2-8), including Trifluridine/Tipiracil in 29.2% of pts. FAS-CORRECT 0-3/4-5/6+ were 32.6%/35.7%/38.1% and Tabernero subgroups BPC/GPC/PPC were 20%/42.3%/37.3%. Median of REG cycles was 3 (range 1-18 cycles). With a median follow up of 23.4 months, median OS was 6.7 months (95% CI, 6.1-7.3 months) with 12- month OS rate 20.8% and median PFS was 2.9 months (95% CI, 2.7-3.0 months) with 6-month PFS rate 14.6%. Overall Response Rate (ORR) and Disease Control Rate (DCR) were 4.6% and 25.4%, respectively. The most common grade 3-4 toxicities were asthenia (12.3%), hyperbilirubinaemia (6.4%), hypertension (3.9%) and hand-foot skin reaction (3.9%). This toxicity was managed with dose reduction in 39.2 % of cases. OS FAS-CORRECT 0-3/4-5/6+ were 9.2 vs. 6.9 vs. 5.3 m (p=0.138) and OS Tabernero subgroups BPC/GPC/PPC were 10.5 vs. 6.9 vs. 5.2 m (p=0.022). DCR FAS-CORRECT 0-3/4-5/6+ were 37.5% vs. 28.5% vs. 22.9% (p=0.121) and DCR Tabernero subgroups BPC/GPC/PPC were 48% vs. 21.1% vs. 24.4% (p=0.004).

Conclusions: OS and PFS observed in our serie were consistent with the CORRECT trial, although in our routine clinical practice they were slightly higher. FAST-CORRECT and, especially, Tabernero's prognostic subgroups identify patients who may benefit from long-term Regorafenib treatment.

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P-64 Incidence of brain metastases in a potentially high-risk group of patients with metastatic colorectal cancer: Results from a pilot study

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Background: Brain metastases (BM) are an uncommon presentation of metastatic colorectal cancer (mCRC) and routine imaging of the brain is not recommended. The majority of patients with BM undergo a palliative treatment course with an expected survival of few months. However, appropriately selected patients could be candidates for metastasis-directed treatment with a potential for a curative outcome. In a registry-based CRC cohort study patients undergoing curatively intended treatment of BM had more frequently rectal cancers with lung metastases. Patients undergoing curative intended treatment of BM achieved a 5-year survival rate of 12.7%. The aim of our pilot study was to prospectively investigate the incidence of BM in a potentially high-risk group of patients with mCRC. Possible prognostic biological aspects were investigated by translational analysis of blood samples.

Methods: A prospective pilot study to investigate if the currently suggested risk factors, rectal cancer and lung metastases, could add to a relevant detection rate of asymptomatic BM from CRC. Inclusion criteria: rectal cancer; lung metastasis diagnosed by histo- or cytopathology, or by clinical and imaging criteria. Exclusion criteria: contraindications for magnetic resonance imaging (MRI); previously treated or known brain metastasis. Patients underwent a standard 3T MRI scan of the brain with intravenous contrast. MRI were described by a specialized radiologist. Positive findings were discussed at the multidisciplinary tumor board for potential treatment options according to best standard of care. The level of total cell free DNA (cfDNA) in plasma samples drawn at inclusion were measured by a direct fluorescence assay (as previously published). Blood samples were available from a cohort of healthy individuals.

Results: Twenty-nine patients were included. Four patients withdraw their consent, and the remaining 25 patients underwent screening MRI of the brain. The median age was 68 years (interquartile range [61-71]) and the majority males (68%). Twenty-one patients had active lung metastases, including six with lung-only disease, whereas four patients were included during follow-up after local ablative treatments. Mutational status in tumor tissue comprised 14 (67%) with KRAS mutations, seven wild-type, and four not done. Evidence of brain metastasis was detected in one patient (4.0%; 95%CI [0.1-20.4]). The cfDNA levels were significantly higher in the study cohort (median 0.73 ng/µl) compared to the healthy cohort (median 0.52 ng/µl, $p < 0.001$) and there was a tendency for higher cfDNA levels in patients with primary tumor in situ (p=0.14) and in patients with liver metastases (p=0.12). The cfDNA level was 0.81 ng/µl in the patient with BM and 0.72 ng/µl in the remaining. Numbers were, however, low for sub-analyses.

Conclusions: A single asymptomatic BM was detected but we did not find an incidence of BM, which justifies routine MRI of all patients in this selected population. Future studies should focus on identifying further characteristics and biomarkers associated with high risk of BM from CRC. This would enable early detection of BM, and thereby a possibility for early intervention, prolonged survival and improved quality of life. In accordance with the literature, we found a significantly higher cfDNA level in patients compared to healthy individuals.

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P-65 Stereotactic radiosurgery for palliative management of hepatocellular carcinoma associated with portal vein thrombosis

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Background: The life expectancy and treatment options for the patients with hepatocellular carcinoma HCC presented with portal vein thrombosis are frustrating. This study aimed at evaluating the efficacy and safety of stereotactic radiosurgery SRS as a palliative treatment for this group of patients.

Methods: Between January 2020 and March 2021, we examined patients who are ineligible for local treatment of HCC (i.e., radiofrequency RF, trans- arterial chemotherapy TACE, or even liver transplantation) because they were diagnosed to have portal vein thrombosis PVT. We offered those patients SRS as palliative treatment. The selected dose of SRS was 40 Gy in 5 fractions while sparing $\geq$ 700 cc of the liver tissue. Patients should have ECOG performance status of 1-2 with no or minimal ascites and total bilirubin of $\geq$ 2.5 mg/dl.

Results: During the study period, 16 patients were enrolled, 12 were males, and only 4 were females. The median age of those patients was 62.4 years (range 48 to 72 years). They were all having Child- Pugh B or early C (7-9). All the patients had suffered from portal vein thrombosis PVT (of the main portal vein or one of its branches). The 6 months overall survival OS was 87.5%, and the radiological response rate RR (stable disease and decreased tumour size) was found in 75% of cases (12/16) by the 3 months follow up. The thrombosed portal vein showed radiological signs of recanalization in 50% of treated patients. Those patients showed reduced levels of alpha fetoprotein and improved levels of local pain compared to the pre-treatment levels. None experienced grade 4 adverse events. By the time of data analysis (September 2021) 8 patients were still alive.

Conclusions: SRS as a palliative treatment for advanced HCC is safe and effective in patients with good performance status. Such results need validation with multicentre randomized studies that would recruit more patients with longer follow up.

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P-66 PET/CT radiomic features to predict clinical outcomes in locally advanced pancreatic cancer

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Background: Innovative biomarkers to predict clinical outcomes in pancreatic cancer would be helpful in optimizing personalized treatment approaches. In this study, we aimed to develop PET/CT-based radiomic biomarkers to predict early progression in patients with locally advanced pancreatic cancer (LAPC).

Methods: Among one-hundred fourteen patients with LAPC treated at our institution with initial chemotherapy followed by curative chemoradiation (CRT) from July 2013 to March 2022, a secondary analysis with baseline 18F-FDG PET/CT images was conducted in fifty-seven patients. All pre-treatment PET/CT were performed at a single PET/CT Centre. Clinical factors as well as semiquantitative PET parameters, including standardized uptake value (SUV), metabolic tumor volume (MTV), and total lesion glycolysis (TLG), were also reported. Early progression (EP) was defined temporally as a progression at the first evaluation, at 3 months from the start of treatment. EP was evaluated by CT scan, resulting in a dichotomous label of progression. A 3D Volume of Interest (VOI) was placed over the primary tumour,

manually delineated. Three families of hand-crafted features were extracted from the VOIs of each patient's images, from both CT and PET acquisitions, thus quantifying grey intensity and tissue texture. Statistical features consisted of the moments up to the fourth-order of the first-order image histogram, i.e., the mean, the standard deviation, the skewness and the kurtosis. Texture features were derived from the 3D gray-level co-occurrence matrix (GLCM) and from the Local Binary Patterns-TOP (LBP-TOP). The final dataset was then created by adding clinical data from each patient. The predictive pipeline consisted of a feature selection phase followed by a sequence of two cascading decision trees in which the second used the predictions of the first as additional features for sample prediction. In the training phase, this model optimised the binarization threshold for classification to be applied later in the testing phase. The whole system follows a ten fold cross-validation approach. The quality of the proposed model was appraised by means of receiver operating characteristics (ROC) and areas under the ROC curve (AUC).

Results: Given each 3D VOI in the images, we computed the radiomics features, taking into consideration 12 statistical features, 230 textural features (182 GLCM, 48 LBP-TOP) extracted from the images, and adding 15 clinical features. We defined the final performance. To the best of our knowledge, this is the first study for feasibility and hypothesis generation of a radiomic strategy to predict early progression in LAPC and our data suggests that a specific signature can be identified (AUC 0.83; prediction accuracy 80.7%).

Conclusions: This model based on clinical and PET/CT radiomic features assessed before treatment can predict the early progression in LAPC patients. It could be a promising pre-treatment, non-invasive, approach that can assist physicians in evaluating the risk of early progression in patients individually, and thus achieving a personalized treatment and better clinical outcomes. The identification of the external validation dataset is actually ongoing.

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P-67 Comparison of the malignant predictors in intrahepatic and extrahepatic intraductal papillary neoplasm of bile duct

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Background: Intraductal papillary neoplasm of the bile duct (IPNB) is a precancerous lesion of cholangiocarcinoma, for which surgical resection is the most effective treatment. We evaluated the predictors of malignancy in IPNB according to anatomical location and the prognosis without surgery.

Methods: A total of 196 IPNB patients who underwent pathologic confirmation by surgical resection or endoscopic retrograde cholangiography or percutaneous transhepatic cholangioscopic biopsy were included. Clinicopathological findings of IPNB with invasive carcinoma or mucosal dysplasia were analyzed according to anatomical location.

Results: Of the 116 patients with intrahepatic IPNB (I-IPNB) and 80 patients with extrahepatic IPNB (E-IPNB), 62 (53.4%) and 61 (76.3%) were diagnosed with invasive carcinoma, respectively. Multivariate analysis revealed that mural nodule $>$ 12 mm ($p=0.043$) in I-IPNB and enhancement of mural nodule ($p=0.044$) in E-IPNB were predictive factors for malignancy. Pathology discrepancy before and after surgery, IPNB has 71.2% of sensitivity and 82.3% of specificity. In the non-surgical IPNB group, composed of nine I-IPNB and seven E-IPNB, 43.7% progressed to IPNB with invasive carcinoma within 876 days.

Conclusions: E-IPNB has a higher rate of malignancy than I-IPNB. The predictive factor for malignancy is mural nodule $>$ 12 mm in I-IPNB and mural nodule enhancement in E-IPNB.

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P-68 Regorafenib monotherapy as second-line treatment of patients with RAS-mutant advanced colorectal cancer (STREAM): An academic, multicenter, single-arm, two-stage, phase 2 study

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Background: Therapeutic options after first-line treatment in patients with RAS mutant metastatic colorectal cancer (mCRC) are limited by poor clinical outcomes and lack of activity of anti-epidermal growth factor receptor drugs. Maintaining angiogenesis inhibition and switching the chemotherapy backbone represents the current therapeutic strategy of second-line mCRC therapy. Regorafenib, an oral broad-spectrum multikinase inhibitor targeting angiogenesis, has been shown to prolong overall survival (OS) and is approved after progression on chemotherapy.

Methods: STREAM trial was an academic, multicentric, phase 2, single-arm, Simon's two-stage design, aimed to establish the activity of regorafenib, defined as the rate of patients alive and progression free after 6months from study entry (6mo-PFS) in patients with RAS mutant mCRC, after progression on fluoropyrimidine, oxaliplatin and bevacizumab.Setting α and β errors at 0.10, defining a 6mo-PFS rate of 30% as p0 and 50% as p1, to consider the study positive $\geqq$8 patients without progression at 6mo, were needed in the first stage (N=22) and $\geqq$18 in the overall population (N=46). Regorafenib was administered orally at the approved schedule of 160mg day1-21 q28. Secondary endpoints were the evaluation of toxicity, objective response rate (ORR), progression-free survival (PFS), OS. Early metabolic response assessed by PET-CT scan after 2 weeks of treatment was an exploratory endpoint. Translational analyses are ongoing and will be presented at a later stage.

Results: Between November 2015, and December 2020, 46 patients were enrolled. median age was 67ys; 80.4% had ECOG performance status 0, 32.6% single organ involvement, 26% lung-limited disease. The study did not meet its predefined primary endpoint. Eight of the first 22 patients and 14 in the overall population were 6mo-PFS, as compared to the 18 required by the study protocol. At a median follow-up of 50.2 months (95%CI=24.2-56.3), ORR was 10.9%, Disease Control Rate (DCR) was 54.6%, median (m)PFS was 3.6mo (95%CI=1.9-6.7).Despite the short mPFS, regorafenib did not preclude a subsequent treatment: mPFS2 (from study entry to progression to subsequent treatment line) was 13.3mo (95%CI=8.4-19.7) and mOS was 18.9mo (95%CI=10.3-35.3). No unexpected toxicity was reported. Grade$\geq$3 AEs occurred in 18 patients(39.1%), mostly hand foot syndrome(13%), fatigue and bilirubin increase(6.5%). Early metabolic response with PET/CT was not associated with ORR, mPFS and mOS. Baseline metabolic assessment, not predictive of ORR and mPFS, was significantly associated with mOS. A subgroup of patients, with single organ involvement, mostly lung-limited disease, low baseline PET-CT parameters, a low rate of early progression in first line ($<$6months=21.4%) and a long mPFS2 (23.3mo 95%CI=13.3-39.9), reported a long disease control with regorafenib: ORR=35.7%; mPFS=10.2mo (95%CI =8.6-13.5), mOS=38.8mo (95%CI=23.9-NR). Conversely, patients with higher radiological and metabolic burden of disease, higher rate of early progression in first-line ($<$6months=56.3%) and a shorter mPFS2 (8.4mo CI95%=6.1-13.3), reported unfavorable outcomes.

Conclusions: Despite the study did not meet its primary endpoint, treatment with regorafenib had no unexpected toxicity and did not preclude efficacy of subsequent treatments. A subgroup of patients characterized by good prognostic features (limited disease, lung metastasis and low metabolic burden) had clinical benefit with regorafenib. Appropriate patients selection might guide the clinical development of regorafenib in an earlier setting, ensuring a chemotherapy-free interval in the treatment sequence.

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