Conclusions: Single organ pulmonary metastasis has better impact on PFS and OS in mCRC patients treated with FOLFIRI and VEGF inhibitors as second-line chemotherapy.

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P-34 Does the chemotherapeutic efficacy of trifluridine/tipiracil plus bevacizumab change depend on pre-treatment vascular endothelial growth factor inhibitors?

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Background: Trifluridine/tipiracil (FTD/TPI) plus bevacizumab (BEV) is widely used as one of salvage line treatment options in metastatic colorectal cancer (mCRC) patients. In Japan, three vascular endothelial growth factor (VEGF) inhibitors, BEV, ramucirumab (RAM), and aflibercept (AFL), are approved for mCRC patients with second-line chemotherapy including irinotecan. It remains unclear the effect of the difference of pretreatment VEGF inhibitors in clinical outcomes of FTD/TPI plus BEV.

Methods: Consecutive mCRC patients who were treated with FTD/TPIplus BEV were retrospectively enrolled. Disease control rate (DCR), progression-free survival (PFS), overall survival (OS), and safety were compared according to the pretreatment VEGF inhibitors. Subgroup analyses of prognostic and predictive efficacy markers were performed.

Results: In total,156 patients (median age, 61.5 years) were included. The DCR was 52.6%, median PFS was 4.2 months (3.2-4.9), and median OS was 12.9 months (10.7-15.3). A total of 73 (46.8%), 50 (32.0%), and 33 patients (21.2%) were treated with FOLFIRI +BEV, RAM, or AFL, respectively. DCR, PFS, OS showed no significant differences between three groups. The most common grade 3 or 4 AEs were neutropenia (29.1%), proteinuria (16.0%) respectively. There were also no significant differences about grade 3 or 4 adverse events rates between three groups.Multivariate analysis revealed poor performance status and liver metastasisas an independent predictor for shorter both PFS and OS (Liver metastasis, PFS: P = 0.002, OS: P = 0.001, Performance status, PFS: P = 0.001, OS: P = 0.00002).

Conclusions: Chemotherapeutic efficacy and safety of FTD/TPIplus BEV did not differ regardless of the pre treatment VEGF inhibitors.

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P-35 An observational study of health-related quality of life (HRQoL) with electronic patient-reported outcome (ePRO) monitoring during nivolumab therapy for advanced gastric cancer as the 3rd or later line treatment: NIVO-G QoL study

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Background: Nivolumab is the first immune checkpoint inhibitor that proves efficacy in advanced gastric or gastroesophageal junction cancer and is approved as the 3rd or later line treatment. However, the patients (pts)'s HRQoL has not been evaluated in this setting. We thus investigated how adverse events (AEs) affect HRQoL decline during nivolumab treatment and assessed the feasibility of symptom monitoring at home using the patient's own smartphone.

Methods: Eligible pts were aged ≧20 years with ECOG-PS of 0-2, diagnosed as advanced gastric cancer, and were scheduled to receive nivolumab every two weeks as the 3rd or later line treatment. Pts assessed symptomatic AEs by themselves with PRO-CTCAE and HRQoL with FACT-Ga weekly through ePRO system using pts' own smartphones or rental devices. Objective AEs were evaluated with NCI-CTCAE v5 at the time of consultation. The observation period was 12 weeks. The primary endpoint was the association between each AE and HRQoL decline. The impact of AE deterioration on HRQoL decline was determined by the longitudinal data analysis using a general linear model. The response variable was FACT-Ga total score changes from baseline for each time point. Explanatory variables were FACT-Ga total score at baseline, time point, and composite grade of each AE based on PRO-CTCAE. After ePRO monitoring, the pts completed the questionnaire about its usability.

Results: Between April 2019 and April 2020, 30 pts were enrolled, out of which 29 were evaluable. Twenty pts had completed ePRO monitoring by the end of the observation period, of which 10 pts had still continued nivolumab. The median age of pts was 71 years, and 58% were male. 97% of the pts were PS 0-1 and treated after the third line of treatment. 37.9% of pts do not use their smartphones on a regular basis, and 52.4% were aware of the difficulty of using them. As a result, only 0.95% of the total timepoints were missing data due to no ePRO input, indicating good compliance. The median time until the definitive deterioration of the FACT-Ga total score was nine weeks (95%CI: 3-NA). AEs such as stomatitis ($p<0.0001$), dysgeusia ($p<0.0001$), pain ($p<0.0001$, malaise ($p<0.0001$, nausea ($p=0.0006$, depression ($p=0.0011$, insomnia ($p=0.0035$), loss of appetite ($p=0.0047$, shortness of breath ($p=0.0052$, and vomiting ($p=0.0123$) were associated with worsening HRQoL, but peripheral neuropathy, diarrhea, and constipation were not. For the questionnaire about the usability of ePRO, no pts answered "not satisfied", but only 33.4% of pts were answered "satisfied". While 33.4% of pts wanted to continue using ePRO, 22.2% did not.

Conclusions: Symptom monitoring with ePRO revealed that certain AEs may be responsible for the decrease in HRQoL in pts with advanced gastric cancer during the 3rd or later line nivolumab treatment. Although compliance in the ePRO input was sufficient, there are still challenges in implementing it in daily practice to meet pts expectations.

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P-36 Real-world outcomes in BRAFV600E metastatic colorectal cancer – the Glasgow experience

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Background: Approximately 8 - 10% of metastatic colorectal cancers (mCRC) have a BRAF V600E mutation. BRAF V600E mutant mCRC represents a distinct clinical subset with a poor prognosis. Previous treatment guidelines have been derived from subgroup analyses of non-designated BRAF V600E trials. Real world studies have shown that outcomes and treatment practices can vary widely. Here, we report on our regional practices and outcomes.

Methods: We undertook a retrospective analysis of all mCRC patients with confirmed BRAF V600E mCRC diagnosed in NHS Greater Glasgow and Clyde Health Board (Scotland, UK) between 01/01/2015 - 31/12/2020. Clinical and pathological features were obtained from electronic records. Univariate analysis of prognostic factors was performed using Kaplan Meier analysis and log-rank test. Multivariate analysis was performed using Cox regression.

Results: A total of 139 patients were identified for study with 1 excluded for missing follow up information. Median age at metastatic diagnosis was 69 years, with a female preponderance (59% female, 41% male). 31% of tumours also had deficient mismatch repair (dMMR) or high levels of microsatellite instability (MSI-H). Primary tumour site was mostly right-sided (n=102, 74%), with less left-sided (n=20, 15%) and rectal (n=15, 11%) tumours. 1 patient had 2 synchronous primaries (1 right colon and 1 rectal). 64% presented with de novo metastatic disease. For those with initial loco-regional disease, the median time to metastatic progression was 10 months. The most common metastatic sites were liver (54%), peritoneal (33%), lymph node (31%), and lung (28%). 36% of patients did not receive any systemic treatment, 36% received 1 line, and 28% received 2 or more lines of treatment. Most (69%) received a cytotoxic chemotherapy doublet as first-line treatment, and 6% received triplet cytotoxic chemotherapy. 7% received immunotherapy. Among the treated patients, only 19% received some form of targeted therapy over their full treatment course, usually a combination containing an anti-EGFR inhibitor. The median overall survival was poor at 7.2 months. Features significantly associated with shorter survival were

performance status (PS) of 2 or worse ($p < 0.01$), the presence of lymph node metastasis ($p = 0.010$) and peritoneal metastasis ($p < 0.01$), a higher modified Glasgow Prognostic Score (GPS) of 2 ($p = 0.035$) and a high neutrophil-lymphocyte ratio >5 ($p = 0.032$). Primary tumour site was also significantly associated with survival ($p < 0.01$), with worse survival for right-sided tumours (6.6 months), compared to 14.0 months for left-sided/rectal tumours. Using multivariate analysis, independent prognostic markers were PS, presence of lymph node metastasis, presence of peritoneal metastasis and right-sided primary tumour location.

Conclusions: This is a representative cohort of BRAF V600E metastatic colorectal cancer patients, which confirms previously known clinical features. Of the common metastatic sites, peritoneal or lymph node metastases confer a poorer prognosis. There was not widespread adoption of more intensive triplet chemotherapy over the study time period. Overall survival is poor, and changed treatment strategies facilitated by recent clinical trial advances with targeted therapies may improve outcomes in this poor prognostic group.

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P-37 Has the COVID-19 pandemic lead to an upshift in emergency presentation and stage migration of colorectal cancer in Uruguay?

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Background: Effective Cancer screening is critical in reducing cancer related mortality in CRC by increasing the detection in earlier stages. Worldwide, practically all cancer pathways have been negatively affected by the implications of the COVID-19 pandemic. Oncological care has not escaped the effects of reprioritization of health care services to handle the surge of COVID-19 patients adequately. Cancer screening programs are no exception as many were temporarily halted to alleviate the pressure on overwhelmed health care systems. In Uruguay, the first COVID patients were detected in March 2020, and since then, the country's Public Health policies have been marked by the COVID-19 public health emergency. The aim of this study is to assess the impact of the COVID-19 pandemic on CRC diagnosis. We further aimed to analyze the effect on the clinical presentation and stage at diagnosis during 2020-2021 compared with previous years.

Methods: This was a single center retrospective cohort study performed at a tertiary center. Patients diagnosed and managed with colorectal adenocarcinoma during the years 2020-2021 were compared with patients from 2018 and 2019. Those enrolled in 2018-2019 were classified as the "pre-pandemic group", and those enrolled in 2020-2021 were classified as the "pandemic group". The primary outcome was the rate of stage IV disease at the time of diagnosis. Mann-Whitney test was used in the comparison of quantitative variables and Fisher's exact test was used for qualitative variables.

Results: A total of 369 patients were included in this study. From March 2018 to 2019 (pre-pandemic), 217 patients were considered, and from March 2020 to 2021 (pandemic), 152 patients. Median age of pre-pandemic and pandemic group was 64.4 and 65.6 years, respectively. There was no statistically significant difference in cancer obstruction or perforation at diagnosis. Other patient demographics were comparable ($p>0.05$). The percentage of surgical candidates was lower during the pandemic (69% vs 62%). There was a significant difference in TNM tumor distribution between pre-pandemic and pandemic subgroups with a higher incidence of advanced (cT4 or cN+ or M1) tumors. T4 tumors and node positive disease were equivalent in both groups but the incidence of disseminated disease (cM1) was significantly higher in the pandemic group (48% vs 36%, $p < 0.001$).

Conclusions: Our study demonstrates how cancer diagnostic variables, mainly stage at diagnosis, have been affected by the impact of the COVID-19 pandemic on cancer screening programs. Therefore, it is of utmost importance that cancer diagnosis and treatment pathways be reinstalled in full to return to and build on pre-pandemic priority to ensure the Uruguayan population benefits from earlier diagnosis and treatment.

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P-38 Proper size and timing of endoscopic dilation in anastomotic stricture after near-total esophagectomy

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Background: The size or timing of endoscopic dilatation for anastomotic stricture after near-total esophagectomy is not clear. The purpose of this study is to find out the target size and the timing of endoscopic dilatation for stenosis after near-total esophagectomy.

Methods: Medical records of patients with endoscopic dilatation for anastomotic stricture after near-total esophagectomy between January 2015 and April 2021 were reviewed. We analyzed the stricture recurrence rate and dilation-free period according to each diameter of dilation.

Results: In the study period, 78 endoscopic dilations in 24 patients were enrolled. The stricture recurrence rate was 91.4% in 13.5mm or less group, 57.9% in 15mm group, and 0% in 16.5mm group. The dilation-free period had a mean of 48.2 (range 14-679) days in 13.5mm or less group and 109.3 (range 14-347) days in 15mm group ($p = 0.045$). No perforation occurred in this study.

Conclusions: In patients with anastomotic stricture after near-total esophagectomy, safely consider 15mm as the target diameter of dilation, and if this is achieved, follow-up endoscopy and dilation can be considered after 3 months.

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P-39 Utility of circulating tumor DNA (ctDNA) to assess tumor response in patients with locally advanced rectal cancer undergoing neoadjuvant therapy

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Background: The current tools to assess tumor response in patients with locally advanced rectal cancer (LARC) undergoing neoadjuvant therapy (NAT) are suboptimal. As the 'watch and wait' (W&W) approach for patients who achieve complete clinical response (cCR) is being widely considered, accurate tumor response assessment is critical. We retrospectively explored whether circulating tumor DNA (ctDNA) can aid in tumor response assessment in patients with LARC undergoing NAT.

Methods: In this multicenter, retrospective study, patients aged ≥18 years with histologically confirmed LARC undergoing NAT, either with chemoradiotherapy (CRT) or total neoadjuvant therapy (TNT), a combination of systemic chemotherapy (CT) and CRT, were included. Patients had baseline (obtained within 7 days before starting NAT), and serial blood samples were drawn during and after the completion of treatment. A tumor-informed, personalized ctDNA assay (SignateraTM, bespoke mPCR-NGS assay) was utilized to measure plasma ctDNA level expressed as mean tumor molecules (MTM)/mL. Tumor response was assessed with imaging studies, including MRI and proctoscopic examination. A correlation between complete ctDNA clearance and tumor response was explored.

Results: The study included 12 patients with LARC (clinical stage II=5, stage III=7) with a median age of 56 years (range: 44 to 68 years); 59% of patients were male. Total 34 blood samples were collected from 12 patients. In this cohort, 4 patients were excluded from the analysis, due to insufficient tissue to design the ctDNA assay (n=2) and lack of detectable ctDNA at baseline (n =2). Among 8 patients who had a baseline ctDNA level, ctDNA clearance was observed in 7 patients after a median interval of 46 days (range: 30-76 days) from the onset of NAT. The patient with persistent ctDNA level discontinued treatment within 1 month of onset of NAT due to noncompliance unrelated to treatment toxicity. Among the patients who cleared ctDNA, 3 patients have completed NAT and achieved cCR, 3 patients are currently on NAT with interim pelvic MRI showing significant shrinkage of the tumors, and 1 patient was lost to follow-up before the completion of NAT with interim MRI showing considerable tumor response. There was an agreement between the ctDNA clearance and tumor response, indicating a Cohen's kappa of 1 for reliability.

Conclusions: In this small cohort of patients, a high degree of correlation was observed between ctDNA clearance and response assessed by MRI and proctoscopy. However, these data are preliminary and hypothesis-generating. Larger prospective studies are warranted to further explore the potential of ctDNA-based tumor response assessment in patients with LARC undergoing NAT.