(basal cohort) and 55 patients assessed after anti-EGFR treatment (post-EGFR cohort). KRAS, NRAS and BRAF mutation analysis in plasma was performed using a fully automated real time PCR-based platform (Idylla™ Biocartis). We evaluated the performance of this technique compared to tissue analysis and correlated the results to patients' clinical features.

Results: The overall agreement between tissue analysis and liquid biopsy in the basal cohort was 81.13%, with a higher concordance in patients with liver metastases (88.57%). In patients with liver metastases, sensitivity, specificity, and positive predictive value (PPV) of liquid biopsy were 84.21%, 93.75%, and 94.12%, respectively. Circulating mutational fraction (CMF) for KRAS was significantly higher in patients with liver metastases. In one case of metachronous metastases, the detection of a RAS mutation in plasma but not on tissue analysis predicted the lack of response to anti-EGFR treatment. In the post-EGFR cohort, 13/55 patients presented detectable mutations in KRAS (9 cases), NRAS (3 cases) or BRAF (1 case) in plasma. Among the KRAS mutants, the prevalence of non-exon2 mutations was higher in the post-EGFR cohort (44%) compared to the basal cohort (21%). CMF values for KRAS increased significantly (*P*: 0.0313) in patients receiving a rechallenge anti-EGFR treatment.

Conclusions: Real time PCR-based testing of RAS/BRAF mutations in plasma is feasible and reliable in mCRC patients in a clinical setting. Liver involvement increases the reliability of the technique. Plasma detection of RAS mutations has a strong clinical value in case of metachronous metastatic disease. Liquid biopsy is useful to monitor the onset and fluctuations of RAS mutations in patients receiving anti-EGFR therapy.

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462P Treatment trends and clinical outcomes of left sided, RAS/RAF wild type metastatic colorectal cancer in the United States

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Background: Retrospective analyses suggest that anti-EGFR therapy (panitumumab or cetuximab) may be superior to bevacizumab when added to first-line (1L) chemotherapy in patients with metastatic colorectal cancer (mCRC) who have left sided primary tumors (LSPT). In this study we evaluated trends in the management of left sided, RAS/RAF wild type (WT) mCRC in the United States (US) and compared clinical outcomes among the most commonly used treatment strategies.

Methods: The nationwide Flatiron Health EHR-derived de-identified database was reviewed for patients diagnosed with mCRC between 2013 and 2018. Patients who were RAS/RAF WT and had a LSPT determined by ICD coding were included for analysis. Treatment trends over time were visually assessed. Kaplan-Meier and Cox proportional hazards modeling were used to compare survival outcomes stratified by 1L therapy. Models were adjusted for chemotherapy backbone, primary tumor site, age, gender, stage at diagnosis, mismatch repair status, and performance status.

Results: Out of 9,753 patients with mCRC, 1,607 were reported as left sided, RAS/RAF WT. Of these, 456 (28%) received 1L chemotherapy alone, 965 (60%) chemotherapy plus bevacizumab, and 186 (12%) chemotherapy plus an anti-EGFR agent. A visual trend over time in these percentages was not observed. Median overall survival for patients treated with an anti-EGFR agent was 42.9 months (mo) (95% CI 36.0 — not reached) compared to 27.5 mo for those treated with bevacizumab (95% CI 25.8 — 28.9), and 27.3 mo for those treated with chemotherapy alone (95% CI 24.8 — 32.3) (p = 0.0018). Compared to chemotherapy alone, multivariate analysis showed an improvement in survival with the addition of an anti-EGFR agent (HR 0.52, 95% CI 0.33 — 0.82, p = 0.005) but not bevacizumab (HR 0.88, 95% CI 0.68 — 1.14, p = 0.33).

Conclusions: This analysis of real-world data showed no clear trend over time in the management of patients with left sided, RAS/RAF WT mCRC. Chemotherapy with bevacizumab remains the most widely used 1L treatment strategy in the US. Despite this preference, our analysis suggests that survival outcomes may be superior with the addition of a 1L anti-EGFR agent. Prospective trials are needed to clarify the optimal treatment strategy for these patients.

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463P The prognostic role of tumour inflammation markers in patients (pts) with colorectal cancer (CRC) treated with trifluridine/tipiuracil hydrochloride: Real-world data (RWD) from Greater Manchester

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Background: Trifluridine/Tipiuracil hydrochloride (TFT) has been shown to improve progression free survival (PFS) and overall survival (OS) in pts with stage IV CRC. We evaluated the neutrophil to lymphocyte ratio (NLR), platelet (P) to LR, monocyte (M) to LR and systemic inflammatory response index (SIRI) as a stratification tool for patients (pts) receiving TFT.

Methods: All consecutive pts who received TFT between August 2016 and August 2019 were included. Univariate survival analysis was performed with Kaplan-Meier curve and log-rank test. Cox regression was used for multivariable analysis (MVA). All indexes tested were dichotomised by their median value.

Results: One hundred and eighty-eight pts were analysed; median follow up was 7.1 months (mos). Median age was 66. RAS mutation was identified in 29.8% of pts; 134 (74%), 120 (66%) and 70 (40%) had liver, lung and peritoneal metastasis, respectively; 64 pts (34%) had good prognostic characteristics (GPC) (<3 metastatic sites and ≥18 mos since first metastasis). Median baseline neutrophils (N)s 4.5×10^9/L, lymphocytes (Ls) 1.2×10^9/L, monocytes (Ms) 0.5×10 9/L and platelets (Ps9 218×10^9/L; 14% had performance status (PS) 0 and 78% had a PS1. 5% of patients had PS2 and data was missing in 3%. Neutropenia was observed in 133 pts (71%), 64 (34%) with grade ≥3 and 25 (13.2 %) with febrile neutropenia. Median OS for the cohort was 8.6 mos. Median PFS for pts with low NLR was 3.15 mos (95%CI 2.94-3.35) vs 2.9mos (95%CI 2.56-3.41) in pts with high NLR (*P*=0.037). Median OS for patients with low NLR was 9.49 mos (95% CI 6.71-12.27) vs 8.54 mos in pts with high NLR (95% CI 6.82-10.25) (*P*=0.035). Pts with low SIRI had an increased PFS of 3.2 mos (95% CI 2.67-3.76) and OS of 11.20 mos (95% CI 8.57-13.83) vs PFS of 2.9 mos (95%CI 2.6-3.2) and OS of 7.62 mos (95% CI 5.8-9.4) in pts with high SIRI, (*P*=0.018 for PFS and 0.017 for OS). In OS and PFS, MVA adjusted for GPC and ≥G3 neutropenia, NLR and SIRI were not independent prognostic factors. However, GPC and ≥G3 neutropenia were independent prognostic factors for OS (HR 0.55; 95% CI 0.3-0.8; *P*=0.003 and HR 0.4; 95% CI 0.3-0.7; *P*=0.001, respectively.).

Conclusions: Pts with low NLR or SIRI showed the best PFS and OS outcomes. Thus, these two blood-based tumour inflammatory markers could be useful for stratification of pts with stage IV CRC receiving TFT.

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464P Pharmacokinetic analysis of NUC-3373 with and without leucovorin in patients with previously treated metastatic colorectal cancer (NuTide:302 study)

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Background: 5-FU is a key anti-cancer agent used across a broad range of tumours. The anti-cancer metabolite of 5-FU, fluorodeoxyuridine-monophosphate (FUDR-MP), binds and inhibits thymidylate synthase (TS), disrupting DNA synthesis and repair. 5-FU is often dosed with leucovorin (LV) to enhance binding of FUDR-MP to TS. NUC-3373 is a phosphoramidate transformation of FUDR-MP designed to bypass 5-FU resistance mechanisms associated with transport, activation and breakdown. NuTide:302 is a three-part study in patients (pts) with advanced colorectal cancer (CRC) who have relapsed after ≥2 prior lines of 5-FU-containing regimens, investigating NUC-3373 in combination with agents commonly used to treat CRC.