; p=0,58), ECOG performance status (91 ECOG PS 0 (95%) of 96 group 1 patients versus 52 ECOG PS 0 (93%) of 56 group 2 patients; p=0,72), HIV status (2 HIV-positive (8,7%) of 23 group 1 tested patients versus 1 HIV-positive (4%) of 25 group 2 tested patients; p=0,60) and HPV status (25 HPV-positive (89%) of 28 group 1 tested patients versus 34 HPV-positive (92%) of 37 group 2 tested patients; p=0,74) as well as T (T1-2=60(63%), T3=22(23%) and T4=14(15%) in group 1 patients versus T1-2=34 (61%), T3=15(27%) and T4=7(13%); p=0,84), N (N0=43(45%), N1=20(21%) and N2-3=33(34%) in group 1 patients versus N0=28(50%), N1=12(21%) and N2-3=16(29%); p=0,74). Group 1 median age was 62 years-old and group 2 median age was 67 years old (p=0.009; Student's t-test). With a median duration of follow-up of 51.5 months (range: 4-102) in the group 1 and 27.5 months (range: 7-66) in the group 2, the disease-free survival curves of the two groups did not differ significantly (p=0.70 ; log-rank test).). Group 1 2-years DFS rate (IC95%) was 83.2% and group 2 2-years DFS rate (IC95%) was 81.6%. Rates of patients with at least one grade 3 or more acute toxicity was 36%(n=35) in group 1 and 20%(n=11) in group 2 (p=0.029). Diarrhea was the main grade 3-4 acute toxicity in both groups (20% (n=7) in group 1 and 64% (n=7) in group 2). In group 1, asthenia (n=6; 17%) and epithelitis (n=6, 17%) was important grade 3-4 acute toxicity.

**Conclusion:** Capecitabine associated with mitomycin and SIB-IMRT is a treatment as effective and safer than 5-FU-based chemotherapy for locally SCCAC.

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