P-61 Impacts of salvage chemotherapy after nivolumab therapy (NIVO): A REVIVE substudy

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Background: The primary endpoints met in the REVIVE study have been previously reported, demonstrating the chemotherapeutic efficacy after the progression on NIVO therapy in patients with advanced gastric cancer (AGC). Therefore, the current study evaluated the survival from the NIVO therapy initiation in all registered participants of the REVIVE trial.

Methods: The REVIVE trial was a prospective, multicenter, observational study evaluating the efficacy and safety of chemotherapy for NIVO-refractory or NIVO-intolerant patients with AGC (UMIN000032182). We primarily register the patients who underwent NIVO therapy as primary registration, and the patients formally were registered as formal registration. The previously reported main study analyzed data of formally registered patients who underwent chemotherapy with irinotecan, trifluridine/tipiracil hydrochloride, or oxaliplatin combination regimens. In this study, patients who discontinued NIVO therapy for any reason at data cutoff among primarily registered patients were selected. The survival of patients who received the best supportive care (cohort A) was compared to those included in the main study (cohort B).

Results: Of 395 primarily registered patients, 108 patients in cohort A and 199 patients in cohort B were included, respectively. Those receiving other chemotherapeutic regimens (N = 47) or continuing NIVO therapy (N = 38) were excluded. Median overall survival (OS) and time to treatment failure (TTF) were 9.3 (95% confidence interval [CI], 8.3—10.2) and 1.8 (95%CI, 1.6—2.2) months at 234 and 307 events, respectively, from the initiation of NIVO therapy in the whole population. The objective response rate (ORR) and disease control rate (DCR) were 9.1% and 43.0%, respectively. Patients in cohort B had significantly better prognosis in OS (median, 12.2 vs. 4.8 months; hazards ratio [HR], 0.43 [95%CI 0.34—0.57]; $p < 0.01$). However, the difference in short-term efficacies was not observed: ORR, 6.5% vs. 10.6%; DCR, 38.0% vs. 45.7%; and median TTF, 1.9 vs. 1.8 months (HR, 1.06 [95%CI 0.84—1.35]; $p = 0.62$) (cohort A vs. B). The post-progression survival (PPS) from the date of NIVO therapy discontinuation was significantly better in cohort B than in cohort A (median PPS, 8.1 vs. 1.9 months; HR, 0.22 [95%CI 0.17—0.30]; $p < 0.01$). The proportion of patients who received the best supportive care after NIVO therapy was similar, regardless of the effectiveness of NIVO therapy (transition rate: 25% in complete response or partial response [responders, N = 28] and 33% in stable or progressive disease [non-responders, N = 267]). The difference of OS from the initiation of NIVO therapy in responders was not observed between cohorts A and B; however, the OS of cohort B in non-responders was significantly longer than that of cohort A (median OS, 10.8 vs. 4.8 months; HR, 0.60 [95%CI 0.52—0.69]; $p < 0.01$).

Conclusions: Salvage chemotherapy as much as possible after NIVO therapy could improve the AGC prognosis.

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P-62 Characterization and management of cholangiocarcinoma in a tertiary hospital with a high volume of patients

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Background: The objective of this study is to evaluate the epidemiological characteristics, potential risk factors and local/systemic treatments in a tertiary care hospital with a high volume of patients.

Methods: Unicentric retrospective study; The patients were seen in consultation from January 2020 to January 2022, this being the end date of follow-up. Demographic variables related to tumor, treatment, and death were also collected. For descriptive statistics, percentages with frecuencies and medians were used. Survival was estimated using Kaplan-Meier plots. The SPSS 20.0 program was used for stadistical analysis.

Results: Data from a total of 44 patients were collected. 70.7% men and 29.3% women. All Caucasian. The highest incidence peak was in the decade between 50 and 60 years (59%), with the rest of the cases in the decade between 40 and 50 years. There was no significant history of prior smoking, alcohol consumption, prior pancreatitis, history of cholangistitis, or heavy metal exposure. However, in our series two personal antecedents stand out: 1) 48% of the patients were type 2 diabetics and 23% type 1 diabetics and 2) 61.3% of the patients prior to diagnosis had periodontal disease. 90.2% of the histology was adenocarcinoma, 53.7% of the tumors being resectable, the rest presenting advanced disease. In the case of local surgery, partial hepatectomy with lymphadenectomy was the most used (68%), capecitabine the adjuvant treatment of choice in operated patients (82.3%) and the treatment scheme for advanced disease Cisplatin in combination with Gemcitabine (82.9%), obtaining partial response in 54.5%, stabilization in 18.2% and disease progression in 27.3% in the first tumor evaluation performed. NGS was performed on 100% of the patients, finding potentially actionable mutations: KRAS G12C mutation in 2 patients, IDH mutation in 1 patient, and microsatellite instability in 2 patients. Regarding germline mutations, these were performed in 12 patients due to family history, finding mutations related to the ATM gene (2), BRCA2 (1) and p53 (1) in 4 of them.

Conclusions: The oncological results observed in our series are comparable to those described in the literature. Its etiology is uncertain, advancing the age of diagnosis and requiring the study of more predictive and prognostic factors. Our study reaffirms the role of NGS in this disease, with the intention of increasing future treatment options in this pathology.

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P-63 Efficacy, safety and prognostic subgroups for outcome with regorafenib in patients with refractory metastatic colorectal cancer in the real-world setting: The CORE study

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Background: CORRECT trial has shown a survival benefit for regorafenib over placebo in patients with metastatic colorectal cancer (mCRC) that progressed after standard therapies. We evaluated survival, safety and prognostic subgroups in patients treated with regorafenib in a real-life setting.

Methods: Retrospective, multicenter, observational study of patients (pts) with mCRC treated with Regorafenib (REG) after failure to standard therapies as part of routine clinical practice at 7 hospitals from the Galician Research Group on Digestive Tumors (GITuD).

Results: We recorded 130 pts treated with REG between September 2013 to December 2019. Median age was 63 years (range 27-79), 94.6% ECOG PS0-1, 55.4% RASmt and 1.5% BRAFmt, 18% time since initial diagnosis 3 metastatic locations and 75% liver metastases. Prior therapy included a median of 3 lines of treatment (range

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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Legal entity responsible for the study: The author.

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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,