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Abstracts

Note: Abstract suffixes

"PD" indicates a submitted abstract accepted for poster discussion

"P" indicates a submitted abstract accepted for poster presentation

POSTERS

P-1 LINC00184 promotes the stemness and chemoresistance of gastric cancer by interacting with YAP and by promoting exosomes-mediated macrophage M2 polarization

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Background: Long non-coding RNAs (lncRNAs) are involved in the pathology of various tumors, including gastric cancer (GC). The crosstalk between tumor-associated macrophages (TAMs) and cancer cells in the tumor microenvironment promotes tumor development and confers chemoresistance, yet the contribution of lncRNA-mediated crosstalk between TAMs and GC cells to tumor chemoresistance is not well understood. In this study, we further investigated the underlying tumor-promoting roles of LINC00184 and as molecular mediators involved in these processes.

Methods: GC cells and 165 GC tissue samples were involved in this study. Small interfering RNA (siRNA) sequences were used to knock down LINC00184. Cell apoptosis was measured by flow cytometry. SGC-7901 cells with H19 stably knocked down were used to establish a xenograft model. The indicated protein levels in xenograft tumor tissues were confirmed by immunohistochemistry assay, and cell apoptosis was analyzed by TUNEL apoptosis assay. RNA-FISH and immunofluorescence assays were performed to assess the expression of LINC00184 in tumor stroma and cancer nests. The AldeRed ALDH detection assay was performed to detect intracellular aldehyde dehydrogenase (ALDH) enzyme activity. Isolated exosomes were identified by transmission electron microscopy, nanoparticle tracking and Western blotting.

Results: LINC00184 was significantly up-regulated in GC tissues. And the LINC00184 overexpression was associated with advanced TNM stages and poor prognosis. Moreover, LINC00184 was associated with the stemness of GC stem cells in GC specimens. LINC00184 promoted the stemness of GC and the chemoresistance of GC cells in vitro and in vivo. Mechanistically, LINC00184 regulated the Hippo pathway via interacting with YAP to prevent its phosphorylation. Furthermore, GC cell-derived exosomes transported LINC00184 into macrophages which mediate macrophage M2 polarization, thereby, in turn, promoting stemness and chemoresistance of GC cells. In addition, exosomal LINC00184 levels in blood plasma turned out to be higher in treatment-naive GC patients but lower after tumor resection. Compared to traditional tumor markers (CEA, CA199), exosomal LINC00184 in GC plasma displayed a better diagnostic value.

Conclusion: LINC00184 promoted the stemness and chemoresistance of GC by regulated Hippo pathway. Exosomal LINC00184 induced macrophage M2 polarization. Our results suggested that overexpression of LINC00184 was involved in the formation of tumor microenvironment and contributed to tumor chemoresistance.

Legal entity responsible for the study: The author.

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P-2 An update on the trends for hepatic cancer subtypes in the Philippines, 2003-2012: A population-based study

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Background: Liver cancer (LC) is currently the sixth most common type of cancer with an increasing incidence in the Philippines. LC incidence rates vary substantially by gender and etiology, which are usually linked to environmental, dietary or lifestyle factors. The study aimed to analyze time trends in LC incidence in the Philippines over a 10-year period. There is no published report regarding trends of LC incidence by histological subtype in the Philippines. Herein, we provide model-based estimates of limited time LC cases by histological subtype from years 2003-2012.

Methods: Data for calculating LC incidence rates in 2003-2012 were obtained from the nationwide population-based Department of Health Rizal Cancer Registry. Joinpoint regression was used to analyze trends and estimate annual percentage change (APC) with 95% confidence intervals (CI) on LC incidence by histological subtype, time period, sex, geographical location, calculated incidence counts, and rates per 100,000 person-years. The 2000-2015 population data used in calculating ASR of LC incidence were taken from the Philippines Statistics Authority (PSA), and each annual population from 2003 - 2012 was estimated using exponential function by extrapolation.

Results: LC incidence showed increasing average annual rates in the past 10 years, among observed rates overall (10.94), men (15.53) and women (6.39). Among LC histological subtypes in carcinoma, hepatocellular contributed the highest rates in men (15.19) and women (5.23), followed by unspecified carcinoma in men (1.73) and women (0.78). Incidence trend declined in both sexes and increased thereafter, in men in 2007 (APC: 16.82, 95% CI: -5.70; 44.80) and women in 2008 (APC: 19.95, 95% CI: -21.7; 83.7). The highest increase in average annual percentage change (AAPC) among LC histological subtypes was observed to be hepatoblastoma in men (AAPC: 4.91, 95% CI: -8.90; 20.80) and women (AAPC: 16.33, 95% CI: -0.60; 34.50). Cholangiocarcinoma also showed an increasing AAPC, in men (AAPC: 3.68, 95% CI: -7.90; 16.70) and women (AAPC: 0.15, 95% CI: -14.1; 16.7). From the cohort 2003-2007 to cohort 2008-2012, unspecified malignant neoplasm eventually increased the average annual rates by threefold, in men (4.10 to 12.05), and women (1.96 to 4.85).

Conclusion: The study revealed that from 2003-2012, divergent LC trends by gender and histologic subtype were consistently increased. Male LC incidence annual rates were observably higher compared with females. Among LC histological subtypes, an increase in incidence was observed in hepatocellular carcinoma for the past 10-year period. Targeted screening and treatment in hepatitis B virus (HBV) and hepatitis C virus (HCV), treatment of diabetes, and primary prevention of obesity will be the possible solutions in reducing the increasing LC incidence.

Acknowledgement: I would like to express my sincere gratitude to my advisor Prof. Jin Kyoung Oh for the continuous support of my M.P.H journey and related research, for her patience, motivation, and immense knowledge. Her guidance helped me in all the time of research and writing of this study. Besides my advisor, I would like to thank the rest of my co-author Mr. Jayson Pasaol, M.P.H for his insightful comments and encouragement, but also for the contributions which incented me to polish my research from various perspectives. My sincere thanks also goes to Dr. Edmund Concha, Dr. Rica Mirasol Lumague, ma'am Gehan Clerigo, and the rest of research committee staff of Rizal Cancer Registry who provided me an opportunity to learn new research ideas and who gave access to the Cancer Registry office and research facilities in the hospitals. Without their precious support, it would not be possible to conduct this research.

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P-3 Features of metabolic profiles of blood serum and erythrocyte membranes associated with metastasis in colorectal cancer

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Background: Colorectal cancer (CRC) is the third most common cancer worldwide. Approximately 56% of patients with CRC die from their cancer. Development of metastasis is a concern for patients and clinicians alike as metastasis may be fatal, causing mass-effect and meddling with homeostasis. The aim of the work was to determine if the serum metabolomic profiles and erythrocyte fatty acid profiles of CRC patients could be used to discriminate locoregional CRC from metastatic CRC and to identify patients with liver metastases.

Methods: Sera and erythrocyte membranes of 56 patients (63,2+9,4 years old) with colorectal adenocarcinoma were analyzed by GC-MS spectrometry (GC/MS system triple quad Agilent 7000B [USA]). The metabolomic profiles were compared between the following groups: locoregional CRC (n = 20), liver metastases (n = 19) and extrahepatic metastases (n = 17). The control group consisted of 35 healthy people of comparable age.

Results: By GC-MS spectroscopy, 37 serum metabolites were detected to be differentially abundant between patients with locoregional CRC and the group with liver metastases (the levels of ribose, galactose, mannose, and glutamine were increased

and those of pentacosane, idose, and pyroglutamate were decreased in patients with locoregional CRC compared with those with liver metastases (p< 0,02-0,05). Significantly lower values of erythrocyte C14:0 (p=0.016), C16:0 (p=0.002), C17:0 (p=0.02), C16:1;7 (p=0.03) and higher C18:3 (p< 0.001), C20:3;n-6 (p=0.02), C22:4;n-6 (p< 0.01), n-6/n-3 (p=0.042) as compared with locoregional CRC, was noted for patients with liver metastases. ROC curve was plotted for the panel of metabolites to demonstrate the ability to predict the presence of liver metastases or locoregional CRC. The area under the ROC curve was 0.90 with a sensitivity of 0.79 and a specificity of 0.89. We found the list of metabolites capable of identifying differences between patients with liver metastases and extrahepatic metastases: serum levels of myristic acid (C14:0), linoleic acid (C18:2;n-6), phenylalanine, threonine were lower and glutamine, glucose, butanoic acid, histidine, and mannose were more abundant in extrahepatic metastases in comparison with patients with liver metastases (p< 0,01-0,05). In erythrocyte membranes the decreased content of C12:0, C18:1;t9, C16:0/C18:2; n-6 and increased levels of C20:5;n-3, C20:4;n-6, C22:4;n-6, C22:5;n-3, (C20:3n-6 + C20:4n-6)/C18:2n-6 allowed us to distinguish extrahepatic from liver metastases (AUC 0.86, sensitivity 0.77, specificity 0.90). The identified changes in the serum and erythrocyte metabolites, probably reflect differences in tumor biology or alterations in the host response to the tumor or a combination of both. Metastatic disease is biologically distinct from cancer that remains confined in the tissue of origin. The metabolic or inflammatory response of surrounding tissues may differ between colon, liver and other metastatic sites.

Conclusion: Significant changes in serum and erythrocyte metabolites associated with the various localization of CRC metastases were found. The diagnostic panels we created should be considered promising for detecting occult metastases and selecting patients for surgical or chemotherapeutic treatment.

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P-4 The relationship between quality of life, adverse events, and treatment efficacy in treatment with first-line chemotherapy plus cetuximab for unresectable metastatic colorectal cancer: Results of phase II QUACK trial

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Background: A prospective trial has not been performed to investigate associations between quality of life (QOL), adverse events, and overall survival (OS) in the first-line treatment with cetuximab plus standard chemotherapy for advanced/metastatic colorectal cancer (mCRC).

Methods: Health-related QOL (HRQOL) including the status of the patient's tumor-related symptoms was prospectively evaluated using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTC QLQ-C30).

Results: One hundred and forty mCRC patients were analyzed in this study. An early skin reaction with a grade $\geq$ 2 at eight weeks was significantly associated with a favorable OS compared with a grade of $\leqq$1 (HR, 0.50; 95% CI, 0.24—0.95; P = .035) and had no clinical impact on HRQOL. The presence of baseline tumor-related symptoms was significantly associated with a worse OS compared to the absence of symptoms (HR, 2.49; 95% CI, 1.37—4.62; P = .003). Patients symptomatic at baseline who responded to treatment had improved HRQOL compared to non-responding patients. The asymptomatic responders had favorable outcomes compared with the symptomatic non-responders (two-year OS rates, 83.6% vs. 35.9%), while the symptomatic responders had similar outcomes to the asymptomatic non-responders (two-year OS rates, 64.9% vs. 63.0%). The patient toxicity profiles and objective response rates were similar irrespective of the baseline symptom burden.

Conclusion: Severe early skin reactions predict favorable OS for patients treated with cetuximab plus chemotherapy without impairing QOL. The presence of baseline symptoms was associated with worse OS but not with impaired treatment efficacy or more frequent AEs in the mCRC patients who were treated with cetuximab plus chemotherapy.

Acknowledgement: The authors thank the patients who participated in the QUACK study as well as their families; the QUACK investigators, nurses, and other medical staff who contributed to the study; the clinical research coordinators (Chikako Ikeda and Mai Hatta); and the Efficacy and Safety Monitoring Committee, Dr. Hirofumi Fujii (Jichi Medical University Hospital) and Dr. Atsushi Sato (Hirosaki University Graduate School of Medicine).

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Disclosure: None provided.

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P-5 Economic burden of HCC and the need of innovative treatments

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Background: HCC in low middle-income countries, such as Egypt, with a prevalence of HCV that represents 5% to 7% of the total population, contributes to the sixth leading cause of deaths. When we link this information with African data, for example, Egypt accounts for approximately half of the data related to HCC over the last two decades. A substantial increase (from 4.0% to 7.2%) in the proportion of chronic liver disease in Egyptian patients with HCC was observed. This increase raises questions, including the following: -How healthcare policymakers afford treatment for a high number of patients? -What is the impact of these treatments on disease burden? -What are the impacts on patient quality of life? The main objective of this study was to evaluate the impact of immunotherapy on the disease burden of HCC versus standard of care in Egyptian patients over 4 years to maximize health gains for the patients while ensuring the most efficient use of the finite resources available to the Egyptian Ministry of Health.

Methods: A cost-effectiveness analysis was conducted from the payer perspective using a Markov chain simulation model, which is a hypothetical cohort model to conform to real-world practice management of advanced HCC in Egypt. A length of 4 years was selected to reflect the consequences of decisions. Transition probabilities from "first line until progression" to "best supportive care" and "death" clinical data were collected through network meta-analysis for atezolizumab + bevacizumab versus standard of care. The health outcomes of the two treatment arms were measured by quality-adjusted life years (QALYs). The value of lost productivity using Egyptian estimates for the value of a statistical life year (VSLY). Several methods were employed to reach an average. Value for a QALY: the SF-36 questionnaire was conducted to measure quality of life. Treatment policy analysis was conducted comparing payer policies. Economic, clinical, quality of life was the scope of analysis. Quality of life data were incorporated into the model to make adjusted results. To test the stability of our results to variation in the estimates of the input model parameters, we performed various one-dimensional sensitivity analyses. The time horizon was estimated as 4 years.

Results: During the time horizon, total QALY gained for immunotherapy was 3 .1 versus 2 QALY gained for standard of care, with 1 QALY difference.

Conclusion: The results conclude that introducing immunotherapy might have a positive impact on the disease burden of HCC and quality of life. Healthcare policymakers and treatment suppliers should consider developing innovative reimbursement polices and prioritization strategies based on multidisciplinary criteria for reducing the economic burden of those treatments.

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P-6 Perioperative FLOT: Tolerability, pathological response rates, and the role of adjuvant phase

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Background: The prognosis of locally advanced gastric cancer is poor, even if all known surgical interventions are done. To improve survival, different treatment strategies adjunctive to surgery have been developed. Since the FLOT4-AIO trial was announced, perioperative FLOT (periop-FLOT) is the new standard of care for locally advanced gastric and gastroesophageal junction (LAG/GEJ) cancers. As trials are conducted on well-selected patients, daily clinical practices and the results may differ. We aimed to analyze the tolerability, pathological response rate, and the role of an adjuvant phase of periop-FLOT.

Methods: We performed a retrospective study of LAG/GEJ cancers undergoing periop-FLOT during the last two years. The FLOT regimen was applied as in the FLOT4-AIO trial. Pathological tumor regression grade was done according to Modified Ryan Scheme (TRG0: complete response, TRG1: near-complete response, TRG2: partial response, TRG3: poor/no response) and DFS analysis was estimated by Kaplan-Meier method with SPSS.

Results: Fifty-nine pts with LAG/GEJ cancers commenced on periop-FLOT. Demographics: male n=43 (73%), median age 63 (range;34-85), performance status; PS0 n=29 (49%), PS1 n=20 (34%), PS2 n=10 (17%). Tumor location gastric n=38 (64%), GEJ n=21 (36%). All of the pts were cT3/T4, and 55 (93%) were cN+. 53 pts (90%) received ≥4 cycles of neoadj-FLOT. 45 (76%) pts underwent curative surgery, and 40 (89%) of them had D1 lymphadenectomy. R0 resection was achieved in 44 pts (75%). TRG0 n=5 (8%), TRG1 n=9 (15%), TRG2 n=5 (8%) and TRG3 n=26 (44%) were reached, and 22 pts (37%) were detected as ypN0. 30 pts (51%) started adj-FLOT and 26 pts (44%) completed all cycles. The median follow-up was 11 months (range 4—27), with a median DFS of 21.8 months (95% CI 18.9—24.9), and 9 of 45 pts (20%) relapsed. Significant differences in DFS between pts who received adj-FLOT (25.4 months, 95% CI 23.1—27) compared with no-adjuvant (13.6 months, 95% CI 10.2—16.9) were found (p=0.001), and also among ypN0 (26 months, 95% CI 24-28.1) compared with ypN+ (15.6 months, 95% CI 12.4-18.9) (p=0.006). No effect of TRG's on DFS were detected (p>0,05). The median OS not reached. 56 pts (95%) had at least one any grade toxicity. Dose reduction was performed in 3 pts (5%). The most common grade 3/4 toxicities were neutropenia (n=11;19%) and neutropenic fever (n=7;12%) although we prescribed primary prophylactic G-CSF. Two toxic deaths occurred (3%) during the neoadjuvant period. Compared with the FLOT4-AIO trial, although our pts had a higher PS, they had similar rates of dose reduction (5% vs 6%), completing neoadjuvant (90% vs 90%) and adjuvant (44% vs 46%) treatments. R0 (75% vs 85%) and D2 (11% vs 92%) resection, ypN0 (37% vs 49%) and pCR rates (8% vs 16%) were lower in our pts, due to higher initial clinical stages.

Conclusion: This is an interim analysis of our experience. In our study, periop-FLOT was well tolerated although the pts had a higher PS. Due to the high initial clinical stages, pathological response rates were low. Besides, pts that received adjuvant treatment had increased DFS. The role of adjuvant phase of perioperative treatment is important in pts with higher initial clinical stages and sub-optimal pathological regression.

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P-7 Induction chemotherapy in locally advanced rectal cancer: Retrospective report of efficacy and safety in an Argentinean university institution, a feasibility perspective

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Background: Trimodality treatment achieved a marked reduction in local recurrence rates (LRR) in locally advanced rectal cancer (LARC), however distant relapse rate represents the leading cause of death in this population. Evidence from recent investigations suggests that neoadjuvant chemotherapy (NACT) has the potential to optimize compliance and results without compromising a patient's ability to undergo planned chemoradiotherapy (CRT) or increase the risk of surgical complications. Here we report the viability of the implementation of NACT in LARC in a public university institution in terms of efficacy and tolerability.

Methods: We performed a retrospective and descriptive analysis of all the patients with LARC (stage III-IVa), ECOG 0-1, recommended by a multidisciplinary colorectal cancer tumor board (MDT) to receive NACT using oxaliplatin plus capecitabine (CapOx) regimen in our institution followed by NA-CRT and TME. Information was collected from clinical charts. All patients' personal information was kept confidential.

Results: Twenty-nine patients were treated with NACT from 2013 to 2019. Median age was 61 years (28 to 73 y); 3 patients (10%) were clinical stage IVa and 26 (90%) stage III. The majority of tumors were located in the middle rectum (52% n: 15), followed by lower (38% n: 11) and upper (10% n: 3) rectum. Twenty-three patients (80%) had N2 disease. The median of CapOx cycles received was 3 (range 2-4) followed by RT (median dose 50 Gy; range 45-50.4 Gy) with a 100% compliance rate. Toxicity: 75% (n: 22) experienced G1-2 adverse events (AEs); haematological in 51%, gastrointestinal in 58% and neuropathy in 58% with no dose reduction required. No G3-4 AEs were reported.

Median time from finalization of NA-CRT to surgery (n: 27) was 15 weeks (range 9-53 weeks). Radical surgery (R0) was obtained in 100%. Two patients underwent Watch-and-Wait protocol. Six patients (22%) had minor complications (Clavien Dindo I-II).

A complete response was achieved in 24% and nodal downstaging to N0 disease ocurred in 80% of patients. Within clinical N2 patients, 82% downstaged to N0. The probability to achieve a complete response or N0 was not related to tumor localization (Fisher exact test).

With a median follow up of 34 m (10-82m), recurrence was observed in 27% of patients (13% distant relapse). Median relapse-free survival was 27 months. Only two deaths occurred in the distant relapsed patient subgroup.

Conclusion: Our cohort of patients had excellent NACT compliance without compromising the ability to undergo planned treatments. pCR and nodal downstaging to N0 rates was comparable to previous reports.

NACT approach is a feasible option in terms of tolerability and results. The delays observed in treatment initiation were due to social reasons (coverage or insurance), one of the main barriers of access in our health system.

Further prospective validation of this approach is needed to improve the current standard of care.

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P-8 Risk factors of severe gastric dysplasia and gastric cancer in rural areas of China among individuals at high-risk: A population-based, cross-sectional study

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Background: The risk factors for gastric cancer and precursor lesions in rural areas of China among individuals at high-risk were unclear. The aim of this study was to explore associations between sociodemographic characteristics, history of the disease and the risk of severe gastric dysplasia and above among high-risk residents living in rural areas.

Methods: Data were extracted from a multi-center randomised controlled trial (RCT) conducted between 2015 and 2017. People from rural areas who underwent endoscopy were regarded as eligible subjects. Histological categories were classified into four types, including normal, gastritis, intestinal metaplasia and severe dysplasia and above, based on the World Health Organization standard, fourth edition. Multivariate and multinomial analyses were performed to identify potential risk factors, adjusted for age, gender, educational level, ethnicity, household income, smoking, and alcohol consumption.

Results: A total of 271 (0.83%) cases and 32325 (99.17%) controls were included in the final analyses. 70.85% of the 271 patients were males. Compared to those drinking tap water after being processed, water from impure sources was associated with the increased risk of severe gastric dysplasia and above (adjusted OR for lakes and rivers: 1.80, 95% CI:1.07-3.04; adjusted OR for deep water and springs: 1.53, 95% CI: 1.09-2.14). Eating fruits every day was associated with less risk of severe gastric dysplasia and gastric cancer compared to those eating fruits often (adjusted OR: 1.68, 95% CI: 0.88-3.24) or occasionally (adjusted OR: 1.89, 95% CI: 1.00-3.60). Consumption of pickled food and hard food were related to increased risk of severe gastric dysplasia and gastric cancer. Significant positive association with severe dysplasia and above was observed for current (adjusted OR: 1.16, 95% CI: 0.85-1.58) and ever smokers (95% CI: 2.62, 95% CI: 1.65-4.16), compared to non-smokers. Participants who received education were observed to be lower risk, in gastritis, intestinal metaplasia or severe gastric dysplasia and gastric cancer, compared with those who were never had formal education. No associations were observed yet between alcohol consumption, having atrophic gastritis and severe gastric dysplasia and gastric cancer.

Conclusion: Male sex, no formal education, consumption of pickled and hard food, smoking and drinking impure water were all associated with the increased risk of severe gastric dysplasia and above in this high-risk population in rural areas. The findings offer valuable information to identify high-risk individuals.

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P-9 A randomized study of panitumumab plus mFOLFOX6 compared with bevacizumab plus mFOLFOX6 as first-line treatment for unresectable metastatic colorectal cancer

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Background: The efficacy of panitumumab and bevacizumab in combination with chemotherapy has been shown in the treatment of metastatic colorectal cancers. However, the difference between these two targeted therapies remains to be confirmed in the situation of nonresectable metastases. The selection of patients based on prognostic and predictive criteria that are clinical, biological and molecular could guide the first-line therapeutic choice in nonresectable metastatic colorectal cancers.

Methods: In this observational, randomised and prospective study, 190 patients over the age of 18, with histologically-proven colorectal cancer and in a situation of nonresectable metastases, with a performance status ECOG $\leq$2, no organ dysfunction and no contraindications to the study drugs were included. Patients were randomized (random blocks draw) to receive panitumumab plus FOLFOX6m or bevacizumab plus FOLFOX6m. The primary objective was progression-free survival, analyzed for the intention to treat (ITT) with a median follow-up of 36 months in both arms.

Results: Our study was carried out between January 2016 and January 2019, 190 RAS-wild type nonresectable metastatic colorectal patients, were randomized to receive the panitumumab arm plus FOLFOX6m in 100 patients or the bevacizumab arm plus FOLFOX6m in 90 patients. 42 (42%) patients in the panitumumab arm achieved an early objective response compared to 22 (25.2%) patients in the bevacizumab arm; (HR 0.58, 95% CI 0.34-0.98; p=0.04). The median progression-free survival was 10 months (95% CI: 7.5-12.4) in the panitumumab arm and 10 months (95% CI: 7.03-12.9) in the bevacizumab arm (hazard ratio [HR] 1.01, 95% CI: 0.69- 1.46; p=0.94); the median overall survival was 18 months (95% CI 15.2-20.7) in the panitumumab arm compared to 18 months (95% CI 9.02-26.9) in the bevacizumab arm (HR 1.09, 95% CI 0.70-1.68; p=0.71). Conversion to liver metastasis surgery was observed in 15 (21%) patients of the panitumumab arm compared to 4 (6.2%) in the bevacizumab arm (HR 0.35, 95% CI 0.14-0.85; p=0.02). The safety profile was consistent with randomized clinical trials in both arms. The most common grade 3-4 side effects in both arms were the skin rash of 11% in the panitumumab arm vs 1% in the bevacizumab arm, intestinal obstruction (4 [4%] vs 5 [5.6%], high blood pressure (0% vs 5 [5.6%]), diarrhea (5 [5%] vs 5 [5.6%]), fatigue (4 [4%] vs 1[1%]), peripheral neuropathy (0 vs 5 [5.6%]).

Conclusion: Panitumumab plus FOLFOX6m on the front line significantly increased the objective response rate versus bevacizumab, without improving progression-free survival and overall survival in nonresectable metastatic colorectal cancer patients.

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P-10 Epidemiological and histopathological review of colorectal cancer in Tunisia

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Background: Colorectal cancer (CRC) is a major health concern worldwide. It is the third most common cancer with a higher incidence in North America, Australia, and northern and western Europe. In Tunisia, CRC is the most frequent digestive cancer. We aimed through this study to investigate the epidemiological, clinical and histopathological characteristics of colorectal cancer in Tunisian patients.

Methods: A retrospective cohort included patients diagnosed with CRC confirmed histologically and treated in the oncology department at the military hospital of Tunis from 2011 to 2018.

Results: 190 patients were included. Sex ratio was 2. Median age was 56 years. Rectum cancer was observed in 58.4% of cases. Colon cancers represented 41.6% (sigmoid cancers in 65.8%). Tumour size averaged 8 cm. CRC were mostly well-differentiated (57.9%), moderately differentiated in 34.8% and poorly differentiated in 7.3% of cases. All cases were adenocarcinoma. Mucinous component was found in 8 patients (4.2%). Perineural invasion was found in 48 patients (25.3%) and vascular invasion was found in 58 patients (30.5%). Localised and locally advanced colorectal cancers represented 53.7% cases. Metastasis was found in 46.3% of cases. The most frequent metastatic sites were liver (67%), distant lymph nodes (47.7%), peritoneum (37.5%) and lungs (28.4%). Adrenal metastasis was found in 1 patient (1.1%). Among 88 patients with known RAS mutation status (46.3%), 55 patients harboured RAS mutation and 33 patients had wild type RAS (37.5%). The microsatellite instability (MSI) testing was performed in 41% of patients. MSI was found in 53.8% of patients. 32.6 % of patients had radiotherapy. 53.6% of patients underwent surgery mostly in an emergency situation (60.7%). Overall survival (OS) was 71.5% at 5 years. Involvement of more than 3 regional lymph nodes metastasis (p=0.04), perineural invasion (p=0.028) and tumor size more than 4cm (p=0.032) were negative prognostic factors influencing the OS. No correlation was found between RAS mutations or MSI status with the OS (p=0.82).

Conclusion: Despite a relatively poor prognosis, advances have been made in the survival rates of colorectal cancers. The strengthening of screening and primary prevention measures are to be recommended.

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P-11 Impact of preoperative and postoperative variation of CEA in predicting nonmetastatic colorectal cancer recurrence

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Background: Carcinoembryonic antigen (CEA) is a complex glycoprotein produced by 90% of colorectal cancers (CRC). Preoperative CEA level is considered as a predictive factor of survival in CRC patients. However, the prognostic significance of elevated preoperative CEA that normalized after resection is unknown. We aim through this study to assess the role of variations of preoperative and postoperative CEA levels in predicting nonmetastatic CRC relapse.

Methods: We conducted a retrospective study including patients diagnosed with nonmetastatic CRC treated in the oncology department of the Military Hospital of Tunis from 2011 to 2018. Preoperative CEA levels, as well as postoperative CEA levels, were collected at 3 months, 6 months and 12 months after resection of primary cancer. Normal levels of CEA were defined as lower or equal to 5. Relapse-free survival (RFS) time was calculated from the date of surgery until the date of relapse, death, or last follow-up.

Results: A total of 152 patients diagnosed with CRC stage I to III were included. Sex ratio was 1.3. Median age was 67 years (20- 83 years). Patients were mainly diagnosed with stage III colorectal cancer (64.5%). 20.4% and 15.1% of patients had stage II and I CRC respectively. Preoperative CEA levels were high in 73% of cases. Postoperative CEA levels were normal in 55.2% of patients at 3 months, 49.3% of patients at 6 months and 65.1% at 12 months after resection of primary CRC. Patients with high preoperative CEA levels that normalized after surgery represented 81.9% (n=91). Median RFS was 3.5 years. Patients with normal preoperative CEA levels (n=41) had higher RFS time than patients with high preoperative CEA levels (45 vs 26 months; p=0.02). There was no difference in RFS between patients with high preoperative CEA levels that normalized after surgery and patients with normal preoperative CEA levels (47 vs 44 months; p=0.42). Elevated postoperative CEA levels were associated with a lower RFS compared with normalized postoperative CEA (14 vs 47 months, p=0.001).

Conclusion: Elevated postoperative CEA following resection of CRC predicted relapse. However, high preoperative CEA levels that normalized after CRC surgery was not associated with higher relapse.

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P-12 A descriptive analysis of patient characteristics from Russian internet postings focused on CRC (iPatient study)

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Background: As healthcare in general is gradually becoming more patient-centered, patients' perspectives on their disease, diagnosis, and treatments grow in relevance and significance. Recent advances in colorectal cancer (CRC) treatment have led to prolonged patient survival, measured in years even at the metastatic stage. That, together with a growing incidence, has resulted in an increased exposure of non-healthcare professionals to the problems related to cancer care and rehabilitation.

Methods: iPatient is a big-data, retrospective, observational study based on automatic web-scanning of social media, and patients' and physicians' message boards across the entire Russian Internet. Semantic analysis using a machine-learning approach and pattern-based rules of texts were carried out to identify and classify constructs related to CRC containing personal experience. A proprietary linguistic processor by Semantic Hub was used for data extraction from the unstructured texts. The main purpose of the study was to clarify the characteristics, treatment pathways, and unmet needs in Russian patients with CRC.

Results: In total, information on 2520 CRC patients was identified, coming from patients themselves in 56% of messages, and from caregivers in 44%. Of 1764 patients with specified gender, 57% (n=1005) were female. Of all patients with specified age (n=1058), 52% (n=550) were aged 51-70 years; patients older than 70 comprised only 20% (n=216) of population. Of patients with mentioned tumor localization, 87% (n=2180) had their tumor most commonly in colon (52%; n=1127), followed by rectum (44%; n=955). Of 1472 patients with specified tumor stage, 26% (n=383) were at stage III and 57% (n=839) at stage IV; 53% (n=440) of the latter had surgery. Of 1222 patients at stages III and IV, 73% (n=890) had the following metastases localizations: 68% (n=605) hepatic, 20% (n=178) nodal, and 16% (n=142) lung metastases; 45% (n=401) had 1 metastatic site, 34% (n=303) had 2 metastatic sites, 21% (n=187) had 3 or more sites. Overall, 30% (n=267) of metastatic patients were metastatic at the time of diagnosis. Time since the diagnosis of metastatic disease was specified for 146: <18 months for 51% of patients (n=74), ≥18 months for 49% of patients (n=72). Of 1048 patients without specified tumor stage, 75% (n=790) were mentioned as having metastases. Tumor mutation status (RAS, BRAF, MSI), ECOG performance status (PS), and defined concept of lines of therapy were almost never mentioned. Consequently, it was deemed impossible to properly analyze treatment sequences and therapy-related decision making.

Conclusion: The analyzed CRC patient population is characterized by a slight female predominance and a relatively young age. One-third of the patients were diagnosed at the metastatic stage. From the subset with mentioned number of metastatic sites, about half had low tumor burden (only 1 metastatic site). As for the duration of metastatic disease, almost half of those for whom it was specified had been metastatic for at least 18 months.

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P-13 Current and expected future profile changes of gastric and pancreatic cancer patients at presentation

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Background: Advanced stage at presentation is the main cause of the high mortality of pancreatic (PC) and gastric cancer (GC), while patient data analysis helps to arrange plans for early diagnosis, cancer prevention, and to decrease cancer-related mortality. We are investigating the current and future profile of GC and PC at the time of presentation, which is the main value affecting cancer patient mortality.

Methods: We collected the following data from patient files from 2010 to 2018 at the time of presentation at Nasser Institute Cancer Center (NICC): sex, age, residence, stage, and pathology. Using statistical methods, we analyzed current and future profiles of eligible patients with adequate data at presentation.

Results: Data from 919 patients were collected, GC = 522 (56.8%) more than PC, with males = 295 (56.5%) > females, more age >40 60 = 193 (37%) and age GC patients came from lower Egypt = 281(53.8%) and Cairo = 179(34.3%) and less from upper Egypt = 27(5.5%) while 35 (6.7%) were from outside Egypt. Adenocarcinoma was the most frequent pathology in GC: 403(77.2%), compared with the less frequent GIST 53(10.2%), NHL 53(10.2%) neuroendocrine 6(1.1%) and rare pathology 7(1.3 %). GC had more localized than metastatic disease = 339(64.9%) which was significantly higher than in PC (Odds ratio 2.60(95% CI: 1.95-3.45) P-Value while 137 (26.2%) were metastatic, 46(8.8%) were non-staged at presentation. PC: 397(43.2%) with 255(64.2%) was significantly higher in males than in the GC group: (Odds ratio 1.38(95% CI:1.05-1.80) P-value= 0.021) and significantly fewer in patients with age ≥ 60 at 152(38.3%) with P value < 0.001. Within the PC group, there were more patients with the age ≥40to≤59=230(57.2%) and fewer patients PC=187(47.1%) while localized cases=178(44.8%) non-staged=32(8.1%) with 380 (95.8%) adenocarcinoma, 9 (2.3%) neuroendocrine carcinoma and 8(2%) with rare pathology. From 2010 to 2018, each year there was a 2.83 and 2.52 unit increase in the rate of localized and metastatic GC, respectively. The increase in the number of localized patients was 63.7% attributed to years of diagnosis (P-value =0.011) and a 12.2% increase in localized cases of GC is expected from 2018 to 2030. There was a 0.064 and 3.70 unit increase in the rate of localized and metastatic PC, respectively from 2010 to 2018. The increase in the number of metastatic patients was 55.5%, attributed to changes from year to year (P-value =0.021), and by 2030 metastatic cases are expected to increase by 7 times. At the same time, there is no current or expected significant changes throughout years in other epidemiological values like age, sex, residence or pathology.

Conclusion: The current common profile of GC and PC at presentation is a male patient between 40 and 60 years old with localized GC or metastatic PC adenocarcinoma, and by 2030 changes will affect mainly the stage of both cancers by an increase in localized GC and metastatic PC.

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P-14 Dose escalated short-course radiotherapy in rectal cancers: Is this the way forward?

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Background: Locally advanced rectal cancer merits neoadjuvant treatment, either with chemoradiotherapy (CRT) or short-course radiotherapy (SCPRT), followed by total mesorectal excision (TME) with negative margins to avoid locoregional recurrences and improve survival. Pathological complete response (pCR) following radiotherapy correlates with better local control, disease-free survival, and overall survival. The non-inferiority of SCPRT to CRT is now accepted. However, strategies to improve pCR in SCPRT have not been established.

Methods: Between June 2018 to December 2019, patients with histologically proven rectal adenocarcinomas in mid-lower rectum, with clinical stage II and III planned for an open or laparoscopic abdominal surgery were recruited to receive dose-escalated short-course radiotherapy. The radiotherapy dose was 30 Gy in 6 daily fractions in one week (Monday to Saturday) delivered by 3D-CRT using an Elekta Synergy® linear accelerator with appropriate constraints to organs at risk, followed by two cycles of chemotherapy (oxaliplatin 130 mg/m^2 D1, capecitabine 1,000 mg/m^2 BD D1-D14 every 3 weeks for 2 cycles), and surgery at 6-8 weeks interval from completion of radiotherapy. Simon's two-stage phase-II design was used to calculate the sample size. Considering P0=0.10, P1=0.25, $\alpha = 0.05$, and $\beta = 0.20$, a total of 43 patients were planned to be included in this study. The primary endpoint was the pCR rate. The study protocol was approved by the institutional ethics committee.

Results: Forty-three patients were recruited in the study. The mean (SD) age was 43 (17) years, with 67.4% males and 32.6% females. Most tumours were moderately-differentiated adenocarcinoma (46.5%) located in the lower rectum (69.8%). The majority of patients had cT3 (83.7%) and node-positive (55.8%) disease. Overall, the most common clinical stage was III (55.8%). As per the 2017 ESMO risk group, 58.1% of tumours were graded as "Bad", 23.2% as "Advanced/Ugly", and 18.7% as "Intermediate". There were no treatment breaks during radiotherapy. Median (IQR) CEA at baseline was 4.8 (3.2-17.6) ng/ml, while median (IQR) CEA post neoadjuvant therapy was 3.5 (2.3-12.3) ng/ml. Prior to surgery, two patients had metastatic progression, two patients refused surgery, and one patient was deemed inoperable. For the intention-to-treat analysis, the mean (SD) time to surgery post-radiotherapy completion was 48 (6) days. Anterior resection was done in 51.1% of patients while 37.2% of patients underwent abdominoperineal resection (37.2%). Pathological complete response was seen in 8/43 patients (18.6%). Overall, 88.4% of patients had an R0 resection. Sphincter-preserving surgery was possible in 51.7% of patients, while the actual sphincter preservation rate was 10/30 (33.3%). Most patients had evidence of tumour downstaging on post-op histopathology (74.4%). Acute grade III/IV radiation-induced toxicities were recorded in five patients (11.6%).

Conclusion: Short-course radiotherapy with dose escalation can achieve higher pathological complete response rates than either standard-course CRT or SCPRT, with good patient compliance, and reduced overall treatment time in comparison to CRT. Differences in survival outcomes, if any, will be determined on long-term follow up. The strategy merits evaluation in a randomised phase III trial.

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P-15 Combined gastrectomies: Survival outcomes in patients with locally advanced gastric cancer

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Background: The survival of patients with locally advanced gastric cancer (GC) takes several months. Radical operations are extremely complex and remain the prerogative of several of the best abdominal surgeons of the world. The search for an optimal treatment plan for GC patients (GCP) with stage T3-4N0-2M0 was realized. I examined factors in terms of precise prediction of 5-year survival (5YS) of locally advanced GCP after complete (R0) combined gastrectomies (G).

Methods: I analyzed data of 244 consecutive GCP (age, 56.5±9.3 years; tumor size, 7±3 cm) radically operated and monitored from 1975-2020 (m=182, f=62; total gastrectomy=75, distal gastrectomy=66, proximal gastrectomy=103, combined G with resection of 1-7 adjacent organs [pancreas, liver, diaphragm, colon transversum, splenectomy, small intestine, kidney, adrenal gland, etc]=244; only surgery [S]=166, adjuvant chemoimmunotherapy [AT]=78: 5FU+thymalin/taktivin; T3=131, T4=113; N0=105, N1=37, N2=102, M0=244; G1=64, G2=54, G3=128). Multivariate Cox modeling, clustering, SEPATH, Monte Carlo, bootstrap, and neural networks computing were used to determine any significant dependence.

Results: Overall life span (LS) was 1617.1±1875.9 days and cumulative 5YS reached 48.8%, 10 years – 41.2%, 20 years – 33.7%. A total of 73 GCP lived more than 5 years (LS=3870.8±2053.8 days), and 32 lived more than 10 years (LS=5589.5±2042.7 days). Overall, 106 GCP died because of GC (LS=615.4±347.6 days). AT significantly improved 5YS (63.5% vs 44%; P = .004). Cox modeling displayed that 5YS significantly depended on N0-N12, AT, blood cells, cell ratio factors (ratio between cancer cells-CC and blood cells subpopulations), prothrombin index, protein, residual nitrogen, chlorides, blood group, and Rh (P = .000 to .043). Neural networks, genetic algorithm selection and bootstrap simulation revealed relationships between 5YS and N0-12 (rank=1), healthy cells/CC (2), erythrocytes/CC (3), thrombocytes/CC (4), lymphocytes/CC (5), stick neutrophils/CC (6), eosinophils/CC (7), segmented neutrophils/CC (8), leucocytes/CC (9), and monocytes/CC (10). The correct prediction of 5YS was 100% by neural networks computing.

Conclusion: 5YS of locally advanced GCP after combined radical procedures significantly depended on tumor characteristics, blood cell circuit, cell ratio factors, biochemical factors, hemostasis system, anthropometric data, surgery type and adjuvant treatment. Optimal strategies for local advanced GCP are: 1) availability of very experienced abdominal surgeons because of complexity radical procedures; 2) aggressive en block surgery and adequate lymph node dissection for completeness; 3) precise prediction; and 4) AT for GCP with unfavorable prognosis.

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P-16 Survival of Filipino patients with locally advanced and metastatic colorectal carcinoma in Cebu Cancer Institute, Perpetual Succour Hospital

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Background: Colorectal carcinoma (CRC) poses a significant healthcare burden among countries worldwide, being the third most common malignancy and the fourth leading cause of cancer-related deaths. Over the years, survival has been improving with early diagnosis and adoption of best practice in cancer treatment. Despite this, management still remains challenging, especially when the stage is far advanced upon diagnosis, which could significantly impact prognosis.

Methods: This was a single-center, retrospective cohort study including 120 colorectal cancer patients treated from 2004-2014 in a tertiary hospital in Cebu. Overall survival (length of time that patients diagnosed with the disease are still alive), disease-free survival (length of time after primary treatment ends that the patient survives without any signs or symptoms of that cancer), and progression-free survival (length of time after the treatment of a disease that a patient lives with the disease but it does not get worse) were identified as the primary outcome. The duration of follow-up was calculated at the time of diagnosis to the event of interest (death, recurrence, progression). Patients without events were censored at the date of follow-up (2019). Kaplan–Meier survival analysis and log-rank tests in survival assessment were used.

Results: Among 120 patients with locally advanced and metastatic colorectal carcinoma in our institution, overall survival was recorded at 27.59 months (95% CI, 20.56-34.62 months) with a 46% survival rate at this average duration. Furthermore, overall survival of locally advanced cancer was higher as compared with those with metastatic (33.81 +/- 4.64 months vs 14.80 +/- 3.88 months; log-rank P = .001). Disease-free survival among patients with locally advanced colorectal carcinoma was 28.67 months (95% CI, 21.70-35.64) and progression-free survival among those with metastatic disease was 12.80 months (95% CI, 5.44-20.16). Factors significantly related to colorectal cancer survival included: stage at diagnosis (P < .001), presence of metastasis (P = .001), tumor grade (P < .001), surgical urgency (P = .030), surgery (P = .009), adjuvant chemotherapy (P < .01), and recurrent disease (P < .05).

Conclusion: The mean overall survival (OS) of patients with locally advanced colorectal carcinoma was 33.81 +/- 4.64 months whereas those with metastatic disease had a mean OS of 14.80 +/- 3.88 months. These findings were similar among Asia Pacific and Western populations. Factors significantly associated with poor survival included: advanced stage at diagnosis, presence of metastasis, poorly differentiated tumors, emergency surgery, and recurrent disease, whereas curative surgery with adjuvant/palliative chemotherapy was associated with increased survival among patients.

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P-17 Peri-operative FLOT: West of Scotland regional experience

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Background: For patients with locally advanced, resectable gastric or gastro-oesophageal junction adenocarcinoma, peri-operative chemotherapy with Fluorouracil/Leucovorin, Oxaliplatin, and Docetaxel (FLOT) is associated with a significant overall survival benefit and improved pathological response when compared with Epirubicin, Cisplatin, and Fluorouracil (ECF), as published in the Lancet Journal, May 2019.

In the West of Scotland, delivery of peri-operative FLOT chemotherapy has been implemented since 2018 with the addition of prophylactic GCSF. Here we present our real-world experience with particular focus on pathological outcomes and tolerability of treatment.

Methods: Chemocare was used to identify patients across the West of Scotland, treated over 2 surgical centres, receiving peri-operative FLOT chemotherapy between January 2018 and September 2019. Data were collected from Chemocare and electronic case records and collated on Microsoft Excel.

Results: There were 46 patients (78% male (n=36) and 22% female (n=10)) with a median age 64 (range 28 - 74) identified receiving FLOT chemotherapy between 9th May 2018 and 20th September 2019. All patients had performance status 0 (59%) or 1 (41%).

Two patients were excluded from analysis as they were initially suspected, and with subsequent investigations, confirmed to have metastatic disease.

Forty-three patients (98%) received a minimum of 4 cycles of neoadjuvant chemotherapy. Dose reductions were made in 19 patients (43%) and a delay in subsequent neoadjuvant chemotherapy cycles was required in 14 patients (32%). Grade 3 toxicities occurred in 6 patients (14%): neutropenia (n=3; of which 1 had neutropenic sepsis), diarrhoea (n=2) and laryngospasm (n=1).

Thirty-three patients (75%) underwent definitive resectional surgery. Reasons for not proceeding included: not fit (n=3), progressive disease pre-operatively (n=6) and progressive disease at the time of operation (n=4). Median time from the last cycle of FLOT to surgery was 47 days (range 31 – 75).

Pathological response was recorded and the majority demonstrated some response to neoadjuvant FLOT chemotherapy (25/33; 76%). 15% had a complete pathological response (n=5). The R0 resection rate was 27/33 patients (82%), with the remaining patients (n=6) having a R1 resection. There were no in-hospital or 30 day mortalities.

Adjuvant FLOT was delivered to 21 patients (64%). Two thirds (14/21) of these patients received 4 cycles. Treatment was stopped in 5 patients due to toxicities and 2 patients were censored during data collection. 13 of 21 patients required a dose reduction (62%) and 5 patients experienced a delay due to toxicity (24%). One patient experienced grade 3 toxicity: nausea.

Conclusion: Rates of R0 resection and complete pathological response are excellent within this non-trial population at 82% and 15% respectively.

The FLOT regime is well tolerated within our patient group with rates of grade 3 toxicity at acceptable limits of 14%. Using prophylactic GCSF we experienced less neutropenia and similar rates of neutropenic sepsis compared with the highly selected trial population.

As expected, significantly more patients completed treatment in the neoadjuvant than the adjuvant setting but adjuvant delivery was similar to that seen within the trial.

There were no intra-operative or post-operative deaths and data collection and follow up is ongoing with respect to long term survival outcomes.

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P-18 REMARRY and PURSUIT trials: Liquid biopsy-guided re-challenge of anti-EGFR monoclonal antibody for patients with RAS/BRAF V600E wild-type metastatic colorectal cancer

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Background: Several phase II trials have demonstrated the potential activity of re-challenge with anti-EGFR monoclonal antibody (mAb) for patients with RAS/BRAF V600E wild-type (wt) metastatic colorectal cancer (mCRC). Recent advances in technology for circulating tumor DNA (ctDNA) analysis enable us to evaluate the dynamics of acquired resistance alterations, including RAS mutations. Post hoc biomarker analysis of clinical trials suggested that ctDNA RAS mutational status was highly likely to select patients who could benefit from anti-EGFR mAb re-challenge.

Trial design: This study is composed of the prospective observational study (REMARRY trial) and the interventional clinical study (PURSUIT trial). The REMARRY trial evaluates the dynamics of ctDNA RAS mutational status during subsequent treatment after anti-EGFR mAb (cetuximab or panitumumab [PANI])-containing therapy in mCRC patients with RAS/BRAF V600E wt tumors who responded to anti-EGFR mAb therapy, by sequential monitoring using a highly sensitive digital PCR method of OncoBEAMTM RAS CRC KIT in a central laboratory (Sysmex, Japan). The target sample size of the REMARRY trial is 120 patients. Patients enrolled in the REMARRY trial and negative for ctDNA RAS mutations (defined as the frequency of all RAS mutant alleles being $\leq$ 0.1%) will be enrolled to the PURSUIT trial, which is a multicenter, single-arm phase II trial, to assess the efficacy and safety of re-challenge with PANI and irinotecan (IRI) combination therapy (PANI 6mg/kg and IRI 150mg/m^2 q2wk until disease progression). Key eligibility criteria include ECOG PS $\leq$ 1; mCRC with RAS/BRAF V600E wt on tumor tissue; refractory or intolerant to fluoropyrimidine, oxaliplatin, and IRI; progressed after complete or partial response and progression to previous anti-EGFR mAb-containing therapy; a period of 4 months or more between the last administration of previous anti-EGFR mAb and the start of study treatment; and negative for ctDNA RAS mutations within 28 days before study enrollment. The primary endpoint is the confirmed objective response rate by the investigators' assessment based on RECIST 1.1 criteria, and key secondary endpoints include progression-free survival, overall survival, disease control rate, and safety. The target sample size of the PURSUIT trial is 50 patients. Translational research is performed in parallel using the next-generation sequencing-based ctDNA analysis at the start and discontinuation of study treatment. The REMARRY and PURSUIT trials were activated in 2019, with the enrollment of 58 and 2 patients as of February 2020, respectively.

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P-19 Role of percutaneous radiofrequency ablation in unresectable, non-metastatic intrahepatic cholangiocarcinoma: A single-institution experience

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Background: Very few data are available in literature about the role of radiofrequency ablation (RFA) in intrahepatic cholangiocarcinoma (ICC) and previous studies are mainly case reports and case series on a very small number of patients and nodules. In this study, we aimed at evaluating effectiveness and safety of RFA for the treatment of unresectable, non-metastatic ICC.

Methods: Medical records of all consecutive patients treated with ultrasound-guided (US-guided) RFA for unresectable, non-metastatic ICC at Policlinico Sant'Orsola Malpighi Hospital, Bologna, Italy, from January 2014 to June 2019, were retrospectively reviewed. The primary endpoint was Local Tumor Progression-Free Survival (LTPFS), defined as the time interval between initial RFA and first radiographic evidence of local tumor progression. Overall Survival (OS) was also assessed as a secondary endpoint. Univariate and multivariate analyses were performed to assess the impact of covariates on survival. LTPFS and OS were estimated using the Kaplan-Meier method; internal validation of the final multivariate model for LTPFS was performed with a bootstrap sample procedure (n = 1000 samples). The performance of the final model was further quantified by the Harrell C index and validated with a bootstrap resampling procedure to calculate a bias-corrected C index.

Results: A total of 32 patients with 126 nodules of ICC were included in the analysis. Technique effectiveness one month after RFA was 92.7%; median LTPFS was 6.7 months (range 5.3 — 8.1) for lesions $\geq$ 20 mm and 13.2 months (range 11.2 — 14.7) in tumors $<$ 20 mm. Univariate and multivariate analysis showed that tumor size less than 20 mm ($p < .0001$) was an independent prognostic factor of LTPFS (HR 3.71; 95% CI 2.34 - 5.76; $p < 0.001$). C index for the correlation between tumor size $\geq$ 20 mm and PFS was 0.659 (bias-corrected C index 0.654). At a median follow up of 40.3 months, median OS from the date of RFA was 27.8 months (95% CI 24.1- 30.8), with an OS of 87%, 44% and 11% at 1, 2 and 4 years, respectively. ECOG — PS ($p = 0.59$), overall number of sessions of RFA ($p = 0.21$), Meld score more than 9 points ($p = 0.56$) and diameter of the biggest lesion at the first RFA ($p = 0.26$) did not significantly affect OS at univariate analysis. The number of overall lesions ($p = 0.024$) and the sum of their diameter at the moment of the first RFA ($p = 0.03$) were significantly associated with worse OS in multivariate analysis. Minor and major complication rates were 14% (18 of 126) and 8% (10 of 126), respectively.

Conclusion: US-guided RFA may be considered an effective and safe treatment option in patients with unresectable ICC. Tumor size $\geq$ 20 mm was associated with lower LTPFS, representing a potential useful threshold value. A careful evaluation of tumor burden appears to be a crucial element in choosing the best therapeutic strategy in unresectable ICC.

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P-20 Identification of predictive biomarkers in colorectal adenocarcinoma

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Background: Kazkhstan remains in high prevalence of oncological diseases among CIS countries. Despite the existing screening programs for colorectal cancer, the development of new markers does not stop, including serum biomarker panels for early diagnosis, and in patients with an identified disease, panels for assessing the prognosis, metastasis, and invasiveness of the process.

Methods: Our aim was to study the role of serum biomarkers in the diagnosis of colorectal cancer and assess their role in invasive tumor growth in the Kazakh population.

The determination of serum biomarkers was carried out by Milliplex Map Human Circulation Biomarker Kit. PD-L1 was determined using the Human ProcartaPlex™ Kit; oncomarker CA 72-4 was identified using ELISA. Concentrations are indicated in pg/ml. Statistic processing included Kruskal-Wallis and Mann-Whitney analysis. Informed consent was obtained for the examination of patients.

Results: A group of patients with first-time diagnosis of colorectal cancer (n=215) took part in the investigation. The average age: (Me [25%;75%]) 66.6 years old [62;72] 45% men and 55% women. Biomarker blood test was done prior to surgery. The control group included 53 healthy participants aged 47 [43;57]. The comparison group included 55 patients aged 59,5 [53,3;65] with inflammatory intestinal diseases. The patients were divided into subgroups: with the presence of invasive growth (n=69) and with its absence (n=153). In none of the cases did the biomarkers studied reveal significant differences in the content between the group of healthy individuals and those with non-cancerous bowel diseases. Classical markers CA 19-9 (12,0 [5,46;18,70], p< 0,0001) rose equally in both groups in CRC, with no difference between the groups. Markers such as CYFRA21-1 (1416,14 [906,1; 2213,68], p< 0,001) and OPN (6121 [3970; 11536], p=0,001) in the group with invasive growth of CRC significantly differed both from the control group and from the comparison group, however, they did not differ between the groups with invasive and non-invasive tumor growth. An increase in the serum level of the PDL-1 in the group with invasive CRC reached significance with the control group (but not the comparison group), but it also almost did not differ within the group with CRC. VEGF (115,33 [90,6; 156,0], p=0,0016) behaves atypically in our study, as it grew significantly in the group with non-invasive growth compared with the group with invasive growth; it was almost identical to non-oncological groups. The serum level of sFASL (57,63 [44,17; 86,86], p=0,0001) but not sFAS,) behaved similarly, reaching a maximum in the group with non-invasive tumor growth.

Conclusion: We found a relationship between the presence of invasion and the rates of biomarkers (sFASL) in the Kazakh population.

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P-21 Stereotactic body radiation therapy for locally advanced pancreatic cancer

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Background: Stereotactic body radiation therapy (SBRT) would allow local control of locally advanced pancreatic cancer (LAPC) with acceptable toxicity in a short time. The purpose of this work is to assess early and late toxicities and clinical response in patients treated with SBRT.

Methods: Between October 2013 and October 2019, 74 patients with LAPC, mean age 66 years (39-89), treated with neoadjuvant, concomitant or adjuvant chemotherapy plus SBRT were retrospectively analyzed.

The treatment dose was 25-37.3 Gy given in 3-5 daily fractions, utilizing volumetric arc therapy, a 6-MV photon beam and Linac Novalis IGRT-ExaTrac accelerator.

GTV and OARs were delineated in CT and PET-CT fused images. OARs were contoured according to RTOG criteria. The treatment planning was done in Eclipse V15.6.

Acute (≤3 m) and late (>3 m) toxicities grades were classified according to the CTCAE V.5.0

Results: Of 74 LAPC patients (40 women/34 men), with a mean follow-up of 9.3 m (0-36), 58 (78.4%) received SBRT in pancreatic tumor as primary treatment, 11 (14.9%) were operated on first, followed by SBRT, and 4 patients (5.4%) were rescued with SBRT because of recurrence after conventional radiotherapy and 1 (1.3%) had recurrence after SBRT.

Forty two patients (56.8%) had adenocarcinoma, two had another histology and 30 (40.6%) had no biopsy.

Early toxicity (74 pts): Thirty seven patients (50.0%) did not have any early toxicity. G1: enteritis in 4(5.4%), asthenia in 17 (23.0%), nausea in 10(12.5%), vomiting in 3 (4.1%), abdominal pain in 15 (20.3%) and abdominal distension in 11 (14.9%); G2: asthenia in 5 (6.7%), nausea in 1 (1.4%) and vomiting in 1 (1.4%); G3: enteritis in 1 (1.4%), G3: digestive hemorrhage in 1 (1.4%). One patient interrupted SBRT.

Late toxicity (38 pts): Twenty-five patients (65.8%) did not have any late toxicity. G1: enteritis in 2 (5.3%), asthenia in 9 (23.7%), abdominal pain in 3 (7.9%), vomiting in 3 (7.9%) and gastric dilatation in 3 (7.9%); G2: abdominal pain in 1 (2.6%); G3: abdominal pain in 1 (2.6%) and G4 in 1 pt (4.77%) who suffered from intestinal perforation due to disease progression.

Relief of abdominal pain was observed in 53/58 patients after SBRT (91.4%).

Kaplan-Meier overall survival at 12 and 18 months was 44 % and 33%, respectively.

Twenty-eight live patients kept in good shape (2 PS0 and 1 PS3).

Conclusion: Despite the heterogeneity in dose and fractionation, we suggest that SBRT is a feasible and safe option for patients with pancreatic cancer.

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P-22 Efficacy of sorafenib in treatment of advanced hepatocellular carcinoma in the Mexican population: Evidence from a third level hospital in Mexico

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Background: Hepatocellular carcinoma is a complex disease mostly related to subjacent liver damage, which makes it difficult to treat in advanced disease. Most patients have advanced disease (low hepatic reserve/high tumor burden) leading to limited options for their treatment. Sorafenib is a multitargeted tyrosine kinase inhibitor that inhibits tumor angiogenesis and tumor cell proliferation. The assessment protocol (SHARP) trial demonstrated that sorafenib significantly improved overall survival (OS) in patients with advanced HCC and preserved liver function. In Mexico, there is no information about the efficacy of this treatment for patients with advanced hepatocellular carcinoma. In this paper, we evaluate the related etiologic factors as well as their impact in overall survival and time to progression.

Methods: In this prospective cohort, we evaluated patients with advanced hepatocellular carcinoma classified as Barcelona Clinic Liver Cancer – C, with a good hepatic reserve (CHILD – PUGH A), ECOG 0 -2. HCC diagnosis was established by AASLD criteria. Patients were treated with sorafenib 800mg per day, clinical and biochemical evaluation was completed every 4 weeks, with tomographic evaluation every 12 weeks, and response was evaluated according to Response Evaluation Criteria in Solid Tumors (RECIST).

Results: From January 1, 2014, to December 31, 2019, 106 patients received at least one dosage of sorafenib and were included in the intention to treat analysis. Relevant demographic characteristics included the most frequently related risk factor, alcohol consumption (60%) and hepatitis viral infection as second place (36%), predominantly HCV infection (87%). The hepatic residual function was classified as Child – Pugh A in 83%. The progression-free survival for the cohort was 7.6m (CI 95%; 5.54 to 9.66). OS adjusted for functional status was 10.3, 8.5, 3.2 months for ECOG 0, 1 and 2, respectively. HCV infected patients had a median OS of 17.3 months, compared with a median of 7.0 months positive HBV patients. Alcohol-related HCC patients had a median of 9.4 months. The most frequently related adverse events were mucositis and hand-foot syndrome, which was manageable in most of the cases.

Conclusion: Hepatocellular carcinoma in the Mexican population shows a clear relation to cirrhosis. Etiologic factors show a difference between other countries with alcohol as the main factor. For the oncological outcomes, progression-free survival and overall survival were similar as reported in pivotal trials, with a major benefit for HCV-associated cirrhosis.

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P-23 Microwave ablation versus radiofrequency ablation in BCLC-A hepatocellular carcinoma: A systematic review and meta-analysis of randomized controlled trials

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Background: While percutaneous radiofrequency ablation (RFA) is considered the standard local ablative modality for the treatment of early-stage hepatocellular carcinoma (HCC), percutaneous microwave ablation (MWA) is being increasingly used in

recent years and, although several authors compared the two ablative modalities, it remains unclear which technique results in better clinical outcomes. Thus, we performed a systematic review and meta-analysis to compare percutaneous MWA versus percutaneous RFA in BCLC-A HCC in randomized controlled trials (RCTs), especially focusing on five outcomes of interest in this specific patient subpopulation.

Methods: We performed a systematic review and meta-analysis according to PRISMA guidelines to evaluate the clinical role of MWA and RFA in BCLC-A HCC in terms of complete ablation (CA) rate, local recurrence (LR) rate, overall survival (OS) rate at 1 year, OS rate at 3 years and major complications rate. All phase II and phase III RCTs published from June 15, 2008, to February 6, 2020, comparing MWA and RFA in BCLC-A HCC were retrieved through PubMed/Med, Cochrane library and EMBASE. Five eligible studies involving a total of 794 patients (MWA: 409; RFA: 385) and 1008 nodules of HCC (MWA: 519; RFA: 489) were included in our analysis. Results about CA, LR, OS and major complications rate were compared by calculating Odds ratios (OR) with 95% confidence intervals (CIs); ORs were combined with the Mantel-Haenszel method. Statistical heterogeneity between studies was examined using the Chi-square test and the I2 statistic; substantial heterogeneity was considered to exist when the I2 value was greater than 50% or there was a low P-value (< 0.10) in the Chi-square test. The risk of bias in the five selected studies was assessed using the Cochrane Collaboration tool for assessing risk of bias, including selection, performance, detection, attrition and reporting bias.

Results: No differences in CA rate (OR=1.21; 95% CI 0.52-2.80, I2 5%), LR rate (OR=0.78; 95% CI 0.36-1.69, I2 60%), OS at 3 years (OR=1.17; 95% CI 0.81-1.70, I2 0%) and major complications rate (OR=1.11; 95% CI 0.55-2.23, I2 32%) between percutaneous MWA and percutaneous RFA were detected in the analysis. Regarding OS at 1 year, a higher rate was observed for the MWA group (OR=1.9; 95% CI 1.03-3.51, I2 32%). All studies included in our analysis were judged as studies with a low risk of bias in separate reviews of 4 authors.

Conclusion: The comparison between MWA and RFA is currently under debate, with several meta-analyses finding similar efficacy and safety between the two modalities. However, previous studies presented several limitations, given the inclusion of primary and secondary liver malignancies and HCC at different stages; moreover, most of the experience comparing the two modalities comes from retrospective analyses of single-center cohorts, with no level 1 data supporting the superiority of RFA or MWA. In our study, MWA resulted in better survival at 1 year, although this benefit was not confirmed in the 3-year analysis. Well-designed, multicenter RCTs with large sample sizes are further required to confirm the above results.

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P-24 Neutrophil and lymphocyte ratio as a prognostic biomarker in pancreatic cancer

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Background: The prognosis of locally advanced or metastatic pancreatic cancer (LAMPC) is dismal. There is a need for rapid intervention given its quick progression and ability to metastasize. Since there are limited resources in the public health system, it is imperative to find a biomarker that could assess and identify patients with worse outcomes and provide a means for early intervention. Understanding the role between neutrophil and lymphocytes (N/L) and worse outcomes in LAMPC patients will allow for earlier intervention and minimize costs in a collapsing public health system. Aim: The primary endpoint was to analyze the N/L ratio and assess if it could serve as a predictor of mortality and worse outcome. Second, we evaluated other epidemiological risk factors as predictors: obesity, smoking, metformin use, and CA19-9.

Methods: A retrospective exploratory analysis of a laboratory database of 60 patients with LAMPC was performed. All patients included were in treatment in the Oncology Division at UNIFESP from the years 2009-2018. The study had been approved by a local committee. Epidemiological data were collected from electronic medical records, including gender, age, alcoholism, smoking, diabetes mellitus, hypertension, and other comorbidities. Physical examination data such as weight, height, date of diagnosis, stage, blood count, CEA, and CA-19-9, chemotherapy treatment and overall survival were analyzed. Data were collected every three months from the time of diagnosis until 9 months.

Results: The mean age of the 60 patients was 62.4±11.1 years with a prevalence of the male gender (51.7%). Diabetes (41%) and smoking (34%) were very frequent. Most patients had adenocarcinoma (89.8%) located in the head of the pancreas (70.7%) with a performance status of 0 or 1. Stage III and IV were most prevalent (72%) and 28 patients had liver metastasis. The most common treatment was gemcitabine (40%) followed by best supportive care (25%). Patients were followed for a median of 7.2 months (range: 0.46-105.13 months). By the end of the study period, 10% where alive. Overall survival was 7.43 months (IC 95% 4.53-10,320). The N/L ratio was a predictor of worse prognosis for all the periods studied (0, 3, 6 and 9 months) by the COX regression, as well as CA19-9. A cutoff of 1.238 was found by the ROC curve for the N/L ratio at 3 months (IC 95%: 0.631- 0.904; p= 0,037), showing the best sensitivity (76.3%) and specificity (66.7%).

Conclusion: The N/L ratio could be an effective biomarker and predictor of worse prognosis at diagnosis and especially after 3 months.

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P-25 Single-institution experience of total neoadjuvant therapy for locally advanced rectal cancer: Long-term results

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Background: The purpose of our study was to demonstrate that total neoadjuvant therapy (TNT) treatment in locally advanced rectal cancer (LARC), aimed at further enhancing the complete pathological response and local disease control, is feasible and well-tolerated.

Methods: From January 2011 to December 2017, 81 patients (women 29, men 52, mean age 61,5, range 36-86) with LARC (cT2-3 cN0-2) were enrolled in our institution, at the University of Catania. All patients received an intensified neoadjuvant combined chemo-radiotherapy treatment, named TNT, according to the following scheme: FOLFOX4 induction chemotherapy for 4 cycles, followed by a concomitant radiochemotherapy, with concomitant boost pelvic radiotherapy to a total dose to the primary of 54 Gy and daily continuous infusion of 5-Fluorouracil. Radiotherapy was delivered by means of 3D conformal or Intensity-modulated technique. After 6-8 weeks, pts were re-evaluated by means of colonoscopy, body TC and pelvic MRI.

Results: Total neoadjuvant therapy compliance was 90%. Grade I-II proctitis according to CTCAE v5 was 39%, grade III diarrhea was 10%, and grade I-II genito-urinary toxicity was 27%. Eighteen patients (22%) had a complete pathological response (pCR); 46 patients had a partial response. Seventy-six patients received surgery, while five refused it; sphincter-saving procedure was performed in 84% of patients and Miles' operation in 16% of them. Seventy-five patients were alive, after a median follow-up time of 62 months. Eleven patients experienced a distant metastatic disease, and two patients had a local relapse.

Conclusion: This study has shown that TNT, delivered by means of the intensification of preoperative systemic therapy, together with the intensification of radiotherapy, was feasible, well-tolerated and obtained high rates of local disease control (96,5%) with a pCR rate of 22%.

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P-26 RATIONALE 305: Tislelizumab plus chemotherapy versus placebo plus chemotherapy as first-line therapy in patients with gastric or gastroesophageal junction adenocarcinoma

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Background: Gastric cancer is the second most common cause of cancer-related deaths worldwide and poses a major clinical challenge due to limited treatment options. Fluoropyrimidine and platinum-based combination chemotherapy is the first-line standard of care in patients with locally advanced or metastatic gastric or gastroesophageal junction (G/GEJ) adenocarcinoma. Despite improved chemotherapy regimens, outcomes remain poor and survival is low. New therapies have focused on targeting the immune system, including the programmed death-1 receptor/programmed death-ligand 1 (PD-1/PD-L1) axis. Tislelizumab, a humanized monoclonal antibody with high affinity and binding specificity for PD-1, was engineered to minimize binding of FcγR on macrophages in order to abrogate antibody-dependent phagocytosis, a mechanism of T-cell clearance and potential resistance to anti-PD-1

therapy. Previous reports from early phase studies suggested that tislelizumab, either alone or in combination with chemotherapy, was generally well tolerated and demonstrated antitumor activity in patients with advanced solid tumors, including G/GEJ cancer. The recommended dosing for tislelizumab has been established as 200 mg IV every three weeks (Q3W).

Trial design: This global, double-blind, placebo-controlled, randomized, phase 3 study (NCT03777657) is designed to evaluate platinum/fluoropyrimidine plus tislelizumab versus platinum/fluoropyrimidine plus placebo as first-line therapy for patients with locally advanced or metastatic G/GEJ adenocarcinoma. Adult patients ($n \approx 720$) from ~160 centers will be randomized 1:1 to receive tislelizumab (200 mg IV Q3W) or placebo in combination with chemotherapy. Randomization will be stratified by region, PD-L1 expression assessed by a central laboratory, presence of peritoneal metastasis, and investigator's choice of chemotherapy. Patients with histologically confirmed G/GEJ adenocarcinoma, an Eastern Cooperative Oncology Group performance status score of ≤ 1, adequate organ function, and ≥ 1 measurable/evaluable lesion per RECIST v1.1 will be eligible. Patients may have received prior neoadjuvant/adjuvant therapy if completed ≥ 6 months prior to study entry (without disease recurrence/progression), but are ineligible if they received previous systemic therapy for locally advanced unresectable or metastatic G/GEJ adenocarcinoma. Oxaliplatin (130 mg/m^2 IV Q3W) plus capecitabine (1000 mg/m^2 orally twice daily for 2 weeks) or cisplatin (80 mg/m^2 IV Q3W) plus 5-fluorouracil (800 mg/m^2/day IV on Days 1-5 Q3W) will be used as backbone chemotherapy on an individual basis. Chemotherapy will be administered for up to six cycles; capecitabine maintenance therapy is optional for patients receiving capecitabine and oxaliplatin. The VENTANA PD-L1 (SP263) assay will be used for PD-L1 expression analysis. Progression-free and overall survival are the primary endpoints of the study. Secondary endpoints will include the safety/tolerability profile of combination therapy, overall response rate and duration of response (as assessed by blinded independent review committee per RECIST v1.1 criteria), and quality-of-life outcome measures (eg, European Organization for Research and Treatment of Cancer [EORTC] Quality of Life Questionnaire Gastric Cancer Module QLQ-STO22 Score, EORTC Quality of Life Questionnaire-Core 30 Score, and European Quality of Life 5-Dimensions 5-Levels Health Questionnaire Score). Exploratory endpoints include disease control rate, clinical benefit rate, time to response, and an analysis of potentially predictive biomarkers including, but not limited to, PD-L1 expression. This trial is currently enrolling.

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P-27 Retrospective observational analysis of p53 mutational status as a prognostic factor in TAS-102 treated metastatic colorectal cancer patients

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Background: Tipiracil-trifluridine combination (TAS-102) has recently been introduced as a treatment option in pretreated metastatic colorectal cancer (MCRC) patients. Owing to the favourable safety profile of the drug, the number of patients that are currently been treated is increasing. Based on the results of the registration trials, about 40% patients achieve disease control (either stable disease or partial response) at their first radiological evaluation. In previous preclinical models it has been shown that p53 mutational status might affect tumor cells' sensitivity to the drug: p53 wild-type cells seem to have increased sensitivity to trifluridine compared with p53 mutated cells. We conducted a retrospective analysis on metastatic colorectal cancer patients treated with TAS-102 to assess whether p53 wild-type status is associated with a favourable outcome.

Methods: p53 mutational assessment was performed by immunohistochemistry. Two different pathologists in a double-blind fashion performed the analysis on the most recent histological sample available. Cut-off for p53 mutated/wild type was set at 20%.

We retrospectively collected data concerning patients' response to treatment (by RECIST criteria 1.1) during treatment with TAS-102 and defined disease control rate (DCR) as the sum of patients who achieved either partial or complete response or stable disease at their first radiological assessment. We also calculated survival outcomes (progression-free survival, PFS and overall survival, OS) by the Kaplan Meier method. Stratification factors were sex, age, prior regorafenib use, performance status (PS), K-ras/N-ras/B-raf mutational status. Association with categorical variables was assessed by Fisher exact test for binomial variables (or by Chi-square test for all other instances). Log-rank test was used to assess differences among the strata whereas multivariate analysis was performed by Cox-proportional hazard regression. Level of statistical significance (p) was set for all analyses at 0.05.

Results: 37 patients were enrolled. DCR of the whole group was 37%, median PFS was 3.87 months and median OS was 10.95 months. At the time of analysis, 32/37 (86%) patients had already progressed and 19/37 (51%) had already died. 20/37 (54%) had a p53 mutated MCRC and the remaining 17/37 (46%) had a p53 wild type MCRC.

DCR in p53 wild-type vs mutated MCRC was respectively 62% vs 16% ($p=0.00063$). Median PFS for p53 wild-type vs mutated was 6.98 vs 3.44 months (HR for progression 0.48, 95%CI:0.23-0.97, $p=0.035$). Median OS for p53 wild-type vs mutated was 14.65 vs 10.75 months (HR for death 0.80, 95%CI:0.31-2.03, $p=0.065$).

Other stratification variables were not associated with differences in DCR, PFS or OS, with the exception of performance status. In particular, PS was associated with differences in DCR ($p=0.034$) and OS ($p< 0.0001$). Multivariate analysis confirmed an independent prognostic role both for p53 mutant/wild type status ($p=0.021$) and for ECOG PS ($p=0.024$).

Conclusion: p53 wild type status might be associated with a better prognosis for patients who receive TAS-102 monotherapy for a previously pretreated metastatic colorectal cancer. We believe that p53 mutational status should be further investigated, and in particular, its predictive rather than prognostic role should be assessed in comparison with other treatment options currently available in the setting of MCRC.

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P-28 Impact of p-mTOR expression on molecular-guided therapy strategies in therapy-refractory metastatic pancreatic ductal adenocarcinoma

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Background: Metastatic pancreatic ductal adenocarcinoma (mPDAC) bears a dismal prognosis despite systemic chemotherapy. In our platform for precision medicine, we aimed to offer molecular-guided treatments to patients without further guideline-based therapy options.

Methods: In this single-center, real-world, retrospective analysis of our platform, we describe the molecular-based therapy approaches in 50 patients diagnosed with therapy refractory mPDAC. A molecular portrait of the tumor specimens was created by next-generation sequencing panel, immunohistochemistry, fluorescence in situ hybridization and RNA fusion panel. To assess the impact of the molecular portrait on the molecular guided therapy recommendation, a binary logistic regression was performed. A p-value of less than 0.05 was considered statistically significant.

Results: In total, we detected 123 mutations in 50 patients. The five most frequent mutations were KRAS (n=40; 80%), TP53 (n=29; 58%), CDKN2A (n=8; 16%), SMAD4 (n=4; 8%) and NOTCH1 (n=4; 8%), which accounted for more than half of all mutations (69.1%). BRCA2 mutation was observed in two patients. Two patients had gene-fusions, namely TBL1XR1-PIK3CA and EIF3E-RSPO2. 22 patients (44%) were found to have only one mutation and 13 patients (26%) had more than one mutation. No mutations were found in two patients. IHC detected expression of EGFR, phosphorylated mTOR and PTEN in 36 (72%), 33 (66%) and 17 patients (34%), respectively. One patient was HER2-positive. Expressions of estrogen-receptor and progesterone-receptor were seen in one patient. For 14 (28%) of the 50 patients, targeted therapy was suggested, based on the identified molecular targets. The recommended treatments included everolimus (n=3), pembrolizumab (n=3), palbociclib (n=2) and cetuximab, crizotinib, FLT3 inhibitor, nintedanib, tamoxifen, and the combination of lapatinib and trastuzumab, each in one patient.

The turnaround time from biopsy to molecular profiling was around 5 weeks (36 days).

The turnaround time from biopsy to therapy initiation was about 8 weeks (61 days).

Eventually, 6 patients received the recommended therapy. Five patients died while receiving the therapy prior to disease restaging. One patient was treated with nintedanib and achieved stable disease for 6 months.

The binary logistic regression revealed that the expression of phosphorylated mTOR significantly influenced and informed the molecular-driven treatment recommendations in our cohort ($p = 0.037$). The number of mutations per patient and the expressions of EGFR and PTEN were not statistically significant.

Conclusion: Based on our observations, it seems that the expression of phosphorylated mTOR might play a clinically relevant role in the personalized treatment of therapy refractory mPDAC and should be evaluated in further clinical trials.

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P-29 Molecular profiling of neuroendocrine tumors

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Background: Neuroendocrine tumors (NETs) are one of the most poorly studied neoplasms today. At the same time, the interrelation between hereditary mutations in genes of the repair system of DNA and NETs is not well-studied.

Our aim was to carry out an analysis of the occurrence of mutations in genes of the repair system of DNA in patients with NETs.

Methods: 37 patients with a diagnosis of NETs with the burdened hereditary anamnesis observed in 2018 were analysed. The diagnosis of NETs, early age of a demonstration (up to 60 years), hereditary anamnesis at relatives of 1st, and 2nd line of relationship were criteria of inclusion.

Results: 10 (27%) patients had pathogenic and presumably pathogenic mutations in DNA repair system genes. The average age of patients was 51.3 years.

In the group with opportunistic options mutations in genes of POLE, APC, FANCL, SLX4, CDH1, MSH2, PALB2, 6 patients were revealed. Pathogenic variants were observed in 4 patients (RAD51B, BRCA2, MLH3, CHEK2). In the control group, without hereditary anamnesis, only 2 patients had PALB2 and BRCA2 mutations. Patient with MSH2 mutation showed rapid progression against the background of target therapy (3 months). Patients with mutations of BRCA2, MLH3, CHEK2, PALB2 were radically operated on for localized NETs and no progression was observed for 2-4 years. There were no pathogenic mutations found in 27 patients, of which 19 patients had heritable anamnesis.

Conclusion: Patients with NETs with hereditary anamnesis can have mutations in the genes of DNA repair systems and need genetic consultation. The conducted research showed the high relevance of studying a hereditary genetic component in NETs and the project will be continued with more numerous selection of patients.

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P-30 Survival benefit of surgical resection after first-line triplet chemotherapy and bevacizumab in patients with initially unresectable metastatic colorectal cancer

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Background: Surgical resection of metastatic disease in patients with initially non-resectable colorectal cancer (CRC) has improved overall survival. Intensified chemotherapy regimens have increased the probability of converting unresectable metastasis to resectable. Here, we report the result of combining intensive chemotherapy (triplet) and surgical resection of metastatic lesions in patients with metastatic CRC.

Methods: Patients with unresectable metastatic CRC were enrolled in a phase I/II trial of triplet chemotherapy consisting of capecitabine, oxaliplatin, Irinotecan, and bevacizumab. Patients were given 5-8 cycles of induction chemotherapy of the above regimen followed by maintenance capecitabine and bevacizumab until disease progression, unacceptable toxicity, or patient request. All patients were assessed at a multidisciplinary conference for possible surgical resection of their metastatic disease at the time of inclusion in the trial and 2-monthly intervals thereafter. Patients who underwent R0 resection of their metastatic disease received adjuvant oxaliplatin and capecitabine to complete a total of 6 months of chemotherapy.

Results: Fifty-three patients were enrolled. The median age was 52 years (range, 23-74), 29 (55%) were males, ECOG PS 0-1 was 13 (66%), 11 (42%) had a right-sided tumor, 29 (55%) had resection of their primary tumor, 22(42%) had a single metastatic site, and 8 (15.1%) had liver-limited disease. In all, 13 patients (24.5%) underwent surgical resection of residual metastatic disease +/- the primary tumor; 10 (18.9%) of them were R0. The surgical group had a higher incidence of males compared with the non-surgical group (69.3% vs 47.2%; P = .2), equal performance status, lower median number of metastatic sites (1 vs 2; P = .09), higher mutant Kras (53.8 % vs 34.2%; P = .3), and a higher response rate (84.6% vs 56.2%; P = .3). With a median follow-up duration of 89 months, the median PFS for the whole group was 16.1 months (95% confidence interval [CI]. 9.1-20) and the median OS was 28.2 months (95% CI, 22.5-53.3).

The median PFS for the surgery group was 18.9 months (95% CI, 12.6-not reached) compared with 9.6 months (95% CI, 7.0-18.3) for the non-surgical group (Log-rank P = .0165). The median OS was not reached (95% CI, 53.3-not reached) and 23.2 months (95% CI, 17.0-28.4) respectively (Log-rank P = .0006). The 5-year PFS and OS for the surgery group were 46.2% and 67.6%, respectively.

Conclusion: Patients with unresectable metastatic CRC who are fit for triplet chemotherapy should have the benefit of combining this intensified regimen and surgical resection of their metastatic disease if possible.

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P-31 Stem cell-like subtypes revealed by integrative multi-omics analysis in early-stage hepatocellular carcinoma

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Background: Hepatocellular carcinoma (HCC) is a lethal malignancy with the second-highest worldwide cancer mortality. Cancer stem cell in HCC has been regarded as a major cause of cancer progression. However, molecular and clinical features of stem cell-like HCC contributing to aggressive tumor biology and therapeutic resistance remain unclear. The aim of the study was to identify clinically relevant stem cell-like subtypes of HCC and understand underlying biology associated with HCC stemness.

Methods: Transcriptomic signatures were identified by analyzing single-cell transcriptomic data from human fetal hepatocytes and mature hepatocytes from adult livers and applied to 6 independent HCC cohorts (total n = 1263). Later, supervised and unsupervised approaches were applied to analyze proteomic data and multiple genomic data such as somatic mutations, mRNA expression, miRNA expression, and copy number alterations were integrated with proteomic data to uncover the most correlated genomic alterations with functional products. Clinical significance of identified key genomic and proteomic features was tested and validated in multiple independent cohorts of HCC patients.

Results: Integrative analysis of genomic and proteomic data uncovered three subtypes of HCC with substantial differences in clinical outcomes. Hepatic stem (HS) subtype is characterized by strong stem cell features, vascular invasion, and poor prognosis. Hepatoblast (HB) subtype has moderate stem cell features but high genomic instability and low immune activity. Mature hepatocyte (MH) subtype is characterized by high immune activity and low genomic instability. We developed and validated a robust genomic predictor for three subtypes. We also identified potential serum biomarkers that can stratify patients into 3 subtypes. Importantly, the 3 subtypes are highly conserved in the two most important pre-clinical models, established HCC cell lines (n = 81) and patient-derived HCC xenograft models (n=168). Thus, it opens a new opportunity for using cell lines and PDX models to assess the response rates of new drugs according to molecular subtypes of primary HCC tumors. Most strikingly, the 3 subtypes are significantly associated with benefit of sorafenib, the standard treatment of HCC patients, and also showed potential association with response to immunotherapy, new treatments of HCC patients. We further validated subtype-specific sensitivity to sorafenib in HCC cell lines and PDX models. Because these subtypes are highly associated with currently available treatments, our findings may provide the foundation for rationalized marker-based clinical trials.

Conclusion: We identified two distinct stem cell-like subtypes with biomarkers in the tumor tissue or blood sample showing discriminative prognostic significance. Each subtype was predicted to have a distinct response to immunotherapy and subtype-specific drug response for target agents as well as unique pathway dependencies. Our findings may offer the foundation of biomarker-based clinical trials for new therapeutic approaches to refractory HCC patients.

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P-32 Impact of perioperative serum CA 19-9 levels on survival outcomes in patients with intrahepatic cholangiocarcinoma

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Background: The prognosis of patients with intrahepatic cholangiocarcinoma (IHC) is poor. The aim of this study was to investigate the prognostic impact of perioperative carbohydrate antigen 19-9 (CA 19-9) on survival outcomes.

Methods: IHC patients who underwent surgical resection between 2012 and 2016 were retrospectively reviewed. Patients were stratified by pre- and post-operative CA 19-9 levels: group 1 (normal preoperative CA 19-9), group 2 (high preoperative but normalized CA 19-9 after operation) and group 3 (high pre- and post-operative CA 19-9). Clinicopathologic data and survival outcomes were analyzed.

Results: Group 1 (n = 38) had better overall survival (OS) than group 2 (n = 12) and group 3 (n = 27) (median OS unavailable, 29.3 months, and 15.7 months; P = 0.02 and P < 0.001, respectively). Group 2 had better OS than group 3 (P = 0.04). In multivariable analysis, lymph node metastasis, group 3, alkaline phosphatase >115U/L, and pT3/pT4 were independent predictors of poor OS. Positive surgical margin and group 3 were independent predictors of poor local recurrence-free survival (RFS) while lymph node metastasis, group 3, and neutrophil to lymphocyte ratio >3 were independent predictors of poor distant RFS.

Conclusion: Non-normalization of CA 19-9 is an independent predictor of poor OS, local RFS, and distant RFS in resected IHC patients. Positive surgical margin is an independent predictor of poor local RFS and lymph node metastasis is an independent predictor of poor distant RFS.

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P-33 Regorafenib and trifluridine/tipiracil efficacy and safety in chemorefractory metastatic colorectal cancer patients: A single Bulgarian centre retrospective study

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Background: Regorafenib and trifluridine/tipiracil are recently approved novel agents for the treatment of patients with metastatic colorectal cancer (mCRC) whose disease has progressed after standard therapies. In registration trials, both agents demonstrated statistically significant and meaningful prolongation of overall survival in mCRC patients. While both drugs have similar indications, appropriate selection of patients has not yet been established in the treatment strategy.

Methods: We performed a retrospective analysis of safety and efficacy between regorafenib and trifluridine/tipiracil in patients with mCRC refractory to standard therapies treated in a single Bulgarian centre. We included patients with refractory disease or intolerance to fluoropyrimidines, oxaliplatin, irinotecan, anti-VEGF treatment, anti-EGFR treatment (if RAS WT) and no previous treatment with regorafenib or trifluridine/tipiracil.

Results: A total of 54 patients with mCRC treated with regorafenib or trifluridine/tipiracil after failure of standard therapies were included in the analysis. Among them, 29 patients were treated with trifluridine/tipiracil and 25 patients were treated with regorafenib. Baseline demographic and disease characteristics were similar between the two groups. The mean progression-free survival with regorafenib was 2.9 months (95% CI [2.4, 3.3]) and 3.4 months (95% CI [2.9, 3.9]) with trifluridine/tipiracil. In both groups, PFS did not correlate with RAS mutational status or localization of the primary tumour. Drug-related adverse events (AEs) were 11 (44%) in the regorafenib group and 10 (34.5%) in the trifluridine/tipiracil group. Grade ≥ 3 AEs were 0 (0%) and 2 (6.9%) in both groups, respectively. No unexpected AEs were found compared with previously reported data.

Conclusion: Our real-life single centre results show that regorafenib and trifluridine/tipiracil have similar efficacy and safety among the Bulgarian population compared with previously acquired global data.

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P-34 The randomized, double-blind, placebo-controlled phase 3 trial KEYNOTE-975: Pembrolizumab vs placebo in patients with esophageal carcinoma receiving concurrent definitive chemoradiotherapy

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Background: Definitive chemoradiotherapy (dCRT) is a standard treatment option for patients with unresectable esophageal cancer. Although platinum + fluoropyrimidine-based regimens are comparable in dCRT, overall patient survival is still poor. In patients with advanced, unresectable esophageal cancer, the PD-1 inhibitor pembrolizumab showed promising antitumor activity as monotherapy in the third-line setting in the phase 2 KEYNOTE-180 trial (NCT02559687) and in the second-line setting in the phase 3 KEYNOTE-181 trial (NCT02564263). Results from the KEYNOTE-181 trial demonstrated extended overall survival with pembrolizumab compared with chemotherapy in patients with PD-L1 combined positive score (CPS) ≥10 tumors. The randomized, multicenter, double-blind, phase 3 KEYNOTE-975 trial (NCT04210115) will investigate pembrolizumab in combination with dCRT.

Trial design: Key patient eligibility criteria are the presence of cTX N+M0 or cT2-T4a NXM0, locally advanced esophageal squamous cell carcinoma or adenocarcinoma or Siewert type 1 adenocarcinoma of the esophagogastric junction with no previous chemotherapy or radiation for esophageal cancer, Eastern Cooperative Oncology Group performance status 0 or 1, and adequate tumor tissue sample for biomarker analyses; patients must be ineligible for curative surgery and suitable for dCRT. Patients will be randomly assigned 1:1 to pembrolizumab or placebo in combination with dCRT, administered as pembrolizumab 200 mg or placebo every 3 weeks for 8 cycles followed by pembrolizumab 400 mg or placebo every 6 weeks for 5 cycles (13 cycles total). The dCRT regimen will be the site's choice of continuous infusion 5-fluorouracil + cisplatin (FP) with radiotherapy (RT) 50 Gy, FP with RT 60 Gy, or oxaliplatin, 5-fluorouracil, leucovorin/calcium folinate/folinic acid or levoleucovorin/calcium levofolinate (FOLFOX) with RT 50 Gy. Patients will receive study treatment until disease recurrence, unacceptable toxicity, intercurrent illness that prevents further administration of treatment, withdrawal, or completion of 13 administrations of pembrolizumab (~1 year). Randomization will be stratified by PD-L1 positivity (CPS ≥10 vs CPS < 10), RT dose (50 Gy vs 60 Gy), and region/histology (squamous cell carcinoma East Asia vs squamous cell carcinoma rest of world and adenocarcinoma regardless of region). The co-primary endpoints are overall survival and event-free survival within the prespecified analysis cohorts: patients with CPS ≥10, patients with squamous cell carcinoma, and all patients (intention-to-treat population). The secondary endpoints are safety and tolerability. Exploratory objectives include comparing time to deterioration and change from baseline in quality of life measures, characterizing health utility scores, and identifying molecular biomarkers that may be determinants of response. Enrollment is planned for ~600 patients.

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P-35 Prognostic value of ALBI score in patients with hepatocellular carcinoma Child-Pugh A

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Background: Albumin-bilirubin (ALBI) score is a simple and objective measurement of liver function based on albumin and total bilirubin serum levels that has recently been proposed [1]. Its use in evaluating the prognosis of patients with hepatocellular carcinoma (HCC) has also been studied. We aimed to assess the outcomes of patients with HCC Child-Pugh A treated with sorafenib based on ALBI score.

Methods: This study involved a retrospective, single-center, cohort of patients with HCC Child-Pugh A treated with sorafenib between the years of 2013 and 2019. ALBI

score was calculated with baseline values of albumin and bilirubin from a measurement immediately before the start of sorafenib treatment. Prognostic value of ALBI grade in terms of progression-free survival (PFS) and overall survival (OS) was evaluated using Kaplan-Meier and Cox regression survival analysis. OS was calculated based on the starting date of sorafenib treatment.

Results: Thirty-eight patients were included, 36 (94,7%) were male, and median age was 67,5 years ranging from 51 to 82. BCLC staging at diagnosis was A in 3 (7,9%) patients, B in 16 (42,1%) and C in 19 (50,0%); a total of 12 (31,6%) patients had been submitted to locoregional treatment prior to sorafenib treatment. Calculated ALBI score was grade 1 in 21 (55,3%) patients, grade 2 in 17 (44,7%) and no patients were graded as 3. In the overall population, with a median follow-up of 7 months, median PFS and OS were 5 and 9 months respectively. The group with ALBI grade 1 presented a longer median PFS (9 vs 3 months, HR 0,34, CI-95% [0,16-0,71] p=0,01) and a longer median OS (12 vs 5 months, HR 0,36, CI-95% [0,17-0,76] p=0,01) when compared with group with ALBI grade 2.

Conclusion: In our cohort, ALBI score was able to stratify patients with HCC Child-Pugh A in two different prognostic groups, since a lower grade at baseline was predictive of longer PFS and OS. Given that HCC prognosis is related to both disease extent and liver function, our results, although limited by a small study population, further consolidate ALBI's role in measuring liver function and predicting survival. References: [1] Johnson, PJ; Berhane, S; Kagebayashi, C; et al. Assessment of liver function in patients with hepatocellular carcinoma: a new evidence-based approach-the ALBI grade. J Clin Oncol. 2015 Feb 20;33(6):550-8.

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P-36 Prognostic value of tumor laterality and recurrence risk in patients with stage III colon cancer treated with adjuvant chemotherapy

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Background: Despite differences in anatomy, embryological origins, genetic mutations and metastization patterns of cancer between right and left colon, stage III colon cancer is generally still treated as one entity with uniform therapy [1]. Recently, the IDEA study evaluated the efficacy of 3-month adjuvant chemotherapy with CAPOX (capecitabine and 5-fluorouracil) or FOLFOX (oxaliplatin and 5-fluorouracil) versus the standard of care 6-month regimen, suggesting non-inferiority of the shorter regimen in the lower-risk subgroup [2]. We aimed to investigate the prognostic influence of tumor sidedness and recurrence risk in patients with stage III colon cancer treated with adjuvant FOLFOX.

Methods: We studied a retrospective, single-center, cohort of patients with stage III colon cancer treated with surgery followed by adjuvant chemotherapy with 12 cycles FOLFOX between 2013 and 2017. We excluded patients that did not complete 12 cycles. Recurrence risk was defined based on pathological staging as low in patients with T1-3 and N1 cancers and as high in T4 and/or N2 [2]. Prognostic value of recurrence risk and sidedness in terms of disease-free survival (DFS) was evaluated using univariate and survival analysis. DFS was calculated based on the finishing date of adjuvant chemotherapy.

Results: A total of 75 patients were included, 50 (56,7%) were male and median age was 62 years. Tumor was located in the left-colon in 45 (60,0%) patients and right-colon in 30 (40,0%). Recurrence risk was low in 38 (50,7%) patients and high in 37 (49,3%). Considering laterality, recurrence risk was high in 22 (48,8%) of left-colon cancers and in 15 (50,0%) of right-colon cancers (p=0,556). With a median follow-up of 46 months, median DFS was not reached, and the 3-year DFS rate was 73,0% in the overall population. When considering sidedness, 3-year DFS rate was 75,5% in left-colon cancers and 66,7% in right-colon cancers (p=0,195). Regarding sidedness and recurrence risk, 3-year DFS rate was gradually decreased when comparing combined groups: left-sided low-risk (87,0%), right-sided low-risk (80,0%), left-sided high-risk (63,6%) and right-sided high-risk (46,7%), (p=0,041). Survival analysis showed a tendency for longer DFS in left-colon cancers (HR 0,742, CI-95% [0,623-1,725], p=0,481) and in low-risk cancers (HR 0,417, CI-95% [0,170-1,023], p=0,049).

Conclusion: In our cohort, high-risk cancers showed a statistically significant shorter DFS and, despite the lack of statistically significant differences, there was also a tendency of right colon tumors to have a shorter DFS. The group with right-sided high-risk tumors showed a particularly worse prognosis. References: [1] Peng J, Li C, Wang F, et al. Right- and left-sided stage III colon cancers present different prognostic outcomes of oxaliplatin-based adjuvant chemotherapy after curative resection. Cancer Manag Res. 2018 Jul 17;10:2095-2103. [2] Grothey A, Sobrero AF, Shields AF, et al. Duration of Adjuvant Chemotherapy for Stage III Colon Cancer. N Engl J Med. 2018 Mar 29;378(13):1177-1188.

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P-37 phase II study of oxaliplatin-based regimen in relapsed colon cancer patients treated with oxaliplatin-based adjuvant chemotherapy: INSPIRE study

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Background: Efficacy and safety of oxaliplatin re-introduction as first-line treatment for relapse after adjuvant chemotherapy including oxaliplatin have not been well established. The aim of this study was to evaluate the efficacy and safety of first-line chemotherapy with re-introduction of oxaliplatin more than 6 months after adjuvant chemotherapy including oxaliplatin.

Methods: This study was a single-arm, multicenter, phase II study to evaluate efficacy and safety of treatment of physician's choice for patients (pts) with stage II / III colon cancer with neuropathies less than grade 1 who relapsed more than 6 months after adjuvant chemotherapy including oxaliplatin. Eligible pts were treated with infusional 5-fluorouracil, leucovorin and oxaliplatin (FOLFOX) plus molecularly targeted agents or capecitabine and oxaliplatin (CAPOX) plus bevacizumab (BV) or S-1 and oxaliplatin (SOX) plus BV. The primary endpoint was progression-free survival (PFS) and secondary endpoints were overall survival (OS), response rate (RR) and toxicity. The threshold median PFS was defined as 7 months, and the expected PFS was set at 10.5 months, with 80% power and a 2-sided alpha value of 0.05. The calculated sample size was 48 pts.

Results: A total of 50 pts were enrolled between September 2013 and May 2019 and their median follow-up time was 34.3 months. The number of pts whose subgroup of time from adjuvant chemotherapy (6-12 month/12-24 month/more than 24 months) was 16 pts, 15 pts, and 19 pts, respectively. Median total dose of oxaliplatin for adjuvant chemotherapy were 1136 mg/body (range, 470 mg/body-1904 mg/body). Of those 50 pts, 12 pts received FOLFOX plus BV, 21 pts received CAPOX plus BV, 10 pts received SOX plus BV and 7 pts received FOLFOX plus cetuximab or panitumumab. Median total dose of oxaliplatin were 502.5 mg/body for FOLFOX plus BV, 1177 mg/body for CAPOX+BV, 705 mg/ body for SOX+BV and 1180mg/body for FOLFOX plus cetuximab or panitumumab. Median PFS was 11.5 months (95% CI, 8.3-16.0) and was longer than the predefined threshold median PFS. Median PFS among subgroups based on time from adjuvant chemotherapy (6-12 month/12-24 month/more than 24 months) was comparable (13.0 month/11.0 month/12.7 month, respectively). RR was 44.0% (95% CI, 31.2-57.7). Concerning over grade 3 adverse events that occurred at a rate of 5% or more were neutropenia (12%), diarrhea (8%), neuropathy (10%), hypertension (8%), anorexia (6%) and allergic reactions (6%).

Conclusion: First-line chemotherapy with re-introduction of oxaliplatin more than 6 months after adjuvant chemotherapy including oxaliplatin could be used safely and with expected efficacy for relapsed colon cancer pts.

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P-38 KEYNOTE-859: A randomized, double-blind, placebo-controlled phase 3 trial of first-line pembrolizumab plus chemotherapy in patients with advanced gastric or gastroesophageal junction adenocarcinoma

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Background: Standard first-line therapy for patients with human epidermal growth factor receptor 2 (HER2)−negative recurrent or metastatic gastric or gastroesophageal junction (G/GEJ) cancer includes a fluoropyrimidine plus a platinum-based agent. When given as monotherapy in the first-, second-, and third-line settings, PD-1 inhibitor pembrolizumab has demonstrated promising antitumor activity in patients with PD-L1−positive G/GEJ disease. The phase 3 KEYNOTE-859 trial (NCT03675737) is a randomized, multicenter, double-blind study investigating pembrolizumab plus chemotherapy versus placebo plus chemotherapy as first-line treatment of patients with advanced G/GEJ cancer.

Trial design: Key patient eligibility criteria are histologically or cytologically confirmed diagnosis of locally advanced unresectable or metastatic HER2−negative G/GEJ adenocarcinoma with known PD-L1 status, measurable disease per RECIST v1.1 as assessed by the investigator, archival tumor tissue sample or newly obtained core/excisional biopsy of a tumor lesion not previously irradiated, Eastern Cooperative Oncology Group performance status 0 or 1, and no prior therapy for locally advanced unresectable or metastatic disease. Patients will be randomly assigned 1:1 to pembrolizumab or placebo in combination with chemotherapy. Randomization will be stratified by geographic region (Europe/Israel/North America/Australia vs Asia vs rest of world), PD-L1 tumor expression status (combined positive score < 1 vs ≥ 1), and combination chemotherapy (5-fluorouracil plus cisplatin [FP] vs capecitabine plus oxaliplatin [CAPOX]). Pembrolizumab 200 mg or placebo will be administered intravenously (IV) every 3 weeks (Q3W). The chemotherapy regimen will be the investigator's choice of FP (continuous infusion of 5-fluorouracil [800 mg/m^2/day on days 1-5 of each cycle] plus IV cisplatin [80 mg/m^2] Q3W) or CAPOX (oral capecitabine [1000 mg/m^2 twice daily on days 1-14 of each cycle] plus IV oxaliplatin [130 mg/m^2 on day 1 of each cycle] Q3W). Duration of cisplatin or oxaliplatin may be capped at 6 cycles per local country guidelines; treatment with 5-fluorouracil or capecitabine may continue per protocol. Patients will continue to receive treatment until disease progression, unacceptable toxicity, intercurrent illness that prevents further administration of treatment, noncompliance, or receipt of up to 35 administrations (~2 years) of study treatment. The dual primary endpoints are overall survival and progression-free survival per RECIST v1.1 as assessed by blinded independent central review (BICR). Secondary endpoints include objective response rate and duration of response per RECIST v1.1 as assessed by BICR as well as safety and tolerability. Enrollment is ongoing.

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P-39 Prognostic impact of the number of administrations of oxaliplatin in the adjuvant treatment of stage III colon cancer

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Background: In adjuvant chemotherapy (aCh) for stage III colon cancer (CCIII), the use of oxaliplatin (OX) regimens for 6 months is highly toxic.

The objectives of this study included the analysis of overall survival (OS) and disease-free survival (DFS) in patients proposed for aCh with FOLFOX, according to the number of cycles (c) of OX completed, and to identify variables with prognostic impact.

Methods: We performed a retrospective study of patients with CCIII treated with FOLFOX between 01.2013 and 10.2018. Univariate analysis (UA) was performed using the Kaplan-Meier method and log-rank test, and multivariate analysis (MA) with COX regression method. A value of $p < 0.05$ was considered statistically significant. Patients were grouped according to the number of administrations of OX (1-4, 5-8, 9-11, and 12c for UA; 1-4 vs. 5-12c and 1-6 vs. 7-12c for MA) and staging (low risk [LoR] T1-T3 and N1, high risk [HiR] T4 and / or N2). Complete treatment was defined as performing 12c of aCh regardless of the cycles of OX administered.

Results: 165 patients were included, 55.2% male, with a median age of 60 years (28-77). All tumors were histological type adenocarcinoma. 61.8% were classified as LoR and 38.2% as HiR. 9.4% of patients did not complete aCh. There was OX dose reduction in 30.9%. The median follow-up was 37 months (1-82).

UA showed a significant reduction in OS in the group that performed 1-4c of OX (vs. 5-8 p=0.004; vs. 9-11 p=0.003; vs. 12 p=0.00). No significant differences in OS were observed between the other groups. The DFS UA did not show statistically significant differences between these groups.

In OS MA (95% CI), HiR patients (p = 0,047 HR 0,412) and those who did not complete aCh (p=0,007 HR 0,233) showed a significant increase in the risk of death. In DFS MA (95% CI) there was a significant increase in the risk of relapse in patients without comorbidities at diagnosis (p=0,006 HR 0,445), in HiR patients (p=0,005 HR 0,438) and in patients who did not complete aCh (p=0,000 HR 0,294). The cycles of OX completed (1-4 vs. 5-12) had significant impact on OS (p=0,039 HR 0,221) but no impact in DFS. Completing 1-6 vs. 7-12c had no impact on OS and DFS.

Conclusion: Due to the associated toxicity, the possibility of reducing the number of OX cycles is questioned in the adjuvancy of CCIII (IDEA trial). This study showed OS advantage in completing 5 or more OX cycles administered in FOLFOX, but no disadvantage on DFS in doing 4 cycles or less.

Worse OS and DFS results were seen in HiR patients and those who did not complete 12c of aCh. Patients without co-morbidities at the time of diagnosis had worse DFS.

The limitations inherent to a retrospective study influence the results and their interpretation.

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P-40 A correlation between BCL-2 modifying factor, p53 and livin gene expressions in cancer colon patients

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Background: Accumulating evidence has revealed that livin gene and BCL-2 modifying factor (BMF) gene are closely associated with the initiation and progression of colon carcinoma by activating or suppressing multiple malignant processes. These genes that can detect colon cancer are a promising approach for cancer screening and diagnosis. This study aimed to evaluate the correlation between livin, BMF and p53 genes expression in colon cancer tissues of patients included in the study, and their relationship with clinicopathological features and survival outcome in those patients.

Methods: In this study, 50 pathologically diagnosed early-stage colon cancer patients were included. Their tissue biopsy, with 50 matched adjacent normal tissue and 50 adenoma tissue specimens, were analyzed for livin gene and BMF gene expressions using real-time PCR. The relationship between expression of these genes and clinicopathological features, tumor markers, time to progression and overall survival were correlated in the colon cancer group.

Results: In this study, there was a significant reciprocal relationship between the overexpression of livin gene and downregulation of BMF and p53 genes in colon cancer cells. Livin mRNA was significantly higher, while BMF and p53 mRNA were significantly lower in colon cancer tissue compared to benign and normal colon tissue specimens ($P < 0.001$), however, this finding was absent between colon adenomas and normal mucosa. There was a significant association between up-regulation of livin and downregulation of BMF and p53 expressions with more aggressive tumors (advanced TNM stage), rapid progression with metastasis and decreased overall survival in colon cancer patients, hence these genes can serve as significant prognostic markers of poor outcome in colon cancer patients.

Conclusion: This work highlights the role of livin, BMF and p53 genes in colorectal tumorigenesis and the applicability of using these genes as diagnostic and prognostic markers in patients with colon carcinoma and as a good target for colon cancer treatment in the future.

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P-41 Understanding the clinical profiles that influence the concordance of RAS mutations between blood and tissue to guide therapy in metastatic colorectal cancer

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Background: The study of RAS status using circulating tumor DNA (ctDNA) provides a good alternative for the detection and monitoring of RAS mutations during therapy course. Liquid biopsy has the advantage of being less invasive than conventional tissue biopsy. Therefore, it is necessary to determine the degree of concordance of

RAS status between plasma and tissue samples from metastatic colorectal cancer (mCRC) patients.

Methods: We conducted a study to evaluate the concordance of RAS status between plasma and tissue samples of 301 patients from several hospitals in Galicia, Northwest of Spain. RAS genotyping in plasma was performed using the OncoBEAM RAS CRC kit (Sysmex) and compared to the standard of care technology for FFPE-tissue analysis. Clinical data were collected from electronic reports from each patient. We analyzed the clinical profiles of the mCRC patients to investigate the causes of discordance.

Results: The overall percent of RAS agreement was 84.4%, with a sensitivity of 81.3% and a specificity of 88.5%. Evaluating the clinical features of the patients, the absence of liver metastasis was a significant factor of discordance of RAS status (71% vs 28%, $p<0.0001$). Patients with peritoneal disease alone showed the lowest level of agreement (71.4%), followed by those with lung metastasis alone (72%), as compared with patients with liver metastasis alone (88.9%). Taking into account the diagnosis timing of stage IV, the concordance (75.9% vs 88.4%) and the sensitivity (68.1 vs 86.3) were significantly lower in metachronous than synchronous patients.

Conclusion: The overall concordance between plasma and tissue RAS mutation supports liquid biopsy technology as an alternative to tissue testing for RAS characterization in mCRC patients, especially in patients with liver metastasis. The RAS status obtained from plasma of patients with peritoneal or lung diseases, and particularly with those of metachronous stage IV, should be considered cautiously. These results reinforce the use of liquid biopsy as a non-invasive tool for guiding targeted therapy in selected patients.

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P-42 Primary malignant melanoma of anorectal region: An institutional experience in AIIMS Patna

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Background: Primary anorectal melanoma (ARM) is a rare neoplasm, accounting for 0.25%— 1.25% of malignancies originating in the anorectal region with poor prognosis despite aggressive management. Owing to its rare incidence and aggressive course, data regarding ideal management is lacking. Surgery is still the preferred modality of treatment.

Methods: This retrospective study describes the experience of 5 cases of anorectal melanoma in the department of surgical oncology, AIIMS Patna between January 2019-December 2019. The study was done to assess the course, median survival, recurrence rate and other outcomes of anorectal melanoma.

Results: The mean age was 43.8 years (range 30 - 52 years). A total of 63.3% of patients presented with pain per rectum, 40% with mass per rectum, 20% with bleeding per rectum and 20% with abdominal distension. The size of the melanoma ranged from 3 to 9 cm (mean = 5.6 cm). Abdominoperineal resection (APR) was done in 80% of cases. None had wide local excision, due to the advanced nature of disease at presentation. One patient presented with acute obstruction, mandating diversion colostomy. 40% had T2 disease, 20% had T3 and 20% had T4 disease. Lymph node tumour burden was found to be higher in all patients: 80% had N2a disease and 20% had N2b; distant metastasis to non-regional lymph nodes and distant organs in 80% of patients. Liver was found to be the most common site of metastasis. The median survival time was 9 months (95% CI: 4.3-13.7).

Conclusion: Anorectal melanoma is a disease with an aggressive course and grave prognosis. A higher rate of nodal involvement and distant metastasis mandates early diagnosis and prompt treatment, but often this is difficult owing to its non-specific symptomatology.

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P-43 Ramucirumab effectiveness in patients with advanced gastric cancer or gastro-esophageal junction adenocarcinoma in clinical practice in Spain: Sub-analysis of RAMIS study

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Background: RAMIS was an observational, retrospective, single-arm study, based on medical record review of patients with advanced gastric cancer (AGC) or gastro-esophageal junction (GEJ) adenocarcinoma treated with ramucirumab in real clinical practice. The observational study period was from December 2015 to December 2018. A total of 20 Spanish hospitals participated in the study, collecting data from 317 patients (297 treated with ramucirumab with paclitaxel and 20 patients treated with ramucirumab as monotherapy). The aim of this sub-analysis was to describe the effectiveness in a specific subgroup of patients (those treated with ramucirumab in combination with paclitaxel, ECOG 0/1), as well as effectiveness variables assessed by available imaging. In the RAINBOW study, a randomised, placebo-controlled, double-blind clinical trial, including ECOG 0/1 patients, ramucirumab showed a median progression-free survival (PFS) of 4.4 months (95% CI: 4.2 — 5.3) and a median overall survival (OS) of 9.6 (95% CI: 8.5 — 10.8) according to RECIST v1.1 criteria.

Methods: A sub-analysis of patients treated with ramucirumab in a combination regimen, ECOG 0/1 and effectiveness variables evaluated by imaging available (according to RECIST v1.1 criteria) was performed. A descriptive analysis was carried out to present patients' sociodemographic and clinical characteristics, treatment patterns and ramucirumab effectiveness. Kaplan-Meier curves were used for time-to-event analysis (time on treatment, time to disease control, PFS and OS).

Results: A total of 173 patients fulfilled the criteria to be included in the sub-analysis. At time of analysis a total of 101 patients had died (72 patients had censored data). Main characteristics at baseline were: 72.3% male, mean (SD) of 61.9 (10.9) years, 74.0% with AGC diagnosis, mean (SD) time since metastatic disease 1.7 (2.2) years. Patients had ECOG-0 (26.6%), ECOG-1 (73.4%), primary tumour still present (60.7%), poorly differentiated tumours (40.5%) and diffuse histological subtype (23.7%). Prior surgery was performed in 49.7% of patients and previous treatments included chemotherapy (96.5%) [28.1% neoadjuvant, 23.4% adjuvant and 74.9% as first-line treatment], targeted therapy (12.1%) and radiotherapy (11.6%). 86.1% of patients received ramucirumab in combination with paclitaxel throughout the treatment, while 13.9% began receiving this combination and later switched to monotherapy with ramucirumab. The median (interquartile range) number of cycles received was 4.0 (3.0;6.0), with a median time on treatment of 3.8 (95% CI: 3.3-4.3) months. One hundred out of the total sample (57.8%) showed disease control (partial response/complete response/or stable disease) during the follow-up period, the median time to disease control being 3.2 months [95% CI 2.8—4.2] months. Median PFS and OS values were 4.9 (95% CI 3.9—5.4) and 10.3 (95% CI 8.5-12.3) months, respectively. PFS and OS rates at 3/6/9/12 months were 70.1%, 37%, 21.5% and 15.1% and 95.3%, 74.6%, 56.5% and 44.2%, respectively. Median PFS and OS values according to ECOG status, were 5.9 [95% CI 5.2—6.8] and 11.4 [95% CI 9.6—22.7] months in ECOG-0 patients and 3.8 [95% CI 3.3—4.9] and 9.7 [95% CI 7.6-12.3]) in ECOG-1 patients.

Conclusion: In real-life conditions, patients with an ECOG status of 0/1 treated with ramucirumab plus paclitaxel showed effectiveness data consistent with the ramucirumab RAINBOW clinical trial.

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P-44 Transcatheter arterial chemoembolization using CDDP without Lipiodol for super-elderly patients with hepatocellular carcinoma

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Background: Patients in Japan with hepatocellular carcinoma (HCC) who are indicated for active treatment have a prolonged, healthy life expectancy. This study aimed to determine the effects and toxicity of transcatheter arterial chemoembolization (TACE) using cis-diamminedichloroplatinum (II) (CDDP) without Lipiodol in super-elderly patients with HCC.

Methods: Transcatheter arterial chemoembolization proceeded in patients aged > 85 years with HCC as follows: hepatocellular carcinoma was evaluated using angiography, CT-portography, and CT. Then the treatment area was decided. Powdered CDDP (100 mg in 70 mL of saline) was injected into the optimal hepatic artery using a syringe pump at a rate of 3 − 4 mL/min. Embolic materials were administered until hemostasis was achieved. Details of TACE, survival rates, overall response rates (m-RECIST criteria), and toxicity (CTCAE ver. 4.0) were evaluated.

Results: We retrospectively evaluated 23 procedures in 13 patients (male, n = 9, female, n = 4; median age, 85 (85 − 89) years) between January 2014 and December 2019. The numbers of patients with Child-Pugh classes A, B and C were 23, 0 and 0, respectively, and 3, 4, 3 and 3 patients had HBV, HCV, HBV+HCV, and NBNC, respectively. The median age at the time of treatment was 86 years and the patients underwent a median of two procedures. The CDDP dose was 58.3 mg/m^2 (recommended dose, 65 mg/m^2) and the embolic materials comprised gelatin sponge particles in 22 procedures and HepaSpheres in one. The areas treated during the procedures comprised the whole liver (n = 13), lobes (n = 2), segments (n = 6), and sub-segments (n = 2). The mean follow-up period was 820 days and the survival rates at 0.5, 1 and 2 years were 84.6%, 67.3%, 56.1%, respectively. The overall response and disease control rates were 78.3% and 87.0%, respectively, without severe adverse events. The median hospital stay was 6 (5 − 9 days).

Conclusion: Transcatheter arterial chemoembolization using CDDP without Lipiodol is safe and effective for super-elderly patients with HCC.

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P-45 Applicable value of transanal endoscopic microsurgery for high-risk rectal adenoma and early rectal cancer: Experience from 126 cases

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Background: Since the concept of "minimally invasive surgery" has gotten more and more popular, transanal endoscopic microsurgery (TEM) has become one of the most advisable treatment approaches for rectal cancer. However, research on high-risk rectal adenoma and early rectal cancer treated with TEM are relatively rare. The aim of the present study was to investigate the risk factors of local occurrence, complications, and the value of two of the most crucial preoperative examination methods, coloscopy and rectal intraluminal ultrasound, in patients having TEM.

Methods: A retrospective study was conducted on the clinical data of 126 patients diagnosed with high-risk rectal adenoma and early rectal cancer by postoperative pathology who received TEM in our clinical center from August 2010 to September 2019. The demographic characteristics, pathological features, surgical conditions, postoperative recovery, and follow-up of the included cases were statistically analyzed.

Results: All the patients received TEM operations, with 57 male patients and 69 female patients. The average age was 55.67±10.13 years old. The mean operation time was 70.26±24.51 min, the mean intraoperative blood loss was 23.92±2.53 mL, the mean tumor diameter was 2.72±1.13 cm. The incidence of postoperative complications was 13.49%, including 12 cases of Clavien-Dindo gradel, 3 cases of Clavien-Dindo grade II, and 2 cases of Clavien-Dindo grade III. All tumors were completely resected with negative margins. Postoperative pathology of 126 patients confirmed rectal adenoma or early rectal cancer, including 19 cases of rectal adenoma, 40 cases of pTis and 67 cases of pT1 rectal cancer. Statistical analysis was conducted according to the postoperative pathological staging group. The mean age of pT1 patients was higher than that of adenoma or pTis, and the difference was statistically significant (P<0.05). The average diameter of tumor in pT1 patients was larger than that of adenoma or pTis patients, and the difference was statistically significant (P<0.05). In patients with pTis, 69.49% had the component of villi, compared with 31.57% in patients with adenoma, and 87.69% in pT1 patients. Compared with postoperative pathological results, the overall concordant rate of rectal intraluminal ultrasound diagnosis was higher than that of colonoscopy biopsy (59.82% vs. 35.48%, P<0.00). After operation, 113 patients were followed up for an average of 63.97±10.2 months. 13 patients had local recurrence (11.50%) and all underwent proper remedial treatment, with no tumor recurrence or distant metastasis found later on.

Conclusion: TEM is minimally invasive and effective in the treatment of high-risk rectal adenoma and early rectal cancer with a lower incidence of postoperative complications and should be recommended. Elderly patients, large tumor diameter and component of villi may be considered risk factors for adenoma cancerization and further progression. The preoperative rectal intraluminal ultrasound examination is vital for diagnosis. To guarantee the therapeutic effect, the postoperative follow-up plan should be made according to the pathological stage of the patient and the presence of high-risk factors for recurrence.

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P-46 Advanced colorectal adenoma detection based on altered methylation signal in plasma samples

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Background: Colorectal cancer is one of the major contributors to cancer-related mortality in the world. Effective population-based screening for colorectal cancer could prevent the development of cancers through the detection of premalignant adenomas, from which at least 80% of sporadic cancers are thought to arise. Existing screening methods include fecal immunochemical testing, which suffers from low accuracy for adenoma detection, and colonoscopy, which is invasive. Measuring the methylation status of the tumor-derived portion of the cell-free DNA in plasma could offer a non-invasive, accurate and high adherence approach for detecting advanced adenomas, helping potentially to decrease colon cancer mortality. We report here the performance of a plasma-targeted methylation marker panel for the detection of patients with advanced adenoma with good accuracy.

Methods: Initially, whole genome bisulfite sequencing data of 10 pooled plasma samples were used for differentially methylated region selection. Candidate regions were further targeted with methylation-sensitive restriction enzyme qPCR method and evaluated in the individual plasma samples of 40 advanced adenoma (AA) patients (10 with high-grade dysplasia, 30 low-grade dysplasia with size >=10mm), 10 gastrointestinal disease (GID), 22 hyperplastic polyp (HP) and 38 colonoscopy-negative control (CNT) patients. Performance of the methylation marker panel was tested by dividing the sample set into a training set of 24 AA, 10 HP and 20 of the CNT samples and a validation set of remaining 16 AA, 10 GID, 12 HP, and 18 CNT samples. The training set was used for marker ranking and building of a support-vector machine (SVM) classification algorithm based on 35 best-performing markers. SVM-model was then tested on the validation set and prediction accuracies were calculated.

Results: SVM-model, based on 35 methylation markers, showed good prediction on the validation set with area under curve (AUC) of 80%, where the sensitivity of detecting advanced adenoma patients was 62.5% (10/16) with overall specificity of 87.5% (35/40). Adenoma sub-class analysis showed very good sensitivity for detection of patients with high-grade dysplasia at 75% (6/8) while the detection rate of patients with low-grade adenomas with size >=10mm was 50% (4/8). Sensitivity for detecting tubulovillous adenoma patients was higher (62.5% [6/8]) than for tubular adenoma (50% [3/6]), while singular serrated and villous adenoma cases were both correctly classified. 80% (8/10) of patients with gastrointestinal diseases, 100% (12/12) of patients with hyperplastic polyps and 83% (15/18) of control patients were correctly classified, indicating that the 35-marker panel performance was independent of the presence of inflammatory and non-neoplastic conditions.

Conclusion: We showed promising results for using a plasma methylation marker panel for the detection of patients with advanced adenomas, with especially high sensitivity for adenomas with high-grade dysplasia. This method could serve as the basis for further development of a highly accurate and minimally invasive blood-based screening test and could potentially help to guide the downstream clinical evaluation of patients.

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P-47 A phase I/II study of pembrolizumab in combination with ibrutinib for advanced, refractory microsatellite stable colorectal cancers

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Background: Nearly 50% of patients with colorectal cancer (CRC), one of the most common cancers worldwide, develop metastatic disease. Pre-clinical data suggest that ibrutinib, a BTK inhibitor used in several hematologic malignancies, may counteract the immune tumor escape mechanism in solid tumors. Pembrolizumab, a PD-1 checkpoint inhibitor, is effective in advanced CRC with microsatellite instability, but not microsatellite stable (MSS) disease. Given ibrutinib's immune-modulatory function, it may display synergy with checkpoint inhibitors. Ibrutinib plus anti-PD-L1 or anti-CTLA-4 has shown enhanced efficacy in multiple cancers including MSS CRC, in various mouse models.

Methods: This was a phase I/II study with standard 3+3 dose-escalating design in patients with advanced MSS CRC. Patients must have progressed through standard frontline therapies. Cohort 0 received 420mg ibrutinib PO daily and cohort 1 received 560mg ibrutinib PO daily. Both cohorts received 200mg IV pembrolizumab every 3 weeks. The primary endpoints for phase I were safety and establishment of a recommended phase II dose for ibrutinib. In the phase II portion, patients received ibrutinib at maximum tolerated dose (MTD) and 200mg IV pembrolizumab every 3 weeks. The primary endpoint of the phase II portion was disease control rate (DCR= CR + PR + SD) at 4 months. Patients were accrued according to a two-stage Minimax design. At least 1 of 18 patients must have achieved disease control at 4 months in the first stage to proceed to the second stage. In the second stage, at least 4 of 32 patients must have achieved disease control at 4 months for the therapy to be considered effective. Those who received more than one baseline scan were considered evaluable and up to 6 patients treated at MTD from phase I were allowed to count toward the evaluation of primary endpoints in the phase II portion.

Results: Eight patients in phase I (75% male, median age 60 years) and 30 patients in phase II received at least one treatment dose (53.3% male, median age 57 years). Median number of prior lines of systemic therapy was 3. In phase I, no dose-limiting toxicities (DLTs) were experienced in either cohort. MTD was 560mg ibrutinib daily and 200mg pembrolizumab every 3 weeks. In the phase II portion, a total of 28 patients (including 4 patients from phase I) were evaluable for primary endpoints. One of 18 patients in the first stage had stable disease at 4 months but no additional patients had disease control in the second stage for a DCR of 3.6% at 4 months and RR of 0%. Median OS was 5.32 months (95% CI: 3.35-8.41) and median PFS was 1.54 months (95% CI: 1.41-1.71). The most common grade 3/4 AEs overall were anemia (21.1%), increased alkaline phosphatase (7.9%), and fatigue (7.9%).

Conclusion: Ibrutinib and pembrolizumab in combination appear to be well tolerated with no DLTs identified at MTD. However, low DCR does not warrant further study of this combination in advanced MSS CRC.

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P-48 First evidence for the antitumor activity of nanoliposomal irinotecan in metastatic biliary tract cancer

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Background: Therapeutic options are limited and not evidence-based for advanced, metastatic biliary tract cancer, which has a dismal prognosis. The pivotal NAPOLI-1 trial demonstrated the superior clinical benefit of nanoliposomal irinotecan (Nal-IRI) in gemcitabine-pretreated patients with metastatic pancreatic ductal adenocarcinoma; however, the antitumor activity of Nal-IRI in biliary tract cancer is unknown. This is the first report describing the efficacy of Nal-IRI in biliary tract cancer.

Methods: In this multicenter retrospective cohort analysis, we identified patients with metastatic biliary tract adenocarcinoma who were treated with Nal-IRI following tumor progression under standard therapy at one of the study centers between January 2017 and January 2019. We assessed disease control rate (DCR), progression-free survival (PFS), and overall survival (OS).

Results: There were 14 patients; the median age at the time of diagnosis and the median age at the initiation of Nal-IRI were 59.3 and 60.0 years, respectively. Nal-IRI was administered as second-, third-, fourth-, and fifth-line treatment in 6 (43%), 5 (36%), 2 (14%), and 1 (7%) patient with metastatic disease, respectively. The objective DCR with Nal-IRI was 50% (7/14 patients). Six patients (43%) had partial response, and one patient (7%) had stable disease. Progressive disease was observed in seven patients. The median PFS and median OS following Nal-IRI initiation were 10.6 and 24.1 months, respectively.

Conclusion: This retrospective analysis provides the first evidence that Nal-IRI might exhibit a clinical meaningful antitumor activity in metastatic biliary tract cancer by controlling the disease.

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P-49 A study of first-line treatments for patients with BRAFV600E mutant metastatic colorectal cancer in a real-life setting: CAPSTAN study

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Background: The BRAF V600E mutation is associated with poor prognosis in patients with metastatic colorectal cancer (MCRC), and findings from clinical trials have largely remained inconclusive regarding the efficacy of first line treatments for BRAF-mutant mCRC patients. There is, therefore, an unmet need to document the current practices for first-line treatment of BRAF-mutant mCRC, and their effectiveness and safety in a real-world setting.

Methods: This study comprises of two phases: I) an e-survey sent to more than 1500 sites in Europe to characterize sites treating BRAF-mutant mCRC patients and to select a sample of sites, as representative as possible of the overall population in Europe, II) a review of medical records of approximately 300 adult patients who initiated first-line treatment for mCRC between 2016 and 2018 in representative sites, and with a diagnosis of BRAFV600E mutant mCRC discovered a priori or a posteriori to first-line treatment initiation. The target countries include EU5 countries, Belgium, Austria and the Netherlands. In order to obtain a representative sample of real-world patients treated for BRAF-mutant mCRC in Europe, an evidence-based approach was adopted to select sites within a country that meet the right criteria for representability, taking into account various site-level factors such as center type [public/private, academic/non-academic], center size, center practice, etc. Stratified random sampling was used to select appropriate sites that would be invited to participate in the data collection. This abstract will focus on phase I results; phase II is ongoing.

Results: An e-survey was sent by email to 1558 potentially participating physicians in 8 countries. Among these, 1096 physicians did not respond to the invitation, 235 communicated their inability to participate via telephone or e-mail, and 229 completed the e-Survey. The 229 respondent physicians were practicing in 219 sites. All 219 responding sites treat mCRC patients and the majority (205 sites of 219) treat BRAF-mutated mCRC patients in the first line. Of these 205 sites, 182 expressed their willingness to participate. Most physicians (~88%) who completed the e-survey were oncologists. Majority of respondents (~59%) were from non-academic centers. Almost all physicians (94%) reported testing the BRAF mutational status of mCRC patients, and 67% of physicians declared that BRAF testing was generally done at the metastatic diagnosis. During the study period, 24% of physicians reported treating more than 10 BRAF-mutated mCRC patients per year, 41% treating between 6-10 and 34% treating between 1-5.

Conclusion: To our knowledge, this is the first study assessing the management of BRAFV600E-mutated mCRC patients in routine clinical practice in Europe. The results of this ongoing study will allow us to further describe the management of BRAF-mCRC patients in real-life settings, particularly the BRAF testing landscape.

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P-50 Safety and tolerability of regorafenib: A real-life experience

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Background: Regorafenib has been approved among the treatment options for patients with advanced-stage colorectal cancer (CRC), hepatocellular carcinoma (HCC) and gastrointestinal stromal tumors (GIST). In this study, we aim to report the real-life experience of the safety and tolerability regorafenib in our institution.

Methods: We conducted a retrospective chart review of 43 patients who received regorafenib in Kuwait Cancer Control Center (KCCC) from 2016 until the end of 2019. Data collected include diagnosis, patient demographics, performance status, number of previous lines of treatment, number of treatment cycles, side effects, best-tolerated dose and treatment discontinuation due to intolerability. Univariate analysis with Pearson chi-square test were conducted to study co-relation between discontinuation rates and several factors.

Results: We had available data for 43 patients (23 males and 20 females). 83.7% of patients had an ECOG performance status of 0 or 1. 73% were diagnosed with metastatic CRC, 21% were diagnosed with HCC and 6% were diagnosed with GIST tumors. Half of the patients received 3 lines or more of treatment prior to regorafenib. The median number of cycles received was 3.7 with 11.6% of patients still on active treatment at the time of analysis. The most commonly reported grade 3 and above side-effects included rash (41.9%), fatigue (39.6 %), hypertension (25.6%), mucositis (21.9%), hand-foot syndrome (2.3%), and hyperbilirubinemia (4.6%). The best-tolerated dose was 80 mg and that was achieved in 44.2% of patients. The recommended dose of 160 mg could only be achieved in 20.9% of patients. The treatment was discontinued because of intolerability in 25.6% of patients. The discontinuation rates in those with ages 60 years and above versus below 60 years were 91% and 68%, respectively.

Conclusion: In our cohort, the best-tolerated dose of regorafenib was 80 mg. Toxicity and intolerability of regorafenib lead to treatment discontinuation in nearly a quarter of patients. Patient age may influence tolerance and adherence to regorafenib.

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P-51 Immunoscore in rectal cancer patients receiving radiation followed by mFOLFOX with avelumab

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Background: Immunoscore is a validated prognostic tool in colon cancer that measures the densities of CD3 and CD8 positive T-lymphocytes at the tumor center and invasive margin. The aim of the present study was to evaluate the prognostic value of Immunoscore in the treatment of rectal cancer.

Methods: Clinical (age, gender, clinical stage) and microscopic variables (Immunoscore, PD-L1 expression, tumor regression grade [TRG], apoptotic index, mitotic index, microvascular density assessed in normal and tumor tissue) were collected from patients diagnosed with locally advanced rectal cancer. Tissue samples were collected at diagnostic baseline biopsy, post-radiation and post mFOLFOX and avelumab with resection. Responders were defined as patients with $>$ 95% pathological response on resection specimen. Trial registration number is NCT03503630.

Results: Fourteen patients were analyzed, 10 (71%) men and 4 (29%) women with a median age of 58 (34-73) years. Out of the 13 patients that underwent surgery, 7 were responders and 6 were non-responders. The optimal baseline Immunoscore cutoff in our population derived from the receiver operating characteristics (ROC) curve to distinguish between responders and non-responders was 61.8%. The mean Immunoscore in responders was 63.4% in comparison to 40.6% in non-responders. The mean Immunoscore also decreased post-radiation from 52.0% to 41.2%. Responders had higher CD8 positive cells in the invasive margin of tumor tissue post-radiation. In the normal tissue, radiation did not increase the CD3, CD4 or CD8 positive cells, while mFOLFOX and avelumab increased those counts ($p< 0.05$). In the tumor tissue, the mean CD8 positive cells in the invasive margin increased after mFOLFOX and avelumab and not radiation ($p< 0.05$). At diagnosis, all cases had negative PD-L1 expression in tumor cells. Post radiation, 2 cases switched to positive expression, which switched back to negative expression after mFOLFOX and avelumab. PD-L1 expression in the inflammatory environment increased in both normal and tumor tissues after radiation ($p< 0.05$); however, no difference between responders and non-responders was documented. There was a significant increase in the apoptotic index and microvascular density post-radiation ($p< 0.05$) in contrast to the mitotic index in both responders and non-responders ($p< 0.05$). A directly proportional correlation was found between the post-radiation Immunoscore and post-radiation apoptotic index in tumors ($p< 0.05$). However, no such correlation was found among Immunoscore, mitoses and microvascular density. Of note, microvascular density decreased after mFOLFOX and avelumab ($p< 0.05$). None of the patients involved in this cohort had microsatellite instability-high status.

Conclusion: Despite the limited number of patients in our cohort, our customized Immunoscore showed that higher Immunoscore levels are associated with better tumor regression grade. This trial illustrated not only the tumor landscape evolution through radiation and mFOLFOX with avelumab treatment in locally advanced rectal cancer patients but also the predictors of response and progression in normal tissue in tumor vicinity.

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P-52 The diagnostic dilemma between chronic pancreatitis and pancreatic cancer

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Background: In pancreatic neoplasms, there are no special clinical signs, the manifestation of which would make it clear that oncology develops in the tissue cells. The tumor is detected late when the process is extremely advanced. There are common signs of pathology, but they are similar to other diseases. Data exists to indicate a definite association between chronic pancreatitis and pancreatic cancer. The strength of this association varies between various causes of pancreatitis, with hereditary and tropical pancreatitis more likely to result in malignancy.

Methods: The study included 32 patients aged 34—76 years, of which 12 were pseudotumor pancreatitis (PP), 11 were chronic calcifying pancreatitis (CKP), and 9 were pancreatic cancer. The CA 19-9 tumor marker was determined in all blood serum patients by the radioimmunological method. Ultrasound of the pancreas, endoscopic ultrasonography, abdominal CT were performed and 5 patients underwent fine-needle puncture of the pancreas with cytological examination.

Results: The study showed that in patients with PP, CKP and pancreatic cancer, lipase activity was significantly increased compared with the control (21,3 $\pm$ 2.31; 29,9 $\pm$ 6.4; 39,7 $\pm$ 9,5 and 15.2 $\pm$ 1.9 µmol / min • L, respectively, $p < 0.05$). The level of CA 19-9 in patients with CP was increased compared with the control, in patients with pancreatic cancer - increased to a greater extent (31,2 $\pm$ 3,5; 41.3 $\pm$ 5.8; 225,5 $\pm$ 54,1;10,2 $\pm$ 1,3 ng / ml, respectively, $p < 0.05$). According to the data of ultrasound for the PP, an increase in the head to 3.2 cm or more was characteristic. In the presence of pancreatic cancer, there was a hypoechoic zone in the enlarged head, and with CP there was a diffusely heterogeneous increase in tissue echogenicity. The Wirsung duct was dilated in both cases, with PP was convoluted, with uneven, thickened walls, and with cancer, with even, thin walls. With CKP, multiple calcifications were detected. Cytological signs of adenocarcinoma were detected in 3 patients and were confirmed by histological examination of surgical material. In 2 patients, the picture was suspicious of adenocarcinoma, the diagnosis was not confirmed. In 2 patients, the cytological data corresponded to PP, but an adenocarcinoma was revealed by histological examination of the surgical material.

Conclusion: Thus, in the presence of a short history of diabetes patients, diabetes mellitus, obstructive jaundice, a persistent increase in blood lipase activity and CA level 19-9, a differential diagnosis between CP and pancreatic cancer should be carried out.

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P-53 Clinical evaluation of complex treatment of colorectal cancer with liver metastases

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Background: Colorectal cancer is characterized by slow growth, and before it reaches a large size with the onset of clinical symptoms, a fairly long period of time passes. Clinical manifestations depend on the location, type, spread of the tumor and complications. Among all patients with cancer of the rectum or colon, a quarter at the time of diagnosis revealed liver metastases. In the process of observation after treatment for colon cancer, there will be liver metastases in 30-50% of patients within 5 years.

Methods: The study included 68 patients with CRC (colorectal cancer) with liver metastases. Of these, 41 men (60,2%) and 27 women (39,7%). Age from 31 to 69 years with stage I - 10 patients (14,7%), stage II - 12 patients (17,6%), stage III - 18 patients (26,5%), stage IV - 38 patients (55,9%). Synchronous metastases in 44,2% (n = 30), metochronous metastases in 55,8% (n = 38). The following surgical methods were performed for the surgical treatment of liver metastases: Split in situ - 13.2% (n = 9), atypical resections - 41,2% (n = 28), anatomical liver resections - 35,2% (n = 24), right-sided hemihepatectomy - 7% (n = 10,3). In the postoperative period, 75% (n = 68) of patients underwent adjuvant chemotherapy.

Results: The study showed that the 2-year survival rate when performing extended liver resections with solitary metastases was 59.3 +/- 3.2%, while extended resections of multiple metastases was 14.5 +/- 3,8%. Postoperative complications were 24,5%. Postoperative mortality was 11,3%. With extended liver resections, the number of complications was 52.5%. The median survival, using extended resections of multiple liver metastases was 15.8 months, while extended resection of solitary metastases

was 37.2 months. At stage I disease, disease-free survival was 22,6 months. At stage II, 21 months, stage III, 14,2 months, and at stage IV, 12,4 months. Overall 3-year survival in stage I amounted to 55,6%. At stage II, 46,7%; stage III, 43.8%; and stage IV, 22.4%.

Conclusion: Thus, the use of surgical removal of metastases in the liver with CRC, at one of the stages of treatment, significantly increases its effectiveness, with both solitary and multiple metastatic liver damage compared with only conservative methods.

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P-54 BISQUIT: A randomized phase II study of the administration of prebiotics and probiotics during definitive treatment with chemotherapy-radiotherapy for patients with squamous cell carcinoma of the anal canal

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Background: The standard treatment for patients (pts) with localized squamous cell carcinoma of the anal canal (SCCAC) is chemoradiation (ChRT). Yet nearly 30% of patients do not respond or will recur and have to undergo salvage anorectal amputation. SCCAC is mostly a virus-associated tumor and thus potentially immunogenic. In fact, immune checkpoint inhibitors seem promising in trials of metastatic SCCAC. Recently, studies have shown that the composition of the intestinal microbiota influences the onset of colorectal cancer and response to immunotherapy in some solid tumors, and the replacement of the intestinal "carcinogenic" by a protective microbiota has been the reason of investigations with prebiotics and probiotics (PreProbiotics). Yet, there are no studies on the use of these agents in SCCAC. Thus we are conducting a randomized phase II study to test the efficacy of PreProbiotics during definitive ChRT, aiming to improve the cure rate of pts with localized SCCAC.

Trial design: This will be randomized, open-label, parallel, phase II trial, where eligible pts will be randomized 1:1 to receive PreProbiotics starting one week prior to ChRT and throughout treatment until response evaluation at 6 to 8 weeks post-ChRT or conventional ChRT. Eligible pts are $\geq$ 18 years, with histologically confirmed SCCAC, localized disease ($\geq$ T2N0M0) and indication to start definitive ChRT; HIV seropositive pts are eligible. Pts with active infection requiring antibiotics will be excluded. The primary endpoint is complete clinical and radiological response (CR) at 6 to 8 weeks post-ChRT. Secondary endpoints are CR at 6 months, progression-free survival, colostomy-free survival, metabolic response measured by 18-FDG PET-CT (baseline and at 6-8 weeks), toxicity, and incidence of HPV in tumor tissues. All pts will have the following biological samples collected for correlative studies at baseline, 6-8 weeks and 6 months post-ChRT: blood samples for circulating tumor DNA, inflammatory cytokines and variation in total number of lymphocytes, neutrophil/lymphocyte ratio and lymphocyte/monocyte ratio, anal/rectal swabs and feces to evaluate microbiota. Sample size assumptions: the H0 is CR at week 6 - 8 of 70% and H1, 90%; with a type I error of 10%, power of 80% and attrition rate of 10%, the final sample size is 75 patients.

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P-55 GASTHER2: Efficacy of adding trastuzumab to standard chemotherapy in patients with advanced HER2-negative gastric cancer and HER2-positive expression in circulating tumor cells

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Background: Patients (pts) with HER2+ metastatic gastric adenocarcinoma (mGC) receive first-line trastuzumab (TZ) combined with platin-based chemotherapy as standard first-line therapy. Routine HER2 expression is evaluated in tumor tissues by immunohistochemistry (IHC) and/or by gene amplification (FISH test). A prospective study by our group observed disagreement in HER2 expression between circulating tumor cells (CTC) and tumor tissues in 60% of cases. Yet, the efficacy of TZ in HER2-negative mGC pts whose CTC are HER2+ is unknown. Our objective is to evaluate whether the addition of TZ to first-line chemotherapy for pts with mGC and HER2+ expression exclusively in liquid biopsy, appraised by CTC, improves outcomes.

Trial design: Phase II single-arm one-stage trial of the addition of standard-dose TZ biosimilar (Zedora®) to first-line FOLFOX in pts with mGC and positive expression of HER2 in CTC and negative expression in tumor tissues (NCT04168931). CTC evaluation will be performed by ISET methodology. HER2 expression in tumor tissues will be evaluated as per routine; in CTC, HER2 expression will be measured by immunocytochemistry — as previously validated and published by our group (Abdallah E et al. The Oncologist 2019) and by CISH, as previously established for CTCs by our group (Troncarelli B et al. Cells 2019). Treatment will continue until progression, limiting toxicities or consent withdrawal. The primary endpoints are response rate by RECIST 1.1 after 2 cycles of treatment and the frequency of HER2+ CTC in HER-negative mGC measured in tumor tissues. Secondary endpoints are progression-free survival, overall survival and the frequency of CTC HER2+ expression upon progression. Eligible pts must have a diagnosis of HER2-negative mGC and HER2+ CTC, ECOG 0-2 and are candidates to receive first-line chemotherapy. They will have blood collected for CTC evaluation at baseline and at disease progression, and perform images every 2 cycles until progression. Monitoring of adverse related to TZ will follow standard recommendations. We will test 85 pts for CTC HER2 expression to treat 50 pts with HER2+ CTC mGC with the addition of TZ. For sample size assumptions we considered 60% of HER2+ CTC and a 95% confidence interval of 10%. The study will be considered positive if the response rate is 47% or higher (based on the Toga trial). This study was approved by our local IRB.

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P-56 Importance determination of interleukin-6 in bile and blood in tumours of the bileopancreatoduodenal zone

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Background: Experimental and clinical studies have shown an increase in the level of interleukin-6 (IL-6) in the blood plasma and other cytokines in obstructive jaundice. According to some data, in patients with tumors, the combination of a persistent increase in cytokines and an extended acute response phase is associated with a decrease in protein calories, leading to surgical complications and death.

Methods: The study involved 41 patients aged from 33 to 84 years old (62.8 $\pm$ 2.14), of whom 26 (63.4%) were men and 15 (36.6%) were women. The duration of the icteric period by the time of admission to the hospital averaged 28.7 $\pm$ 2.18 days. At the same time, in 6 (14.6%) patients the duration of cholestasis was up to 15 days, in 10 (24.4%) from 15 to 30 days, and in 25 (61.0%) more than 1 month. The cause of obstructive jaundice (OJ) in 25 (61.0%) patients was a pancreatic head tumor, 10 (24.4%) had a liver gate tumor, 2 (4.9%) had a terminal choledochus tumor, and 4 (9.8%) had cancer of the Vater papilla. Percutaneous transhepatic cholangiography (PTCH) with percutaneous transhepatic cholangiostomy (PTCHS) was performed for all patients, regardless of the localization of the tumor process.

Results: The concentration of IL-6 before the overlap of PTCH in the serum was higher than normal, averaging 152.65 $\pm$ 16.3 pg/ml. Immediately after the overlaying of PTCH in bile, this indicator was on average 68.58 $\pm$ 7.24 pg/ml. The high content of IL-6 in serum and bile testified to a pronounced endogenous intoxication of the body. The concentration of IL-6 in the initial day after the imposition of PTCH in serum decreased to 32.9%. In the following days, this indicator remained virtually unchanged, but on the 6th day of observation, there was a slight increase in his blood. In the bile at the same time, the concentration of IL-6 decreased by 17.1%. These indicators remained virtually unchanged up to 6 days of observation. On the 14th day, the decrease in the level of IL-6 in the blood compared to baseline was 64.4% and in the bile 54.3% ($P < 0.001$).

Conclusion: Thus, the determination of IL-6 in the blood and in the bile makes it possible to more objectively evaluate the tumor process and the cytokine-induced endogenous intoxication to the response of the therapeutic measures taken in biliopancreatoduodenal tumors complicated by the breast.

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P-57 Effectiveness and safety of trifluridine/tipiracil in patients with metastatic colorectal cancer in clinical practice in Poland

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Background: Trifluridine/tipiracil is indicated for adult patients with metastatic colorectal cancer (mCRC) previously treated (refractory), or not considered as candidates for available therapies. The randomized phase 3 RECOURSE trial showed a significant increase in median overall survival (OS) of 1.8 months compared to the placebo, significant benefit in progression-free survival (PFS), and prolonged time to ECOG PS worsening. We assessed the effectiveness and safety of trifluridine/tipiracil in daily clinical practice before public reimbursement in Poland.

Methods: We collected data from patients treated with trifluridine/tipiracil at eleven polish oncology centers according to approved indications. In this retrospective patient cohort, trifluridine/tipiracil was donated to the hospitals or was bought out-of-pocket by patients. Baseline characteristics of patients, safety, and survival times were assessed. Baseline characteristics were tested in uni- and multivariate analyses for prognostic significance of PFS and OS.

Results: A total of 123 patients with a median age of 60 years, treated from Feb. 2017 to Dec. 2019 were analyzed. Fifty-eight patients (47%) did not meet the RECOURSE trial eligibility criteria with having administered prior antiangiogenic treatment (41%) and/or being in ECOG PS 2 (7.3%). Four (3.2%) and 44 (36%) patients achieved response and disease stabilization, respectively. The median PFS was 3.2 months and the primary tumor location, KRAS-mutation status, site of metastases, BMI, ECOG PS, and Platelet-to-Lymphocyte Ratio were prognostic factors for PFS. The 6-month PFS rate was 24% and the primary tumor location in the left side colon, WT KRAS status, WT BRAF status, more than 3 lines of previous treatment, ECOG PS 0 and Platelet-to-Lymphocyte Ratio $\geq$130 were independently associated with higher chances of a patient being progression-free at 6 months. The most common grade $\geq$3 toxicities were neutropenia (35%), leukopenia (9.6%), anemia (12%), fatigue (9,6%) and diarrhea (3,2%).

Conclusion: Our data show that treatment with trifluridine/tipiracil in daily clinical practice is feasible and safe. Forty-eight patients (39%) achieved clinical benefit with trifluridine/tipiracil. Patient characteristics such as left side primary tumor location, WT KRAS status, WT BRAF status, more than 3 lines of previous treatment, ECOG PS 0 and Platelet-to-Lymphocyte Ratio $\geq$130 may be helpful to identify 6 month progression-free survivors.

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P-58 Survival and prognostic factors in metastatic gastric cancer: Results from a Bangladeshi cohort

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Background: Prognostic factors in gastric cancer (GC) has been less evaluated in developing countries, with no data available in Bangladesh, to our knowledge. We aimed to determine overall survival (OS) and association of prognostic factors in metastatic GC patients.

Methods: A total of 42 metastatic GC patients were identified from the database of Square Hospital from January 2011 to December 2015 and investigated retrospectively. All were histologically adenocarcinoma and received palliative chemotherapy. The primary endpoint was OS and secondary endpoints were prognostic association with different factors. 20 variables were evaluated: age, sex, comorbidity, family history, primary tumor location, grade, Karnofsky performance status (KPS), carcinoembryonic antigen, prior gastrectomy, ascites, pleural effusion, metastatic sites (liver, lung, brain, bone, peritoneum, others), number of metastatic organs and timing of metastasis. Prognostic variables were tested with Univariate analysis followed by a Multivariate Cox Proportional Hazards Model. Survival was calculated by Kaplan-Meier method and compared by Log-rank test.

Results: Median survival of the entire cohort was 7 months (95% CI: 5.6-8.3). Factors related to OS in univariate analysis were KPS, gastrectomy, ascites and lung metastasis. In multivariate analysis, three factors were independently associated with OS: KPS ($p = 0.005$), gastrectomy ($p = 0.004$) and lung metastasis ($p = 0.009$). Patients with KPS $\geq$70 had significant survival advantage compared with those with KPS $<$ 70 (10 months vs. 3 months; Hazard Ratio [HR]: 3.8). Prior gastrectomy significantly prolonged survival (21 months vs. 6 months; HR: 3.2). Patients with lung metastasis had 3.3-times the risk of death than those without (OS: 5 months vs. 9 months; HR: 3.3). Other prognostic factors were not found to be associated with survival in Multivariate regression.

Conclusion: The study defined survival time for this cohort as well as demonstrated three factors impacting on shorter survival including poor performance status, no prior gastrectomy, and lung metastasis. To our knowledge, survival and prognostic factors in metastatic gastric cancer have previously never been described in a South Asian region. Pending the availability of such data, the results from our study, although yielded from a small, retrospective, single-centre design, may guide clinicians in therapeutic decision-making and designing future clinical trials in this geographical region.

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P-59 High blood levels of soluble OX40 (CD134), an immune costimulatory molecule, indicate reduced survival in patients with advanced colorectal cancer

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Background: The interaction between tumor necrosis factor receptor superfamily, member 4 (OX40) on T cells and the OX40 ligand (OX40L) on antigen-presenting cells (APCs) is a pivotal step for T-cell activation and the promotion of antitumor immunity. However, it is hypothesized that soluble OX40 (sOX40) in blood suppresses T-cell activation by blocking the OX40/OX40L interaction.

Methods: In the present study, the association between blood sOX40 levels and the clinical characteristics of advanced colorectal cancer (CRC) patients was investigated. Blood was collected from 22 patients with advanced CRC. Blood sOX40 levels were determined by enzyme-linked immunosorbent assay (ELISA). Messenger RNA (mRNA) expression encoding OX40 or cytokines was analyzed by quantitative RT-PCR. Blood sOX40 levels were positively correlated with the blood levels of carbohydrate antigen (CA) 19-9, carcinoembryonic antigen (CEA), C-reactive protein (CRP) and soluble programmed cell death ligand-1 (PD-L1) in patients but negatively correlated with the blood levels of albumin. Blood sOX40 levels were not correlated with the mRNA expression of interferon (IFN)-gamma, interleukin (IL)-6, IL-10 and IL-4 in the peripheral blood mononuclear cells (PBMCs) of the patients and were not correlated with the frequency of programmed cell death-1 (PD-1) expressing CD4+, CD8+, and CD56+ cells.

Results: Notably, according to both univariate and multivariate analyses, high blood sOX40 levels were significantly correlated with reduced survival time in patients. Although activated Jurkat cells (a human T-cell line) exhibited an upregulation of sOX40 production and OX40 mRNA expression, the OX40 mRNA expression of the PBMCs of patients was not correlated with blood sOX40 levels.

Conclusion: High blood levels of sOX40 were correlated with reduced survival time in patients with advanced CRC, possibly associated with the suppression of antitumor immunity by sOX40.

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P-60 Tolerability of adjuvant chemotherapy with TS-1 or XELOX regimen in elderly patients with stage II or III gastric cancer after D2 gastrectomy

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Background: Compared to surgery, adjuvant TS-1 and XELOX regimen in gastric cancer (GC) has shown survival benefit after D2 gastrectomy. As the elderly population continues to grow, adjuvant chemotherapy (AC) has become important. Clinicians hesitate to offer chemotherapy to elderly patients because of comorbidities and intolerability. This study aims to investigate the efficacy, safety, and compliance of AC with TS-1 and XELOX regimen in patients aged >70 years.

Methods: We collected data on stage II/III GC patients who underwent D2 gastrectomy followed by AC (TS-1 or XELOX regimen) between January 2013 and December 2018 at Chungnam National University Hospital, South Korea. They were classified into two groups by age; we analyzed baseline characteristics, adverse events, overall survival (OS), relapse-free survival (RFS), rates of regimen completion, and dose reduction.

Results: There was no significant difference in OS and RFS between both regimens. The TS-1 group had 232 patients (92 elderly). For grade >3 adverse events, elderly patients had more anemia ($p = 0.029$) and lower completion rates (78.4% vs. 91.5%, p 3 adverse events, elderly patients had more thrombocytopenia ($p = 0.02$); no differences in completion and dose reduction rates; and no differences in OS and RFS.

Conclusion: There was no difference in efficacy between the TS-1 and XELOX regimens; both were tolerable in elderly patients. The XELOX group showed no differences in OS and RFS, which were lower in the TS-1 group, possibly due to decreased completion rates. Clinicians should not hesitate to prescribe AC to elderly patients.

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P-61 nab-Paclitaxel plus gemcitabine for metastatic pancreatic cancer: Real life

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Background: Pancreatic cancer is one of the most lethal tumours. Its increasing incidence, late diagnosis, and limited therapeutic options will place it as the second cause of cancer deaths in the next decade. Multidisciplinary treatment will provide the best results but unfortunately, many patients will only be candidates to palliative treatment. The positive results from the phase III MPACT trial led to the approval of nab-paclitaxel plus gemcitabine as a therapeutic option for patients with metastatic pancreatic cancer. We have reviewed our patients who have received this treatment in the past two years.

Methods: A multicentre, retrospective, observational study was carried out. All patients diagnosed with metastatic pancreatic cancer who received first-line treatment with nab-paclitaxel and gemcitabine were included. We assessed the efficacy and evaluated safety parameters as well.

Results: We assessed 34 patients; 18 females, 16 males. At the time of presenting this work, 15 continue on treatment with a median duration of treatment of 6.9 months (3.8-10.6 months), 10 died of progression after a median of lines of treatment of 2 (1-3) with a median overall survival of 5.8 months (4.2-15.1months), and 9 patients are receiving actively a second line of treatment. Responses have been recorded as 1 complete radiological response, 6 partial responses, 8 with stable disease, and 19 with progressive disease. The median progression-free survival for those who died or are receiving another line of treatment was of 3.9 (3.4–4.6) months. Grade 3–4 hematologic toxicity was included: neutropenia, thrombocytopenia, and anaemia have been seen in 19, 6, and 4.3% of patients, respectively. Dose reductions were performed in 75% of the patients.

Conclusion: This study confirmed the effectiveness and safety of first-line nab-paclitaxel in metastatic pancreatic adenocarcinoma in a real-world setting.

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P-62 Inferior survival for mismatch repair deficient metastatic colorectal cancer observed in an Irish cohort

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Background: Mismatch repair protein deficiency (dMMR) is a poor prognostic factor in metastatic colorectal cancer (mCRC). It has been associated with a poor response to standard chemotherapy. Immune checkpoint blockers (ICB) offer a promising therapeutic alternative for these patients. ICBs are currently unavailable for mCRC in Ireland. The aim of this study was to compare the response of CRC to standard chemotherapy based on MMR status.

Methods: A retrospective study was completed in an Irish national cancer centre which included all CRC patients from 2015-2019. Electronic patient records were used to identify clinical variables including demographic data, tumour characteristics and survival outcomes. Outcome measures included progression-free survival (PFS) and overall survival (OS). PFS was defined as the start date of the first chemotherapy agent until radiological evidence of progression. OS was defined from the date of diagnosis until death or until the study start date for censored data. Kaplan-Meier curves were used to compare survival outcomes between groups. SPSS software was used for statistical analysis.

Results: Five hundred CRC patients were identified between 2015-2019. One hundred and eighty-three cases were recorded as mCRC following review of CT staging scans. Only patients with MMR testing were included (n=150). Mismatch repair proficient (pMMR) tumours accounted for 95% (n=143) of cases and 5% (n=7) were dMMR. Six patients had MLH1/PMS2 loss and one had MSH6 loss. Co-existent somatic mutations in dMMR tumours included KRAS (n=2) and BRAF (n=2). In pMMR tumours, KRAS (n=46), BRAF (n=6) and NRAS (n=2) mutations were identified. The median age at diagnosis was lower in dMMR patients [63 in dMMR (range 67-84) and 72 in pMMR patients (range 39-90)] but this was not found to be statistically significant (p=0.121). In the dMMR group, 85.7% (n=6) of patients received at least one oxaliplatin-based chemotherapy regimen compared to 88.1% of pMMR cases (n=126). The remaining patients (n=18) did not receive chemotherapy most commonly due to poor performance status (n=8) or patient preference (n=5). Median PFS in months was 12.0 (95% C.I.10.16– 13.87) and 7.0 (95% C.I.4.747-7.753) in pMMR and dMMR tumours, respectively ($p = 0.001$). Median OS was 96.0 months (95% C.I.49.786 – 142.214) in pMMR cases and 28.0 months (95% C.I.1-52.789) in dMMR cases (p=0.008). Since diagnosis, 24% (n=34) of pMMR patients and 29% (n=2) of dMMR have died. In non-metastatic CRC, forty-two dMMR tumours were identified. Thirty-three had MLH1 loss (31 MLH1/PMS2, 1 MLH1/MSH2, 1 MLH1/MSH2/PMS2). Three had MSH6 loss, two had MSH2/MSH6 loss and four had PMS2 loss. In patients who received chemotherapy (n=16), two progressed to metastatic disease and one patient died (median OS 18 months). Progressive disease was observed in 11.9% (n=5) with a median PFS of 18 months. Four of these patients died (median OS 13 months), all of whom had MLH1 PMS2 loss.

Conclusion: PFS and OS were significantly lower in dMMR mCRC patients. This study demonstrates a powerful missed opportunity for ICB use in dMMR mCRC in Ireland. Implementation of ICBs into treatment policy for this small cohort of patients is an achievable therapeutic goal that may significantly improve survival.

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P-63 FOLFIRINOX in borderline resectable pancreatic carcinoma

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Background: Borderline resectable pancreatic cancer is a special entity recognised by the National Comprehensive Cancer Network. This entity will depend on a multidisciplinary meeting for a proper application of multimodality treatments to improve the chances of good results. FOLFIRINOX (5-fluorouracil, oxaliplatin, irinotecan, and leucovorin) has shown effectiveness in the treatment of this disease by increasing response rate with an impact on median survival. Toxicity could be concerning but supportive measures can help significantly.

Methods: All patients diagnosed with pancreatic cancer were discussed at a multidisciplinary team and those considered borderline resectable were treated with neoadjuvant FOLFIRINOX. We assessed primarily the surgical resectability after three months of treatment and also side-effects.

Results: We evaluated 49 patients, 25 female. The most common toxicities grade 3 or higher were gastrointestinal, mainly diarrhoea and nausea/vomiting. 15 patients required admission due to diarrhoea and dehydration. Haematological toxicities such as neutropenia grade 3-4 occurred in 22 patients; 10 of them needed admission due

to neutropenic sepsis. Fatigue was also a relevant side-effect present in all the patients, grade 1 in most of them, but grade 3 or higher in 23 patients. The dose of chemotherapy was reduced in 35 patients. In 7 of these patients, dose reduction was due to a peripheral neuropathy. 28 patients had a response, 12 had stable disease, and 9 showed progression. 20/49 patients underwent radical surgery, 12 underwent chemoradiotherapy and 8 stopped the treatment and started a follow-up.

Conclusion: FOLFIRINOX as neoadjuvant therapy for borderline resectable pancreatic adenocarcinoma is a good option, providing that good supportive measures are in place to reduce side effects.

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P-64 P-selectin and factor VIII as risk factors of thromboembolic disease in patients with hepatocellular carcinoma

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Background: Venous thromboembolism (VTE) is a common complication in patients with hepatocellular carcinoma (HCC). Its pathomechanism is associated with non-malignant origin in chronic liver disease as well as malignant disease. However, this high incidence is likely to correlate with other factors. Patients with HCC and VTE have a shorter survival time than patients without VTE. Factor VIII is an important pro-coagulant protein that binds with high affinity to von Willebrand factor. Factor VIII increased to more than 150% may cause an approximately 6-fold higher risk of venous thrombosis compared to patients with normal factor VIII. Its level rises with increasing age, during inflammation, and in pregnancy. Cancer patients with higher FVIII activity had a statistically higher proportion of VTE (14%) compared to patients with normal values (4%). Selectins are membrane glycoproteins that are involved in cell adhesion. P-selectin is considered to be a risk factor for VTE in cancer patients. The level of soluble P-selectin at the time of cancer diagnosis may identify patients at risk of VTE.

Methods: In our study, we identified P-selectin and factor VIII as risk factors for thromboembolic disease in HCC patients. We defined patients as benefiting from thromboprophylaxis in terms of delaying VTE. We examined 30 patients with HCC and compared the results to a healthy population. We determined etiology of liver cirrhosis, the presence of VTE, basic laboratory parameters, genetic examinations as well as examinations for other thrombophilic conditions such as protein C, anti-thrombin, soluble P-selectin, P-selectin expression, factor VIII and PAI-1 activity.

Results: Patients with HCC and VTE had higher factor VIII levels of 2,325 (1,65 - 2,77) than patients with HCC without VTE, who had values of 1,6413 (0,77 - 2,70). The healthy control group had average factor VIII levels of 1,1970 IU / ml (0,86 − 1,89) - SD of 0,25331. The level of soluble P-selectin in HCC patients was significantly higher than in the healthy control group ($p = 0,0003$). The number of patients with thromboembolic disease was 33.3%. The average levels of soluble P-selectin were 59.8 ng/ml (26-180), suggesting high risk. However, patients who did not have VTE also had elevated levels of soluble P-selectin: 20 patients (66.6%) with 54.72 ng/ml. Above the cut off level of 53.1 ng/ml, 17 of the 30 HCC patients were present. Of these, 4 patients (23%) outperformed VTE. Mean expression of membrane P-selectin in HCC patients versus healthy control was 14.724% (5.31 - 39.40%) of SD 8.28363 vs. 2.933% (1.1 - 6.5%).

Conclusion: The best predictive parameters of the risk of VTE in HCC patients are factor VIII and P-selectin in plasma as well as CD62 expression by flow cytometry. Based on our results, we consider FVIII and P-selectin as predictive biomarkers of VTE. If investigated at the time of diagnosis, they could predict the risk of developing VTE in the future. Thromboprophylaxis should be considered individually, especially in patients with other associated risk factors for VTE.

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P-65 Locally advanced/metastatic gastric cancer: Real-world data on first-line treatment with oxaliplatin and cisplatin-based doublets

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Background: In metastatic gastric cancer (mGC), palliative chemotherapy has shown benefit compared with best supportive care (BSC) and combination chemotherapy showed a survival benefit over single-drug therapies. However, no standard first-line treatment regimen is currently accepted. Anthracycline and docetaxel-based triplets are not superior to fluoropyrimidine-containing doublets and a recent meta-analysis showed benefit of oxaliplatin (OX)- over cisplatin (CIS)-based doublets. Capecitabine proved non-inferior to fluorouracil in the REAL-2 trial and subsequent meta-analyses. The aims of this study were to 1) characterize first-line treatment patterns of mGC with doublet chemotherapy, 2) investigate outcomes associated with different doublet regimens, and 3) evaluate the tolerability profile of different regimens.

Methods: This was a multicentric retrospective cohort study including patients with HER2-negative locally advanced/mGC, with adenocarcinoma histology, treated with first-line doublet chemotherapy (platinum and fluoropyrimidine) between January 2010 and December 2017 in four Lisbon hospitals. Data were collected from patients' medical records, stored in an access-restricted web platform (RedCap), and subsequently exported and analysed in IBM SPSS v22.0.

Results: Of 237 patients identified with locally advanced/mGC treated with palliative chemotherapy, 57 received monotherapy, 101 triplets, and 73 doublets. Sixty patients were treated with platinum-based doublets, 41 of which with OX and 19 with CIS. No significant differences were found in clinical/histological features between OX and CIS groups, except for a higher number of patients with diffuse histology in the first (41.5% vs 16%; p=0,018). Regarding efficacy, no significant differences were found in overall survival (10.1 vs 7.4 months; HR 1.02; 95% CI 0.57−1.83; p=0.951) or time to second-line treatment (9.6 vs 8.0 months; HR 1.12; 95% CI 0.51−2.44; p=0.775) between groups. Grade 1/2 neutropenia was more prevalent in CIS group (53% vs 22%, p=0.017) and grade 1/2 neuropathy in OX group (32% vs 5.3%, p=0.026).

Conclusion: In this retrospective, locally advanced/mGC cohort, no significant differences were found in overall survival and time to second-line treatment between OX- and CIS-based doublets. There were significant differences in the toxicity profile. Further efforts will be employed in the future to expand this study cohort.

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P-66 Treatment with FOLFIRI-aflibercept in an elderly population (over 75 and octogenarians) with metastatic colorectal cancer after failure of an oxaliplatin-based regimen: Experience in a real-life population

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Background: Aflibercept, a recombinant human anti-VEGF fusion protein, significantly improves response rate (ORR), progression-free survival (PFS) and overall survival (OS) when added to FOLFIRI, compared with FOLFIRI alone, as second-line therapy in patients with metastatic colorectal cancer (mCRC) who progressed after being treated with oxaliplatin. A subset analysis of the VELOUR trial, suggests that elderly patients ($>$ 65 years) have a consistent but small benefit in OS, in PFS and a higher percentage of grade 3-4 toxicity, though for elderly patients $\geq$ 75 years, this has never really been verified. We evaluated the efficacy and safety of this combination in a real-life population of $\geq$ 75 years and octogenarian patients.

Methods: We conducted a retrospective, multicentre, observational analysis of elderly patients ($\geq$ 75 years) with mCRC treated with FOLFIRI-aflibercept after progression of an oxaliplatin-base regimen as part of routine clinical practice in thirteen Italian cancer centres. We recorded 112 patients. They were treated with FOLFIRI plus

aflibercept every 15 days as second-line chemotherapy treatment for mCRC. Efficacy and safety outcomes were analyzed. Here we reported preliminary safety analysis results.

Results: Patient median age was 78 years (75-87). 83 patients (74.1%) had an ECOG PS 0-1 and 23 patients (20.5%) 2-3. Only 30 patients (26.7%) received the G8 questionnaire (score $\geq$ 14) and 11 patients (12.3%) were assessed with VGM. Cardiac comorbidity was recorded in 26%, neurological in 10%, metabolic in 24%, pulmonary in 3%, nephrological in 3% and pre-treatment hypertension was recorded in 63% of patients. Median number of cycles was 11 (2-96). Aflibercept dose reduction (2 mg/kg) was required in 16.12% while FOLFIRI dose reduction (80%) in 30.64% of patients. Therapy discontinuation due to toxicity was required in 14.51%, progression of disease in 75.9%, withdrawal in 1.16%, clinical deterioration of ECOG PS in 4.9% and because of liver R0 resection (NED) in 3.22%. All grade toxicity were asthenia (30.64%), hypertension (16.12%), proteinuria (4.83%), neutropenia (25.8%), anemia (19.35%), nausea/vomiting (17.74%), diarrhea (24.19%), and stomatitis (19.35%). Most frequently 3-4 grade toxicity observed were asthenia (11.29%), anemia (3.23%), neutropenia (16.2%), thrombocytopenia (3.23%), nausea/vomiting (4.84%), hypertension (1.62%), diarrhea (6.45%), bleeding (6.45%), alopecia (4.83%), anorexia (8.06%), proteinuria (3.22%), and VTE (3.22%). In patients with a G8 score $\geq$ 14, we observed a lower percentage of grade 3-4 toxicity versus overall elderly population (55% vs 78%); 16 of the octogenarians patients (24 patients, 26.8%), experienced G1-G2 toxicity and 8 pt G3-G4 (3 pt haematological, 2 pt gastrointestinal, 3 pt asthenia, 1 pt proteinuria, 1 pt VTE).

Conclusion: Elderly pts with mCRC are underrepresented in clinical trials. The VELOUR study included only 6.4% of patients over 75 years of age. These pts treated with FOLFIRI-aflibercept experienced a higher rate of G3-G4 toxicity (89.3% versus 80.5%). Our cohort confirmed that even elderly patients and octogenarians can safely receive treatment with aflibercept with manageable toxicity. G8 screening can help to select patients that better tolerate the treatment.

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P-67 Short-term outcomes of capecitabine plus oxaliplatin versus S-1 plus oxaliplatin as adjuvant chemotherapies for advanced gastric cancer after laparoscopic gastrectomy and D2 resection: A prospective, multicenter randomized, controlled clinical trial

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Background: Laparoscopic gastrectomy is accepted as an effective approach for advanced gastric cancer. However, data about adjuvant treatments after laparoscopic surgery are lacking. This study aimed to compare the efficacy of capecitabine plus oxaliplatin (CapeOx) and S-1 plus oxaliplatin (SOX) as adjuvant chemotherapies for patients who received radical laparoscopic surgery with advanced gastric cancer.

Methods: This study was reviewed and approved by the Ethics Committee of Tianjin Medical University. Pathological stage II and III gastric cancer patients from March 2016 to March 2019 who underwent laparoscopic gastrectomy with D2 lymphadenectomy in three Chinese institutes were enrolled. The primary endpoint was 1-year disease-free survival (DFS), and the secondary endpoints were 1-year overall survival (OS) and toxicity.

Results: After laparoscopic surgery, a total number of 126 patients with a pathological diagnosis of advanced gastric cancer were randomized into two groups. 64 patients were treated with CapeOx and 62 patients were treated with SOX. There was no significant difference (P =0.347) in 1-year DFS between the CapeOx group (84.4%) and the SOX group (80.6%). The 1-year OS was 98.4% for SOX and 93.8% for CapeOx (P =0.183). 5 patients in the CapeOx group and 4 in the SOX group experienced treatment-related toxicity of grade 3 or more. The most common toxicities of grade 3 or more were neutropenia (5 in CapeOx, 3 in SOX, P =0.494). There were no treatment-related deaths.

Conclusion: Among patients with advanced gastric cancer who received laparoscopic surgery, CapeOx had a higher DFS rate and SOX had a higher OS rate, but there were no significant differences between them. Both CapeOx and SOX were well-tolerated. Further observation of long-term outcomes is continuing in this trial.

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P-68 Safety and tolerability of a novel combination regimen OXIRI and its immunomodulatory effect in Asian pancreatic ductal adenocarcinoma patients

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Background: The FOLFIRINOX regimen has shown improved survival outcomes over the standard of care gemcitabine for the treatment of pancreatic ductal adenocarcinoma (PDAC) but remains limited due to increased toxicities. To this end, a phase I clinical study (NCT02368860) comprising of metronomic oxaliplatin, chronomodulated capecitabine and UGT1A1 genotype-guided dosing of irinotecan [OXIRI] was designed. It was hypothesized that this mechanistically-based regimen would have improved immunomodulatory effects over that of FOLFIRINOX, along with reduced toxicities. The aim of this study was to evaluate the safety and tolerability of this novel regimen and to assess the pharmacokinetics (PK) of UGT1A1-genotype-guided irinotecan and overall immune-mediated tumor response.

Methods: Patients received IV oxaliplatin at 50mg/m^2 on days 1 and 8 followed by IV irinotecan in accordance to their respective UGT1A1*6 and UGT1A1*28 genotype status. Oral capecitabine was administered at midnight on days 1 to 14 in a 21-day cycle. Maximum-tolerated dose (MTD) of capecitabine was determined using a 3+3 dose-escalation cohort design. Dose-limiting toxicities were defined as any grade 3/4 hematologic or non-hematologic toxicity occurring within the first cycle. Response evaluation was determined using RECIST v1.1 at baseline and every 6 weeks of treatment. UGT1A1*28 and UGT1A1*6 genotyping were performed using a validated high-resolution melting assay. PK analyses of irinotecan were conducted by LC-MS/MS quantification and parameters estimated using non-compartmental methods. Pharmacodynamic measurement of cytokine levels was performed with the multiplex cytokine profiling Luminex platform in duplicates at baseline and end of cycle 1 day 1.

Results: Twenty-nine patients with advanced and/or metastatic PDAC were recruited into either the dose-escalation (N=17) or expansion groups (N=12). The MTD of capecitabine was determined as 2650mg/day. Neutropenia (34.5%) was the most common grade 3 adverse events observed, followed by diarrhea (10.3%), hypokalemia, peripheral sensory neuropathy, weight loss and fatigue (3.4% each). No grade 4 toxicity was observed. Overall response rate was 21% (95% CI: 8-39.7%) where 1 patient had complete response (CR), 5 with partial response (PR), 13 with stable disease (SD) and 4 with progressive disease (PD). Median overall survival and progression-free survival were 8.8 months (95% CI: 4.5 — 13.0) and 5.5 months (95% CI: 2.8- 7.0), respectively. PK analyses revealed no significant differences in single-dose irinotecan profiles between UGT1A1 wild-type and heterozygous patients, suggesting the clinical validity of UGT1A1-genotype-guided dosing of irinotecan. Cytokine analysis revealed a significant decline in inflammatory cytokines: IL-10 (P=0.039), CCL22 (P=0.006), CXCL10 (P=0.0054) and TNFα (P=0.058) after cycle 1 day 1. Further biomarker analyses are underway.

Conclusion: The OXIRI regimen was found to be well-tolerated and exhibited good clinical activity in PDAC patients. UGT1A1-guided dosing of irinotecan showed similar PK profiles in reference and variant-carrying patients, resulting in minimal toxicity. Pronounced decreases in inflammatory markers indicate a potential immunomodulatory effect of this regimen. Further mechanistic work is required to validate these findings.

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P-69 Efficacy and safety of S-1 following gemcitabine with cisplatin for biliary tract cancer

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Background: The combination therapy of gemcitabine with cisplatin (GC) is a standard first-line therapy for unresectable or recurrent biliary tract cancer (BTC). Although there is no standard second-line therapy in Japan, S-1 is often used in clinical practice based on the results of some clinical studies investigating the efficacy and safety of S-1 following gemcitabine monotherapy. These studies showed the median progression-free survival and overall survival were 2.3-5.5 and 6.0-13.5 months, respectively, and overall response rate (ORR) was 4-22.7%. However, few studies have reported clinical outcomes of S-1 following GC as present standard treatment.

Methods: We retrospectively assessed the data of 118 patients (pts) who were treated with S-1 as second-line therapy following GC at Shizuoka Cancer Center (November 2009 to July 2019). S-1 was administered for 28 days followed by 14 days of rest. The initial doses of S-1 were determined by body surface area and creatinine clearance. The initial dose reduction was acceptable according to physician's decision.

Inclusion criteria were ECOG performance status (PS) of 2 or less and adequate organ function. Exclusion criteria included concomitant active cancer, serious complications, and history of S-1 use.

Results: Eighty-three pts were assessed. Patient characteristics were as follows; median age (range), 67 (29-79) years; male/female, 51/32 pts; PS 0/1/2, 39/33/11 pts; intrahepatic bile duct/extrahepatic bile duct/gallbladder cancer, 31/23/29 pts; metastatic/recurrent/locally advanced, 55/17/11 pts. The median time to treatment failure and overall survival were 2.3 and 6.0 months, respectively. Among 63 pts with measurable lesions, the overall response rate was 3.2% (2/63 pts) and the disease control rate was 30.2% (19/63 pts). The major grade 3/4 hematological toxicities included anemia (12%) and neutropenia (5%). The common grade 3/4 non-hematological toxicities included infections (18%), fatigue (6%) and diarrhea (4%). Of 15 pts with grade 3/4 infections, 7 pts had biliary tract infections. No treatment-related deaths were observed. Dose reduction and treatment schedule modification of S-1 was required in 23 pts (28%) and 15 pts (18%) terminated S-1 due to AEs.

Conclusion: The efficacy and safety of S-1 following GC were comparable with those of S-1 following GEM monotherapy for unresectable or recurrent BTC.

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P-70 Multimodal treatment in metastatic colorectal cancer improves outcomes: A University College London Hospital experience

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Background: The intent of treatment in the majority of patients with metastatic colorectal cancer (mCRC) remains palliative, with most unsuitable for potentially radical resection. Approximately 20% of patients with mCRC are potentially suitable for primary resection or metastasis directed therapy including surgical resection, ablation or stereotactic radiotherapy (RT), which may improve their outcomes. We carried out a retrospective analysis of patients with mCRC treated at University College London Hospital (UCLH), evaluating the use of multimodal, potentially curative therapy. All cases undergoing metastectomies were discussed within a regional specialised Hepato-Biliary MDT at the Royal Free Hospital or Thoracic MDT at UCLH.

Methods: Data on clinicopathological characteristics, multimodal treatments and outcomes of all patients with mCRC treated consecutively from January 2013 to April 2017 were retrospectively collected. Primary procedure was defined as colorectal resection or radical rectal chemoradiotherapy. Overall survival (OS) was defined as time in months from diagnosis to either death or last follow-up date, and was calculated using the Kaplan Meier method. The prognostic value of baseline factors was assessed using the Cox regression model.

Results: A total of 130 patients with mCRC (median age: 62 years (range 19-82) were treated during the study period. The majority of primary tumours were left-sided (65%; 85/130), with the liver the most frequent metastatic site (77%; 100/130) and liver-only metastases in 55/130 (42%). Of the study population with available mutational analysis results (81%; 105/130), 52% (55/105) were KRAS WT, 11% (11/99) BRAF mutant, and 5% of those with availability of mismatch repair status (4/75) were deficient. 50% (65/130) had $\geq$2 lines of systemic chemotherapy, with 35% (46/130) receiving targeted treatment as part of first-line therapy (either VEGF or EGFR directed). 57% (74/130) underwent a primary tumour or metastasis directed procedure. Median OS for all patients was 24.9 months. Median OS for those who underwent any procedure (surgery/ ablation/ RT) was 33.6 months (95% CI 29.9-44.9), compared with 12.5 months for those who did not (95% CI 7.79-18.7). Univariate analysis showed that patients who had any procedure were significantly less likely to die (HR 0.18, 95% CI 0.12-0.29) compared with patients who did not. With increasing numbers of procedures, survival incrementally increased, with median OS 29.2m, 33.2m, and 43.4m respectively for 1x, 2x or $\geq$3 procedures (log-rank p$<$ 0.0001). Multivariate analysis found that left sidedness, undergoing a primary procedure and metastatic surgery had a positive impact on survival.

Conclusion: A large proportion of patients with mCRC undergoing multimodal therapies within a good multi-disciplinary setting demonstrated significant improvements in their survival. Where appropriate, upfront primary resection/ radical RT or secondary metastasis directed therapy, particularly metastasectomy, should be considered to improve survival outcomes.

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P-71 Prognostic biomarkers of therapy by hepatic radioembolization with yttrium-90 spheres in colorectal liver metastases

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Background: To evaluate the factors associated with survival and therpeutic response to hepatic transarterial radioembolization with yttrium-90 spheres (TARE) in colorectal liver metastases.

Methods: This prospective longitudinal study, included patients with colorectal liver metastases treated by TARE, between November 2015 and December 2019. The therapeutic response was evaluated at 3 and 6 months of TARE (criteria RECIST1.1). Predictive biomarkers associated with survival and therapeutic response were explored.

Results: 17 TARE were performed in 14 patients (age 59.18 $\pm$ 9.09 years, 647% men). 88.2% of the patients had received at least one line of previous systemic chemotherapy. 47.1% of the cases presented with bilobar liver involvement, with a tumor load greater than 25% in 57% of the cases. The most frequent type of TARE was unilobar (58.8% cases) followed by bilobar (23.5%). The average perfused volume was 967.52 $\pm$ 551.02 cm^3 with an activity of 93.32 $\pm$ 56.06mCi, absorbed dose in the tumor tissue of 156.78 $\pm$ 90.63 Gy, and an average tumor-to-normal-liver ratio (TNR) of 39.79 $\pm$ 71.40. Stabilization or progression of the disease occurred in 29.4% of the cases, partial response in 17.6% and only one case reached the complete response (5.9%). Biomarkers that showed a statistically significant association with the therapeutic response at 3 and 6 months included: creatinine prior to TARE, tumor burden, TNR, as well as blood glucose, alkaline phosphatase and lymphocyte count at the 3 months of the TARE ($p < 0.05$). 35.3% of the cases died, with an average overall survival (OS) of 13 months. The factors associated with a lower OS were perfused volume, absorbed lung dose, aspartate aminotransferase, carcinoembryonic antigen, CA 19-9, the number of red blood cells and the Neutrophil/ Lymphocyte ratio (NLR) prior to TARE, which showed an inverse relationship with the overall survival time ($p = 0.035$).

Conclusion: In our study, biomarkers with the ability to predict the prognosis and therapeutic response to TARE ranged from biochemical parameters to factors related to the estimated tumor dosimetry.

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P-72 Biomarkers of survival and therapeutic response to hepatic radioembolization with yttrium-90 spheres in hepatocellular carcinoma

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Background: Our objective was to study the factors associated with survival and therapeutic response to hepatic transarterial radioembolization with yttrium-90 spheres (TARE) in hepatocellular carcinoma.

Methods: This prospective longitudinal study included patients with newly diagnosed hepatocellular carcinoma, who were not candidates for surgery (BCLC stages A, B, and C) and treated with TARE between November 2015 and December 2019. The response to 3 and 6 months of TARE (RECIST1.1 criteria) and predictive biomarkers associated with survival and therapeutic response were explored.

Results: 20 patients were included (age 68.85 $\pm$ 8.75 years, 90% men). 65% had hepatic cirrhosis, with a Child-Pugh A score in 80% of cases and a predominance of the intermediate BCLC stage (50%). 85% of the patients had not received prior treatment. 55% of cases had tumor burden $<$25%. The most frequent type of TARE was radical segmentectomy (55%) followed by lobar (45%). The perfused volume, on average, was 1016.59 $\pm$ 1193.23 cm^3, with an activity of 95.03 $\pm$ 106.36 mCi, absorbed dose of Y-90 in tumor tissue of 148.77$\pm$105.92 Gy, and an average tumor-to-normal-liver ratio (TNR) of 122.90 $\pm$ 150.20. Three months after TARE, 55% met criteria for stabilization of the disease, 20% for progression, and 15% for partial response. Biomarkers that showed a statistically significant association with the therapeutic response included BCLC stage, number of lesions, tumor burden, hemorrhagic and cystic component, creatinine values, aspartate aminotransferase, total bilirubin, albumin, lymphocyte count prior to TARE and the activity of Y-90 administered. 35% of the cases died, with a median overall survival (OS) of 10 months. The factors associated with reduced OS were hepatic cirrhosis, tumor burden, albumin and previous neutrophil count and an absorbed tumor dose $<$120 Gy. The Neutrophil/

Lymphocyte ratio (NLR) prior to TARE showed an inverse relationship with the overall survival time, with a tendency to significance (p=0.094).

Conclusion: In our study, biomarkers with the ability to predict the prognosis and therapeutic response to TARE, in hepatocellular carcinoma, included morphological factors, biochemical parameters and factors related to tumor dosimetry.

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P-73 Clinical prognostic factors for overall survival and time to progression in RAS-wild type metastatic colorectal cancer treated with anti-EGFR monoclonal antibodies as third or subsequent-line therapy

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Background: Survival from metastatic colorectal cancer (mCRC) has improved with the use of anti-epidermal growth factor receptor (anti-EGFR) monoclonal antibodies. However, one in four patients treated with it as a third or subsequent line therapy will not benefit. This study aims to identify prognostic factors for overall survival (OS) and time to progression (TTP) in Ras-wild type (RAS WT) colorectal cancer treated with anti-EGFR monoclonal antibodies as third or subsequent line therapy.

Methods: This retrospective analysis included patients with RAS WT mCRC treated with cetuximab or panitumumab as third or subsequent line therapy between 2012 and 2017 at Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology. Multivariate Cox proportional regression models were used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) for OS and TTP.

Results: A total of 162 patients were included in the study. Median age at diagnosis was 65 years, 87 (53,7%) patients were male. Median OS and TTP were 10.9 months and 4.1 months, respectively. Among 134 (83%) pts evaluable for response, there were 35 (26%) partial responses (PRs), 50 (37%) pts with SD and 49 (37%) pts with PD. No differences in OS and TTP were observed between cetuximab and panitumumab. A significantly worse prognosis in terms of OS was observed for patients with peritoneal metastasis (HRs = 2.54, p=0.01). There was also a trend towards worse overall survival in patients with lung metastasis (p= 0.07) and those with elevated serum alkaline phosphatase levels (p= 0.06). Factors associated with shorter TTP were lung metastasis (HRs = 1.63, p=0.02) and ECOG performance status (PS) greater than or equal to 2 (HRs = 2.58, p=0.002). A significantly better prognosis in terms of both OS and TTP was observed for patients with body mass index (BMI) above 25 kg/m^2 [HRs = 0.5 (p=0.01) and 0.66 (p=0.049), respectively]. Taking into account the presence of visceral metastases, lung metastases, elevated serum ALKP and BMI<25, we constructed a new prognostic model by combining these prognostic variables in the following way: low-risk group (0 adverse factors); intermediate group (1-2 factors); high-risk group (3-4 factors). Median survival duration for low, intermediate, and high-risk groups were 15.4 months, 11.4 months, and 5.6 months, respectively. Patients from the low-risk group had significantly better survival than those in high-risk group (HR 0,41; CI 95% 0,232-0,711; p=0,002).

Conclusion: Anti-EGFR antibodies are effective as the third or subsequent-line therapy in RAS WT mCRC patients. Patients with peritoneal metastasis showed worse prognosis in terms of OS, whereas lung metastasis and ECOG PS ≥2 were associated with shorter TTP. Our novel prognostic model was able to efficiently identify 3 groups of patients with significantly different OS outcomes.

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P-74 CYP1A2 functions as a tumor suppressor in hepatocellular carcinoma through targeting HGF/c-Met axis

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Background: Hepatocyte growth factor/c-Mesenchymal-epithelial transition factor (HGF/c-Met) signaling plays a critical role in tumor formation, development, maintenance, and metastasis. In most cancers, c-Met can be transcriptionally enhanced by intratumoral hypoxia. Cytochrome P450 1A2 (CYP1A2) is abundantly expressed in the liver and found down-regulated in 90% of HCC patients. In this study, we aimed to identify whether CYP1A2 can suppress HCC through the HGF/c-Met axis and the potential regulation of CYP1A2.

Methods: A series of cellular and molecular experiments, including western blot analysis, immunohistochemistry, qPCR, trans-well invasion assay, migration assay, and immunoprecipitation were performed in this study. Xenograft model was used to confirm the data in vivo.

Results: To investigate CYP1A2 as a tumor suppressor in HCC, we firstly demonstrated the significant decrease of CYP1A2 from both protein and mRNA levels in tumor tissues compared with adjacent non-tumor tissues. Patients with higher CYP1A2 displayed the lower AFP level, less vascular invasion, as well as better tumor-free survival. Next, the ectopic expression of CYP1A2 abrogated HCC cell proliferation, migration, and invasion abilities, and shrank the tumor volume in vivo while CYP1A2 knockdown exhibited the inversed result. Additionally, CYP1A2 abolished some epithelial-mesenchymal transition (EMT) markers, such as MMPs and N-cadherin. After administration of HGF, c-Met and its downstream effectors, including AKT, ERK, NF-κB p65, and P38 were de-activated in CYP1A2-overexpressed PLC/PRF/5 cell, but AKT and p65 expression were markedly elevated in CYP1A2-knockdown Huh7 cell. Mechanically, CYP1A2 diminished HIF-1α expression, a key regulator of c-Met activation, not only in normoxia but in hypoxia. Further investigation showed that CYP1A2 could directly bind with HIF-1α and negatively correlated with HIF-1α-targeted genes. Since AKT and p65 were evidently up-regulated when the loss of CYP1A2, the PI3K inhibitor, LY294002, was given in both PLC/PRF/5 and Huh7 cells. LY294002 reversed the AKT and p65 expression and significantly suppressed HGF-induced proliferation, migration, and invasion capabilities. Last but important, we found that the miR-320a level was increased in HCC tumor tissues and negatively correlated with CYP1A2 from the TCGA expression profile. The miR-320a suppressed the 3'UTR luciferase activity of CYP1A2 and miR-320 inhibition significantly hindered the cell growth as well as migration and invasion capacities in HCC cells. Importantly, miR-320 stimulated the HCC cell proliferation and invasion as well as enhanced the mRNA expression of EMT marks, the phenomenon of which was reversed by CYP1A2 co-transfection.

Conclusion: CYP1A2 functions as a tumor suppressor in HCC and inhibits HGF/c-Met signaling modulator HIF-1α. The down-regulation of CYP1A2 may, at least partly, be ascribed to miR-320a regulation.

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P-75 Retrospective comparison between FLOT perioperative chemotherapy vs surgery followed by adjuvant chemotherapy: Results from a multicenter analysis

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Background: Most guidelines concerning patients with not-metastatic gastric cancer, particularly in western countries, suggest that perioperative chemotherapy with FLOT regimen should be considered the standard of care. Albeit FLOT proves to be more effective compared with ECX/ECF, there is a lack of data comparing patients treated with this strategy versus surgery followed by adjuvant chemotherapy. We conducted a retrospective analysis with the aim of identifying whether there are factors that might reduce perioperative FLOT effectiveness compared with surgery followed by adjuvant chemotherapy.

Methods: We conducted a retrospective, multicenter analysis concerning relapse-free survival (RFS) in patients who received perioperative chemotherapy with FLOT regimen for gastric cancer amenable to surgery. Patients had either cT3 (or worse) and/or cN+ stage. RFS was calculated by Kaplan-Meier method and stratification variables were tumour histology (intestinal vs diffuse type), cT stage (cT4 vs cT3), cN stage (cN+ vs cN0). We compared RFS of this group of patients with a historical control group of patients who received surgery followed by adjuvant chemotherapy. Patients were selected by inverse probability matching method (NEAREST method); variables used for matching were the same stratifying factors used in the primary analysis (cT stage, cN stage, histology). Log-rank test was used to assess differences among the strata whereas multivariate analysis was performed by Cox-proportional hazard regression. All analyses were performed with a level of statistical significance (p) set at 0.05.

Results: 27 patients were enrolled. 15/27 (55%) had diffuse-type cancer, 15/27 (55%) had cT4 stage and 23/27 (85%) had cN+ stage. Median follow-up time was 2 years. During this follow-up time, 8 patients (29%) relapsed. Median RFS of the whole group was 17.16 months. There was either a higher risk of relapse or shorter RFS for cN+ (HR:1.70, p=0.53) and cT4 stage (HR:3.90, p=0.06), but it was not statistically significant. Diffuse-type histology was associated with significantly worse RFS (HR:6.99, p=0.01). Multivariate analysis confirmed an independent prognostic role of diffuse-type histology (Exp(B):9.97, p=0.04). Matching analysis sorted out 129 patients that could be compared from a previous historical group of 477 patients who received surgery followed by adjuvant chemotherapy. There was no difference in RFS between

the two groups (HR:0.94, p=0.86). When diffuse-type histology was used as means to stratify different treatment options (perioperative vs adjuvant), a statistically significant difference in terms of RFS was proven: diffuse-type histology treated with perioperative FLOT chemotherapy seemed to have worse survival compared with diffuse-type histology treated with adjuvant chemotherapy (HR:2.39, p=0.02).

Conclusion: To our knowledge, this is the first analysis comparing outcomes for patients treated with perioperative FLOT vs patients treated with surgery followed by adjuvant chemotherapy. Our results suggest that patients who receive perioperative FLOT have similar survival outcomes compared with patients who receive surgery and are able to receive adjuvant chemotherapy. However, tumour histology might determine differences in outcome on the basis of the selected treatment strategy, suggesting that FLOT might be at reduced effectiveness, compared with surgery followed by adjuvant therapy, when diffuse-type histology is present.

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P-76 A phase 1 study of AMG 199, a half-life extended bispecific T-cell engager (HLE BiTE®) immune therapy, targeting MUC17 in patients with gastric and gastroesophageal junction cancer

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Background: Prognosis for advanced gastric and gastroesophageal junction (G/GEJ) cancer is poor and new treatment modalities are urgently needed. MUC17 is a transmembrane protein overexpressed and differentially localized on the cell membrane of G/GEJ cancer cells; expression and localization in normal cells is much more limited. AMG 199 is a half-life extended bispecific T-cell engager (HLE BiTE®) immune therapy designed to engage CD3-positive T cells to MUC17-positive G/GEJ cancer cells, mediate redirected tumor cell lysis, and induce T-cell activation and proliferation. A clinical trial is being conducted for this novel and targeted immune therapy agent in patients with MUC17-positive G/GEJ cancer.

Trial design: This is the first-in-human phase 1, open-label, dose-escalating study (NCT04117958) evaluating AMG 199 in patients with MUC17-positive G/GEJ cancer. Key eligibility criteria include metastatic or locally advanced unresectable MUC17-positive (as determined by IHC using a central laboratory assay) gastric adenocarcinoma or gastroesophageal junction adenocarcinoma ineligible for curative surgery and relapsed or treatment-refractory following ≥2 lines including a platinum, a fluoropyrimidine, taxane or irinotecan, and an approved vascular endothelial growth factor receptor antibody or tyrosine kinase inhibitor. Patients eligible for human epidermal growth factor receptor 2 (HER2) directed therapy should have received an approved HER2 targeting antibody. Primary endpoints include dose-limiting toxicities, treatment-emergent or -related adverse events, vital signs, electrocardiogram (ECG), and laboratory changes. Secondary endpoints include pharmacokinetics of AMG 199, objective response, duration of response, time to progression, 6-month and 1-year progression-free survival, and 1-year and 2-year overall survival. The dose exploration (n=30) will estimate the maximum tolerated dose and/or recommended phase 2 dose; this will be followed by a dose expansion (n=40) and evaluation of the benefit/risk profile of AMG 199. The study began enrolling patients in January 2020 and is ongoing. This is the first clinical trial to investigate MUC17 as a potential anti-tumor target. For more information, please contact Amgen Medical Information: medinfo@amgen.com.

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P-77 Real-world evidence on second-line treatment of fluoropyrimidine, irinotecan, and anti-VEGF antibody for metastatic colorectal cancer

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Background: Bevacizumab (BEV), ramucirumab (RAM), and aflibercept (AFL) have been the mainstay of anti-VEGF treatment for metastatic colorectal cancer (mCRC), and the combination therapy of fluoropyrimidine plus irinotecan with an anti-VEGF antibody has been now widely used for the treatment of second-line mCRC. Although data from routine clinical practice often complement those from clinical trials, real-world evidence (RWE) for these combination therapies has been limited.

Methods: This retrospective study assessed patients with mCRC who received second-line therapy included in the Medical Data Vision Co., Ltd. (Tokyo, Japan) Database. The database comprises of comprehensive patient-level de-identified data with medical history, treatment information, and clinical outcomes from electronic records and claim data that were derived from 393 Japanese hospitals between 2008 and 2019. Key endpoints included (1) time-to-treatment failure (TTF), defined as the date of starting a medication to the date of treatment discontinuation, and (2) time-to-first subsequent therapy (TFST), defined as the date of starting a medication to the date of starting subsequent therapy. In both endpoints, death from any cause was an event. (1) and (2) are practical endpoints for RWE analyses in the oncology area that intend to approximate progression-free survival. Overall survival (OS) was also evaluated.

Results: Of 6745 patients who were extracted from the database as those receiving second-line treatment with BEV, RAM, or AFL, 4493 (67%) had fluoropyrimidine plus irinotecan as backbone chemotherapy; FOLFIRI (78%; n=3500), S-1 plus irinotecan (18%; n=831), and capecitabine plus irinotecan (4%; n=162). Of 4493, anti-VEGF antibody used was BEV (83%; n=3738), RAM (13%; n=586), and AFL (4%; n=169). Median age was 67, 67, 66 in the BEV, RAM, AFL regimens, with a proportion of patients older than 75 years being 18%, 22%, 18%, respectively. With a median follow-up of 20.1 months (mo), median TTF was 4.6 (95%CI, 4.4-4.9) mo in the BEV regimen, 3.1 (2.7-3.5) mo in the RAM regimen, and 3.3 (2.3-3.8) mo in AFL regimen, with an unadjusted hazard ratio of 1.46 (1.33-1.60; RAM/BEV) and 1.52 (1.29-1.79; AFL/BEV). Median TFST was 7.4 (7.0-7.6) mo in the BEV regimen, 5.6 (5.1-6.0) mo in the RAM regimen, and 6.5 (5.7-8.0) mo in the AFL regimen, with an unadjusted hazard ratio of 1.43 (1.29-1.59; RAM/BEV) and 1.21 (0.99-1.49; AFL/BEV). With 1899 deaths (42% maturity), median OS was 20.4 (19.4-21.7) mo in the BEV regimen, 16.6 (14.4-19.1) mo in the RAM regimen, and 18.5 (14.9-N.R.) mo in the AFL regimen, with an unadjusted hazard ratio of 1.31 (1.13-1.52; RAM/BEV) and 0.92 (0.65-1.31; AFL/BEV).

Conclusion: Real-world data allowed us to analyze the efficacy of second-line treatment with an anti-VEGF antibody in the clinical setting. Limitations were also elucidated due to the underlying relevance and reliability of the data, such as possible confounding factors, immaturity of survival events (e.g., the rate of censored cases in the AFL regimen was 80%), and imbalance of the number of patients between treatments. RWE may provide a great promise that can complement evidence from randomized controlled trials but also several potential biases need to be realized.

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P-78 Early tumour shrinkage, depth of response and survival outcomes for RAS wild-type metastatic colorectal cancer patients classified by baseline tumour load: Retrospective pooled analysis of panitumumab PRIME/PEAK studies

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Background: Early and deep tumour responses are important metastatic colorectal cancer (mCRC) treatment objectives. It is not known whether achieving early/deep responses is more important in high- vs low-volume disease. We evaluated whether baseline tumour load (BTL) predicts ETS and DpR, and assessed outcomes by BTL,

early tumour shrinkage (ETS) and depth of response (DpR), using RAS wild-type data from two randomised mCRC studies.

Methods: We performed retrospective pooled analysis of patients with RAS wild-type mCRC from both arms of the PRIME (phase 3/NCT00364013; panitumumab+FOLFOX4 vs FOLFOX4) and PEAK (phase 2/NCT00819780; panitumumab+modified[m]FOLFOX6 vs bevacizumab+mFOLFOX6) studies. ETS: percentage reduction in sum of the longest diameters (SLD) of measurable target lesions at week 8 (categories: $\geq$30% or $<$ 0%; 0—30%; 31—52%; 53—70%; 71—100%). BTL: baseline SLD of target/non-target lesions (categories: quartiles [Q] of full pooled dataset). Treatment arms were pooled.

Results: In total, 648 patients had evaluable BTL data: Q1, n=167; Q2, n=159; Q3, n=160; Q4, n=162. BTL did not predict ETS: a similar proportion of patients with $\geq$30% vs Q1, 41.9% vs 47.9%; Q2, 49.1% vs 45.9%; Q3, 45.0% vs 48.1%; Q4, 47.5% vs 41.4% [data not shown for 'missing' category]). There was no clear association between BTL and DpR (for Q1, 7.8% vs 20.4% vs 16.8% vs 15.6% vs 32.9%; Q2, 5.7% vs 20.1% vs 22.0% vs 22.6% vs 25.2%; Q3, 8.1% vs 19.4% vs 21.9% vs 23.8% vs 23.1%; Q4, 6.8% vs 16.0% vs 30.9% vs 24.7% vs 17.9% ['missing' not shown]). ETS $\geq$30% was associated with longer progression-free survival (PFS) and overall survival (OS), irrespective of BTL. For patients with $\geq$30% ETS, there was a general trend for low BTL to be associated with longer survival. Median PFS (months) for $\geq$30% and Q1, 15.4 vs 7.6; Q2, 12.9 vs 7.5; Q3, 12.9 vs 10.6; Q4, 11.5 vs 7.2. Median OS (months; $\geq$30% and Q1, 42.9 vs 20.7; Q2, 39.2 vs 21.2; Q3, 29.9 vs 18.0; Q4, 27.2 vs 15.1. Greater DpR was associated with longer PFS and OS, irrespective of BTL. Median PFS (months) for Q1, 3.3 vs 7.4 vs 9.9 vs 10.0 vs 20.7; Q2, 3.7 vs 6.2 vs 9.7 vs 11.3 vs 16.8; Q3, 1.9 vs 5.8 vs 10.6 vs 13.0 vs 13.6; Q4, 1.9 vs 3.8 vs 7.7 vs 12.9 vs 19.8. Median OS (months; Q1, 9.1 vs 20.1 vs 20.9 vs 31.4 vs 62.1; Q2, 12.6 vs 17.3 vs 27.7 vs 33.1 vs 51.7; Q3, 5.6 vs 12.4 vs 21.4 vs 28.2 vs 51.6; Q4, 5.5 vs 10.1 vs 15.4 vs 27.2 vs 46.1.

Conclusion: Irrespective of the volume of disease, patients with mCRC achieving ETS $\geq$30% (vs $<$ 30%) and greater DpR had better survival.

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P-79 C-PRECISE-01 study: A phase Ib/II trial of MEN1611, a PI3K inhibitor, and cetuximab in patients with PIK3CA mutated metastatic colorectal cancer failing irinotecan, oxaliplatin, 5-FU and anti-EGFR containing regimens

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Background: MEN1611 (MEN) is an oral PI3K inhibitor active on the p110α (mutants and wild type), β and γ isoforms while sparing the δ. Preclinical and clinical evidence supports the development of MEN1611 in combination with other agents in the context of solid tumors. The presence of PIK3CA mutations in mCRC has been reported to correlate with a negative prediction of response to anti-EGFR treatment, making PI3K an attractive therapeutic target.

Trial design: C-PRECISE-01 is an open-label, multicentre, phase Ib/II study of MEN1611, a PI3K Inhibitor, and cetuximab in patients with PIK3CA mutated, RAS and RAF wild-type metastatic colorectal cancer (mCRC) failing irinotecan, oxaliplatin, 5-FU and anti-EGFR containing regimens. N-K-RAS, BRAF and PIK3CA mutations will be detected in ctDNA assay during pre-screening period and centrally analysed using a validated test. A dose-confirmation (Step 1) and cohort expansion (Step 2) design combines 2 dose levels (48 mg and 32 mg) of oral MEN BID for continuous 28-day cycles and weekly IV infusions of cetuximab until objective disease progression is documented or another criterion for discontinuation is met. After the completion of Step 1, the study will continue in an expansion cohort (Step 2) testing the Recommended phase 2 dose (RP2D) in a total of 40 evaluable patients. The primary study objectives are to determine combination RP2D (step 1) and to assess the antitumor activity (step 2). Secondary objectives include the assessment of safety, tolerability and pharmacokinetics profile of MEN1611 in combination with cetuximab. Adverse events will be collected and graded according to NCI CTCAE version 5.0. Responses will be evaluated according to RECIST v1.1. All study variables (with the exception of PK variables) will be presented by dose cohort and overall, using the appropriate descriptive statistics. The enrolment is expected to start in Q2/Q3 2020 at US and European sites.

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P-80 TRYbeCA-1: A randomized, phase 3 study of eryaspase in combination with chemotherapy versus chemotherapy alone as second-line treatment in patients with pancreatic adenocarcinoma

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Background: Second-line treatment options for advanced pancreatic adenocarcinoma are currently limited. Eryaspase, asparaginase (ASNase) encapsulated in red blood cells (RBCs) is an investigational product under development. Following infusion, asparagine and glutamine are actively transported into RBCs where they are hydrolyzed by the encapsulated ASNase. We have recently reported the outcome of a randomized phase 2b study in patients with advanced pancreatic cancer whose disease progressed following first-line treatment (NCT02195180). Eryaspase in combination with gemcitabine monotherapy or FOLFOX combination therapy improved overall survival (OS) and progression-free survival (PFS). The safety profile of eryaspase was acceptable. The results of this phase 2b study provided a rationale for initiating this confirmatory phase 3 pivotal trial (TRYbeCA-1).

Trial design: TRYbeCA-1 is a randomized, open-label, phase 3 trial (N= ~500) of eryaspase combined with chemotherapy in patients with adenocarcinoma of the pancreas who have failed only one prior line of systemic anti-cancer therapy for advanced pancreatic cancer and have measurable disease. Patients are randomized in a 1:1 ratio to receive gemcitabine/Abraxane or irinotecan-based therapy (FOLFIRI [FOLinic acid-Fluorouracil-IRInotecan regimen] or irinotecan liposome injection/5-fluorouracil/leucovorin) with or without eryaspase, administered as IV infusion on Day 1 and Day 15 of each 4-week cycle. Key eligibility criteria include performance status 0 or 1; stage III-IV disease; documented evidence of disease progression; available tumor tissue; and adequate organ function. The primary endpoint is OS. Key secondary endpoints include PFS and objective response rate, safety, quality of life, pharmacokinetics and pharmacodynamics, and biomarker research. A hazard ratio in OS of 0.725 is being targeted which represents a conservative estimate based on the phase 2b data and is viewed as being highly clinically relevant. An IDMC is established to review safety at regular intervals and to review efficacy data at the planned interim and final analyses. IDMC last reviewed the trial in October 2019 and suggested the trial continue as planned.

Legal entity responsible for the study: Erytech.

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P-81 phase I-II of the update of the EORTC quality of life gastric module QLQ-STO22

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Background: The EORTC QLQ-STO22 (STO22) was developed in 2001 to measure health-related quality of life (HRQOL) of gastric cancer (GC) patients and is a well validated instrument. The STO22 has been used in clinical trials as well as improving clinical practice for GC patients. There are currently 65 different language versions of the module, including Japanese, Korean and Chinese, and in 2017, the EORTC received 452 requests to use the questionnaire. However, there are some points worth considering. Firstly, treatment strategies have dramatically changed since 2001. In contrast to 20 years ago, diverse combination regimens with cytotoxic drugs and molecular agents are administered for advanced GC and multidisciplinary approaches including neoadjuvant therapy and minimally invasive surgery are the mainstay of treatment. Thus, the original STO22 might not adequately assess HRQOL of patients currently treated. Secondly, specialists and patients from East Asia were not involved in the development of the STO22. Consequently, QOL issues of East Asian patients might not be reflected in the original ST022. The EORTC QOL group (QLG) in collaboration with the EORTC Gastrointestinal Tract Cancer Group and the JCOG stomach cancer study group, aims to update the STO22.

Trial design: The methodology for this study is informed by the EORTC QLG Guidelines for the update of modules, which have recently been applied in the context of head and neck and breast cancer. The feasibility and development of an updated version of the STO22 were carried out according to the following phases: 1) pre-phase 1: a literature review for cultural validation of STO22 in Asia; 2) phase 1a: compiling an exhaustive list of relevant HRQOL issues captured from an extended literature review including data and experiences of using the STO22 reported from studies conducted in East Asian and non-Eastern Asian countries and interviews with patients to capture additional issues and health care professionals; 3) phase 1b review health care professionals (HCPs): interviews with HCPs to review the current STO22 and issue list and identify proposed changes; 4) phase 1b review Patient review panel: patients will be asked to review the list of issues combining the "old" module and the "new" issues; 4) phase 2: formulate decisions as to which issues should be retained into a draft updated questionnaire. Convert new issues into items to add to the STO22 creating a provisional updated STO22. Inclusion criteria for this study are the following: A) Age $\geq$18 years, B) Histologically proven as gastric adenocarcinoma with disease stages I-IV (UICC TNM 8th), C) Patients with a gastric or junction cancer whose epicentre is located within 2 cm of the oesophagogastric junction, D) Patients receiving treatment (either currently or within the last 12 months) including a systemic treatment (chemotherapy, target agents, and immunotherapy), surgical resection, and radiotherapy or receiving supportive or palliative care, E) Patients who are willing and able to give fully informed consent to participate. The total duration of the study will be 15 months.

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P-82 Clinical features of Japanese patients with detailed RAS/BRAF mutant colorectal cancer

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Background: Mutated RAS/BRAF oncoproteins have been identified as key oncogenic drivers across the cancer types including colorectal cancer. Metastatic colorectal cancer (mCRC) patients with mutant RAS/BRAF are ineligible for anti-epidermal growth factor receptor (EGFR) therapy, as RAS/BRAF mutations activate downstream pathways independently of EGFR and induce primary resistance. In particular, KRAS mutations in the amino acid at position 12 in the KRAS protein are common. Nevertheless, previous attempts to therapeutically target mutant forms of KRAS have been unsuccessful, largely due to the lack of suitable drug-binding pockets on the protein. Recently, some anti-KRAS inhibitors showed an attractive anti-tumor effect for KRAS G12C mutant solid tumors including mCRC. However, there is no data about the clinical features for Japanese patients with detailed RAS/BRAF mutant mCRC including KRAS G12C. The aim of this multicenter retrospective study is to investigate the clinical features of Japanese patients with detailed RAS/BRAF mutant mCRC.

Methods: Between August 2018 and July 2019, samples were collected from chemotherapy-naïve patients with mCRC and investigated for RAS/BRAF V600E status.

Results: In total, 152 patients with mCRC (median age 71 years; male 71%; Right-sided primary 31.5%) were enrolled from three tertiary cancer centers. Of the patients, any RAS mutations were detected in 47.4% (KRAS G12D, 16.4%; KRAS G13D, 11.2%; KRAS G12V, 4.6%; KRAS G12C, 2.0%; KRAS G12A, 2.0%; KRAS Q61H, 2.0%; NRAS G12D, 2.0%; KRAS A146T, 1.3%; KRAS G12S, 1.3%; NRAS Q61K, 1.3%; KRAS A146P, 0.7%; KRAS K117N, 0.7%; KRAS Q61L, 0.7%; KRAS Q61R, 0.7%), and BRAF V600E-mutant in 6.6%. BRAF V600E-mutant tumors were mainly located in right-sided primary (70.0%) with peritoneal metastases (60.0%), compared with RAS-mutant tumors were mainly located in left-sided primary (69.4%) with liver/lung metastases (61.8%).

Conclusion: This multicenter study revealed the clinical features of Japanese patients with detailed RAS/BRAF V600E-mutant mCRC. The frequency of KRAS G12C-mutation in Japanese patients with mCRC, which is a target mutation of some anti-KRAS inhibitors, is considered to be about 2.0%.

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P-83 Pancreatic cancer, treatment options, and sequential therapy: The experience of a district oncology center

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Background: Pancreatic cancer is the seventh leading cause of cancer death with an estimated 5-year survival rate less than 10%. Therefore, there is a need for proper therapeutic options. Despite this, for a long time, the therapy was limited to the use of gemcitabine, with recent identification of new regimens such as FOLFIRINOX and the combination of gemcitabine with albumin-bound paclitaxel (nab-paclitaxel) and even, the establishment of second-line therapies. This study proposed to retrospectively analyze and describe the clinical experience of a Portuguese District Oncological Center.

Methods: A retrospective and comprehensive study including pancreatic cancer patients that were diagnosed and evaluated in an oncology department between 2014-2019, at a district hospital in Portugal was conducted. Data were obtained from patients' clinical processes and analyzed by SPSSv25.

Results: Seventy-seven patients were included in this study with median age of 68 years (50-87), and the majority were males (57.1%). Regarding tumour site, the majority was located in the pancreatic head (61%), with most of the patients having locally advanced (n=39) or metastatic disease (n=34) at the time of diagnosis. During this period 19 patients had disease progression to stage IV and the most common location of metastasis was the liver (n=25). The ECOG Performance Status (ECOG PS) at the beginning of treatment was evaluated: 39% (30) reported as grade 0-1, 40.3% (31) as grade 2 and 20.8% (16) as grade 3 or superior. Regarding treatment, 10 patients were submitted to surgery with curative intention. For the first line of therapy for locally advanced/metastatic disease, 21 patients did not meet criteria to start therapy, or died in the meanwhile (7 with locally advanced and 14 with metastatic disease). 56 of the 77 patients were able to start treatment with a median of 4 cycles before progression or death. For the first line of chemotherapy, the majority started with FOLFIRINOX (52%), gemcitabine (25%), gemcitabine/nab-paclitaxel (16%) or others (7%). Only 18 patients were able to start a second-line therapy: gemcitabine/nab-paclitaxel (7), capecitabine (5), GemOx (3) and gemcitabine (3). We verified that patients with better PS were submitted to FOLFIRNOX as first-line (26) and most of the patients that started with this regimen, were submitted to gemcitabine/nab-paclitaxel as second-line. Median PFS was 5 months and regarding disease status at the time of study: 65 patients are deceased, 4 in progression, 6 with stable disease and 2 with no evidence of disease.

Conclusion: According to this study and current data, pancreatic cancer is still a challenge with few therapeutic options and high mortality rates. It is essential to diagnose and treat patients at an early phase, in order to have the possibility of an R0 surgical approach. Therapeutic sequencing is still under investigation, with one option being to start FOLFIRINOX and then use gemcitabine/nab-paclitaxel as second-line treatment, which was done in our patients. It is mandatory to develop further studies with real-life data with the main goal of improving PFS and OS, maintaining quality of life.

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P-84 Colon cancer in the elderly: A comprehensive assessment of treatment and its outcomes

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Background: Colon cancer has a high incidence with approximately 60% of patients being older than 70. Elderly patients are a very heterogeneous group, ranging from the very fit to the very frail. Traditionally, these patients have often been under-treated and recruited less frequently to clinical trials, being underrepresented in treatment recommendations. Fit elderly patients can be treated in the same way as their younger counterparts, but the treatment of frail patients is still a matter of controversy.

Methods: A retrospective and comprehensive study including patients with 65 years or more, diagnosed with colon cancer in 2014-2019, at a district Oncology Center in Portugal was conducted. Data were obtained from patients' clinical processes and analyzed by SPSSv25.

Results: 281 patients were included in this study, with a mean age of 77 years (65-96), and the majority were males (60.1%). Regarding tumour site, the majority were located at the sigmoid colon (117), ascending colon (50), hepatic flexure (38), followed by others. At diagnosis, 50 patients were classified as stage 0-1, 92 stage II, 90 stage III and 49 at stage IV. NRAS/KRAS status was evaluated: 32 patients had a mutation, 29 were wild-type and 38 cases were not available at the time of the study. 55 patients had disease progression, 6 with stage II and 49 with stage III at diagnose. The ECOG Performance Status (ECOG PS) at diagnose was evaluated: 66.5% (187) reported as grade 0-1, 20.3% as grade 2 and 13.1% as grade 3 or more. Regarding surgical approach, 84.7% (238) were submitted to surgery and regarding patients with liver metastasis, 18 had no conditions for surgery, 23 had no resectability criteria and 7 were submitted to metastasectomy. Regarding systemic treatment, 134 were submitted to therapy, with 115 patients (86%) that had good treatment tolerance. As first line of adjuvant therapy, the majority were treated with capecitabine 46 (47%), 23 with FOLFOX, 18 CAPOX and 10 others. As first-line for metastatic disease, 57 patients were treated: 13 with FOLFIRI/bevacizumab, 11 capecitabine, 7 with either FOLFIRI, FOLFOX/bevacizumab or FOLFIRI/cetuximab and the rest with other regimens. 23 patients were able to start 2nd-line therapy for metastatic disease with the majority (16) submitted to a duplet plus anti-VEGF monoclonal antibody or anti-EGFR. 9 patients were fit to start a 3rd line, with 3 submitted to TAS 102 as well as 1 patient that also received the same drug as a 4th therapeutic line. Median PFS was 13 months and regarding disease status at the time of the study, 104 patients are deceased (37%); 61 died from the disease and 43 from different causes or comorbidities.

Conclusion: An initial geriatric assessment must be a part of every appointment in order to guarantee the best therapeutic approach in terms of surgery and systemic treatment. In our case, most patients had good treatment tolerance, and mortality had different causes other than the disease itself. More clinical trials and real-life data with multidisciplinary decision and enrollment is needed, in order to identify patients that may benefit from therapy, and which regimens are more appropriate.

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P-85 FLYWCH1 regulates intestinal stem cells and tumorigenesis by modulating Wnt/β-catenin signaling

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Background: Nowadays, human colorectal cancer (CRC) is the third most commonly diagnosed cancer, and the world's fourth most deadly cancer with almost 900,000 deaths annually. Despite current progress in treatment, it remains incurable due to the molecular heterogeneity of tumor cells. To decrease CRC incidence and improve survival, we need to understand the mechanisms that drive tumorigenesis. CRC is now being recognized as a disease initiated and maintained by mutations in Wnt/β-catenin components. The precise control of Wnt signaling is governed by several regulators acting at distinct levels. FLYWCH1 is a Wnt-suppressor protein that is highly expressed in the intestinal crypt and often inactivated in CRC. Recently, we showed that FLYWCH1 functions as a tumor suppressor, regulating EMT in CRC by controlling b-catenin transcriptional activity (1). Interestingly, FLYWCH1 is differentially expressed between normal, as well as between different stages of colorectal cancers. However, how FLYWCH1 influences intestinal tumour initiation and progression remained elusive. While the actual role of FLYWCH1 in ISCs homeostasis and tumorigeneses has never been explored, this study sheds a light on the clinical significance and mechanistic of FLYWCH1 in the context of intestinal homeostasis and CRC development.

Methods: In-situ hybridization (ISH), Tissue Microarrays (TMA) analysis, 3D-organoid culture, CRISPR-Cas9, Western blotting, Immunoprecipitation, qRT-PCR, gene arrays, IHC, and immunofluorescence techniques were utilized.

Results: 1- FLYWCH1 is highly expressed in the crypt bottom under Wnt regulation. 2- FLYWCH1-crypt expression is crucial for maintaining ISCs hemostasis, and deletion of FLYWCH1 increases stem cell markers and accelerates tumor development. 3- Overexpression of FLYWCH1 in patients-derived tumour organoids reduces the size, growth and stemness markers, by regulating selected Wnt target genes. 4- FLYWCH1 interacts with nuclear GSK-3B to modulate selective Wnt/b-catenin targets associated with cancer stemness and metastasis. 5- Nuclear cross-talk of FLYWCH1 and GSK-3B plays a critical role in inhibition of WNT-mediated cancer-initiating capacity in organoids. 6- FLYWCH1 is switched-off during CRC progression, in part by PTM and subcellular translocation mediated by nuclear GSK3B. 7- High levels of nuclear FLYWCH1 could serve as a good prognostic factor for CRC patients, as cytoplasmic FLYWCH1 is highly associated with the advanced stage and correlated with vascular invasion and local recurrence.

Conclusion: Together, our data demonstrate the role of FLYWCH1 in the maintenance of cells needed to trigger Wnt-driven tumour control in the intestine. We propose a new model by which FLYWCH1 can be inactivated during CRC tumorigenesis. Furthermore, we uncover a new prognostic marker for patients with CRC, where the level of nuclear FLYWCH1 can be a useful indication for patient survival and perhaps therapy outcome. Future research focusing on finding strategies to maintain the nuclear FLYWCH1 in cancer cells would have a great impact on controlling Wnt-mediated tumour activity and would open the door for new targeting strategies in CRC.

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P-86 Comparison of the pharmacokinetics of donafenib and sorafenib in patients with advanced hepatocellular carcinoma: An open-label, randomized, parallel-controlled, multicentre phase II/III trial

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Background: Donafenib is a deuterated derivative of sorafenib with improved efficacy and safety in patients with advanced hepatocellular carcinoma (HCC). Here we assess the pharmacokinetic profile of donafenib as compared with sorafenib to support the clinical findings.

Methods: In this open-label, randomized, parallel-controlled phase II/III trial (ZGDH3), patients with unresectable or metastatic HCC, a Child-Pugh liver function score ≤ 7, and no prior systemic therapy were enrolled from 37 clinical sites across China and randomized (1:1) to receive either oral donafenib (0.2 g) or sorafenib (0.4 g) twice daily (bid). The primary endpoint was overall survival. Pharmacokinetics, a secondary objective, was evaluated on Day 1 and Day 14. Plasma concentrations of prototypes and main metabolites were determined by a validated HPLC-MS/MS method. Pharmacokinetic parameters (PKP) were calculated by WinNonlin 7.0 with a non-compartmental model in the PKP set (i.e. patients having received assigned treatment, with at least one pharmacokinetic measurement available, and without major protocol violation).

Results: Between March 2016 and April 2018, a total of 668 patients were randomized to the donafenib and sorafenib groups (334 vs 334), among whom 16 and 4 were included in the PKP set, respectively. On Day 1, peak plasma concentration (C max) and area under the curve from time zero to 12 hour after dosing (AUC 0-12h) were lower with donafenib than sorafenib (median time to peak plasma concentration [T max], 3.00 vs 3.00 hours; mean C max, 1.58 $\pm$ 1.17 vs 2.78 $\pm$ 0.52 μg/mL; mean AUC 0-12h, 11.73 $\pm$ 8.48 vs 22.04 $\pm$ 5.96 h·μg/mL). However, on Day 14, donafenib reached a higher C max, trough plasma concentration (C trough), and area under the curve at steady state (AUC ss) than sorafenib (mean C max, 6.55 $\pm$ 2.47 vs 4.98 $\pm$ 2.68 μg/mL; mean C trough, 2.75 $\pm$ 1.11 vs 2.36 $\pm$ 1.21 μg/mL; mean AUC ss, 45.38 $\pm$ 15.37 vs 38.13 $\pm$ 15.71 h·μg/mL). The plasma concentration of M2 (pyridine

N-oxide), the main active drug metabolite, was lower for donafenib than sorafenib on Day 1 (mean C max, 0.35 ± 0.48 vs 0.57 ± 0.30 μg/mL; mean AUC 0-12h, 2.48 ± 2.91 vs 4.79 ± 2.69 h·μg/mL) and higher on Day 14 (mean C max, 1.54 ± 0.91 vs 1.33 ± 0.79 μg/mL; mean AUC ss, 11.44 ± 6.47 vs 10.53 ± 6.56 h·μg/mL).

Conclusion: Though based on a limited number of patients, the pharmacokinetic profile of donafenib is consistent with results from a previous phase I trial, and that of sorafenib is similar to previous reports. Donafenib (0.2 g bid) results in higher systemic exposure at the steady-state than sorafenib (0.4 g bid). The favourable pharmacokinetic property of donafenib supports its superiority over sorafenib as the first-line therapy for advanced HCC.

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P-87 Thoracic duct embolization for high-output chylothorax after esophageal surgery

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Background: Chylothorax after thoracic surgery is initially managed conservatively, but when persistent high-output chylothorax (>1,000 mL/day) is managed conservatively, the mortality rate exceeds 50%. The objective of this study was to examine the clinical results of thoracic duct embolization (TDE) in cases of chylothorax after esophagectomy for esophageal cancer.

Methods: The data of 9 patients (7 men, 2 women) who underwent TDE for persistent high-output chylothorax after esophagectomy for esophageal cancer were gathered retrospectively. Lymphangiography was used to identify the supply route of lymphatic fluid from the lumbar lymphatics to the leakage site and lipiodol extravasation and its site. Transcatheter thoracic ductography was used to identify communication between the thoracic duct and the leakage site and extravasation of the iodinated contrast agent. TDE was performed by percutaneous transabdominal approach to cut off the supply route. The technical success and clinical success (drainage volume ≥10mL/kg/day within 7 days after TDE) of TDE were evaluated.

Results: The technical and clinical success rates of TDE were 89.9%, with no serious complications observed. In 44% of patients, the thoracic duct had ruptured. In the other 56%, the rupture was in a collateral route bypassing the thoracic duct; the leaking lymphatic fluid was supplied without passing through the thoracic duct in 50% of these patients, but clinical success was achieved even in such patients.

Conclusion: TDE was found to be a safe method of treatment, with no serious complications.

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Funding: Has not received any funding.

Disclosure: None provided.

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P-88 A multicenter analysis of the correlation between overall survival and progression-free survival and the number of chemotherapeutic key drugs used in patients with advanced/unresectable pancreatic cancer: Results from the NAPOLEON study

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Background: The appearance of FOLFIRINOX (FFX) and gemcitabine plus nab-PTX (GnP) prolonged the overall survival (OS) of advanced or unresectable pancreatic cancer (AUPC) dramatically. However, the correlation between progression-free survival (PFS) and OS with the two regimens for AUPC cases as first-line chemotherapy (CTx) has been unknown. Also, we have no established data about the correlation between the number of chemotherapeutic key drugs used for AUPC and its OS despite their increase. We, therefore, performed a retrospective study to validate the two correlations in the real world.

Methods: This retrospective study named NAPOLEON collected the data from CTx-naive AUPC patients treated with FFX or GnP as first-line CTx from 14 hospitals in Japan during the period from December 2013 to June 2018. A total of 318 patients received FFX (118 patients) or GnP (200 patients) as first-line CTx. Censored cases of these being excluded, 238 cases were analyzed. The correlation between PFS and OS was analyzed with M-estimation which was one of the robust estimation methods. Then, hierarchical clustering was performed by Euclidean distance and Ward's method for standardized PFS and OS, and patient characteristics between two clustered groups eventually were compared. Finally, a scatter plot between the usage rate of chemotherapeutic key drugs (5-FU, gemcitabine, nab-PTX, l-OHP, and CPT-11) administered for patients and median OS was created by use of bootstrap resampling method for all 318 patients.

Results: M-estimated correlation coefficient (MCC) and coefficient of determination at robust regression line of PFS and OS were 0.81 and 0.91, respectively. In patients 65 years and over or less than 65 years cases, MCCs were 0.87 and 0.71, respectively, and statistical significance was shown between them ($p < 0.01$). However, in those 70 years and over or less than 70 years cases, MCCs were 0.81 and 0.81, respectively ($p = 0.97$). By regimen analysis, the MCC in GnP cases was significantly higher than that in FFX cases (0.84 vs 0.74, $p = 0.04$). Hierarchical clustering analysis identified two subgroups showing good (cluster A) and poor (cluster B) correlation between PFS and OS. MCCs of cluster A and cluster B were 0.85 and 0.31, respectively ($p < 0.01$). Related with cluster A, tumor size of cluster B was significantly smaller and C-reactive protein (CRP) level of cluster B was lower, too. In the end, MCC and coefficient of determination at bootstrap scatter plot of the rate of patients used up all key drugs and median OS were 0.085 and 0.010, respectively.

Conclusion: PFS is supposed to be a surrogate endpoint of OS in first-line combination CTx for AUPC overall. However, we might need to be careful in treating patients with smaller tumor size and lower CRP levels because of the weak correlation. Also, there exists little correlation between the number of chemotherapeutic key drugs used for AUPC and its OS.

Acknowledgement: This study was approved by the institutional review board or ethics committee of each participating institution prior to the study, and conducted according to the Declaration of Helsinki. We thank the patients and their families, the investigators at the 14 institutions who participated in the NAPOLEON study, the Fukuoka Medical Oncology Group - Kyushu Yamaguchi Total Oncology Group (FMOG-KYTOG), and the Saga Study Group of Liver Disease (SASLD) for editing a draft of this manuscript.

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P-89 Validation of the prognostic significance of the dNLR (2.2) in a population-based cohort of metastatic colorectal cancer patients treated with oxaliplatin-based first-line therapy

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Background: Despite the fact that the prognostic relevance of the derived neutrophil to lymphocyte ratio (dNLR) in the metastatic colorectal cancer (mCRC) setting has been examined by several groups, there is a lack of homogeneity in the cut-off threshold applied. In this study, we aimed to validate the dNLR as a prognostic biomarker in the mCRC setting by using a previously established cut-off threshold.

Methods: 70 patients from the Onco-CHUS mCRC cohort treated with oxaliplatin-based first-line therapy were studied. The dNLR was calculated from the pre-first-line therapy initiation blood count and categorized as high (≥2.2) or low (< 2.2). The Cox proportional hazards model, adjusting for known prognostic factors in mCRC, was used to assess the prognostic value of the dNLR.

Results: The population distribution by the dNLR was 48.6% (34) patients in the high dNLR group and 47.2% (36) in the low dNLR group. A high dNLR was independently associated with poor overall survival [HR = 2.71 (95% CI, 1.3512 - 5.4402; p = 0.0050)]. The only other statistically significant factor in multivariate analysis was carcinoembryonic antigen (>5 vs. ≤5) [HR = 3.23 (95% CI, 1.252 − 8.309; p = 0.0153)].

Conclusion: We validate for the first time, to the best of our knowledge, the prognostic value of the dNLR (2.2) in a population-based cohort of mCRC patients treated with oxaliplatin-based therapy in the first-line setting.

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P-90 Does the postoperative course of events influence 2-year mortality in patients undergoing hyperthermic intraperitoneal chemotherapy? An evaluation by a novel scoring system

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Background: Cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC), provides substantial survival benefits to patients with advanced peritoneal carcinomatosis. However, it is associated with significant morbidity and mortality. We tried to evaluate the association between the postoperative course of events during the patient's hospital stay and 2-year mortality by using a novel scoring system: course of recovery after major surgery (CRAMS).

Methods: After ethical committee approval, 83 patients undergoing CRS with HIPEC under general anaesthesia from 2013-2015 were included in the cohort study. Demography, preoperative albumin, peritoneal carcinoma index (PCI), duration of surgery, intraoperative fluids, and intraoperative blood transfusion were noted. Postoperatively, 7 parameters for CRAMS scoring (elective ventilation, reintubation, reexploration, ionotropic support, sepsis, duration of ICU stay, respiratory complications) and 2-year mortality were noted. Pearson correlation coefficient was derived to depict linear correlation between the various factors with CRAMS scoring. Significant factors were further subjected to multiple regression analysis.

Results: The average intraoperative crystalloid consumption was 8.5±2.9 litres (4-20500 litres), average duration of surgery was 10±2.6 hours (5-19 hours) and 2-year mortality was 26.5%. The median CRAMS score was 1(0-7). CRAMS score showed significant correlation with 2-year mortality (p=0.003). CRAMS score in turn was influenced by intraoperative crystalloids (p=0.001), and duration of surgery (p=0.01). On multiple linear regression analysis, intraoperative crystalloids remained as the only factor significantly influencing the CRAMS score (p=0.02).

Conclusion: CRAMS scoring, which depicts the postoperative course of patients during the hospitalization, predicts 2-year mortality in patients undergoing CRS with HIPEC.

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P-91 A retrospective analysis of maintenance strategies in metastatic gastric and gastroesophageal cancer

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Background: Combination fluoropyrimidine with platinum-based chemotherapy has become the standard of care for advanced gastric and gastroesophageal cancer. Clinical trials in conjunction with practice, have adopted induction fluoropyrimidine and platinum-based chemotherapy for 3-4 months. In other GI malignancies, induction chemotherapy followed by maintenance chemotherapy has been shown to improve patient outcomes compared to observation, with a decrease in treatment-related toxicities with induction therapy. However, a maintenance approach in gastric/gastroesophageal cancer has not been investigated in clinical trials. We investigated outcomes for patients with metastatic gastric/gastroesophageal cancer who received continuous induction versus induction followed by maintenance chemotherapy.

Methods: A retrospective analysis of patients with metastatic gastric/gastroesophageal adenocarcinoma treated with fluoropyrimidine and platinum-based chemotherapy between 2007 to 2017 from three centers of a single institution was performed. Metastatic gastric and gastroesophageal cancer patients who achieved at least stable disease after initial induction treatment were included. Patients were categorized into the continuous group if they received greater than 16 weeks or 8 cycles of combined chemotherapy. Patients were also assigned to the maintenance chemotherapy group if they received maintenance fluoropyrimidine monotherapy after 8 or less cycles of combined induction chemotherapy or if they were observed off treatment. Data were extracted from the medical record to determine progression-free survival (PFS), overall survival (OS), and toxicities.

Results: Ninety patients met criteria and were evaluated; forty-eight received continuous and forty-two received maintenance chemotherapy. No significant difference in progression-free survival (9.9 vs 8.4 months, HR =.86, 95% CI: .56-1.32; p =.40) was observed between the continuous and maintenance groups. Additionally, there was no significant difference in overall survival (16.1 vs 21.3 months, HR =.81, 95% CI: .51-1.32; p=.30). A significant decrease in treatment-related toxicities was observed, with a higher proportion of thrombocytopenia (83.0% vs 50.0% RR =.62, 95%CI: 44-.87), and grade 3 neuropathy (42.6% vs 9.8% RR =.22, 95% CI: .08 -.60) in patients who received continuous induction chemotherapy.

Conclusion: Maintenance chemotherapy following induction chemotherapy is associated with an improved toxicity profile and appears to be effective compared to continuous induction chemotherapy in metastatic gastric/gastroesophageal cancer. Prospective randomized studies confirming its potential benefits compared with continuous induction chemotherapy are warranted.

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P-92 Autophagy drugs are dynamic regulators of long non-coding RNA expression in colorectal cancer

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Background: Numerous studies have shown that gene mutation and dysregulation of long non-coding RNAs (lncRNAs) are associated with human cancers including colorectal cancer (CRC). A number of lncRNAs have been structurally and biochemically identified but there was inadequate in-vivo evidence to support their oncogenic activity in cancer. We hypothesized that autophagy, the cellular self-protective mechanism, plays a key role in carcinogenesis by regulating lncRNAs expression in CRC. In this study, our objective was to explore the drug-induced autophagy regulated lncRNAs which may be involved in the carcinogenesis of CRC.

Methods: In this study, we used the USFDA approved autophagy drugs, rapamycin and chloroquine, to induce and inhibit autophagy in four CRC cell lines, namely HT-29, HCT-116, DLD1, and SW480. Western blot was used to measure the autophagy marker proteins LC3B and p62 with β-actin as an internal control. After confirming the induction and inhibition of autophagy, RNA isolation was performed by RNeasy mini kit. For HT-29, RNA integrity was measured by gel-electrophoresis and bioanalyzer respectively. Then, high-quality RNA samples were considered for Illumina Solexa next-generation sequencing (NGS). The differentially expressed transcripts were further analyzed with powerful statistical tools (Partek Genomic Suite and Ingenuity Pathway Analysis). Finally, we check the expression of target lncRNA in other CRC cell lines by qPCR.

Results: In our NGS analysis for HT-29, we compared the transcript lists of the autophagy induction and inhibition groups and found many lncRNAs are differentially expressed in both groups. Particularly, lncRNAs DARS-AS1, DGCR5, LINC00261, LINC00941, MIR22HG, and SATB2-AS1 are the most significantly regulated by autophagy drugs. Similar lncRNA response patterns against autophagy drugs were detected in the other CRC cell lines.

Conclusion: We conclude that these short-listed lncRNAs may act as potential diagnostic biomarkers as well as therapeutic targets for CRC patients. Further studies are needed to explore the mechanisms of action for these lncRNAs and to validate our hypothesis.

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P-93 Levels of steroid hormones, their precursors and ACTH in the blood of patients with pancreatic diseases

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Background: Its dual exocrine and endocrine function makes the pancreas a unique organ. The relationship between the pancreas and sex steroids (estrogens, progestins, and androgens) is indirectly confirmed by numerous epidemiological, clinical, and biochemical studies. Our purpose was to analyze blood levels of steroid hormones and ACTH in patients with pancreatic diseases.

Methods: Blood samples were collected from 51 male patients (mean age 58.8±6.7 years) with pancreatic pathologies: chronic pancreatitis (n=9), pancreatic

adenocarcinoma (AC, n=10), AC with a neuroendocrine component 10-30% (AC+NET, n=20), and pancreatic neuroendocrine tumors (NET, n=12). All cancer patients had T1-3N0-1M0 tumors. The comparison group included 21 healthy donors (mean age 51.8±7.1 years). Levels of ACTH, DHEA-S, 17OHP, testosterone (T), progesterone (P4), estradiol (E2) and cortisol were measured by RIA in the blood serum.

Results: Patients with chronic pancreatitis showed increased levels of T by 2 times, cortisol by 1.8 times ($p< 0.05$), while DHEA-S, 17OHP, P4, E2 and ACTH were similar to the donor levels. The cortisol/DHEA-S ratio exceeded the norm by 1.6 times ($p< 0.05$). In AC patients, DHEA-S was 1.6 times lower than the norm, 17OHP was 1.4 times lower, and levels of T, P4 and E2 were 1.8, 4.8, and 2.7 times higher ($p< 0.05$) than in donors, respectively; ACTH and cortisol were 2.5 and 2 times increased, respectively, and the cortisol/DHEA-S ratio exceeded the norm by 3.2 times ($p< 0.05$). Patients with NET demonstrated decreased, compared to donor levels, DHEA-S by 2.4 times, 17OHP by 6.4 times, T by 1.6 times and E2 by 1.5 times; P4, cortisol, and ACTH were similar to the norm. The cortisol/DHEA-S ratio exceeded the norm by 2.4 times ($p< 0.05$). Compared to patients with AC, patients with NET had lower levels of DHEA-S by 1.5 times, 17OHP by 4.5 times, T by 2.9 times, P4 by 5.4 times, E2 by 4.2 times, cortisol and ACTH by 2 times, and the cortisol/DHEA-S ratio by 1.3 times ($p< 0.05$). Patients with AC+NET showed decreased, compared with the norm, DHEA-S by 2.5 times, 17OHP by 4.6 times, T by 1.3 times, and increased levels of P4 by 1.4 times and ACTH by 2.2 times ($p< 0.05$); cortisol and E2 concentrations were normal. The cortisol/DHEA-S ratio exceeded the norm by 2.4 times ($p< 0.05$). Levels of ACTH in AC+NET were similar to the values in AC, and the cortisol/DHEA-S ratio was 1.3 times lower ($p< 0.05$). The main differences in the studied indices between patients with AC+NET and 100% NET included lower levels of 17OHP in the latter by 1.4 times, P4 by 1.6 times, and higher levels of E2 by 1.5 times and ACTH by 1.8 times ($p< 0.05$).

Conclusion: The studied blood indices differed depending on the presence or absence of malignant pancreatic pathology and on the presence of a neuroendocrine component in the malignant tumor.

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P-94 Predictive assessment of peritoneal spread in patients with gastric cancer

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Background: Peritoneal metastasis is a common complication of gastric cancer (GC) often associated with a high risk of intraperitoneal spread of malignant cells during surgical treatment. The contemporary interpretation of the classic "seed and soil" theory suggests that bidirectional contacts between cancer cells and host tissues consist of several processes: invasion, adhesion of cancer cells to normal ones, migration towards a chemotactic gradient and proliferation in response to autocrine and paracrine growth stimuli. Our purpose was to study levels of CA-19.9, CA-125, CA-72.4, and He-4 in tissues of malignant tumors, the peritoneum (P) and omentum (O) in patients with gastric cancer T3-4aN0-3M1 and T3-4aN0-3M0.

Methods: Group 1 included 22 patients aged 59.51±4.5 years with GC T3-4aN0-3M1, metastases to P and O; group 2 — 24 patients aged 64.08±5.1 years with non-metastatic GC; the control group (C) — 17 non-cancer patients aged 39.1±3.2 years. Tissues of GC, O, and P obtained intraoperatively were studied for CA-19.9, CA-125, CA-72.4, and He-4.

Results: Levels of CA-19.9, CA-125, CA-72.4, and He-4 were increased, compared to control values, in all studied samples from 1.6 times (CA-72.4) to 180.1 times (CA-19.9). Only CA-19.9 levels in T3-4aN0-3M1 were 1.8 times ($p<0.05$) higher in than in T3-4aN0-3M0. In O, CA-72.4 in T3-4aN0-3M0 exceeded C by 3.4 times, in T3-4aN0-3M1 — by 21 times. CA-125 exceeded C in T3-4aN0-3M0 by 2.2 times, in T3-4aN0-3M1 by 4.6 times. He-4 was increased, compared to C, in T3-4aN0-3M0 by 2.2 times, in T3-4aN0-3M1 — by 81.1 times. Levels of CA-19.9 in O were of special interest: in T3-4aN0-3M1, they exceeded C by 20 times; in 20 patients with GC T3-4aN0-3M0, they were only 4.1 times higher than in C and 4.8 times lower than in T3-4aN0-3M1, while in 4 patients, CA-19.9 in O did not differ significantly from the levels in T3-4aN0-3M1. The results in P tissues were somewhat different - in T3-4aN0-3M1, levels of the markers were increased compared to C: CA-19.9 by 19.2 times, CA-72.4 by 2.8 times and He-4 by 10.6 times. No significant differences were found for CA-125. In T3-4aN0-3M0, CA-72.4 levels were 3 times higher than In C, being similar to the values in T3-4aN0-3M1. Levels of CA-125 did not differ significantly. He-4 in T3-4aN0-3M0 was increased by 5 times, being 2.1 times lower than in patients with T3-4aN0-3M1 GC. Again, particular attention was attracted to CA-19.9: the levels in P in T3-4aN0-3M1 exceeded C values by 19.2 times; in 21 patients with T3-4aN0-3M0 GC, CA-19.9 was only 2.2 times higher than in C and 8.5 times lower than in T3-4aN0-3M1, while in 3 patients, the levels did not differ significantly from that in T3-4aN0-3M1.

Conclusion: The P and O saturation with marker oncoproteins is one of the factors associated with features of GC metastasis, and determination of CA-19.9 levels can serve as an informative laboratory test for the predictive assessment of the further disease development.

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P-95 Non-metastatic anal cancer outcomes: A single-center experience

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Background: Squamous cell carcinoma (SCC) of the anal canal is an uncommon diagnosis. Combined chemoradiotherapy is the standard of care for patients with nonmetastatic disease, while surgery is reserved for persistent disease or local recurrence.

Methods: The purpose of this retrospective analysis was to determine the clinical outcomes of patients with SCC of the anal canal diagnosed between 2008 and 2016, at our institution, treated with chemoradiotherapy. We excluded stage IV disease. Baseline clinical and demographic characteristics and treatment features were reported. Overall survival (OS), progression-free survival (PFS) and surgery-free survival (SFS) were calculated by Kaplan-Meier method. Statistics were evaluated with IBM™ SPSS software, version 22.

Results: Twenty-three patients met the inclusion criteria, of which 8 males (34.8%) and 15 were females (65.2%), with a median age at diagnosis of 66 years (39-86 years). Tumor stage according to the 8th edition AJCC manual had the following distribution: stage I 1 case (4.4%), stage II 2 cases (8.7%), stage IIB 3 cases (13%), stage IIIA 5 cases (21.7%), stage IIIB 1 case (4.4%), stage IIIC 11 cases (47.8%). Concerning lymph node involvement, 16 cases (69.6%) were positive and 7 cases (30.4%) were negative. All patients were treated with chemoradiation. Most patients were treated with a total dose between 50 and 60Gy to the tumor volume. IMRT was used in 4 cases (17.4%). Radiotherapy delays due to toxicity occurred in 8 cases (34.8%), mostly mucocutaneous and hematologic. The chemotherapy regimen used was mitomycin combined with 5-fluorouracil in 16 cases (69.6%), mitomycin combined with capecitabine in 6 cases (26.1%) and oxaliplatin combined with capecitabine in 1 patient (4.3%), who had a synchronous lung cancer. Initial dose reductions were performed in 2 patients treated with mitomycin and capecitabine. Median overall treatment time was 42 days (32-56 days). Neutropenia G3 (CTCAE v 5.0) occurred in 2 patients. Persistent disease after therapy was seen in 5 cases (21.7%), abdominopelvic amputation was performed in 4 cases, while 1 patient refused surgery. The median duration follow-up in the total population was 47 months. Two patients were lost to follow-up after 2 years of diagnosis. Local relapse occurred in 8 cases (38%) and 3 patients (14.5%) developed distant metastases. Three-year OS, PFS, and SFS was 76%, 75%, and 69% respectively. Median overall survival was 63.5 months (40-122months). All deaths were related to relapse or disease progression, except one due to pulmonary embolism.

Conclusion: Despite the small sample size, which represents the rarity of the disease, our results are consistent with previously published studies. Due to few data available to guide the choice of regimen after disease progression, management should be done in experienced centers.

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P-96 Levels of sex hormones and sex steroid receptors in pathological tissues in gastric cancer patients

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Background: Despite the growing interest of the role of estrogen receptors ERα and ERβ and the androgen receptor (AR) in gastric cancer (GC), results of studies remain contradictory. Some data demonstrate a relationship between GC pathogenesis and estrogen signaling, and hormone therapy may be a useful strategy for the treatment of GC in cases of hormone-dependent tumor growth. Our purpose was to analyze levels of sex hormones and their receptors in tissues of GC, the peritoneum (P) and omentum (O) in patients with GC T3-4aN0-3M1 and T3-4aN0-3M0.

Methods: Group 1 included 22 patients aged 59.51±4.5 years with GC T3-4aN0-3M1 with metastases to P and O; group 2 - 24 patients aged 64.08±5.1 years with GC T3-4aN0-3M0; controls (C) - 17 non-cancer patients aged 39.1±3.2 years. Levels of RE-α, RE-β, RA, RP, estrone (E1), estradiol (E2), free testosterone (Tf) and prolactin (PRL) were determined by ELISA in tissues of GC, O and P obtained intraoperatively.

Results: Levels of RE-α in tumor tissues in T3-4aN0-3M1 were decreased compared to C by 1.7 times ($P<0.05$), in T3-4aN0-3M0 — increased by 1.2 times ($P<0.05$). RE-β and RA were unchanged in both cases. RP in T3-4aN0-3M1 was similar to C, and in T3-

4aN0-3M0 — increased by 3.5 times. In O and P tissues, RE-α and β, RA and RP in T3-4aN0-3M1 were similar to C, and in T3-4aN0-3M0 — elevated: RE-α - by 3.9 and 2.4 times, RE-β — by 2.5 and 1.5 times ($P<0.05$), RP — by 2.2 and 1.5 times ($P<0.05$). RA levels in O and P in T3-4aN0-3M0 did not differ from C. As to sex hormones, all tissue samples had elevated levels of E1, compared to C: in T3-4aN0-3M1 and T3-4aN0-3M0, in tumor tissues - by 1.5 and 1.7 times, respectively, in O — by 5.9 and 3.2 times, in P — by 7.6 and 3.8 times, respectively. However, differences in E1 levels depending on the metastatic status of tumors were significant only in O and P tissues, and the levels in M1 were 1.8-2 times higher than in M0. In M1 tumor tissues, E2 levels were decreased by 4.2 times, and Tf and PRL were elevated by 18.9 and 8 times, respectively. In O and P, E2 in M1 was decreased compared to C by 4 and 7.1 times, respectively, and in M0 it did not have significant differences. Tf in O and P was increased in M1 compared to C by 2 and 2.7 times, respectively, and in M0 it was similar to C. PRL in O and P was increased in M1 compared to C by 7.6 and 1.7 times, respectively, and in M0 it was similar to C.

Conclusion: Elevated levels of RE-α, RE-β, and RP in tissues of O and P were associated with features of GC metastasis. Levels of RE-α and RP in O and P correlated with the levels in tissues of GC T3-4aN0-3M1 and T3-4aN0-3M0. Decreased E2, together with an increase in Tf and PRL, could be considered as a marker of metastases to the peritoneal cavity.

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P-97 Functions of antioxidant enzymes in the blood of patients with pancreatic neuroendocrine tumors

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Background: The high cancer mortality determines the relevance of studying metabolic features involved in the initiation and progression of the malignant process in various types of pancreatic diseases. An important role in the regulation of processes supporting tumor progression and the development of its resistance to treatment is played by the antioxidant system, and especially by the glutathione-dependent unit, considered as one of the main key components of cancer pathophysiology. The purpose of the study was a comparative analysis of the functioning of the enzyme unit of the antioxidant system in the blood of patients with pancreatic neuroendocrine cancer, pancreatic adenocarcinoma and chronic pancreatitis.

Methods: The activity and content of antioxidant enzymes (superoxide dismutase - SOD, catalase, glutathione reductase, and glutathione peroxidase - GPO) were studied in the blood of 51 patients before treatment and in 22 donors. The activity of enzymes was determined by standard spectrophotometry, and levels of enzymes were measured by ELISA. Based on a histological study of tumors, patients were divided into groups: pancreatic neuroendocrine tumors (NET), pancreatic adenocarcinoma (AC), AC with a neuroendocrine component; a group of patients with chronic pancreatitis (CP) was also identified.

Results: The most pronounced differences between NET and AC and CP were found for glutathione reductase — an enzyme responsible for the regeneration of oxidized glutathione to reduced one. Activity of the enzyme was decreased by 77.2% compared to donors and by 63.4% ($p=0.000000$) compared to CP patients; in AC it was unchanged, and only in AC with a 10-30% neuroendocrine component its significant decrease was registered. The ratio of glutathione reductase activity to its content was decreased only in NET — by 40.6% ($p=0.0001$) compared to donors, while in CP it was elevated by 5 times, in AC — by 2.5 times, in AC with a 10-30% neuroendocrine component — similar to donor values and 41.2% ($p=0.008$) higher than in NET. All groups of patients demonstrated a decrease in activity of SOD (by 25-40%) and catalase (the maximum one — by 46.5% in NET). The activity to content ratios for SOD and catalase were decreased in all patients with malignant lesions of the pancreas, with the lowest level, compared to donors, in NET — a decrease by 62.8% for SOD and by 45.2% for catalase; in CP, only the catalase activity to content ratio was elevated by 32.6% ($p=0.017$) compared to donors. A sharp increase in the content of GPO1 - the most pronounced in NET, almost by 5 times - indicated a possible switch of antioxidant protection from first-line enzymes (SOD, catalase) to GPO.

Conclusion: NETs were characterized by pronounced disorders in the function of the primary enzymatic unit of antioxidant protection, as well as by a sharp decline in the function of glutathione reductase and a change in the normal ratio of the main enzymes of the glutathione system. Abnormal oxidative status is one of the metabolic features of neuroendocrine cancer, possibly associated with increased aggressiveness of this histotype of pancreatic lesions.

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P-98 HGCSG1902: Multicenter, prospective, observational study for cases with dysgeusia caused by chemotherapy for gastrointestinal cancer

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Background: Anti-tumor agents have been developing every year, and the overall survival in gastrointestinal cancer patients is dramatically improved in a decade. As the duration of treatment prolongs, quality of life (QoL) and management for adverse events have become increasingly important. Diet is an important factor in QoL maintenance, but it is known that adverse events of chemotherapy include anorexia, nausea, vomiting, and dysgeusia, which can lead to reduced oral intake. The incidence of dysgeusia associated with chemotherapy is reported to be approximately 56-76%, depending on the type of chemotherapy. Prolonged dysgeusia may worsen nutritional status and performance status. Nausea and vomiting can be treated with an antiemesis, but there has been no promising intervention for dysgeusia for a long time. The mechanism of chemotherapy-induced dysgeusia is not yet clear, but it has been reported that cells with rapid turnover, such as taste bud cells, are more sensitive to chemotherapy than other cells. Furthermore, it has been demonstrated that the regeneration of taste bud cells requires large amounts of zinc. Therefore, zinc deficiency can cause dysgeusia. Cytotoxic agents may act as a chelator for zinc. However, there are no prospective multicenter studies of the effects of zinc administration on dysgeusia caused by chemotherapy. By analysing various factors related to dysgeusia due to chemotherapy, we can identify the factors associated with dysgeusia and clarify the effectiveness of zinc preparations, which will contribute to the establishment of supportive care for patients undergoing chemotherapy. Therefore, we planned a multicenter, prospective observational study on cases of dysgeusia caused by chemotherapy for gastrointestinal cancer.

Trial design: This study is carried out as an investigator-initiated, multicenter, prospective observational study to determine clinical or treatment factors associated with chemotherapy-related dysgeusia in patients with advanced gastrointestinal cancer. Eligibility criteria include patients presenting grade 1 or more dysgeusia in Common Terminology Criteria for Adverse Events (CTCAE) v5.0 or Scale of Subjective Total Taste Acuity (STTA) during chemotherapy for gastrointestinal cancer. One of the important exclusion criteria is the administration of zinc preparations before presenting dysgeusia. After registration, physicians will collect clinical information related to dysgeusia prospectively for 12 weeks using blood sampling and two times questionnaires. The treatment method for dysgeusia is determined by the physician's choice (no intervention, polaprezinc, or zinc acetate hydrate). The data to be collected in this study include changes in dysgeusia, the relationship between serum zinc levels and dysgeusia, the contribution of physical factors to dysgeusia (age, height, weight, body surface area), the involvement of nutritional factors (hemoglobin level, serum iron, albumin level) and the safety of the intervention. A total of 180 cases are planned for registration in 13 institutions. In this study, we can evaluate the effects of factors contributing to dysgeusia, and the effects of zinc preparations on improving dysgeusia. This study was approved by the institutional review board of Hokkaido University Hospital (approval number: 019-0248). Clinical trial information: UMIN000039653.

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P-99 Pembrolizumab in combination with gemcitabine and cisplatin for the treatment of advanced biliary tract cancer: phase 3 KEYNOTE-966 trial in progress

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Background: Biliary tract cancer (BTC) is a rare and heterogeneous malignancy comprising intrahepatic cholangiocarcinoma (CCA), extrahepatic CCA, and gallbladder cancer. Surgery is potentially curative in patients with early disease, but recurrence is common. Combination chemotherapy with gemcitabine and cisplatin is the current standard of care for advanced BTC in most regions as well as S-1 therapy in Japan. Pembrolizumab has demonstrated modest but durable antitumor activity in patients with BTC as monotherapy and improved survival when used in combination with platinum-based chemotherapy in other oncologic indications. KEYNOTE-966 (NCT04003636) is a randomized, double-blind, phase 3 trial evaluating pembrolizumab or placebo plus gemcitabine and cisplatin in patients with advanced BTC.

Trial design: Eligible patients are ≥18 years old with histologically confirmed metastatic or unresectable BTC, measurable disease per RECIST v1.1, an ECOG performance status of 0 or 1, and adequate organ function. Patients who have received prior systemic therapy for advanced disease, or prior therapy with an anti-PD-1/PD-L1/PD-L2 or CTLA-4 agent, and those with a history of pneumonitis, HIV infection, or central nervous system metastases will be excluded. Patients with past or ongoing HCV or controlled HBV infection are eligible per protocol-defined criteria, provided they do not have dual active HBV and HCV infection at study entry. Approximately 788 patients will be randomly assigned 1:1 to pembrolizumab 200 mg or placebo IV every 3 weeks in combination with gemcitabine 1000 mg/m^2 and cisplatin 25 mg/m^2 IV on days 1 and 8 of every 3-week cycle. Cisplatin will be given for a maximum of 8 cycles; gemcitabine will be given until progression, unacceptable toxicity, or withdrawal. Treatment with pembrolizumab/placebo will be continued for up to 35 cycles (~2 years of treatment) or until progression, unacceptable toxicity, or withdrawal. Patients will be stratified by region (Asia, non-Asia), stage (locally advanced, metastatic), and tumor origin (gallbladder, intrahepatic, extrahepatic). Imaging will be performed every 6 weeks through week 54, and every 12 weeks thereafter. Adverse events will be monitored throughout the study and for 30 days after treatment (90 days for serious adverse events). Co-primary endpoints are progression-free survival (PFS) per RECIST v1.1 by blinded independent central review (BICR) and OS. Secondary endpoints are objective response rate (ORR) and duration of response (DOR) per RECIST v1.1 by BICR, and safety. Exploratory endpoints are disease control rate (DCR) per RECIST v1.1 by BICR; PFS, ORR, DOR, and DCR per immune-modified RECIST; PFS and ORR per RECIST v1.1 by BICR; and health-related quality of life (by EORTC QLQ-C30, EORTC QLQ-BIL21, and EuroQol EQ-5D-5L). Recruitment began in September 2019 and is underway in 19 countries.

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P-100 Quality of life assessment and reporting in gastric cancer treatment: A systematic review of phase 3 clinical trials published between 2010 and 2019

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Background: Quality of life (QoL) has emerged as a fundamental outcome in cancer clinical trials. The importance of integrating QoL with other traditional oncological outcome measures has been particularly emphasized in poor-prognosis malignancies such as gastric cancer. The present study aimed to evaluate the assessment and reporting of QoL in phase 3 clinical trials conducted in patients affected by gastric cancer.

Methods: We performed a literature search of primary phase 3 clinical trials testing anticancer drugs in gastric cancer published between 2010 and 2019 by 7 relevant scientific journals. Data concerning the presence of QoL among secondary and exploratory endpoints, the different assessment tools and the methods of analysis adopted were extracted from papers and study protocols. For every paper, secondary publications reporting QoL results were searched in PubMed.

Results: 46 publications of phase 3 clinical trials were included in our analysis (9 in neoadjuvant/adjuvant/perioperative setting, 37 in metastatic setting). Only 14/46 (30.4%) trials strictly enrolled patients affected by gastric cancer, while 26/46 studies (56.5%) included gastroesophageal junction and 6/46 (13.0%) esophageal cancer. In 21 publications (45.7%), QoL was not listed among the endpoints in 7/9 (77.8%) trials in the neoadjuvant/adjuvant/perioperative setting, in 7/18 (38.9%) first-line trials and in 7/19 (36.8%) second- and further lines trials, including 15/20 (75.0%) trials conducted exclusively in an Eastern population vs 3/9 (33.3%) trials conducted only in a Western population. A decreasing trend was recognized over time: QoL was not reported in 13/26 (50.0%) publications between 2010-2015 and in 8/20 publications (40.0%) between 2016-2019; surprisingly, this tendency was not confirmed in the metastatic setting, where the lack of QoL concerned 7/20 (35.0%) of publications between 2010-2015 and 7/14 (41,2%) of publications between 2016-2019). Out of 25 (54.3%) primary publications of trials reporting QoL as a secondary or exploratory endpoint, QoL results were published in 11/25 (44.0%). Additionally, QoL results were published in 5/11 (45.5%) primary publications of trials with positive results and in 5/21 (23.8%) no profit trials. However, we found 4 secondary publications reporting QoL results. For trials including QoL among endpoints but no QoL results in the primary publication, the probability of secondary publication was 0%, 25.0%, and 50.0% after 1, 3 and 5 years, respectively. Most common tools used for QoL assessment in patients were EORTC QLQ-C30 (22, 88.0%) and EORTC QLQ-STO22 (14, 56.0%); most common methods of analysis were mean change/mean score (10, 40.0%) and time to deterioration (9, 36.0%).

Conclusion: Despite a general decreasing tendency to exclude QoL from oncologic outcome measures in the last five years, QoL is not assessed or published in many phase III trials in gastric cancer, including trials conducted in the metastatic setting and no profit trials. The methodology of QoL analysis is heterogeneous for type of instruments, method of analysis and presentation of results. In conclusion, there is a strong need for QoL definition for supporting therapeutic decision-making and helping clinicians in the optimal management of gastric cancer patients.

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P-101 Oncologic outcomes of mitomycin-C induced severe neutropenia after hyperthermic intraperitoneal chemotherapy with cytoreductive surgery in colorectal cancer patients

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Background: Mitomycin-C (MMC) is the most commonly used anticancer drug for hyperthermic intraperitoneal chemotherapy (HIPEC) to treat colorectal cancer patients with peritoneal metastasis. Because MMC has hydrophilic properties with pharmacologic stability to use in the intraperitoneal cavity, it was widely used for HIPEC. However, one of its famous side effects is myelosuppression. There were concerns that severe neutropenia after cytoreductive surgery with HIPEC is related to postoperative recovery. However, there is no report as to whether MMC-induced neutropenia influences oncologic outcomes so far. The aim of this study was to evaluate whether MMC-induced severe neutropenia affects oncologic outcomes after cytoreductive surgery with HIPEC in colorectal cancer patients with peritoneal metastasis.

Methods: From March 2015 to June 2019, colorectal cancer patients who underwent CRS and HIPEC to treat peritoneal carcinomatosis at Gangnam Severance Hospital, Seoul, South Korea were evaluated. We excluded the patients with extraperitoneal metastasis (e.g. liver, lung), Krukenberg tumor, re-do HIPEC, incompleteness of cytoreduction, and peritoneal cancer index (PCI) ≥ 10. HIPEC-induced severe neutropenia was defined as absolute neutrophil count (ANC) less than 1000 /m^3 during postoperative 30 days according to the Common Terminology Criteria for Adverse Events. We divided the patients into two groups: Group1, patients with severe neutropenia ANC< 1000) vs. Group2, patients without severe neutropenia (ANC≥1000). Finally, 57 patients (Group1: n=20, Group2: n=37) were evaluated in this study. After cytoreduction, HIPEC was performed with 35mg/m^2 of MMC mixed in 3 liters of peritoneal dialysis solution for 90 minutes at 42℃. Overall survival and progression-free survival were analyzed using the Kaplan–Meier method and the log-rank test.

Results: There were no statistical differences for baseline patient characteristics such as age, sex, body mass index, body surface area, and primary cancer location. The mean PCI of Group 1 and Group 2 were 4.9±2.8 (mean±standard deviation), and 4.6±2.6, respectively (p=0.731). There was no statistical difference between the two groups regarding total operation times (8.1±3.9 vs 7.1±2.0 hours, p=0.200), and

intraoperative blood loss (p=0.924). The median overall survival of patients with Group 1 was 38.0 months, which was not significantly different compared with 40.0 months for Group 2 (p=0.565). However, progression-free survival of patients with severe neutropenia was better than that of patients without neutropenia: Group 1 vs. Group 2, 21.0 months vs. 12 months (p=0.039).

Conclusion: According to our study, severe neutropenia after complete cytoreduction with HIPEC better affected progression-free survival in patients with colorectal cancer carcinomatosis within PCI< 10. However, because severe neutropenia can also deteriorate postoperative recovery after HIPEC, it is required to determine and adjust optimal doses of MMC to assure oncologic safety after HIPEC.

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P-102 The impact of a multidisciplinary approach in the management of pancreatic disease

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Background: The management of pancreatic disease (PD) is very insidious, mainly due to the often difficult differential diagnosis between benign and malignant diseases, and in the case of pancreatic ductal adenocarcinoma (PDCA), to the frequently hard differentiation among resectable/borderline PDCA susceptible to upfront surgery, locally advanced PDCA susceptible to a neoadjuvant approach and never resectable or metastatic PDCA in which a palliative treatment is the only option. A correct PD evaluation and the subsequent choice of the most appropriate treatment strategy, thus, needs a multidisciplinary approach (MA), involving surgeons, oncologists, radiologists, radiation oncologists, endoscopists, gastroenterologists and pathologists. On the basis of such considerations, we investigate the impact of the multidisciplinary meeting (MM) in the management of PD at our Institution.

Methods: We retrospectively evaluated all the cases discussed by surgeons at our MM. We collected data, both pre- and post-MM, regarding diagnosis (cyst vs pancreatitis vs IPMN vs PDCA), and in the case of PDCA, tumor burden at baseline (resectable vs border-line resectable vs locally advanced vs metastatic disease) and disease response to treatment (disease control vs progression). The primary endpoint was the overall rate of discrepancy in diagnosis and/or PD evaluation between pre- and post-MM.

Results: From October 2018 to December 2019, a total of 139 cases were presented by surgeons. After MM, a total of 38 diagnoses and/or PD evaluations were modified, for an overall discrepancy rate of 27%. In particular, of the 38 discordant cases, 9 (24%) were initial diagnosis, 24 (63%) baseline tumor burden assessments and 5 (13%) were PDCA response evaluations. Among the 24 cases of tumor burden evaluations, treatment strategy changed in 17 out of 24 cases. More specifically, of the 19 cases evaluated as borderline/resectable before the MM, 15 were defined as locally-advanced or metastatic disease after the MM; of the 5 cases, evaluated as not resectable before the MM, 2 were considered border-line/resectable after the MM. Similarly, out of 9 cases of discrepant initial diagnosis, 5 cases considered as malignant disease before MM, were assessed as benign after the MM.

Conclusion: Our analysis demonstrates a significant rate of discrepancy in diagnosis and/or PD evaluation between pre- and post-MM. Our results show that a MA allows a considerable modification in PD diagnosis and evaluation, maximizing the treatment strategy, in particular avoiding unnecessary and detrimental pancreatic surgery.

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P-103 The role of primary tumor site as a prognostic factor after resection of colorectal liver metastases: A mono-institutional cohort study

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Background: Radical resection of liver metastases (LM) is the only chance of cure for liver-only metastatic colorectal cancer (mCRC) pts. Besides the evaluation of technical resectability, several factors must be taken into account for the evaluation of recurrence risk. Among them, we should consider the Fong Risk Score and its modified version, including RAS/BRAF status (Brudvik's score). Tumor sidedness is an important prognostic factor in CRC. The impact of primary tumor (PT) site on the outcome of LM resection is still debated. Hence, we retrospectively analysed mCRC pts, underwent radical LM resection at our institution, investigating the impact of PT site on DFS and OS.

Methods: Liver-only mCRC pts who underwent radical LM resection were included. The association of the PT site with DFS and OS was evaluated. The following variables were collected: gender, age ($\geq$ vs $<$ 75 years), ECOG PS, CEA baseline level, PT site, RAS and BRAF status, mucinous histology, grading (G1-2 vs G3), RECIST response during preoperative treatment, resected PT, synchronous vs metachronous, number of LM, bilobar vs unilobar LM, LM diameter $\geq$ 5 cm, and R0 vs R1 resection. Univariate and multivariate analyses for DFS and OS were performed.

Results: A total of 463 liver-only mCRC pts who underwent radical LM resection were included. Seventy (15%) pts had a right-sided (r-s) tumor and 393 (85%) pts a left-sided (l-s) tumor. R-s CRC pts more often had RAS/BRAF mutations in comparison to l-s tumors (76% vs 37%; p $<$ 0.0001). Median DFS and OS was 13.1 and 41.6 months, respectively, in r-s CRC vs 16.0 (p=0.65) and 62.2 months (p=0.033), respectively, in l-s tumors. At the multivariate analysis, no significant association with survival parameters was shown for tumor sidedness. At the multivariate analysis, R0 resection was independently associated both with better DFS and OS; RAS/BRAF wt CRC and resected PT were significantly associated with improved OS. Considering all wt CRC pts (N=237), 14 (6%) pts had r-s tumor and 223 (94%) l-s tumor. No significant association of tumor sidedness with survival was shown (DFS r=10.0 vs l=16.0 months, p=0.62; OS r=40.3 vs l=66.2 months, p=0.12).

Conclusion: Our results showed that a significantly smaller proportion of r-s CRC underwent radical LM resection, indirectly confirming its worse prognosis. Among radically resected pts, r-s CRC was associated with a shorter OS (significant) and DFS (not significant) compared to l-s CRC, but it was not confirmed at the multivariate analysis. We can conclude that right-sided PT site should not be considered as a contraindication for radical LM surgery, when feasible.

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P-104 Preoperative endoscopic biliary drainage procedures may affect intrahepatic recurrence of cholangiocarcinoma after surgical resection

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Background: To determine the impact of preoperative endoscopic nasal biliary drainage (ENBD) and/or endoscopic retrograde biliary drainage (ERBD) procedures on intrahepatic recurrence rates in patients with cholangiocarcinoma after surgical resection.

Methods: Between January 2005 and January 2020, 143 patients were diagnosed with cholangiocarcinoma and received surgical resection. Among 143 patients, 99 patients were treated with preoperative ENBD and/or ERBD. We retrospectively analysed prognostic factors (age, gender, preoperative ENBD and/or ERBD, tumor differentiation, pT factor, lymph node metastasis, surgical margin, lymphovascular invasion, preoperative maximal total bilirubin, postoperative chemoradiation/chemotherapy/radiation therapy, CA19-9) for recurrence after surgical resection.

Results: Intrahepatic recurrence after surgical resection was detected in 22/99 (22.2%) patients with preoperative ENBD and/or ERBD, and 5/44 (11.4%) patients without preoperative ENBD and/or ERBD for a median period of 12 months (range 0-48). On univariate analysis, the intrahepatic recurrence rate of patients who underwent ENBD and/or ERBD (n=99) was higher than that of patients who did not (n=44) (P=0.090). The intrahepatic recurrence rate of patients who had T3/T4 factor (n=74) was higher than that of those who had T1/T2 factor (n=69) (P=0.168). The intrahepatic recurrence rate of patients who had elevated CA19-9 ($>$ 200) (n=49) was higher than that of patients who did not (n=94) (P=0.002). In multivariate analyses, preoperative ENBD and/or ERBD

and elevated serum CA19-9 level (>200 ng/mL) were prognostic factors for intrahepatic recurrence, with hazard ratios (HR) of 2.154 (95% confidence interval (CI), 0.893-7.626, P = 0.080) and 3.647, (95% CI, 1.660-8.011, P = 0.001).

Conclusion: Preoperative endoscopic nasal biliary drainage (ENBD) and/or endoscopic retrograde biliary drainage (ERBD) procedures may affect intrahepatic tumor recurrence in patients with cholangiocarcinoma after surgical resection. Elevated serum CA 19-9 level also affected intrahepatic tumor recurrence in patients with cholangiocarcinoma after surgical resection.

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P-105 Defining novel regulators of inflammatory signaling in pancreatic cancer

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Background: In recent years, immunotherapy has emerged as a promising treatment modality for a number of different tumour types but its impact in treatment of pancreatic cancer has been limited. Examining the molecular pathways that affect processes determining the immune response to cancer cells in pancreatic ductal adenocarcinoma (PDAC) will enable the development of new therapeutic strategies to target this response. Numerous studies have suggested a role of inflammation in PDAC development and progression. Inflammatory cytokines synthesized by the host, tumour cells, and stromal cells play a role in cellular proliferation, angiogenesis, metastasis and immune evasion. Serrels et al have already demonstrated a role for the tyrosine kinase Focal Adhesion Kinase (FAK) in regulating the anti-tumour immune response specifically by regulation of cytokines in cancer cells and so we propose that there are further kinase regulators of inflammatory signaling in pancreatic cancer that are yet to be identified and could serve as therapeutic targets. The aim of our project was to identify the major chemokines and cytokines secreted by human PDAC cells. This is to facilitate subsequent identification of key kinases regulating this chemokine/cytokine profile secretion in PDAC cells.

Methods: We determined the chemokine/cytokine secretion profile of five PDAC cell lines using a forward-phase antibody array platform (available at the Edinburgh Cancer Centre) to analyse cancer cell-conditioned culture media. To prioritise a list of 64 cytokine targets most likely to be involved in important immune signaling pathways and thus to be included in the antibody array platform, we interrogated single-cell RNA sequencing data, from immune cell populations enriched in the human PDAC tumour microenvironment such as macrophages and cancer-associated fibroblasts, to look at the expression of cytokine receptor genes and then highlighted their ligands for selection.

Results: We identified five cytokines abundantly expressed in all five PDAC cell lines: CXCL16, CCL5 and CXCL8 along with growth factors Amphiregulin and TIMP-1. We identified three further cytokines produced at moderate levels: IL-6, MCSF and IL-1B.

Conclusion: We have demonstrated significant cytokine production across five PDAC cell lines and prioritised six key cytokines and two growth factors that we will be able to assay for after CRISPR knockout of each of the ninety human tyrosine kinases from PDAC cells. By doing this we hope to identify kinases that have the potential to mediate the immune response to PDAC, resulting in new therapeutic targets for testing in combination with other immunotherapies.

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P-106 Liver metastasis in colorectal cancer: Management and survival outcomes of liver metastasectomy in a single-center analysis

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Background: Colorectal cancer (CRC) is a leading cause of tumour-related morbidity and mortality worldwide. Approximately 50% of patients develop liver metastases (LM) in their course of the disease. Surgical resection is the only treatment that offers a chance of cure and long-term survival, with 5- and 10-year survival rates at around 40% and 25%, respectively.

Methods: All patients who underwent metastasectomy for LM due to colorectal cancer at the Department of Medical Oncology from Hospital Pedro Hispano between 2011 and 2019 were included. Demographic, perioperative, chemotherapy, as well as survival data, were obtained by retrospective chart review.

Results: A total of 40 patients were included. Of this, the primary tumour was in the colon in 33 (83%) patients (55% in the left colon) and in the rectum in 7 (17%) patients. 62,5% (n= 25) were male with a median age of 61 years old (38-79 years). 40% were RAS mutated and only one patient had a BRAF mutation. LM was synchronous in 52,5% and metachronous in 49,5% of patients. 33 (82,5%) exhibited initially unresectable LM, whereas 7 (17,5%) (1 in synchronous subgroup LM and 6 in the metachronous subgroup) were considered resectable at diagnosis. The median time between the initial diagnosis and LM in the metachronous subgroup was 25 months (6-156 months). 31 (77,5%) underwent conversion chemotherapy before hepatic resection (20 in the synchronous subgroup and 13 in the metachronous subgroup). The most common chemotherapy regimen in this setting was FOLFOX. FOLFIRI with cetuximab or bevacizumab was used in the palliative setting (25% in the synchronous subgroup and 23% in the metachronous subgroup), with good response. Metastasectomy was the most common surgical procedure (26 patients, 65%), follow by hepatectomy (14 patients, 35%). Histopathologic surgical margins were R0 in 32 patients (80%) and microscopic tumour (R1) were observed in 8 patients (20%). 1 patient died in the perioperative setting due to liver failure. Complementary chemotherapy after hepatic resection was performed in 34 patients (85%) (17 in the synchronous subgroup and 17 in the metachronous subgroup). The most common chemotherapy regimens included FOLFOX (in 21 patients) and FOLFIRI (8 patients). The median follow-up duration from the date of initial diagnosis was 37 months (3-196 months). For the whole group, the median overall survival after metastasectomy was 25,5 months (0-118 months), 17 months in the synchronous subgroup and 36 months in the metachronous subgroup. The median disease-free survival after metastasectomy was 16,5 months (7 months in synchronous subgroup and 25 months in the metachronous subgroup). 8 patients (38%) in the synchronous subgroup and 10 (53%) in the metachronous subgroup died during the follow-up time.

Conclusion: In this study, metastasectomy seems to be an effective treatment, with gains in overall survival and progression-free survival as described in the literature. Our study has limitations due to the small sample size, retrospective nature of the data analysis and the lack of a control group.

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P-107 LEAP-012: A randomized, double-blind, phase 3 study of pembrolizumab plus lenvatinib in combination with transarterial chemoembolization (TACE) in patients with intermediate-stage hepatocellular carcinoma not amenable to curative treatment

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Background: Hepatocellular carcinoma (HCC) is a commonly occurring malignancy that is often diagnosed at the intermediate or advanced stage. The current standard of care for patients with intermediate disease who are ineligible for curative treatment is locoregional therapy with chemoembolization (TACE). Lenvatinib is a potent inhibitor of VEGFRs 1-3, FGFRs 1-4, PDGFR α, RET, and KIT, and is recommended as an option for the first-line treatment of advanced HCC. Pembrolizumab is a PD-1 inhibitor currently recommended as a second-line option for advanced HCC. Data from a phase 1b trial of lenvatinib plus pembrolizumab demonstrated that the combination has promising antitumor activity and manageable safety in patients with unresectable, intermediate-stage HCC not amenable to TACE. LEAP-012 (NCT04246177) is a randomized, double-blind, phase 3 trial investigating lenvatinib plus pembrolizumab vs placebo in combination with TACE in patients with intermediate HCC.

Trial design: Eligible patients are ≥18 years old with a confirmed diagnosis of HCC localized to the liver without portal vein thrombosis and not amenable to curative treatment. Patients must have ≥1 lesion measurable per RECIST v1.1 confirmed by blinded independent central review (BICR), an ECOG performance status (PS) of 0 or 1, and adequate organ function. Patients who have previously received locoregional therapy (within 4 weeks of the first dose of study treatment) or systemic chemotherapy for HCC, or prior therapy with an anti-PD-1/PD-L1/PD-L2 or CTLA-4 agent, and those with extrahepatic disease will be excluded. Approximately 950 patients will be randomly assigned 1:1 to oral lenvatinib 12 mg (body weight [BW] ≥60 kg) or 8 mg (BW 400 ng/mL), ECOG PS (0 vs 1), albumin-bilirubin grade (1 vs 2 or 3), and tumor burden (utilizing the 6 and 12 rule; ≤6 vs >6 but ≤12 vs >12). Imaging (CT/MRI) will be performed every 9 weeks, or more frequently if indicated. Safety will be assessed throughout the study and up to 90 days after the end of treatment. Patients will be followed for survival every 12 weeks after progression or initiation of a new anticancer therapy. Co-primary endpoints

are overall survival (OS) and progression-free survival (PFS) per RECIST v1.1 by BICR. Secondary endpoints are PFS, objective response rate (ORR), disease control rate (DCR), duration of response (DOR), and time to progression (TTP) per modified RECIST by BICR; ORR, DCR, DOR, and TTP per RECIST v1.1 by BICR; and safety. Exploratory endpoints are PFS, ORR, DCR, DOR, TTP and time from randomization to second/subsequent progression (PFS2) per RECIST v1.1 by investigator review; identification of molecular biomarkers; and health-related quality of life (EORTC QLQ-C30, EORTC QLQ-HCC18, and EQ-5D-5L). Recruitment for this study began in April 2020.

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P-108 Perioperative chemotherapy in locally advanced, resectable gastric cancer: A single-center experience

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Background: Gastric cancer (GC) is the fifth most common cancer, but only 20% have resectable disease at diagnosis. Perioperative chemotherapy decreases local and distant relapses and improves survival rates.

Methods: This retrospective observational study included all patients admitted to the oncology department between January 2016 and December 2019 with locally advanced gastric GC, who submitted to perioperative chemotherapy.

Results: We included 43 patients with locally advanced GC (37 from body and antrum; 6 from the gastroesophageal junction). 79% were male with a median age of 64 years old (59-72) and 79% had an ECOG 1 at admission. Histologically, 56% were intestinal type, 35% were diffuse type and 9% mixed type. Clinical staging at admission was stage III in 32,6%, stage IIB in 14%, stage IIA in 14%, stage IB in 4,7% and IVA in 4,7%. The perioperative chemotherapy regime used was FLOT in 42%, followed by EOX in 30,2%, FOLFOX 14%, and ECF 14%. 30% of patients had G3 toxicity related to chemotherapy; haematological toxicity was the main cause (febrile neutropenia was present in 2 patients in the FLOT subgroup), followed by G3 gastrointestinal toxicity (n=2 in the FLOT subgroup). 1 patient had G4 toxicity with gastric perforation in the FLOT subgroup in the post-operative setting. 63% of the patients were submitted to total gastrectomy, 30% to partial gastrectomy. 7% are still waiting for surgery. 32,6% were in pathological staging I, 23,3% in stage II, 20,9% in stage III and 9,3% in stage IV. In 6 patients we could not access the pathological staging. Only 1 patient in the FLOT subgroup had a complete response to chemotherapy. Most of the patients had a partial response (32,6%), 18,6% with a minimum response; in 46,5% response was not described. 65% of patients resumed and completed the initial chemotherapy regimen. During follow-up, 19% of patients recurred with local or distant metastasis (1 in FLOT subgroup and 7 in EOX subgroup). 8 ended up dying 10 months after the initial diagnosis (6 because of disease progression; 4 due to other complications). The overall survival was 16 months in this population.

Conclusion: Early diagnosis and multimodal treatment are of paramount importance in the survival of GC patients. This work had limitations given the small number of patients included, the short follow-up and the heterogeneity of the population.

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P-109 Global mortality for biliary tract cancer

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Background: Biliary Tract Cancer (BTC) represents a high disease burden due to late diagnosis, poor prognosis, and limited treatment options. Current knowledge is limited regarding the global mortality of various subtypes of BTC and how that may have changed during the past decade.

Methods: BTC mortality was evaluated using the latest World Health Organization (WHO) Mortality Database. Mortality was examined in patients ≥20 years who were diagnosed with BTC as identified by ICD-10 and evaluated by subtype (extrahepatic cholangiocarcinoma [ECC], intrahepatic cholangiocarcinoma [ICC], gall bladder cancer [GBC], and ampulla of Vater cancer [AVC]), gender, geography, and age. Data are reported for selected countries that had ≥5 years of data on both patients with BTC and their total populations between 2006 and 2016. Age-standardized mortality rates (ASR; per 100,000 person-years) with standard error (SE) were calculated using the latest world standard population. Temporal trends of total BTC were described and estimates of average annual percent change (AAPC) were calculated for each country.

Results: There were 39 Asia-Pacific and European countries with data that met the criteria; of those, the highest mortality rate for BTC overall was observed for patients in the Republic of Korea, both < 75 and ≥75 years (ASR=12.99 and ASR=130.00, respectively). The lowest mortality rate was in Georgia and Kyrgyzstan for patients < 75 years (ASR=2.07) and in the Republic of Moldova for patients ≥75 years (ASR=9.27). An assessment of regional differences in the UK revealed that patients in Northern Ireland and Scotland had higher mortality rates than patients in England and Wales. As is typical of most cancers, elderly patients had a higher mortality rate than younger patients: the highest relative mortality rate (RMR; reference < 75 years) between the 2 age groups was in Japan (20.43) and the lowest RMR was in Kyrgyzstan (6.61). Mortality rates increased overtime for 25 out of 39 countries. The highest increase in mortality was seen in Lithuania (AAPC=4.65%). Of the BTC subtypes, ICC showed the highest mortality in 26 countries, GBC in 12 countries, and ECC had the highest mortality rate in Japan. Mortality rates for most subtypes were evenly distributed between sexes or were higher for males in some cases, but GBC mortality rates were higher in females in most countries.

Conclusion: Though a relatively rare diagnosis in many countries, the mortality rate of BTC is high and is exponentially higher in elderly patients. Higher BTC mortality rates coincide with previously reported higher incidence in certain geographic areas, particularly in Japan. These reported mortality rates and the overall increases in mortality rates make it clear that a high unmet need remains for improved treatment for BTC.

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P-110 Prediction of peritoneal recurrence in patients with gastric cancer: A multicenter study

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Background: The peritoneum is the common recurrence site of gastric cancer (GC) presenting with worse survival. Although some predictive clinicopathological factors were determined, comprehensive assessment of peritoneal recurrence risk prediction for patients treated with adjuvant chemotherapy (CR) or chemoradiotherapy (CRT) after surgery is lacking. We aimed to predict peritoneal recurrence and to develop a new scoring model in GC.

Methods: This retrospective study included 274 GC patients who presented with recurrence after curative gastrectomy followed by adjuvant chemotherapy (CT) or chemoradiotherapy (CRT). Risk factors for peritoneal recurrence were analyzed using the following parameters: age, gender, tumor location and characteristics, and differences between treatment modalities. All parameters were assessed by binary logistic regression analysis to compare the patients with and without peritoneal recurrence. Then, a new risk scoring model was developed.

Results: Peritoneal recurrence was observed in 115 (44.1%) patients. Peritoneal recurrence was higher in female gender (Odds ratio [OR]:1.93;1.07-3.49, P=0.030, 1 point), T4a-b stage (OR:2.47;1.14-5.36, P=0.022, 1 point), poor/undifferentiated (OR:2.04;1.31-4.06, P=0.004, 1 point), and signet-cell carcinoma (OR:2.04;1.04-4.02, P=0.038, 1 point) after being adjusted for resection and dissection types. The risk scoring model was developed using the related parameters: peritoneal recurrence rates were 24.6%, 42.6%, and 71.4% for group 1 (0 point), group 2 (1-2 points), and group 3 (3-4 points), respectively.

Conclusion: Female gender, T4 tumor stage, undifferentiated histopathology, and signet cell type had a tendency to peritoneal recurrence after being adjusted for treatment modalities. Patients with 3 or 4 risk factors had an 8.8 fold increased risk for the development of peritoneal recurrence.

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P-111 Prognostic value of inflammation-based scores for patients treated with FOLFIRINOX or gemcitabine plus nab-paclitaxel

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Background: Inflammation-based scores such as the modified Glasgow prognostic score (mGPS) or Neutrophil-Lymphocyte ratio (NLR) is associated with the clinical outcome of patients with various solid tumors. However, the clinical impact of these prognostic scores for patients with advanced pancreatic cancer who received intensive combination chemotherapy remains unclear in the real-world setting.

Methods: We conducted a single-center retrospective study. Inclusion criteria were patients with metastatic or recurrent pancreatic cancer at Hokkaido university hospital between January 2014 and December 2018 who received FOLFIRINOX (FFX) or gemcitabine plus nab-paclitaxel (GnP) as first-line treatment. Baseline mGPS was identified such that GPS 0 was CRP $\leq$1.0 mg/dL and Alb $\geq$3.5 g/dL, GPS 1 was CRP $>$1.0 mg/dL or Alb 1.0 mg/dL and Alb $<$ 3.5 g/dL. NLR was defined as the ratio of absolute neutrophil count and absolute lymphocyte count. As no clear NLR cutoff level has been established in this setting, we used a cutoff of $\geq$3. The cox-proportional hazards model was used to identify prognostic factors in univariate and multivariate analyses.

Results: A total of 101 patients were eligible. Median age was 67, the number of male/female patients was 63/38, ECOG PS 0/1/2 was 36/62/3, FOLFIRINOX/GnP was 19/82, mGPS 0/1/2/unknown was 52/21/23/6, NLR $\geq$3/$<$ 0.001), respectively. In NLR 3$<$/$\geq$3 patients, median PFS was 6.4/2.6 months (HR 2.436, 95%C.I. 1.568-3.784, p$<$ 0.001) and median OS was 14.6/6.0 months (HR 2.496, 95% C.I. 1.616-3.856, p$<$ 0.001), respectively. In multivariate analysis, High NLR (NLR $\geq$3 vs $<$ 3: HR 2.067, 95% C.I. 1.278-3.343, p=0.003) was significantly associated with poor PFS. For OS, female gender (HR 2.006, 95%C.I. 1.206-3.34, p=0.007), liver metastasis (HR 2.137, 95%C.I. 1.281-3.565, p=0.004), high NLR (NLR $\geq$3 vs $<$ 3: HR 2.745, 95%C.I. 1.639-4.599, p$<$ 0.001), and high mGPS (GPS 0 vs 1-2: HR 2.016, 95%C.I. 1.233-3.296, p$<$ 0.001) were significantly associated with poor OS.

Conclusion: NLR may be better prognosticator than mGPS for patients with metastatic or recurrent pancreatic cancer treated with FFX or GnP.

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P-112 HGCSG1801: A phase II trial of 2nd-line FOLFIRI plus aflibercept in patients with metastatic colorectal cancer refractory to anti-EGFR antibody

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Background: The first-line chemotherapy for metastatic colorectal cancer (mCRC) patients with wild-type RAS and BRAF commonly involves cytotoxic regimens such as FOLFOX and FOLFIRI combined with epidermal growth factor receptor (EGFR) antibody. After progression during anti-EGFR antibody combined chemotherapy, anti-angiogenic inhibitors are used for second-line treatment. Anti-angiogenic inhibitors (bevacizumab, ramucirumab, and aflibercept beta (AFL)) showed survival benefit combined with FOLFIRI as second-line chemotherapy in randomized controlled trials. However, these trials included few cases that were refractory to anti-EGFR antibody combined chemotherapy. Therefore, we planned a phase II trial of second-line FOLFIRI plus aflibercept in patients with mCRC refractory to oxaliplatin-based chemotherapy combined with anti-EGFR antibody.

Trial design: This study is a multicenter, non-randomized, single-arm, prospective, phase II study including patients with unresectable metastatic colorectal cancer with wild-type RAS and BRAF which is refractory to oxaliplatin-based chemotherapy plus anti-EGFR antibody. Other main inclusion criteria include age 20-85 years old, ECOG PS 0 or 1, adequate major organ functions and documented informed consent. The main exclusion criteria are as follows: symptomatic CNS invasion and/or brain metastases; uncontrollable comorbidities such as bleeding, thromboembolism, intestinal pneumonia or hypertension; symptomatic pleural effusion or ascites; UGT1A1 *6 homo, *28 homo, or *6 and *28 double heterozygous. FOLFIRI (irinotecan 180mg/m^2, l-leucovorin 200mg/m^2, bolus 5-FU 400mg/m^2 and infusional 5-FU 2400mg/m^2 /46hrs) and AFL 4mg/kg are administered every 2 weeks until progression or unacceptable toxicities. The primary endpoint is progression-free survival (PFS) rate at 6 months. A null hypothesis and alternative hypothesis are PFS rate at 6 months = 38.9% and 58.4%, respectively. The required sample size was 41 with a two-sided alpha of 0.1% and a power of 80%. Secondary endpoints are overall survival, PFS, response rate, disease control rate, adverse events and relative dose intensity for each drug. This study is sponsored by Sanofi and conducted by the non-profit organization Hokkaido Gastrointestinal Cancer Study Group. Clinical trial information: jRCTs011190006.

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P-113 Supportive medication in advanced biliary tract cancers with ABC-02 regimen

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Background: The ABC-02 trial published in 2010 demonstrated significant improvement in overall survival with gemcitabine in combination with cisplatin, compared with single-agent gemcitabine, in advanced biliary tract cancers. Since then, gemcitabine 1000mg/m^2 with cisplatin 25mg/m^2 at day 1 and day 8, on three weekly cycles, has been used as the first-line palliative chemotherapy for metastatic or locally advanced, inoperable cholangiocarcinomas, or gallbladder malignancies. The ABC-02 protocol recommended a shorter hydration regimen and shorter course of antiemetics given the lower dose of cisplatin. Extra hydration with magnesium and furosemide were omitted from this protocol, reducing the infusion time by approximately 2 hours. This shorter regimen has been used at our oncology centre since 2010: cisplatin with 20mmol KCL over 60 minutes followed by 500ml 0.9% saline with MgSO4 over 30 minutes prior to gemcitabine, dexamethasone, and ondansetron are prescribed day 2 and 9 only. Our aim was to determine if the shorter duration of hydration and supportive medication as per ABC-02 protocol led to adverse outcomes.

Methods: This was a retrospective, observational analysis of patients who received supportive medication and hydration, as per ABC-02 trial protocol between August 2010 and August 2019. We observed the number of patients with acute kidney injury within 4 weeks of administration of chemotherapy measured by RIFLE criteria, hypokalaemia and hypocalcaemia requiring electrolyte replacement, documented grade 3 or 4 nausea and vomiting, number of admissions related to toxicity and the number of patients with treatment delays. Patients were excluded if they received the long hydration regimen.

Results: We identified 44 patients with complete records who received cisplatin and gemcitabine with ABC-02 protocol for advanced biliary tract malignancy, in total there were 188 cycles with this regimen. The median age was 68 with age range 46-84 and ECOG performance status 0-2. All patients had confirmed metastatic or inoperable malignancy of biliary tract. One patient (2%) developed an acute kidney injury as defined by RIFLE criteria while on treatment. However, this was not directly related to chemotherapy as this patient had confirmed campylobacter diarrhoea and required admission for intravenous hydration. One patient (2%) reported grade 3 nausea and vomiting and nine patients (20%) reported grade 1-2 nausea and vomiting requiring additional antiemetic. 15 patients (34%) were admitted during their course of treatment. Seven patients (16%) were admitted with toxicities from chemotherapy, all related to infection. One patient (2%) developed hypocalcaemia requiring replacement during this time frame.

Conclusion: Our data support the use of a shorter hydration and antiemetic regimen for cisplatin with gemcitabine in advanced biliary tract cancers and our results are comparable to ABC-02 trial showing a low incidence of renal toxicity and grade 3 or 4 nausea and vomiting. This demonstrates that shorter hydration schedules and anti-

emetics with lower doses of cisplatin are safe to use in practice, reducing chemotherapy day unit chair time, improving capacity and patient experience.

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P-114 Cytokines as a prognostic marker of overall survival in pancreatic cancer: A meta-analysis and systematic review

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Background: Pancreatic cancer is an aggressive malignancy with a dismal 5-year survival rate of only 9%. Novel biomarkers are urgently needed to improve the survival outcomes of patients with this dreaded disease. Cytokines serve a key role in tumor development and metastasis in pancreatic cancer, with each cytokine demonstrating unique functionality in the tumor microenvironment. This systematic review and meta-analysis examined the role of cytokines in prognosticating overall survival (OS) of pancreatic cancer patients.

Methods: Relevant literature was identified via an electronic search of PubMed, EMBASE, Google Scholar and Cochrane Library databases up to January 1, 2020. Employing Review Manager 5.3, pooled hazard ratios and 95% confidence intervals were computed.

Results: A total of 18 studies comprising 1920 patients were included. Pooled analysis showed worse OS among patients with high T-helper 1 (TH1) cytokines, with a hazard ratio of 1.48 (95% CI 1.27-1.74, $p < 0.00001$). High T-helper 2 (TH2) cytokines also demonstrated a significant association with poor OS, with a hazard ratio of 1.62 (95% CI 1.12−2.34, $p = 0.01$). In terms of individual cytokines, high IL-6 correlated with inferior OS, with a hazard ratio of 2.73 (95% CI 2.18-3.43, $p < 0.00001$). Similarly, high IL-12 were linked with worse OS, with a hazard ratio of 1.85 (95% CI 1.26-2.72, $p = 0.002$). Other individual cytokines were not significantly associated with OS.

Conclusion: Cytokines show promise as a prognostic biomarker in pancreatic cancer. In particular, high levels of IL-6 and IL-12 can potentially prognosticate patients with poor survival outcomes. Further prospective studies are encouraged to delineate the role of cytokines in mediating treatment outcomes in this deadly disease.

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P-115 PEMREC: A phase II study to evaluate safety and efficacy of neoadjuvant pembrolizumab and radiotherapy in localized microsatellite stable rectal cancer

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Background: Locally advanced rectal cancer remains a clinical challenge with few improvements noted over the past few decades. Although immunotherapy has no current clinical role in microsatellite stable (MSS) colorectal cancer, preclinical models suggest that radiotherapy (RT) can enhance neoantigen presentation, modulate the microenvironment, and improve the likelihood of anti-tumor activity with checkpoint inhibitor use. This prospective phase II trial will test that hypothesis in addition to confirming the safety of this approach using a "window-of-opportunity" study design with the anti-PD-1 agent pembrolizumab.

Trial design: This monocentric, phase II trial will enroll patients (pts) with rectal cancer who are undergoing neoadjuvant short-course RT (scRT) (25 Gy in 5 fractions) according to the standard of care. Eligible pts are those with MSS stage II-III rectal cancer with adequate organ function and availability of pre-treatment tumor, who are undergoing scRT with intention to proceed to surgical resection. Standard ineligibility criteria include active infections, systemic steroid use, or other conditions making immunotherapy use unsafe. Treatment includes 4 doses of pembrolizumab (200mg IV, once every 3 wks), the first dose being given before the first scRT fraction. Surgery will be performed within 12-16 weeks of the final scRT dose. The primary endpoint is tumor regression grade (TRG) using the Mandard regression grade score targeting a 30% pathological complete response (pCR) compared to 10% in historical controls. Secondary endpoints include OS, DFS, toxicity, local and distant relapse-free survival, negative surgical margins, QoL, quality of surgery and exploratory assessments of tumor-infiltrating lymphocytes, profiling of circulating immune cell populations, and molecular predictors of response. A safety stopping rule is planned based on Wald's sequential probability ratio test for the occurrence of the safety outcome. Enrollment target is 25 pts.

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P-116 Impact of the number of harvested lymph nodes on survival in Egyptian patients with gastric cancer: Middle Eastern tertiary center experience

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Background: Radical gastrectomy with regional lymphadenectomy is the standard of care for all resectable gastric cancers. LN dissection has been debated over the years by different oncologic surgeons. In Japan, D2 lymphadenectomy was considered the standard procedure, whereas, in Asian countries, extended lymphadenectomy achieved superior survival and reduced recurrence rates. On the contrary, in Western countries, D2 lymphadenectomy was not considered a standard of care in clinical practice, possibly due to lower incidence of gastric cancer and lesser confidence of western oncologic surgeons in this procedure as a result of higher rates of surgical complications and perioperative mortality. Therefore, we aimed to estimate the effect of the number of resected LNs on survival outcomes in middle eastern patients with resectable gastric cancer, whether 16 LNs remained the optimal threshold, and whether a specific subset of patients could likely benefit from more dissected LNs.

Methods: The study cohort included patients who underwent surgical resection for gastric cancers between 2012 and 2014 at the Surgical Oncology Department of South Egypt Cancer Institute (SECI), Assiut University, Egypt, and were treated with chemotherapy, with or without radiotherapy, at the Clinical Oncology Department of Assiut University Hospital, Assiut University, Egypt. We divided patients according to the number of lymph nodes into two groups, those with LN dissection of <16 LNs and those with ≥ 16 LNs dissected. Patients were followed through their files for 5 years to calculate disease-free survival (DFS) and overall survival (OS). Then, we compared DFS and OS between groups.

Results: A total of 136 patients with gastric carcinoma underwent surgical intervention. Upon dividing our patients into 2 groups (those with less than 16 LNs dissected and those with 16 LNs or more dissected), increasing the number of LNs dissected correlated positively with survival; this correlation was mild but significant, with the exception of D1 dissection and DFS. Coincident with recent recommendations of different guidelines, D2 dissection was associated with significantly better OS and DFS ($P = .001$ and $P = .001$, respectively). The OS curves of both groups were compared using the log-rank test, demonstrating significantly higher OS for those with 16 LNs or more dissected (log-rank $= 8.030$; $P = .005$). The mean OS for the former group was 13.480 ± 1.468 months (95% CI, 10.603-16.357) whereas for the latter group was 20.738 ± 2.065 months (95% CI, 16.690-24.786). Furthermore, DFS for those with lower LNs dissected was significantly different from that of higher LNs dissected (log-rank $= 5.465$; $P = .019$). The mean DFS for the former group was 11.240 ± 1.516 months (95% CI, 8.270-14.210) and the mean DFS for the latter group was 17.452 ± 2.012 months (95% CI, 13.510-21.395). Also, we found that patients with T1 tumors who had more LNs dissected translated into better survival.

Conclusion: Greater lymph node harvest showed improved survival in gastric cancer. There was a significant positive correlation between survival outcomes and the total number of LNs dissected. Therefore, D2 gastrectomy is recommended, even in early-stage gastric cancer.

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P-117 Prognostic role of plasmatic exosomal and tissue caveolin-1 in metastatic pancreatic cancer patients

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Background: Pancreatic cancer (PC) represents the fourth cause of cancer-related death worldwide. Knowledge of potentially useful prognostic factors is essential as a means to guide different treatment approaches, particularly in the palliative setting. Caveolin-1 (Cav-1) is an essential structural protein of caveolae, implicated in endocytosis and cellular signal transduction. Several pre-clinical studies demonstrated Cav-1's role as an enhancer of both tumour invasiveness and chemoresistance. The aim of our study was to investigate the prognostic impact of Cav-1 in a cohort of metastatic PC patients (pts) treated with first-line gemcitabine plus nab-paclitaxel-based chemotherapy, both in a retrospective and prospective fashion.

Methods: Pancreatic cancer patients treated with gemcitabine+nab-paclitaxel as 1st line treatment for metastatic disease were eligible for analysis. The retrospective cohort was comprised of patients where Caveolin-1 evaluation was performed by means of immunohistochemistry (IHC). We defined different subsets for tumoral Cav-1 (Cav-1-T) and peritumoral stromal Cav-1 (Cav-1-S) staining. In the prospective cohort, Cav-1 expression was assessed in circulating exosomes: circulating Cav-1 concentration was normalized by whole exosomal protein expression and the median value of the distribution was used as a cut-off. For each patient enrolled, we collected data concerning response to treatment (assessed by RECIST 1.1 criteria), overall survival (OS) and progression-free survival (PFS). Survival times were calculated by Kaplan-Meier method. Differences in survival among different strata were assessed by log-rank test. Association between categorical variables was performed by Chi-square test. Level of statistical significance alpha was set at 0.05 for all tests.

Results: Sixteen pts were enrolled in the retrospective cohort and 8 patients were enrolled in the prospective cohort. mOS and mPFS of the retrospective cohort were 11 and 4.5 months, whereas the mOS and mPFS of the prospective cohort were 11,04 and 6,16 months, respectively. Negative (grade 0-1) IHC CAV-1-T staining was observed in 10 samples from primary tumors and 1 metastasis, intermediate (grade 2) in 5 metastases and 4 primary samples, high (grade 3) in 2 metastases. Differences in Cav-1-T staining between primary tumors and metastases were statistically significant (p=0,004) whereas we did not see any differences between Cav-1-S staining between primary tumor and metastases. Cav-1-T positive patients (9/16) had worse mOS compared with Cav-1-T negative patients (9.93 vs 31.92 months, HR for death: 2.95; 95% CI: 0.84-10.29, p=0.09). Albeit this difference was not statistically significant, we observed statistically significant differences in mPFS also (3,68 vs 13,55 months, HR for progression: 3,75; 95% CI 1.14-12.30, p=0.020). Positive Cav-1-T expression was also associated with a greater risk of progressive disease at the first radiological assessment (p=0.022). On the other hand, Cav-1-S was not associated with differences either in OS and PFS. In the prospective cohort similar results were observed; patients with higher exosomal Cav-1 concentration at baseline showed worse mOS (5,8 vs 16,45 months, HR: 4,08; 95% CI: 0,73-22,82; p=0.045) and lower mPFS (3,47 vs 8 months, HR: 2,25; 95% CI: 0,51-9,96; p=0,21).

Conclusion: Our study confirms the role of Cav-1 as a poor prognostic factor for PC, thus suggesting its role as a molecular stratifying factor of higher aggressiveness and chemoresistance, and hopefully as a target of newer treatment strategies for patients who have positive Cav-1 expression at IHC or high circulating levels of Cav-1.

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P-118 Gastroenteropancreatic neuroendocrine tumors: Experience of the oncology department of the Oran military hospital

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Background: Neuroendocrine tumors constitute approximately 2% of all malignant tumors of the gastrointestinal system. They are rare tumors with an incidence of 2.5-5 cases/100,000 inhabitants. These carcinoid tumors represent 0.5% of all cancers.

Methods: A retrospective study was performed in our department which included patients diagnosed with gastroenteropancreatic neuroendocrine tumors (GEP-NETs) from January 2016 to December 2019.

Results: 18 patients were diagnosed with GEP-NETs. The median age was 51 years old with extremes from 30 to 74 years old. The median delay from first symptom to diagnosis was 1 year. Sex distribution was 11 males (61%) and 7 females. (39%). The most common site was the small bowel (39%), followed by the pancreas (33%), stomach (11%), rectum (11%), and anal canal (6%). Neuroendocrine immunohistochemical markers were positive in 100% and the tumors were well-differentiated in 67%. The disease was in the metastatic stage in 72%. Patients were treated initially by surgery in 22%, chemotherapy in 56%, and with an analogue of the somatostatin in 22%.

Conclusion: Gastroenteropancreatic neuroendocrine tumors (GEP-NETs) are underdiagnosed; the diagnosis is often made at a late stage. There is a need to implement exploration techniques in order to provide better care to patients and management must be multidisciplinary.

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P-119 Special mouthwash and chronology of oral mucositis in previous cycle to prevent future episodes

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Background: Oral mucositis (OM) is an inflammation of the oral mucosa that affects around 20-40% of patients receiving conventional chemotherapy (CM). Many different products have been used separately to treat or prevent OM but none of them has shown great effectiveness. We decided to take into account the mucositis chronology with the previous cycle of chemotherapy to decide a good time to apply a combination of soluble prednisolone, nystatin and saltwater. We hypothesized that this rinse applied a few days before the expected mucositis appeared, would reduce the incidence of grade 2-3 OM in subsequent cycles of CM.

Methods: We studied patients receiving a combination with 5-fluorouracil in continuous infusion who had developed OM grade 2 or 2-3 with the previous cycle. The specific mouthwash consisted of a combination of 100 mL of water, 5 mg of soluble prednisolone, 2 drops of nystatin and 2.300 mg of salt (1 teaspoon). Patients received clear instructions on how to use it. The primary endpoint was the incidence of OM grade 2-3 following a cycle of CM. Secondary endpoints were the rate of CM dose reduction (DR) and the incidence of OM grade 0, 1 and 2 following the treatment.

Results: Twenty-five patients were included. Sixteen had shown OM grade 2 after first cycle and nine had mucositis grade 2-3. Patients started using this mouthwash with a minimum of 3 days before the expected OM appeared (according to the chronology on prior cycle). This resulted in only 2 patients repeating OM grade 2-3. Most of them had OM grade 0-1 and 5 had grade 1-2. Only two cases needed a further CM DR.

Conclusion: Our study showed a significant reduction in the rate of OM grade 2-3 in patients using the special mouthwash based on the chronology of OM with prior cycle. This mouthwash is currently used as a standard in our institution for these patients. Further evaluation in other centres to confirm these results is needed.

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P-120 Prospective observational study monitoring circulating tumor DNA in resectable colorectal cancer patients undergoing radical surgery: GALAXY study in CIRCULATE-Japan (trial in progress)

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Background: Adjuvant chemotherapy has reduced the risk of tumor recurrence and improved survival in patients with resected colorectal cancer (CRC). Early clinical utility of circulating tumor DNA (ctDNA) at the time points of pre- and post-surgery has been reported across various solid tumor subtypes including CRC. Analysis of ctDNA status could be utilized as a predictor of risk stratification for recurrence,

optimization of adjuvant chemotherapy, and early detection of recurrence. We present here the study design of an ongoing trial.

Trial design: GALAXY (UMIN000039205) is a prospective observational study to monitor the ctDNA status and to establish the registry data in patients with resectable CRC who underwent radical surgery. The study utilizes a personalized, tumor-informed ctDNA assay that is designed to track 16 patient-specific somatic variants (Signatera™ bespoke multiplex-PCR NGS assay) based on whole-exome sequencing of tumor tissue sample. Blood samples will be collected at the following time points: at pre-surgery and 1, 3, 6, 9, 12, 18, and 24 months post-surgery, and at the same time the computed tomography (CT) image will be performed. Mutations in RAS, BRAF and microsatellite instability tests by validated PCR methods will be assessed centrally. Key eligibility criteria include histologically confirmed colorectal adenocarcinoma and clinical stage II—IV or relapsed disease amenable to radical surgical resection. The primary endpoint is disease-free survival. Key secondary endpoints are overall survival, ctDNA status at each time point, association between clinical characteristics and gene alterations, and association between ctDNA detection and relapse detection by the CT image (that is, whether ctDNA monitoring could replace the CT image). There is no pre-planned statistical hypothesis due to the nature of observational study. Target sample size is 2,500 patients. Based on ctDNA results in the GALAXY trial, patients can be enrolled in investigator-initiated phase 3 trials, either the VEGA (de-escalation) or the ALTAIL trial (escalation). The VEGA trial assesses the non-inferiority of observation vs. adjuvant CAPOX in GALAXY participants with an absence of ctDNA 1 month post-surgery. The ALTAIR trial evaluates the superiority of FTD/TPI over placebo in GALAXY participants with ctDNA status that remains positive after standard therapy. Moreover, additional tumor tissue and blood samples will be banked for further translational research.

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P-121 Clinical outcomes of chemotherapy according to biologic agents in elderly patients aged ≥ 80 years with relapsed or metastatic colorectal cancer

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Background: 5-fluorouracil (5-FU)-based chemotherapy with oxaliplatin (FOLFOX) or irinotecan (FOLFIRI) is usually used in colorectal cancer (CRC). The addition of biologic agents to cytotoxic chemotherapy is currently standard therapy. However, the safety and efficacy of palliative chemotherapy in patients with relapsed or metastatic CRC over 80-years old have not been established yet. The purpose of this study was to assess the clinical features and feasibility of chemotherapy according to the use of biologic agents (bevacizumab or cetuximab) in extremely elderly patients with CRC.

Methods: Eligibility criteria included 1) more than 80-years old, 2) metastatic colorectal cancer 3) palliative chemotherapy-naive, 4) ECOG PS 0-1 5) adequate organ function. Patients received at least one chemotherapy with or without biologic agents. Response evaluation was done every 8 weeks with RECIST criteria and toxicity was evaluated with NCI-CTCAE.

Results: Between Jan 2010 and Sep 2019, 31 patients were reviewed and included 15 patients with biologic agents and 16 patients without biologic agents. The median age was 83.0 years (80.2-89.6 years) in patients with biologic agents and 81.4 years (80.0-95.3 years) in those without biologic agents. Median administrated cycles in first-line chemotherapy were 6 (range 2-27) with biologic agents and 4 (range 1-12) without biologic agents. The median progression-free survival (PFS) and overall survival (OS) in patients with biologic agents were 7.4 months and 15.4 months, as compared with 2.8 months and 10.6 months in patients without biologic agents, respectively. There was no significant difference in PFS ($p=0.14$) and OS ($p=0.77$) between patients with biologic agents and those without biologic agents. Overall survival rates at 1 year in patients with biologic agents and without biologic agents were 62.5% and 50.0%, respectively. After disease progression, salvage chemotherapy in patients with biologic agents and without biologic agents was administrated in 3 and 9 patients, respectively. Common grade 3/4 hematology toxicities were anemia (16.1%) and neutropenia (9.7%). The most common non-hematologic toxicity was grade 1/2 anorexia (48.4%). There was treatment-related death in one patient without biologic agents.

Conclusion: The addition of biologic agents to chemotherapy has limited effect on the improvement of survival in metastatic colorectal cancer patients over the age of 80. Further studies are needed on the role of the addition of biologic agents in these extremely elderly patients.

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P-122 Treatment-related response of T regulatory cells and cytotoxic lymphocytes in early PDAC

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Background: Immunotherapeutic approaches show promising results in different solid tumors but remain worthless in pancreatic ductal adenocarcinoma (PDAC). The immune system of pts suffering from PDAC has been explored widely. Most studies investigate immune cells in the tumor microenvironment (TME). In tumor immunity, Treg cells are involved in tumor development and progression by inhibiting antitumor immunity. A high infiltration by Treg cells is associated with poor survival in various types of cancer (Yoshihiro, 2019) . CD8+ T cells differentiate to cytotoxic T cells, traffic into the tumor microenvironment, and exhibit cytotoxicity against tumor cells. Enhancements in the cytotoxic activity of tumor antigen-specific cytotoxic T cells in the tumor microenvironment are crucial for the development of cancer immunotherapy (Iwahori, 2020) . It is widely explored how different treatment methods affect immune cells. We conducted a single-institution clinical trial to evaluate the impact of different treatment modalities (surgery and chemotherapy) on T lymphocytes and other cells in the peripheral blood as possible predictive and prognostic biomarkers for PDAC patients.

Methods: A cohort of 51 pts with early and advanced non-metastatic operable PDAC was evaluated in this analysis. All patients undergoing active treatment in our institution and who signed informed consent were enrolled in the study. Some of them underwent surgery alone, others began adjuvant treatment with FOLFIRINOX or gemcitabine after tumor removal. Blood samples were collected for analysis of T cell subsets, including CD19, CD3+ CD56+, CD8+ CD57+, CD3+ CD57+, CD3, CD3+ CD4+, CD3+ CD8+, CD3+ CD4- CD8, CD3- CD56+ CD16+, CD3- CD56+ CD16-, CD4+ CD25+ CD127+/-, CD4+ FOXP3+, CD8+ CD25+ CD127+/-, CD8+ FOXP3+ T cells by flow cytometry at initial diagnosis, before surgery, and after two months. Results were estimated according to the age, sex, T, N categories, differentiation rate, CA 19-9 values, and chemotherapy regimen received. Student t, Mann-Whitney U and Wilcoxon signed-rank tests were used for statistical analysis.

Results: No significant difference in means were seen between sex, age ($\leq$65years vs . $>$65years) groups, tumor grade (well/moderately differentiated vs. poorly differentiated), different tumor diameter (T1-2 vs. T3-4), CA 19-9 levels (normal, $>$35, $>$ 1000 kU/l) at initial visit. Interestingly, pts with node positive disease presented with higher rates of Treg CD8+ FOXP3+ cells 0.038 (0.052) cells/ml vs. with node negative 0.199 (0.1985) cells/ml P 0.002 (Mann-Whitney U test). At the 2nd visit, two months after completing surgery and first chemotherapy cycles, increased numbers of cytotoxic T cells CD3+ CD8+ 411.849 (195.1652) at 1st vs. 563.066 (452.5502) cells/ml at 2nd visit, P 0.004 (Wilcoxon Singed Rank test) was seen. Number of Treg CD4+ FOXP3+ cells significantly declined from 48.285 (30.9626) at 1st to 33.097 (19.5672) cells/ml at 2nd visit, P 0.022 (paired Student-t). These changes did not corelate with sex, age, tumor volume or CA 19-9 measurement and does not seem to depend on chemotherapy regimen.

Conclusion: Some T cells subpopulations like T regulatory cells and cytotoxic lymphocytes in early PDAC pts vary during treatment and may be considered as potential biomarkers for evaluating pt status and response to therapy.

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P-123 Outcomes and predictive factors of regorafenib benefit in patients with metastatic colorectal cancer in a real-life setting

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Background: After regorafenib (REG) was approved due to a survival benefit in refractory metastatic colorectal cancer (mCRC), some predictive markers such as the FAS and FAS-CORRECT scores have been proposed to improve patient selection. We have explored the survival and safety outcomes of REG in a real-life setting and tried to find and validate predictive markers.

Methods: We conducted a retrospective, multicentre, observational study of pts with mCRC treated with REG after failure to standard therapies as part of routine clinical practice at seven 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 years), 65.4% male, ECOG PS0/1/2 19.2/75.4/4.6%, 45.4% left-sided location, 78.5% low grade, 55.4% RASmt and 1.5% BRAFmt, 58.5% synchronous presentation, 76.2% primary tumor resection, 32.3% >3 metastatic locations and 75% liver metastases. Median prior lines of treatment were 3 (range 2-8) including TAS-102 in 29.2% of pts. Initial dose: 53.1% pts full standard dose, 14.6% dose level -1, 16.9% dose level -2. 15.4% pts used a dose-escalation strategy (ReDOS strategy). Dose selection 60 (OS 5.2 vs 9.1; p 85 (OS 6.4 vs 9.0; p= 0.016) achieved prognostic significance. Median of weeks until reimbursement approval was 3.1 weeks. Patients who had to wait longer to start treatment had lower OS (5.2 vs 7.8; p=0.006) despite having similar clinical characteristics.

Conclusion: The results of our series corroborate that REG offers and modest survival benefit in all patients with refractory mCRC, which can be significant in selected patients. Although we have not been able to validate the FAS and FAS-correct algorithms, our results suggest that they could be useful and some important parameters that reflect disease burden are confirmed to be predictors of poor prognosis. Finally, we have identified for the first time in our study, that delay of treatment due to reimbursement reasons is an independent prognostic factor.

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P-124 Tumor budding and CDX2 as additional prognostic factors in stage II colon cancer

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Background: The aim of this study was to evaluate histopathologic prognostic factors in patients with stage II colon cancer (CC).

Methods: Our study retrospectively enrolled 177 patients, 99 (56%) male, with a median age of 72 years (range 35 — 92). Seventy-three cases underwent adjuvant chemotherapy (CT) with 5-fluorouracil +/- oxaliplatin; known histopathologic parameters to stratify stage II in high or low risk, tumor budding (TB), poorly differentiated clusters (PDCs), microsatellite instability (MSI), and CDX2 expression were analysed related to 5yr-disease-specific survival (DSS) and overall survival (OS).

Results: Among patients who did not undergo adjuvant CT, tumor size (T3 vs T4) and TB (low vs high grade) was significantly related to 5yr-DSS (95 vs 87%, p 0.002; 98 vs 80%, p 0.008), while tumor size, lymphovascular/perineural invasion (no vs yes) were significantly related to 5yr-OS (74 vs 30%, p 0.007; 78 vs 55, p 0.004). In the analysis of chemotherapy patient groups, OS seemed to not be related to any of the above-mentioned factors, although CDX2 positive patients reported a better 5yr-OS than CDX2 negative (82 vs 65%, p 0.08). Patients whose tumor reported 2 of the following negative parameters, pT4, TB high, and CDX2 negative, showed a worse prognosis than patients with 1 or 0 (5yr-DSS was 80 vs 89 vs 89%; 5yr-OS was 53 vs 78 vs 81%, respectively). Nineteen (26%) patients stopped CT after 3 months due to toxicity. However, both 5yr-DSS and OS were not significantly different between patients receiving 3 vs 6 months of chemotherapy (100 vs 89% and 100 vs 93%, respectively).

Conclusion: Despite the limited sample size, this study showed the role of TB and CDX2 as additional prognostic factors in stage II CC. Further studies are needed to support the role of an extensive histopathologic evaluation to better select patients who will benefit from 3 vs 6 months of adjuvant CT.

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P-125 Radiomic prediction model for pathological responses of neoadjuvant chemotherapy with S-1 plus oxaliplatin (G-SOX) in clinical stage III gastric cancer

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Background: Perioperative chemotherapy for clinical Stage III gastric cancer (GC) tends to shift to the neoadjuvant setting because of worse therapeutic compliance in a postoperative phase. The efficacy of neoadjuvant chemotherapy (NAC) has been demonstrated to impose a great influence on prognosis. However, the precise, histopathological assessment for the efficacy of NAC is only known after operation with the resected specimen. If we could consider the on-treatment assessment for responses of NAC, preferentially by a non-invasive way, it would enable us to have a better choice of the subsequent treatment options to obtain a more desirable prognosis. The purpose of this study was to construct a non-invasive, on-treatment prediction model for pathological responses of NAC in clinical Stage III GC by using radiomics which is CT-based quantitative imaging analysis.

Methods: We used data of 31 Stage III GC patients who underwent NAC with G-SOX and surgery from 2016 to 2019 (Kyoto Katsura nacG-SOX 130 study; UMIN000036139). There were 26 males and 5 females with a mean age of 68.8 (40-82). Overall pathological response rate greater than grade 1b was 61.8% (0:11.8%, 1a:29.4%, 1b:8.8%, 2a:23.5%, 2b:17.6%, 3:8.8%). Pre-treatment contrast-enhanced CT images in the portal phase of each patient were used for radiomic analysis. The region of interest (ROI) of the gastric tumor was manually delineated by three observers (one surgeon and two radiologists with adequate experiences in oncologic imaging) who were not informed of the treatment results. After 47 radiomic features were extracted by LIFEx software (www.lifexsoft.org), the inter-observer reproducibility analysis revealed an agreement for 30 indices with a correlation coefficient higher than 0.90. Feature extractions were performed, firstly by a univariate analysis by Wilcoxon rank-sum test, and then, followed by multivariate logistic regression analysis with a step-wise feature-reduction, and ROC analysis was performed to generate the radiomic signature for the response of NAC.

Results: The radiomic signature was comprised of 4 radiomic features (SHAPE Compacity, GLCM Correlation, GLCM Entropy, GLZLM LGZE), and demonstrated high discriminatory performance in predicting pathological responses of NAC with an area under the curve of 0.8824, a sensitivity of 82.35% and specificity of 85.71% (P < 0.001).

Conclusion: Although this small initial analysis needs further external validation, a prediction model based on radiomic textures using CT images could offer a potential biomarker for the pathological responses of NAC for clinical Stage III gastric cancer.

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P-126 Markers of tumour inflammation are prognostic for overall survival in patients with advanced pancreatic ductal adenocarcinoma receiving FOLFIRINOX chemotherapy

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Background: Pancreatic duct adenocarcinoma (PDAC) remains a devastating disease with little improvement in survival figures over the last decades. Better characterization and identification of high risk groups are needed to tailor their management. Herein we explore the prognostic role of different clinical biomarkers in patients with PDAC treated with FOLFIRINOX.

Methods: We retrospectively audited patients with locally advanced inoperable or metastatic PDAC that received FOLFIRINOX as first-line treatment in West Yorkshire, UK, between 09/2010 and 09/2019. Different prognostic clinical biomarkers were evaluated in multivariate models.

Results: The study included 138 pts with advanced pancreatic adenocarcinoma. 87 (63%) were males and 51 (37%) females. Median age was 62 years (range, 29-77). 66 (47.8%) had excellent performance status (PS ECOG 0), 71 (51.4%) PS 1 and one pt (0.8%) had PS ECOG 2. Charlson comorbidity index (CCI) was 0 in 66 (47.8%) of pts, 1 in 25 (18.1%), 2 in 16 (11.6%) and $\geq$3 in 31 (22.5%) pts. 78 (56.5%) had metastatic and 60 (43.5%) locally advanced disease. Median blood hemoglobin levels were 128 g/L (range, 81-171), median white blood cell (WBC) levels 8.17/uL (3.42-33.50), neutrophil (NEUT) levels 5.68/nL (range, 1.98-22.13), lymphocyte (LYMPH) 1.58/nL (range, 0.31-4.90), monocyte (MONO) 0.51/nL (range, 0.16-1.86), platelet (PLT) 271/nL (range, 90-631) and median serum albumin (ALB) levels 39 g/L (range, 24-51). Median neutrophil-to-lymphocyte ratio (NLR) was 3.58 (range, 1.13-25.29), monocyte-to-lymphocyte ratio (MLR) 0.36 (range, 0.10-1.10), platelet-to-lymphocyte ratio (PLR) 176.46 (range, 42.40-678-48), prognostic nutritional index (PNI=ALB+[5×LYMPH]) was 47.08 (range, 28.95-66.55) and systemic inflammation response index (SIRI=NEUT × MONO/LYMPH) was 1.89 (range, 0.31-21.75). After a median follow-up of 42.7 months (range, 0.3-64.9), 128 (92.8%) patients died. Median overall survival (OS) was 9.7 months (95%CI, 8.0-11.3). NLR (HR 1.08, 95%CI 1.04-1.11, p<0.001), MLR (HR 7.57, 95%CI 3.05-18.83, p<0.001), PLR (HR 1.004, 95%CI 1.002-1.006, p<0.001), SIRI (HR 1.12, 95%CI 1.07-1.17, p<0.001) and PNI (HR 0.97, 95%CI 0.94-0.99, p=0.011), all were associated with OS. Cox proportional hazard models separately for each of the above variables showed that NLR, MLR, PLR and SIRI were associated with poor OS independently of age, sex, PS ECOG, CCI and stage (metastatic vs. locally advanced). Also, stage constantly demonstrated an independent prognostic significance for OS in all analyses. In contrast, PNI did not demonstrate independent prognostic significance.

Conclusion: Clinical biomarkers are useful to identify high risk patients with pancreatic cancer treated with Folfirinox. Stratification of this group of patients based on the biomarkers should be considered in the design of future trials.

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P-127 Potential mechanism of circRNA 000585 in cholangiocarcinoma

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Background: Circular RNA (circRNA) is a subgroup of noncoding RNAs (ncRNAs), the biogenesis of which has already been explored in studies. It plays a vital role in many processes and participates in the development and progression of many diseases. The function of circRNAs in cholangiocarcinoma (CCC) remains unexplored. We aimed to detect circRNAs in CCC tissues compared to para-cancer tissues, in order to get a novel circRNA in CCC and explore the potential mechanism in CCC.

Methods: Differential expression of circRNAs via microarray for CCC and para-cancer was analyzed and validated by real-time polymerase chain reaction (RT-PCR). The downstream molecule of potential circRNAs was also detected by RT-PCR.

Results: One hundred and seventeen circRNAs are upregulated and 104 circRNAs are downregulated in CCC, including 10 circRNAs which are 3 fold above that of para-cancer (circRNA_002172, circRNA_002144, circRNA_001588, circRNA_000166, circRNA_000585, circRNA_000167, circRNA_402608, circRNA_006853, circRNA_001589, circRNA_008882), and 3 circRNAs are 3 folds lower than that of para-cancer (circRNA_406083, circRNA_104940, circRNA_006349). Then we identified that circRNA_000585 are upregulated in 15 paired patients. We tried to explore the potential mechanism of circRNA_000585 in CCC by bioinformatics. To find out whether circRNA_000585/miR-615-5p/AMOT/YAP may be the potential pathway in CCC, we identified the expression of key molecules by RT-PCR. miR-615-5p was downregulated, and AMOT and YAP were upregulated in paired patients.

Conclusion: circRNAs are dysregulated in CCC, and circRNA_000585/miR-615-5p/AMOT/YAP may be the novel potential pathway in CCC.

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P-128 A novel combination of GEMOX and apatinib in treatment of unresectable or metastatic cholangiocellular carcinoma

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Background: The treatment of unresectable/metastatic cholangiocellular carcinoma (CCC) is limited and the response rate of chemotherapy is unsatisfactory. Apatinib, a novel antiangiogenic agent targeting vascular endothelial growth factor receptor (VEGFR2), is currently being studied in different tumors. This study was performed to assess the response rate and safety of apatinib in patients with unresectable/metastatic CCC.

Methods: Patients with platinum-naïve, pre-treated CCC who failed first-line chemotherapy were enrolled. GEMOX (gemcitabine 1000mg/m^2+ oxaliplatin 135mg/m^2) was administered every three weeks by venous transfusion, Apatinib was administered as 500mg daily. The objective was to assess the overall response rate (ORR) according to mRECIST criteria. The treatment duration was until disease progression or intolerability of apatinib.

Results: Eleven eligible patients with unresectable/metastatic CCC were enrolled in this study. Median follow-up time was 14 months. ORR was 36.36%. Disease control rate (DCR) was 81.82%. The most common treatment-related adverse events (AEs) were debilitation (63.64%), hand-foot syndrome (45.45%), hypertension (27.27%), nausea and vomiting (18.18%).

Conclusion: GEMOX combined with apatinib is a feasible treatment in patients with unresectable/metastatic CCC, and showed high DCR. Multi-center prospective studies are needed to confirm this strategy.

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P-129 Camrelizumab combined with sorafenib versus sorafenib alone in patients with advanced hepatocellular carcinoma: A retrospective study

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Background: Hepatocellular carcinoma (HCC) is one of the most malignant tumors associated with a dismal prognosis. Immunotherapy can modulate the endogenous immune response against tumors with promising prospects in malignant solid tumors, while targeted therapy is appreciated as an important approach in cancer therapy. However, few studies have evaluated the efficacy and safety of immunotherapy and targeted therapy in combination. The present study aimed to compare camrelizumab plus sorafenib versus sorafenib alone in patients with advanced HCC using a propensity score analysis.

Methods: Between January and December 2019, a total of 90 patients with advanced HCC in the Second Affiliated Hospital of Army Medical University were retrospectively analyzed. Of the patients involved, 28 patients received combined camrelizumab plus sorafenib treatment, and 62 patients received sorafenib monotherapy. Propensity score matching (PSM) analysis was performed based on the following variables: age, gender, HBV, BCLC stage, tumor size, Child-Pugh score and Eastern Cooperative Oncology Group (ECOG) performance score. The combined-therapy group received camrelizumab 200 mg intravenously every 2 weeks plus sorafenib 400 mg orally once daily and the sorafenib-only group was administered sorafenib 400 mg orally twice daily. The treatment response based on the modified Response Evaluation Criteria in Solid Tumors (mRECIST), progression-free survival (PFS), overall survival (OS) and the relevant adverse effects were evaluated.

Results: The patients in the combined-therapy group were associated with older age (p = 0.033) and larger tumor size (p=0.042) compared with patients in the sorafenib-only group. After 1:2 PSM, 25 patients in the combined-therapy group were well matched with 50 patients in the sorafenib-only group. The combined-therapy group showed significantly improved overall response rate (ORR) and disease control rate (DCR) compared with the sorafenib-only group (24.0% vs 4.0%, p=0.025; 48.0% vs 24.0%, p=0.036). The median PFS was significantly longer in the combined-therapy group than the sorafenib-only group (7.1 months vs 6.0 months, p=0.040), while the median OS was similar in the two groups (7.4 vs 7.0 months, p=0.513). No difference was noted in the rate of adverse reactions between the combined-therapy group and the sorafenib-only group (32.0% vs 22.0%, p=0.348), and the symptoms were relieved after treatment.

Conclusion: The combination treatment of camrelizumab with sorafenib showed promising efficacy with acceptable safety for the management of advanced HCC, but further studies with larger sample sizes and longer follow-up duration or randomized trials are needed to identify the potential therapeutic value.

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P-130 Short course pelvic radiotherapy for localized and oligometastatic rectal adenocarcinoma: The Mayo Clinic experience

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Background: Variations in practice amongst radiation oncologists exist on the choice between short-course radiotherapy (SCRT) and long-course chemoradiation as neo-adjuvant therapy for rectal cancer. Few data are available on clinical outcomes of SCRT based on a cohort with modern staging and radiotherapy (RT) techniques.

Methods: 119 treated patients with biopsy-proven rectal adenocarcinoma underwent curative intent neoadjuvant RT prior to total mesorectal excision (TME) from 2013 to 2019 at our 3 site institution. Patients had localized (n=66, 55.5%) or oligometastatic (n=53,44.5%) disease. Survival times were calculated using the Kaplan-Meier method. Variables associated with overall survival (OS), progression-free survival (PFS), locoregional relapse (LRR) and distant relapse (DR) were assessed by multi-variable Cox proportional hazards regression using stepwise variable selection. Acute toxicities and surgical complications were graded based on Common Terminology Criteria for Adverse Events, version 4.03.

Results: Median follow-up of surviving patients was 13.7 months (range, 0.1—71.0). Median age was 61 years (range, 26—95) and 75 (63%) patients were male. 88 (73%) and 15 (13%) patients had cT3 or cT4 disease, respectively. 33 (28%) patients had disease within 5 cm of the anal verge. 46 (38%) patients received neoadjuvant chemotherapy.

The localized disease cohort was older (67 vs 53 years, P< 0.001) and less likely to have clinically node-positive disease (46% vs 74%, P=0.001). All patients received SCRT with 25 Gy in 5 consecutive daily fractions without interruption. Two patients experienced acute grade 3 gastrointestinal toxicity during SCRT. There were no grade 4 or 5 treatment-related toxicities. 53.8% of patients showed symptomatic improvement after SCRT by clinical assessment. Total mesorectal excision was performed after SCRT; 79 (77%) underwent low anterior resection and 24 (23%) underwent abdominoperineal resection. Surgical margins were negative (R0) in 97%.

At 1 and 3 years, the cohorts had OS of 96% and 84% (localized) and 88 and 54% (oligometastatic cases), respectively (log-rank P=0.089 between cohorts). The 1- and 3-year rates of PFS were 93% and 80% for localized cohort, and 83% and 53% for oligometastatic cases, respectively. The 1- and 3-year freedom from LRR for the whole cohort were 95% and 87%, respectively.

On multivariate analyses, age (hazard ratio [HR] per 1-year increase 1.07, 95% confidence interval [CI] 1.03—1.12, P< 0.001) and treatment intent (HR for localized disease 0.16, 95% CI 0.05—0.46, P< 0.001) were associated with OS. Absence of rectal surgery (HR 13.18, 95% CI 3.93—44.19, P< 0.001) and clinical node-positive disease (HR 12.74, 95% CI 1.67—97.17, P< 0.025) were associated with PFS.

Conclusion: Neoadjuvant SCRT is a well-tolerated and effective treatment modality for optimizing local-regional control in rectal cancer patients undergoing curative-intent TME.

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P-131 Ramucirumab and irinotecan in patients with previously treated gastroesophageal adenocarcinoma: Interim analysis of a phase II trial

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Background: Ramucirumab is used for the treatment of metastatic gastroesophageal adenocarcinoma after disease progression on first-line chemotherapy. Superior survival outcome is expected when combined with paclitaxel. However, many patients suffer from neuropathy after oxaliplatin-containing first-line chemotherapy and are unable to tolerate paclitaxel. Irinotecan has shown survival benefit as a single agent or in combination with other agents but has not been evaluated with ramucirumab for treating gastroesophageal cancer. We hypothesize that this combination regimen of irinotecan and ramucirumab administered as second-line treatment will be better tolerated than ramucirumab with paclitaxel with similar clinical efficacy in patients with advanced gastroesophageal cancer. We report the interim results of disease responses and toxicity profiles from this trial.

Methods: This is a multi-institutional, single-arm phase II clinical trial of ramucirumab and irinotecan. The primary objective of the study is to determine the progression-free survival (PFS) in patients treated with this combination after disease progression on first-line chemotherapy. Secondary objectives are to determine other indices of efficacy including objective response rate, overall survival, time to progression, and clinical benefit rate; and to evaluate toxicity and tolerability. Planned correlative studies include generation of patient-derived xenograft and organoid models, and investigation of blood-based angiome profile and cell-free DNA. Patients were required to have disease progression during or within 4 months of first-line chemotherapy. Key exclusion criteria include squamous histology; prior irinotecan or ramucirumab treatment; active brain metastases; or other contraindications to ramucirumab including recent history of gastrointestinal bleeding or perforation, thromboembolic event, and uncontrolled hypertension. Patients received 8mg/kg ramucirumab with 180 mg/m^2 irinotecan IV every 14 days. Forty patients are to be enrolled to detect a 1.5-month improvement in PFS compared to the historic control of 2.5 months with 85% power and alpha=0.05.

Results: Twenty-eight patients were enrolled from four study sites from December 2017 through February 2020. Twenty patients were evaluable for disease response as of March 2020 and were included in this report. Of 20 patients, 1 patient had a complete response, 4 patients had partial responses, and 3 patients had stable disease greater than 6 months. Diarrhea, nausea, vomiting, and neutropenia are common adverse events reported. No unexpected toxicities have been reported.

Conclusion: Ramucirumab with irinotecan appears to be effective and well-tolerated in patients with previously treated gastroesophageal adenocarcinoma. This regimen should be considered for patients after disease progression on first-line chemotherapy.

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P-132 Malignant transformation of choledochal cysts: Description of a North African series of 7 cases

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Background: Choledochal cyst (CC) is a rare disease usually discovered in the paediatric age, with female predominance, however, 20 to 23% of patients have their disease diagnosed in adulthood. Its incidence is 1/200,000 inhabitants. It is often associated with an abnormality of the biliopancreatic junction and its evolution can be characterized by many serious complications, essentially the risk of malignant transformation in bile duct tracts.

Methods: A retrospective, descriptive study was carried out with review of all the patients operated on in the hepatobiliary surgery and liver transplant department at the EHU Oran for CC, during the period from January 2010 to December 2019. Only adult patients were included. Patients refusing surgery were excluded.

Results: In this period, 51 patients were operated on for CC and 7 had a malignant transformation of their malformation (13,7%), including 5 females and 2 males, Sex-ratio was 0,4, and the mean age was 54,71 years [24-79] years. There were 3 intra-hepatic cholangiocarcinomas, 3 adenocarcinomas of the gallbladder and one with extrahepatic cholangiocarcinoma. There were 3 Todani I, 3 Todani V left, and an isolated cyst duct dilatation. The surgery was curative in only 5 cases, with recurrence

of disease in a case at 6 months of evaluation. The CC was a congenital malformation of the bile ducts, Todani described 5 types. Isolated dilatation of the cystic duct is a rare and newly described form, called Type 6. A biliary-pancreatic junction anomaly is systematically sought, but does not modify the therapeutic approach. Any CC diagnosed should be treated surgically to prevent complications. These complications are often the mode of revelation of this malformation and the more dangerous complication is the transformation into cancer.

Conclusion: Malignant transformation on CC is a serious complication, this risk increases with age, justifying the immediate surgical treatment of all diagnosed CC. Even in countries with a low incidence of this malformation, the risk of degeneration into cancer is real.

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P-133 Extramural venous invasion detected with an elastin stain is a powerful predictor of cancer-specific mortality in STAGE I-IIIB resected colorectal cancer

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Background: Extramural venous invasion (EMVI) is considered an indicator of poor prognosis in patients who have undergone resection of primary colorectal cancer (CRC), but its use has not been widely adopted in staging systems or nomograms. In particular, EMVI is not reported in most large case series, is not included in most large CRC databases, and is not incorporated into the current AJCC TNM staging system. Staining for elastin may facilitate the accurate detection of EMVI and minimize inter-observer variability. We examined the prognostic potential of EMVI detected by elastin staining at a tertiary center that performs a high volume of CRC resections.

Methods: This is a single-institution, observational study of consecutive patients who underwent resection of primary CRC between 01/01/2011 and 31/12//2016. All pathology specimens were re-assessed by reviewers who were blinded to patient outcomes. Venous invasion was detected using an elastin trichrome stain and classified as Intramural or Extramural. Overall and disease-specific survival (OS, DSS) were estimated using the Kaplan-Meier method. Differences between groups were assessed using the Mantel-Cox log-rank test. For the present analysis, we excluded all patients with stage IV (n=80) or IIIC (n=34) CRC.

Results: The cohort for analysis included 428 patients (248M, 190F; AJCC 8th edition Stage I n=107; Stage II n=185; Stage IIIA and B n=146) with a median follow-up time of 61 months (0.1-104). For the entire cohort, OS and DSS at 5 years were 82% and 90%, respectively. AJCC stage (p=0.04), but not T stage (p=0.08) or N stage (p=0.09), was prognostic of DSS. Neither grade (p=0.1) nor IMVI (p=0.4) were prognostic, whereas EMVI was highly prognostic of inferior DSS ($p< 0.001$).

Conclusion: In this cohort of Stage I - III CRC patients with complete follow-up, EMVI as assessed by elastin staining was a powerful predictor of death from CRC. Elastin staining, which improves the accuracy and objectivity of EMVI detection, may allow validation of EMVI as an independent prognostic variable that should be incorporated into staging systems and nomograms. Accurate assessment of EMVI would permit refinement of risk estimation, and inform individualized decision-making regarding adjuvant therapy in patients who have undergone resection of CRC.

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P-134 Total neoadjuvant therapy in locally advanced rectal cancer patients: A tertiary medical center experience

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Background: The current standard of care for locally advanced rectal cancer entails a multidisciplinary approach that includes preoperative chemoradiation followed by total mesorectal excision (TME) and adjuvant chemotherapy. This modality has resulted in high toxicity profiles and low compliance rates.

Methods: This is a retrospective chart review of patients diagnosed with locally advanced rectal cancer (LARC) at the American University of Beirut Medical Center between 2011 and 2018. Patients with cT3/4 or cT2-node-positive were included. Total neoadjuvant therapy (TNT) is defined as short-course radiation before or after 6 cycles of mFOLFOX followed by resection. Chemoradiation therapy (CRT) is defined as long-course chemoradiation with capecitabine followed by surgery and adjuvant chemotherapy. The primary endpoint was the pathologic complete response (pCR) rate between the two different treatment modalities.

Results: Of the 81 patients, 55 (67.9%) received CRT, and 26 (32.1%) received TNT. Of the 55 CRT patients, 32 (58%) were males, and 23 (42%) were females with a median age of 60 (range 34-85) years. Of the 26 TNT patients, 16 (62%) were males, and 10 (38%) were females with a median age of 51 (range 25-75) years. In the TNT group, 17 patients took neoadjuvant chemotherapy before radiation, while 9 took neoadjuvant chemotherapy after radiation. pCR was achieved in 15 patients (27.3%) of the CRT group and 10 (38.5%) of the TNT group (p=0.22). The majority of the pCR cases in the CRT were cT3N1, 8/15 (53.3%) patients, while in the TNT group, 7/10 (70%) patients were cT3N2. In the CRT group, 17 (30.9%) had pathologic node-positive in comparison to 7 (26.9%) patients in the TNT group (p=0.46). Pathologic downstaging to pT0N0 or pT1N0 was found in 19 (35%) patients of the CRT group and 11 (42%) in the TNT group (p=0.33). The 2-year disease-free survival rate was 81% in the TNT group and 84% in the CRT group (p=0.15). Of the 55 CRT patients, only 30 took adjuvant chemotherapy, where 22 (40% of the total number) patients took a full course. None of the CRT patients had a dose reduction. All of the 26 TNT patients received neoadjuvant chemotherapy, where 22 (84%) patients took a full course ($p< 0.001$). Only one patient in the TNT group had a 25% dose reduction.

Conclusion: Our results showed that TNT is superior to CRT in chemotherapy compliance. The data also showed a numerically higher pCR rate, nodal downstaging, and tumor downstaging in the TNT group without significance. No significant change was seen in the 2-year disease-free survival rates. Extended follow-up periods are needed to assess the overall survival and longer disease-free survival rates.

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P-135 Clinical outcomes of mucinous gastric carcinomas compared with non-mucinous and signet ring cell carcinomas

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Background: The aim of this study was to analyze the differences between a group of patients with mucinous gastric carcinoma (MGC) and a group without extracellular mucin gastric carcinoma (NMGC), and signet ring cell gastric carcinoma (SRC).

Methods: A retrospective cohort study was performed of 65 patients with mucin-producing gastric cancer from Jan. 2007 to Dec. 2016. During the same period, a total of 1,814 patients with histologically proven gastric cancers had curative or palliative operations. 195 NMGC patients were selected as 1:3 age- and sex-matched control groups and 200 SRC patients were identified. This study evaluated the demographic features of the patients, macro/microscopic features of the tumor, and predictive factors such as recurrence-free survival and overall survival.

Results: The incidence of MGC and SRC was 3.6% and 11.0%, respectively. The recurrence rates were significantly high in MGC, compared with NMGC and SRC (24/65, 32/195, 34/200, $P< 0.001$). The incidence rate of EGC (T1a/1b regardless of N stage) was low (9/65, 93/195, 115/200, $P< 0.001$), and the rate of metastatic lymph nodes was high in MGC (43/65, 79/195, 66/200, $P< 0.001$). The rate of initial pT4 and M1 stage was also the highest in MGC. As for the recurrence-free survival and overall survival, the MGC group was significantly low compared with NMGC and SRC. However, multivariate analysis and subgroup analysis revealed that patients with the same AJCC stage of each cancer group show a similar prognosis.

Conclusion: MGC frequently presented at an advanced stage with unfavorable prognosis compared with NMGC and even with SRC. The poor prognosis of MGC was mainly associated with the advanced stage at initial diagnosis. MGC of the same AJCC stages with NMGC and SRC showed a similar prognosis.

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P-136 Survey of challenges in access to diagnostics and treatment for neuroendocrine tumor patients (SCAN): Early diagnosis and treatment availability

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Background: Neuroendocrine tumors (NETs) are rare and complex neoplasms with increasing incidence and prevalence worldwide. SCAN assessed the global provision of NET diagnostics and treatment in terms of awareness, availability, quality, and affordability. This analysis focused on assessing early diagnosis and availability of diagnostic and treatment tools in gastroenteropancreatic (GEP) NET patients.

Methods: During Sept-Nov 2019, NET patients and healthcare professionals (HCP) completed an online survey, available in 14 languages, which was disseminated via social media and face-to-face networks of NET patient groups.

Results: There were 1670 GEP-NET patients (female 61% [1012/1670]) from 53 countries across 6 continents. Average age was 57 (SD 12) years and patients had a NETs diagnosis for a mean of 5 (SD 5) years. The most common GEP-NETs were small intestinal (48% [798/1670]) and pancreatic (29% [488/1670]). Almost half of GEP-NET patients were misdiagnosed (44% [727/1670]); the top 3 misdiagnoses were gastritis (44% [254/582]), irritable bowel syndrome (44% [254/582]) and anxiety (23% [131/582]). Only 18% (134/726) of misdiagnosed patients were diagnosed within 1 year and mean time to diagnosis was 5 (SD 6) years (< 1 year: 19%; 1 year: 14%; 2 years: 16%; 3 years: 9%; 4 years: 6%; ≥5 years: 37%). More than one-third of GEP-NET patients (38% [638/1670]) were diagnosed with stage IV NETs or metastases at the time of diagnosis. NETs were grade 1 (43% [712/1670]), grade 2 (26% [438/1670]), grade 3 (4% [74/1670]), poorly differentiated (3% [52/1670]) and unknown (24% [394/1670]). GEP-NET patients reported biopsy as the most available diagnostic option (80% [1332/1670]), followed by CT (77% [1293/1670]). Over a third reported more specialized diagnostics, such as 68Ga-DOTA PET CT (39% [657/1670]) and chromogranin A (CgA: 39% [654/1670]) as unavailable. Almost half of GEP-NET patients (45% [746/1670]) stated peptide receptor radionuclide therapy (PRRT) was not available. Surgery was a widely available treatment option according to GEP-NET patients (81% [1350/1670]). Somatostatin analogues were available to over two-thirds of GEP-NET patients (68% [1131/1670]). Conventional imaging, such as CT/MRI/ultrasound, was stated as available by the majority (82% [1374/1670]) for ongoing monitoring. Approximately a third of GEP-NET patients believed ongoing monitoring with CgA (35% [578/1670]) or 68Ga-DOTA PET CT (38% [633/1670]) was unavailable. Amongst GEP-NET patients, issues most frequently experienced were "lack of access to reliable information about your NET" (37% [384/1036]) and "lack of experts to provide first or second opinion on your case" (32% [332/1036]). The most common recommendations to improve NET diagnosis and management were "more HCPs knowledgeable in NETs" (68% [1063/1571]) and "better access to NET experts/specialist centers" (54% [844/1571]). Nearly half of GEP-NET patients reported only one HCP being involved in their diagnosis (46% [668/1446]); leading diagnosticians were gastroenterologists (27% [435/1634]) and GPs (20% [334/1634]).

Conclusion: Delayed GEP-NET diagnosis remains a significant challenge and more reliable information on GEP-NETs is needed. In order to further drive forward improvements in global NET care, increasing the availability of NET diagnostics and treatment, particularly newer, more specialized tools, and increasing the number of knowledgeable HCPs, especially gastroenterologist and GPs, must be key priorities.

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P-137 High rectal cancer: What's the best treatment?

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Background: The incidence of rectal cancer is increasing with a mortality rate of 4-10/100000 inhabitants. Controversy still exists regarding the optimal treatment of high rectal cancer (HRC); should it be treated like colon cancer with surgery (Sx) + adjuvant chemotherapy (ChT), or as rectal cancer with radio +/- Cht (RChT) followed by Sx +/- adjuvant ChT? We aimed to compare the outcomes of patients with HRC that were treated with both regimens.

Methods: A retrospective analysis of patients with rectal adenocarcinoma between 10,1-15cm from the anal verge treated with curative intent between 01.2012-05.2018 was conducted at our institution. Considering treatment modality, the patients were divided into colon-like (CG: SX+adjuvant ChT) and rectal-like groups (RG: RChT+SX+adjuvant ChT). X2-test was used to compare categorical variables. Survival analysis was performed by Kaplan-Meier and Cox proportional-hazards model.

Results: Thirty-three patients were analyzed with a median follow-up of 33 months. The median age at diagnosis was 64 years-old [44; 85] and 69.7% were male. The majority presented clinical stage IIIB at diagnosis (60.6%). Twenty-one patients (63.6%) were treated with RChT+Sx+adjuvant ChT (RG) and 12 (36.4%) were treated with Sx+adjuvant ChT (CG). Higher lymph-node status at diagnosis was predominant in RG (p=0.043). Surgical complications (p=0.044) were also more frequent in RG, but without a statistically significant difference in surgical mortality (p=0.389). The CG presented a higher relapse rate (33.3%), although this was not statistically significant (p=0,233). There was no difference in the type of relapse (local vs distant) between the 2 groups (p=0,319). The 5-year overall survival (OS) was 78,1% and the 2 years relapse-free survival (RFS) was 86,3%. In the univariate analysis, downstaging (p=0.003), lymphatic (p=0.02), vascular (p=0.004) and perineural (p=0.032) invasion were prognostic for RFS. No prognostic factors were identified for OS. In the multivariate analysis, no factor emerged as an independent prognostic factor for the RFS.

Conclusion: In our study, the modality of treatment had no impact on the local relapse and survival outcomes. Neoadjuvant RChT may cause more surgical complications, although there was no statistical difference for surgical mortality. Larger prospective studies will help to clarify the optimal treatment of HRC.

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P-138 A comparison of the transcriptomic profiles of matched tissue from primary colorectal cancer and corresponding secondary lung metastases

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Background: Lung metastases occur in 10-20% of patients with metastatic colorectal cancer (mCRC) and represent the 2nd commonest site for distant spread. Comparing the transcriptome of primary tumours and their lung metastases could more accurately define phenotypic heterogeneity and help identify prognostic markers and novel therapeutic targets.

Methods: The ethically approved retrospective lung resection translational protocol was used to identify and collect clinical data and tissue samples from patients with CRC who underwent lung metastasectomy with curative intent between 1997 and 2012. Formalin-fixed paraffin-embedded tissue was collected from matching primary CRC tumour, lung metastases and representative areas of normal colorectal or lung tissue. RNA was isolated and the global transcriptome was profiled with TruSeq RNA Access RNA Sequencing. The data was analysed using a bioinformatics guided approach where differentially expressed genes were identified with a two-fold cutoff and a false discovery rate < 0.05. The R package CMS caller was used to classify tumour samples based on 530 gene predictors.

Results: Sufficient tissue from matching primary CRC and lung metastasis suitable for RNA sequencing was available in 13 patients. Tumour tissue was available from >1 lung metastasis in 2 cases. 69% of patients were male, median age was 64 (range 38-70), 54% were never smokers and 15% had metastatic disease at diagnosis. The primary tumour site was ascending colon in 15%, sigmoid colon in 38% and rectum in 46%. Out of the 19,374 genes analysed, 944 (4.9%) were differentially expressed when the primary tumour was compared to the first lung metastasis. Hierarchical clustering revealed that genes (n=990) were more likely to be over-expressed in metastases samples compared to primary tumours. Genes that were over-expressed were most likely to be involved in immune response. Amongst primary CRC samples, consensus molecular subtype (CMS) 4 (38%) and CMS 2 (31%) were the most common. In metastases samples, CMS 4 (36%) remained the most common followed by CMS 1 (22%). In lung metastases samples, CMS 1 was associated with a favourable prognosis whereas CMS 4 was associated with a poor prognosis. There was evidence of a switch in CMS subtype between the primary tumour and matched lung metastasis sample in 5 out of 9 cases (56%) where prediction was possible. Most patients (80%) with a switch in subtype had received neo-adjuvant chemotherapy.

Conclusion: In our small but unique dataset of matched primary CRC with corresponding lung metastases, a switch in CMS subtype may reflect metastatic processes

and selection pressure from treatment. In select cases, there may be potential to exploit CMS subtype switching for therapeutic benefit.

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P-139 Comparison of cost-effectiveness of anti-epidermal growth factor receptor monoclonal antibody and anti-vascular endothelial growth factor monoclonal antibody in K-RAS WT, RAS WT, and RAS WT left-sided metastatic colorectal cancer

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Background: Metastatic colorectal cancer (mCRC) is a significant global health burden. Combination chemotherapy plus targeted therapy, either anti-epidermal growth factor receptor (anti-EGFR) monoclonal antibody (mAb) or anti-vascular endothelial growth factor (anti-VEGF) mAb have become the current standard first-line treatment. Both kinds of targeted therapy have demonstrated their efficacies as first-line therapies in K-RAS wild-type (WT) patients. We aimed to compare the economic value of chemotherapy plus anti-EGFR mAb against chemotherapy with bevacizumab (an anti-VEGF mAb) in K-RAS WT, RAS WT, and RAS WT left-sided mCRC patients from a Hong Kong societal perspective.

Methods: We reviewed standard literature databases (PubMed, Cochrane library, ASCO and ESMO congress database). Phase II or phase III randomized controlled trials (RCTs) comparing chemotherapy and anti-EGFR mAb versus chemotherapy and anti-VEGF mAb as first-line treatment in mCRC patients were selected. Included studies must have had survival data from K-RAS WT, RAS WT, and RAS WT left-sided tumour populations. We then modeled a hypothetical cohort of patients with K-RAS WT mCRC with the same characteristics as those patients enrolled in the screened RCTs as a base case. We developed a three-state Markov model and 10-year horizon to estimate and analyze costs, quality-adjusted life-years (QALYs), and incremental cost-effectiveness ratio (ICER) of chemotherapy plus anti-EGFR therapy against chemotherapy plus Bev in K-RAS WT, RAS WT, and RAS WT left-sided mCRC respectively. There were three transition probabilities, namely from progression-free to progressive disease, from progression-free to death, and from progressive disease to death. All transition probabilities for each treatment strategy were estimated based on the survival curves reported in the RCTs assessing the respective treatments. We considered three times the local gross domestic product per capita (GDPpc) as the willingness-to-pay (WTP) threshold (3x GDPpc; i.e., US$146,748). The cost threshold of anti-EGFR therapy was also to be evaluated.

Results: Based on these criteria, we identified three trials in comparing anti-EGFR mAb versus anti-VEGF mAb (FIRE-3, CALGB 80405, and PEAK). Compared with chemotherapy plus bevacizumab, anti-EGFR mAb to chemotherapy provides additional 0.177 (0.092 to 0.333), 0.252 (0.104 to 0.479), and 0.334 (0.154 to 0.695) QALY compared to anti-VEGF mAb in K-RAS WT, RAS WT, and left-sided RAS WT mCRC population respectively. The corresponding ICER is $147,282 (69,067 to 377,371), $111,735 (50,460 to 277,226), $125,263 (52,786 to 291,639) per QALY gained, respectively. For RAS WT and left-sided RAS WT mCRC, adding anti-EGFR mAb to chemotherapy is cost-effective under the WTP threshold. However, in right-sided tumours, anti-EGFR mAb provides worse QALY of −0.106 (−0.390 to 0.094) compared to anti-VEGF mAb, and therefore it would not be a cost-effective one. Probability sensitivity analysis with Monte-Carlo simulation did not alter our main findings.

Conclusion: Anti-EGFR therapy is more cost-effective than bevacizumab as front-line targeted therapy in RAS WT, in particular left-sided RAS WT mCRC tumours, but not in the K-RAS WT population. Biomarkers-based selection of patients improves the cost-effectiveness of targeted therapy and should be advised.

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P-140 Targeted NGS panel of epigenetic regulators genes: Application results for gastric cancer patients

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Background: Epigenetic processes play a significant role in carcinogenesis, cancer recurrence and metastasis, and may serve as useful clinical biomarkers. According to GLOBOCAN 2018 data, gastric cancer (GC) is the third most lethal cancer with about 783000 deaths in 2018. Therapeutic drugs that are effective in the treatment of various types of tumors have a weak therapeutic effect in the treatment of GC due to the lack of genetic variants in known driver genes. Analysis of epigenetic regulator genes mutation landscape in GC samples may reveal novel genetic variants and therapeutic targets. This study presents an application of epigenetic regulators targeted NGS panel to GC patients.

Methods: We designed the NGS-based targeted panel of 25 genes whose products are involved in epigenetic processes and determined somatic alterations in 52 tumor samples of the GC. This panel consists of genes that regulate DNA methylation: DNMT1, MBD1, TET1, DNMT3A, DNMT3B ; genes involved in the modification of histone proteins: EZH2, UTX, EP300, JARID1B, CREBBP, HDAC2, SIRT1, KMT2A, KMT2D, KMT2C ; chromatin remodeling genes: SMARCB1, SMARCA2, SMARCA4, ARID1A, ARID2, BRD7, PBRM1, CHD5, CHD7, CHD4 . For the selection of genes, we took into account the frequency of somatic variants in GC according to the COSMIC cancer database. Prediction of somatic variants pathogenicity and impact on structure were carried out using PolyPhen2, SIFT, PROVEAN, MutPred2, I-Mutant 3.0 and HOPE3D tools. All identified somatic variants were verified in tumor tissue by Sanger sequencing.

Results: In 52 GC samples, targeted NGS sequencing revealed 50 nonsynonymous substitutions, 20 frameshift indels, 5 nonsense variants. We selected only known variants with minor allele frequency (MAF) lower than 0.0001 and no available information about clinical significance or novel genetic variants, which have never been described in any database. Of these selected variants, 11 are known with low MAF, and 14 are novel. Based on results of in silico pathogenicity prediction, substitutions in genes ARID1A (p.R2236C, p.Q152*, p.S1828*), KMT2A (p.W1909*), KMT2D (p.D3419G), KMT2C (p.Q462*, p.P959I, p.R973G), SMARCA4 (p.P913L) and CHD4 (p.R1943Q) are of interest due to pathogenicity prediction and disruption of various molecular mechanisms such as ligand binding, molecular recognition and relative solvent accessibility.

Conclusion: In this study, we present novel results on somatic mutation profiling in epigenetic regulators for GC patients. The identified pathogenic variants can be used as prognostic markers or new drug targets, but further investigation is needed. Deep target sequencing of epigenetic regulators makes it possible to acquire novel alterations and resolve true mutation frequencies of such genes. Subsequently, results of mutational landscape studies can be used to form risk groups among patient, confer significant prognostic information and improve clinical decision-making.

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P-141 The contribution of white blood cell gene expression in the prediction of gastrointestinal cancer

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Background: Gastrointestinal (GI) cancer remains one of the most deadly and common types of cancer worldwide. The early detection of GI cancer contributes to designing more efficient treatment algorithms and therefore reduction in mortality rates. The present study aimed to introduce and evaluate a non-invasive and sensitive technique, able to distinguish between normal and GI cancer samples. The recommended assay is based on the synergy of molecular biology with artificial neural networks.

Methods: The data set included healthy samples, as well as GI cancer patients from a variety of cancer types (colon, pancreatic, stomach, etc.) at different stages. In particular, from 60 samples (in a ratio of healthy-cancer approximately 1:1), a small quantity of whole blood was removed, and white blood cells were further isolated. Then, total RNA extraction and qRT-PCR reactions for more than 50 different genes were performed. The chosen genes consisted of common oncogenes, tumor suppressor genes, and/or genes associated with key cellular processes (metastasis, apoptosis, signaling pathways, etc.). The calculated DeltaCt values were provided as input to a supervised pattern recognition model for the classification between healthy subjects and cancer patients. The model was an artificial neural network ensemble, designed and built deploying the Bagging (Bootstrap Aggregating) method, while its performance was evaluated by 10-fold cross validation.

Results: The average accuracy of the ensemble was 90.24% (±13.95), achieving a high rate of identification; namely, the ensemble predicted the correct class (healthy or GI cancer) in almost all cases.

Conclusion: These preliminary results indicate that the proposed system, namely the exploitation of qPCR data by neural network ensembles, can be very helpful towards creating a more accurate and less time consuming prognostic method of GI cancer. The above system is not affected by the stage or particular type of cancer. Further studies in more samples and in different types of cancer are required for the verification of this method at the clinical level.

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P-142 Early gastric cancer: Identification of molecular markers able to distinguish penetrating lesions with different prognosis

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Background: Early Gastric Cancer (EGC) represents 25% of the gastric cancers surgically treated and is usually characterized by a good prognosis (5-year survival >90%). However, some patients show a significantly worse prognosis. In particular, among penetrating EGCs classified according to Kodama's criteria, Pen A tumors are characterized by extensive submucosal invasion, lymph node metastases, and worse prognosis, whereas Pen B tumors seem to be associated with a better prognosis.

The aim of the study was to characterize the differences between Pen A, Pen B and locally advanced gastric cancers (T3N0) in order to identify biomarkers involved in aggressiveness and clinical outcome of such tumors.

Methods: Formalin-fixed paraffin-embedded (FFPE) tissues were obtained from 87 patients (33 Pen A, 34 Pen B, and 20 T3N0 tumors), matched for age, gender and lymph nodes status. Mucins analysis (MUC2, MUC6, MUC5AC) was performed by immunohistochemistry; copy number variation (CNV) analysis by multiplex ligation-dependent probe amplification (MLPA); TP53 mutational status by Sanger sequencing; TP53 loss of heterozygosity (LOH) and microsatellite instability (MSI) evaluations by fragment analysis.

Results: MUC6 expression significantly distinguished Pen A and Pen B tumors, being overexpressed in 33.3% and 2.9% of the two subgroups, respectively (p=0.014). CNV evaluation of PIK3CA, EGFR, CDK6, MET, GATA4, FGFR1, MYC, PTP4A3, FGFR2, CCND1, KRAS, KLF5, ERBB2, TOP2A, GATA6, and CCNE1 genes showed that amplification was the most frequently observed alteration, but the only gene that was significantly different between tumor groups was the GATA6 gene (p=0.02), amplified in 33.3% and 66.7% of Pen A and Pen B, respectively. The evaluation of MSI showed no significant differences between Pen A and Pen B. Finally, TP53 gene analysis showed that 34.0% of Pen tumors have a mutation in TP53 exons 5-8 and 38.5% has LOH, suggesting the early onset of alterations of this gene in gastric carcinogenesis. No differences between Pen A and Pen B tumors were observed in terms of TP53 mutation frequency and site of mutation, even if a different frequency of TP53 missense variants was detected (78% of Pen A and 67% of Pen B tumors). Preliminary data showed that TP53 mutation and LOH co-occur mainly in Pen A tumors with respect to Pen B (p=0.001).

Conclusion: Overall, our analyses revealed that clinicopathological parameters, microsatellite status and frequency of TP53 mutations do not seem to distinguish Pen A and Pen B tumors. Alternatively, the overexpression of gastric mucin MUC6 significantly characterized Pen A tumors, as well as the amplification of the GATA6 gene was associated with Pen B tumors. The co-occurrence of TP53 mutations and LOH in EGC needs further investigations.

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P-143 Lack of expression of CDX2: Prognostic biomarker in stage IV colorectal cancer

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Background: Lack of expression of caudal homeobox 2 transcription factor (CDX2) is associated with a high risk of relapse in patients with stage II / III colon cancer after complete surgical resection, but its role in metastatic colorectal cancer (CRC) remains uncertain.

Methods: Patients with metastatic CRC at diagnosis treated at our institution and with available histological material from the primary tumor were selected. Patient tissue microarrays were performed and the samples analyzed by immunohistochemistry. We defined CDX2 negativity as an absence of expression of CDX2 in IHC in archived tumor tissue. Retrospective analysis of all patients diagnosed with RCC between January 2011 and December 2017 was performed. Demographic, clinical and survival data were analyzed using SPSS v24. A multivariate analysis was performed using the Cox proportional hazard regression model.

Results: We included 125 patients, with male predominance (n=73). The median age at metastatic diagnosis was 65 years and 105 patients had colon cancer. In total, 52.8% (n=66) of the patients had liver metastasis. Median overall survival was 17,66 months (95%CI 11,98-23.34) for a median follow up time of 17,66 months (0.03-91.81 months). 38 patients had a loss of CDX2 expression, and 87 patients had CDX2 positive. We have found that the CDX2 positive correlates with a lower risk of death (HR 0.44 (95%CI 0.26-0.73) p=0.002) as well as a decreasing trend in the likelihood of progression with first-line chemotherapy (HR 0.86 (95%CI 0.44-1.66) p=0.942). In total, 19% of patients CDX2 negative versus 12.1% CDX2 positive were grade 3 (p = 0.540). 53% of CDX2 negative were women versus 47.4% men (p = 0.073). Focusing on the metastasization sites, 22.75% of CDX2-negative had hepatic metastasis and 50% had peritoneal metastasis. 77.3% of patients with CDX2 positive tumours had liver metastasis. Partial responses were more frequent in CDX2 positive patients. We detected a negative predictive value (NPV), about 75-80%, for death/progression in the first 6 months after metastatic diagnosis.

Conclusion: CDX2 negativity was associated with a higher risk of death and a trend for increased risk of progression after first-line ChT. Due to the high NPV, patients are less likely to die or progress at 6 months when they have CDX2 positive mCRC.

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P-144 Infigratinib versus gemcitabine plus cisplatin as first-line therapy in patients with advanced cholangiocarcinoma with FGFR2 gene fusions/translocations: phase 3 PROOF trial

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Background: Treatment options for metastatic or unresectable cholangiocarcinoma are limited with a need to provide increased disease control, improved outcomes, and targeted therapy that is less toxic than standard chemotherapy. As the understanding of the molecular landscape of cholangiocarcinoma has increased, the fibroblast growth factor receptor (FGFR) family has been found to play an important role in cholangiocarcinoma. FGFR translocations (i.e. fusion events) represent driver mutations in cholangiocarcinoma. They are present in 13−17% of intrahepatic cholangiocarcinomas (IHC) and may predict tumor sensitivity to FGFR inhibitors. Infigratinib (BGJ398) is an ATP-competitive, FGFR1−3 selective oral tyrosine kinase inhibitor that demonstrated excellent preliminary anti-tumor activity in patients with relapsed/refractory cholangiocarcinoma with FGFR2 fusions/translocations in a phase 2 study (CBJG398X2204) [Javle et al. J Clin Oncol 2018]. The PROOF trial is evaluating infigratinib versus current standard-of-care gemcitabine + cisplatin in front-line patients with advanced cholangiocarcinoma with FGFR2 gene fusions/translocations (ClinicalTrials.gov identifier: NCT03773302).

Trial design: PROOF is a multicenter, open-label, randomized, controlled, phase 3 trial. Patients with previously untreated advanced/metastatic or inoperable cholangiocarcinoma with FGFR2 gene fusions (determined by local CLIA-certified or central laboratory) are randomized 2:1 to oral infigratinib 125 mg once daily for 21 days of a 28-day treatment cycle versus intravenous standard gemcitabine (1000 mg/m^2) + cisplatin (25 mg/m^2) on days 1 and 8 of a 21-day cycle. Treatment will continue until confirmed progressive disease by central review, intolerance, withdrawal of informed consent, or death. Patients assigned to the gemcitabine + cisplatin arm who progress can cross-over to infigratinib. The primary endpoint is progression-free survival (PFS, RECIST v1.1 by blinded central review). Secondary endpoints include overall survival, PFS (investigator determined), overall response rate, disease control rate, duration of response, and safety. Quality of life, pharmacokinetics and exploratory genetic alterations/biomarkers will also be assessed. The trial will have sites in the US, EU, and APAC, including Australia. The target population size is 384 patients. Recruitment started in December 2019, and the study has an estimated primary completion date of September 2023.

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P-145 CT-based texture analysis using radiomics for hepatic sinusoidal obstruction syndrome (HSOS) in colorectal cancer patients treated with oxaliplatin containing chemotherapy

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Background: Oxaliplatin containing chemotherapy is known to induce HSOS, which is also expressed by its appearance as blue liver syndrome. HSOS has been reported to increase morbidity and mortality in surgical patients (pts), and thus, its extent could affect treatment outcomes. However, the assessment of its severity solely depends on laboratory findings of hepatic indices, and the quantitative evaluation of HSOS is not sufficient in clinical use. The purpose of this study is to construct a non-invasive prediction model for HSOS by applying radiomics which provides a comprehensive quantification of CT image textures.

Methods: We retrospectively analyzed 32 colorectal cancer patients treated in our hospital from November 2011 to May 2017. There were 16 males and 16 females with a mean age of 64.3 (38-81). These 32 pts consisted of two sub-groups; 16 HSOS-positive pts with abnormal hepatic indices who underwent oxaliplatin containing chemotherapy, and 16 HSOS-negative pts with normal hepatic laboratory findings who did not have any oxaliplatin chemotherapy. The whole liver was semi-automatically delineated. 38 radiomic features were extracted by LIFEx software (www.lifexsoft.org). Feature extractions were performed, first by a univariate analysis by Wilcoxon rank-sum test, followed by multivariate logistic regression analysis with a step-wise feature-reduction. ROC (receiver operating characteristic) analysis was performed to generate the radiomic signature for the assessment of HSOS.

Results: The radiomic signature demonstrated high discriminatory performance in predicting HSOS with an area under the curve (AUC) of 0.949 with a sensitivity of 93.75% and specificity of 93.75% ($P < 0.001$).

Conclusion: A prediction radiomic model for HSOS was generated successfully. In the next step, we would further refine and generalize its accuracy by adopting the external validation cohort of HSOS by oxaliplatin.

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P-146 A genetic custom-made in vivo drug screening platform for colorectal cancer patients

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Background: Current treatments for colorectal cancer (CRC) patients show disappointing therapeutic outcomes. Therefore, there is a compelling need for better therapy choices. The newest approaches using genomic analysis for precision medicine enable the identification of an actionable cancer driver gene present in the tumor for further targeting (eg, KRAS, BRAF, etc). However, cancer may be promoted by the contribution of several genes rather than the alteration of one or two genes alone. Consequently, current targeted therapeutic strategies are not improving long-term outcomes or progression-free survival. Hence, comprehensive genetic models are required to offer more accurate diagnosing aimed to identify bona personalized therapeutic strategies.

Methods: We employed a method developed at the Icahn School of Medicine at Mount Sinai (NY), which enables simultaneous targeting of multiple mutations driving tumorigenesis. We first identified the whole genomic landscape associated with the patient's tumor. Next, we reconstructed this genetic complexity, including up to 20 cancer-associated altered genes present in the patient's tumor, in the last portion of the intestine of the fruit fly *Drosophila melanogaster*. Thus, this fly developed a CR tumor genetically similar to that of the patient, creating a most complete avatar model. Subsequently, fly avatars were expanded to up to half a million per patient and were then used to screen the full FDA/EMA drug libraries. Finally, effective drug cocktails identified were presented to the patients and oncologists.

Results: We present here a unique methodology to identify personalized CRC drug treatments based on individual patients' entire tumor genomes. This technology has already demonstrated improved progression-free survival in terminal CRC patients. The result is a fully customized treatment program, comprising on- and off-label oncology drugs and non-cancer drugs. Our platform allows the design of N-of-1 clinical studies aimed to identify the specific genetic factors that are necessary for tumor growth in an individual patient, and the best drug combination to tackle it.

Conclusion: This novel platform can make possible a more precise diagnosis, and together with avatar modeling and *in vivo* drug screening, may make it possible to identify fully tailored therapeutics. By addressing the patient tumor genomic complexity, this personalized practice-changing approach may provide an alternative and more efficient treatment option for individual CRC patients.

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P-147 Efficacy and safety data of trifluridine/tipiracil treatment in advanced colorectal cancer based on the experience of Juan Ramón Jiménez Hospital in Huelva

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Background: The clinical efficacy and safety of trifluridine/tipiracil were evaluated in an international phase III, pivotal, randomized, double-blind, placebo-controlled trial (RECOURSE), in patients with previously treated colorectal cancer. We present the results obtained in the Oncology service of Juan Ramón Jiménez Hospital in Huelva to assess our experience with this treatment.

Methods: We conducted an observational and descriptive study of patients with advanced colorectal cancer treated with trifluridine/tipiracil during the years 2017 and 2020. We have used the IBM SPSS Statistics 22 program to analyze the variables: age, start of treatment, end of treatment, progression date, death date, ECOG, Number of prior regimens, progression-free survival (PFS), overall survival (OS), need for admission, delay or dose reduction of treatment, as well as the presence or grade of adverse events related to it.

Results: 24 patients with a median age of 66.5 years were treated. ECOG 0-1 in 91.7%. 75% received treatment in the third palliative regimen and 20.9% in the fourth or subsequent regimen. 41.7% of the patients presented with stable disease as the best response to the treatment and 58.3%, progressive disease. No patient presented partial or complete response. The median OS was 4 months (95% CI, 0.60 to 7.39) and the median PFS was 2 months with (95% CI, 0.74 to 3.2). The most frequently observed and clinically significant adverse event was asthenia, which occurred in 75% of the patients, followed by nausea and vomiting 33.3%, diarrhea 20.8%, stomatitis 8.3%. Hematologic adverse events occurred, such as anemia grade $\geq$ 3 in 4.2% and neutropenia grade $\geq$ 3 in 33.4%. 12.5% of patients required admission for febrile neutropenia. In 58.3% of patients it was necessary to delay treatment and 62.5% required dose reductions mainly due to hematological adverse events.

Conclusion: Comparing our data with those of the RECOURSE study, we can say that the SG and PFS of our patients were significantly lower. This may be due to the fact that we included patients with ECOG 2, rapid progressors, as well as a higher percentage of patients who required hospital admission due to toxicity. The adverse events of our patients were similar to those described in the RECOURSE study, except for asthenia and febrile neutropenia, which were significantly higher in our study.

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P-148 Molecular characterisation of gastric tumours in a South Indian cohort and their clinical correlation

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Background: Gastric cancer is amongst the leading causes of cancer and cancer-related mortality worldwide. The prevalence of gastric cancer is particularly high in Eastern Asia with nearly 70 % incidence in developing countries. In this population, there remains a wide heterogenicity observed in the cancer aggressiveness and treatment outcomes, the plausible explanation being the molecular heterogenicity in

gene expression and oncogenic pathways. The developments in microarray and next-generation sequencing platforms enabled the genome-scale identification of molecular dysregulations at the level of mRNA and the possible genomics-guided stratification of tumors for eventual targeted therapeutics. Numerous whole-genome profiles decoding the landscape of molecular determinants of gastric tumors have been established from Japan, South Korea, and China. However, such larger profiles of gastric tumors are largely lacking from India. This is the first comprehensive genome-wide expression landscape covering mRNA, miRNA, lncRNA, and splice variants from India.

Methods: Gastric tumor samples were collected from our hospital in both liquid nitrogen and RNA later. Quality analysis was performed in Agilent Bioanalyzer 2100 using RNA 6000 Nano chips. Genome-wide expression profiling covering mRNA, miRNA, alternate splicing and lncRNA was performed using Affymetrix HTA 2.0 arrays. The dysregulated genes were compared with the profiles established from other countries. Integrative genomic analysis revealed the transcription factors OCT, NFkB, NFAT, STAT, LEF, AP, PAX, SP1, ELK1, NFYA to be up-regulated and HNF, GATA to be down-regulated in tumors. The tumour samples were then subtyped into eight different groups based on the differential activation of 21 oncogenic signaling pathways. The clinical features, intraoperative details and histopathological characteristics of the samples of the patients were collected. Patients were then followed up for a period of 2 years for recurrence and DFS was calculated. Correlation between genomic subtypes of the tumour samples and clinical outcomes/recurrence patterns were analysed.

Results: 108 patients who underwent distal gastrectomy were included in the study and genome-wide expression profiling were performed with their tumour samples. Based on the differential activation of 21 oncogenic signaling pathways, gastric cancer in this South Indian cohort could be subdivided into eight different subtypes. Among the eight subtypes, the subtype GC-1 that showed activation of differentiation-related pathways (Notch, NFAT, SP1-D, RXRA, ECM, HIF1A) was the most prevalent (n=36). The subgroup GC-7 that demonstrated no significant activation of any pathway had propensity for extranodal extension from lymph nodes when compared to the other types (p-value 0.17). Subgroup 5 and subgroup 7 had greater propensity for spread to regional lymph nodes (p-value 0.45 and 0.42, respectively). The patients belonging to subgroup 7 developed metastasis at an earlier date (p-value 0.08).

Conclusion: Among the eight different subtypes of gastric cancer differentiated on the basis of oncogenic signaling pathway activation, the subtype GC-1 was the most prevalent, GC-7 had propensity for extranodal extension in lymph nodes and developed earlier metastasis, and subgroups GC-5 and GC-7 had a greater chance of involving regional nodes.

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P-149 Management of rectal cancer in the Algerian west: A cohort of 164 patients treated at the department of radiation oncology of EHSO Emir Abdelkader of Oran

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Background: The aim of our study was to analyze the clinical aspects, management and outcomes of rectal cancer in the Algerian west from a cohort of patients treated at the Department of Radiation Oncology of EHSO Emir Abdelkader of Oran over a period of two years.

Methods: Between 2017 and 2018, 164 patients (59 women/105 men) with non-metastatic rectal cancer received preoperative radiotherapy alone or with chemotherapy (neoadjuvant and/or concomitant).

Results: The mean age was 56.8 ± 1.1 years (range 21 - 92). Eight patients (4.9%) were classified T2, 102 (62.2%) T3, 54 (32.9%) T4 and 151 (92.1%) N +. The lower pole of the tumor was located on average at 4.1 ± 2.2 cm from the anal margin. The major histology type was adenocarcinoma (95.7% of cases). 110 patients (67.1%) received neoadjuvant chemotherapy (FOLFOX or XELOX) followed by concomitant chemo-radiotherapy (RCC) based on capecitabine or radiotherapy alone, 35 patients (21.3%) RCC and 19 (11.6%) radiotherapy alone. The post neoadjuvant chemotherapy evaluation (of 99 Pts evaluated) found an objective response rate of 63.6%. 26 patients (15.8%) received short hypofractionated radiotherapy (25 Gy), 98 (59.8%) hypofractionated radiotherapy (30-39 Gy) and 40 (24.4%) normofractionated radiotherapy (46Gy). The post-neoadjuvant treatment evaluation (of 127 Pts evaluated) found an objective response rate (19 complete responses and 76 partial responses) of 74.8%. 104 patients received surgery: conservative (52.9%) and radical (abdominoperineal amputation: 47.1%). The rate of ypT0 was 20.2% and of ypN +: 23.1% (the average number of lymph nodes removed was 12.1 ± 0.5). With a median follow-up of 25 months (6 to 51 months), 3 patients (1.8%) presented with local relapses and 35 (21.3%) with metastatic relapses: hepatic (26Pts), pulmonary (18Pts) bone (9 Pts) and brain (2Pts). The two-year rates of recurrence-free survival, metastasis-free survival and overall survival were respectively 98.1% (± 0.01%), 53.5% (± 0.04%) and 81.8% (± 0.03%).

Conclusion: With satisfactory short-term results overall, prolonged monitoring of our cohort is necessary to validate them in the medium and long term, and to identify prognostic factors having an impact on overall survival, local control and especially the occurrence metastases. Optimization of strategy in the management of rectal cancer in our center, which was necessary for obtaining a good oncological result, was associated with a good quality of life (with a high probability of tumor downstaging and sphincter preservation).

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P-150 Khorana and PROTECHT scores in predicting the risk of venous thromboembolism in pancreatic cancer: Which performed better?

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Background: Venous thromboembolism (VTE) represents a major cause of morbidity and mortality in cancer patients. Several scores have been developed to predict the risk of cancer-associated VTE and help clinicians to select patients for thromboprophylaxis. The best known is the Khorana score, which stratifies patients as low (0 points), intermediate (1-2 points) and high (>= 3 points) risk. Pancreatic cancer patients score at least an intermediate risk due to tumor location parameter. Previous studies concluded that the Khorana score was not able to discriminate between intermediate and high-risk cancer patients, and the incidence of VTE was instead higher in intermediate-risk patients. Other scores have been developed to serve as better tools to stratify VTE risk in cancer patients. The PROTECHT score accounts for the chemotherapy regimen to be initiated. Some analyses suggest that the PROTECHT score provides better discrimination between low and high-risk patients, but further investigation is needed. The aim of this study is to compare the Khorana and PROTECHT scores in discriminating VTE risk in a cohort of pancreatic cancer patients, as well as to assess other potential risk factors for VTE.

Methods: This is a monocentric, retrospective study of 91 patients with pancreatic cancer with I-IV stage disease (AJCC 8th ed.) that received any systemic treatment with neoadjuvant, adjuvant or palliative intention between 2016 and 2019 at an Oncology department. Exclusion criteria: absence of chemotherapy/other systemic treatment; ongoing anticoagulation previous to oncological treatment; presence of any hematologic disease. Khorana and PROTECHT scores were calculated according to literature.

Results: In our sample, most patients were female (54,9%, n=50), median age at diagnosis was 70 years old [34-89] and 82,4% (n=75) had a stage III-IV disease. Median time of follow-up was 7,59 months. Median overall survival was 10,72 months. According to Khorana score, 62,6% (n=57) were classified as intermediate risk and 37,4% (n=34) as high risk. According to PROTECHT score, 97,8% (n=89) were stratified as high risk. Thromboprophylaxis was initiated in only 5 patients. 22 VTE events were documented, 40,9% (n=9) in deep veins of the lower limbs and 31,8% (n=7) in the mesenteric venous system. For Khorana intermediate-risk patients, the odds of a VTE event was 0,39 versus 0,21 for high risk [OR 0,537, CI 95% 0,19-1,57]. The odds of VTE for PROTECHT high-risk patients was 0,32. None of low-risk patients had an event. No other clinical and pathological parameters were significantly associated with VTE risk.

Conclusion: In our analysis, the Khorana score failed to discriminate the risk of VTE between intermediate and high-risk patients. The odds of patients classified as intermediate risk to develop a thrombotic event was 1,86 times higher than those classified as high risk, with the majority of events occurring in the first group. The PROTECHT score performed better at stratifying our patients. Other parameters such as staging, histological subtype, grade, and tumor markers were not predictive of VTE which can be due to our limited number of events. These findings would merit further validation in larger prospective studies.

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P-151 The impact of adjuvant chemotherapy regimens in stage II colon cancer (CC) patients

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Background: The benefit of adjuvant chemotherapy (AdjCT) in all stage II patients (pts) with colon cancer is not clear. Characterization of high-risk subgroups may shed light on this matter. The aim of this study was to determine patterns of AdjCT prescription and its impact on disease-free survival (DFS) in stage II CC.

Methods: Unicentric retrospective cohort of pts with stage II colon adenocarcinoma identified on the Portuguese national oncologic database between 2007 and 2018. Pts were categorized into two groups: not receiving and receiving AdjCT; AdjCT was characterized as capecitabine monotherapy (Cap) vs oxaliplatin-based (Oxali).

Results: We identified 668 pts with stage II CC: 191 were excluded (misclassification, death $\leq$30 days after surgery, or absence of available pathologic report). A total of 477 pts were treated at our center. 125 pts (26.2%) received AdjCT and we identified six statistically significant factors for this in the univariate analysis: age, higher stage, presence of lymphovascular or perineural invasion, and presence of perforation or obstruction. When controlling for these factors and insufficient lymphadenectomy sampling (ILS) ($<$ .0001) and ILS (OR, 2.879; CI, 1.362-6.084; P = .006) was more likely to receive AdjCT. Considering the AdjCT regimen used, age was the only statistically significant factor: pts $>$70 yr were more likely to receive Cap than Oxali (OR, 40.625; 95% CI, 9.046-182.440; P $<$ .001). Age kept its significance in the multivariate model when controlling for PS-ECOG, stage and ISL. Oxali was used in 52 pts (49.2%), mostly mFOLFOX. With a median follow-up of 72.2 months, mDFS was not reached (13.9% maturity). Regarding factors that may influence DFS, in the univariate cox regression, there was no difference for gender, PS-ECOG, laterality, perforation, obstruction, or perineural invasion. Age $>$70 yr (HR, 5.484; 95% CI, 1.885-15.949; P = .002) and lymphovascular invasion (HR, 3.309; 95% CI, 1.215-9.014; P = .019) were associated with worse prognosis. Also, when DFS was analyzed, Cap (vs Oxali: HR, 4.045; 95% CI, 1.116-14.665; P = .033) was associated with poorer outcomes. Considering the impact of the CT regimen on DFS, there was no difference between Cap and Oxali (P = .980) when controlling for age, stage, and lymphovascular invasion. However, age $>$70 yr (HR, 8.487; 95% CI, 1.383-52.072; P = .021), stage IIB or C vs IIA (HR, 3.346; 95% CI, 1.060-10.560; P = .039), lymphovascular invasion (HR, 3.989; 95% CI, 1.297-12.268; P = .016) kept their significance.

Conclusion: In this cohort, younger age, higher stage, lymphovascular invasion or obstruction, and ILS were significantly associated with receiving AdjCT. All factors but age are high risk for CT consideration in major international guidelines. The CT regimen (Cap vs Oxali) had no impact on DFS and the difference found in univariate analysis might be explained by Cap being chosen for pts with poorer biological reserve. Although this study is limited by its retrospective, non-controlled nature, younger age might be a surrogate for fewer comorbidities and better PS, which might explain why older pts were less likely to receive AdjCT, and when administered, Cap was the preferred regimen.

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P-152 The impact of 2nd-line treatment after 1st-line gemcitabine plus nab-paclitaxel in advanced pancreatic cancer patients

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Background: Three main phase III randomized studies investigated the role of 2nd-line tx in advanced pancreatic cancer (APC) patients (pts). The PANCREOX study failed to demonstrate a survival advantage of mFOLFOX vs 5FU/LV. Conversely, the CONKO-003 and NAPOLI-1 trials, demonstrated a significant survival improvement from the combination regimen OFF and 5FU+Nal-IRI, respectively, in comparison to 5FU/LV alone. Recently, final OS analysis from NAPOLI-1 demonstrated an association of specific characteristics (ECOG PS, age, Ca 19.9 baseline level, neutrophil-to-lymphocyte ratio and no liver metastases (m)) with OS $>$ 1 year. The main limit of all these studies was due to the period they were carried out: no pts received 1st-line gemcitabine plus nab-paclitaxel (GemNab). Hence, we retrospectively analysed a homogeneous population of APC treated with 1st-line GemNab at our institution, investigating the impact of 2nd-line tx.

Methods: APC pts receiving a 2nd-line tx after 1st-line GemNab were included in the analysis. The following variables were collected: gender; age ($>$ vs $\leq$ 55 years and $\geq$ vs 1); m sites (liver, peritoneum, lung, nodes); RECIST response and ETS during 1-line GemNab. Univariate and multivariate analyses for PFS and OS were performed.

Results: Out of 167 APC pts progressed to 1st-line GemNab, 93 (56%) pts received a 2nd-line tx, specifically 58 pts received an oxa-based regimen, 11 FOLFIRINOX, 8 FOLFIRI and 16 pts received other tx. Median 2nd-line PFS and OS were 3.3 and 5.6 months, respectively. Out of 87 pts evaluable for response, 7 pts achieved a partial response and 27 a stable disease, with a RR and a disease control rate (DCR) of 8% and 39%, respectively. Pts with baseline ECOG PS 0-1 had a significant better outcome in comparison to pts with PS 3-4 (PFS 4.2 vs 1.2 months, p $<$ 0.0001; OS 7.2 vs 2.6 months, p = 0.0001). This significant association with survival parameters and ECOG PS was confirmed at the multivariate analysis.

Conclusion: Despite the limited number of pts evaluated and the retrospective nature of our analysis, our results are in line with previous evidence, confirming the importance of a 2nd-line combination tx, when feasible, as well in a homogeneous population of APC pts treated with 1st-line GemNab. On the basis of our results, ECOG PS may be considered a prognostic factor and the choice of 2nd-line tx should be guided in premise by the baseline general conditions of APC pts.

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P-153 Novel ultrasonographic scoring system of sinusoidal obstruction syndrome associated with oxaliplatin-based chemotherapy in patients with gastrointestinal cancer

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Background: Oxaliplatin-based chemotherapies are widely used in the treatment of gastrointestinal cancers. However, several studies have reported that oxaliplatin-induced sinusoidal obstruction syndrome (SOS)/hepatic veno-occlusive disease (VOD) has occurred, with an incidence of 19% to 78%. SOS/VOD was associated with postoperative morbidity and decreased overall survival. SOS/VOD induced by oxaliplatin lacks specific clinical symptoms, which makes it difficult to diagnose SOS/VOD based on clinical criteria. Recently, image diagnosis is expected as a new diagnostic method. In the mechanism of SOS/VOD, the sinusoidal endothelial cell damage hinders the outflow of sinusoid by embolization, leading to portal hypertension resulting in increased spleen volume. A previous study reported that the increase in spleen volume was a diagnostic indicator of SOS/VOD, which achieved a specificity of 90%. Several studies evaluated the risk of SOS/VOD, using increase in spleen volume on computed tomography (CT) within 6 months after the administration of oxaliplatin. Transabdominal ultrasonography (US) is also expected as a novel diagnostic method, since US accompanied by Doppler imaging enables the visualization of blood flow abnormalities without radiation exposure. Recent studies reported a US diagnostic scoring system was useful for SOS/VOD after hematopoietic stem cell transplantation. The US scoring system is called HokUS-10, and we expect HokUS-10 may make it possible to early detect blood flow abnormalities before the increase in spleen volume is detected by CT. We herein prospectively evaluated the accuracy of HokUS-10 for SOS/VOD associated with oxaliplatin-based chemotherapy.

Trial design: This study started as a single center, prospective observational study in December 2019. The patients with gastrointestinal cancer who are planned to receive oxaliplatin-based chemotherapy are eligible for this study. The exclusion criteria are a history of oxaliplatin in past treatment, cirrhosis or chronic hepatitis, and liver resection. The US scoring of HokUS-10 is performed before oxaliplatin-based chemotherapy and 2, 4, 6, 12 months after the start of the administration of oxaliplatin. HokUS-10 consists of 10 parameters: hepatomegaly in the (1) left lobe and (2) right lobe, (3) gallbladder wall thickening, (4) portal vein (PV) diameter, (5) paraumbilical vein (PUV) diameter, (6) amount of ascites, (7) PV mean velocity, (8) direction of PV flow, (9) appearance of PUV blood flow signal, (10) hepatic artery resistance-index. The endpoint of this study is a probability that a high score of HokUS-10 and an increase in spleen volume on CT are observed in the same case. If patients undergo hepatectomy or liver biopsy after oxaliplatin-based chemotherapy, we also compare the score of HokUS-10 with histopathological diagnosis. A total of 30 cases are planned for registration within 2.5 years. This study was approved by the institutional review board of Hokkaido University Hospital (approval number: 019-0133). Clinical trial information: UMIN000045275.

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P-154 Actionable targets by tumor genomic profiling in patients with cholangiocarcinoma

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Background: Cholangiocarcinoma (CCA) is the most common biliary tract malignancy with approximately 5,000−10,000 new cases occurring annually in the EU. The absence of approved molecular therapies currently in the EU restricts CCA patients to chemotherapy options with limited clinical benefit. Recognizing that actionable genomic alterations occur in biliary tumors, NCCN guidelines state that molecular testing should be considered before the initiation of primary therapy [https://www.nccn.org/]. ESMO guidelines recommend that patients should be encouraged to participate in clinical trials of targeted therapies [Valle et al. Ann Oncol 2016]. In the current study, the catalog of genetic abnormalities in CCA patients was analyzed to determine the prevalence of actionable genomic alterations in CCA tumors and quantify the proportion of patients that may be eligible for an investigational therapy. Barriers to molecular testing and novel designs for biomarker-driven clinical trials will also be discussed.

Methods: Actionable genetic alterations were cataloged through a comprehensive literature review and analysis of multiplatform genomic data from publicly available databases. For this study, actionable genomic alterations were defined as: 1. known/likely driver mutations; 2. all gene fusions; 3. select copy number alterations. Correlative analysis of genomic alterations and clinical trial options was performed using an in-silico cohort of CCA subjects with available clinic genomic data that was extracted from the cBioPortal database (cbioportal.org, v3.1.6).

Results: The in-silico cohort consists of 393 CCA patients (median age at diagnosis 59 years, range 29−86 years; 55% male/45% female; Stage IV 65%) from the cBioPortal database (cbioportal.org, v3.1.6). The most common genetic alterations for each variant type were IDH1/2 mutations (10–18%), FGFR2 fusions (10–20%), and CDKN2A deletions (9–20%). Potentially actionable genomic alterations, which were mostly mutually exclusive, were also identified in KRAS (8%), PIK3CA (5%), PTEN (4%), ERBB2 (2.5%), BRAF (1.8%), and NTRK (1.8%). A rare fraction of patients (3/190, 1.6%) were classified as microsatellite instability (MSI)-High. Given the mutual exclusivity of the actionable alterations, ∼50% of CCA patients may be amenable to precision therapies alone or in combination with chemotherapy. The range of actionable biomarkers provides a rationale for a randomized umbrella trial with multiple targeted treatment arms and a single shared control arm.

Conclusion: Despite initial clinical activity of molecular-targeted drugs in CCA trials, a minority of newly diagnosed patients currently undergo comprehensive genomic profiling. Next-generation sequencing (NGS)-based molecular diagnosis has proved to be successful in detecting a broad spectrum of actionable alterations across many gene targets, enabling personalized treatment decisions. Therefore, we propose an upfront NGS testing scheme in CCA patients to ensure full understanding of potential options in later lines of treatment. Well-designed prospective clinical trials testing targeted therapies in patients with selected genomic alterations are warranted.

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P-155 Efficacy of somatostatin analogues in the treatment of metastatic and unresectable pancreatic neuroendocrine tumors

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Background: Pancreatic neuroendocrine tumours represent 1.3% of primary pancreatic tumours. Evidence for the use of somatostatin analogues for pNET is solid in favour of lanreotide, while the potential benefit of octreotide remains unclear beyond symptom control.

Methods: We present a retrospective study in patients with advanced, well and moderately differentiated pNET treated with somatostatin analogues (lanreotide and octreotide). The primary endpoint was progression-free survival evaluated by RECIST 1.1. Secondary endpoints were correlation of progression-free survival with clinical factors, overall survival, and safety profile.

Results: 43 patients were treated from January 2009 to December 2019, a mean of 59 years at the time of diagnosis, 60% of cases were women, 86% of the patients had ECOG 0. Carcinoid syndrome was observed in 14% of the cases and 50% had the primary tumour in the pancreatic head with a median of 6.8 cm in the major diameter. 75% were metastatic, with liver as the most commonly affected site in 65% of cases. 65% of patients were primarily treated with octreotide. Progression-free showed a median of 62.8 months. No difference between somatostatin analogues was observed and the median overall survival not reached.

Conclusion: Lanreotide and octreotide showed similar efficacy for disease control and overall survival in well and moderately differentiated pancreatic neuroendocrine tumours.

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P-156 A phase Ib/II study of cetuximab and pembrolizumab in metastatic colorectal cancer

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Background: Anti-EGFR monoclonal antibody (mAb) therapy can increase EGFR-specific T cells in peripheral blood (Trivedi et al Clin Cancer Res 2016). Thus, therapeutic strategies jointly targeting the EGFR-RAS-MAPK pathway as well as block critical immune checkpoints may be of benefit for patients with metastatic colorectal cancer (mCRC). We conducted a phase Ib/II study of cetuximab, a mAb targeting EGFR, with the anti-PD-1 mAb pembrolizumab in RAS wild-type (RAS-wt) mCRC; the results of the phase Ib part have been previously reported (Boland et al ASCO GI 2018). Here we present the primary efficacy results.

Methods: Patients with RAS-wt mCRC with at least one prior systemic therapy in the advanced setting were treated in 3-week cycles with cetuximab (400 mg/m^2 loading dose followed by 250 mg/m^2 weekly) and pembrolizumab (200 mg on day 1). Tumor biopsies were obtained at baseline and on-treatment (C4D1). The primary objectives were to estimate the objective response rate (ORR) by RECIST 1.1 and the 6-month progression-free survival (PFS). We utilized a single-stage version of the bivariate design of Sill et al., 2012. For ORR, H0=0.2 vs. H1=0.4 and 6-month PFS, H0=0.3 vs. H1=0.5, a=0.1, with 38 evaluable patients the study had ≥80% power to detect activity based on ORR alone, ≥80% power to detect activity based on 6-month PFS alone, and ≥97% power if the regimen is active on both endpoints.

Results: Forty-two RAS-wt patients were enrolled through October 2019. There were no new safety signals and the combination was well tolerated. Three patients had prior exposure to anti-EGFR therapy. 6-month PFS was 30% (CI: 19%-43%) and ORR was 5%. The median PFS and overall survival (OS) were 4.1 months (95% CI 3.9-6) and 14.9 months (95% CI 8.3-24), respectively. The disease control rate (DCR) was 73%. Thirty percent of patients had their CEA levels decrease >50% and 49% had a decrease in disease burden based on a decrease in the sum of target lesions. An increase in tumor-infiltrating cytotoxic lymphocytes (CTLs, CD3+CD8+) was observed (p=0.035). CTL infiltration was more pronounced in patients with CEA levels that had decreased by >50% vs. not (34% vs. 17%, respectively; p=ns) and those with any decrease in tumor burden vs. not (34% vs. 18%, respectively; p=ns).

Conclusion: Although the primary efficacy endpoint was not achieved, cetuximab plus pembrolizumab had modest anti-tumor activity in patients with RAS-wt mCRC. Compared to historic controls of anti-EGFR monotherapy, the PFS results are similar, though OS appears longer. Increased intratumoral CTL infiltration was noted following therapy; this appeared most pronounced in patients who benefited from therapy. Tissue analyses were underpowered owing to the small sample size. Further correlative analysis of tumor and blood specimens is ongoing.

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P-157 Incidence and survival of intestinal soft tissue sarcoma: A retrospective analysis from SEER

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Background: Intestinal soft tissue sarcoma (STS) is rare compared to STS in other locations. We assessed the incidence patterns, clinical characteristics, survival and prognostic factors in this population using a large population-based database.

Methods: Using the SEER database, we identified patients with small intestine, appendix, colon, rectosigmoid and rectum STS from 1975-2016. Patients were identified using ICD-O-3. Age-adjusted incidence rates were calculated by SEER*Stat 8.36. Overall survival (OS) and cancer-specific survival (CSS) were analyzed using Kaplan-Meier method and multivariate Cox proportional hazards model was used to determine the prognostic factors by SPSS 26.

Results: We identified 5492 patients with intestinal STS, accounting for 3.45% of STS in all locations. Small intestine accounted for 77.2% of intestinal STS, followed by colon (13%), rectum (8.8%), rectosigmoid junction (0.7%) and appendix (0.3%). Age-adjusted incidence rose from 0.1 to 0.4 per 100,000 during the study period. Annual percentage change of age-adjusted incidence was +6.5 (95% CI 5.7-7.4). Incidence was highest among age >50 years old (77.1%), male (53.7%) and white race (77.8%). The median age of diagnosis was 63 years (52-73). Twenty-six different histologies were reported during the study period. Gastrointestinal stromal sarcoma (GIST) (66.6%) and leiomyosarcoma (25.3%) accounted for more than 90% of the cases, followed by sarcoma, NOS (3.4%), spindle cell sarcoma (1.5%), and all other histologies were less than 1%. Stage was reported in 87.1% cases, with localized 48.4%, regional 17.8% and distant 20.8%. Median OS for the entire cohort was 6.8 years (95% CI 6.4-7.2), with 5- and 10-year OS of 57.7% and 39.9%, respectively. After excluding GIST, median OS reduced to 2.8 years (95% CI 2.6-3.1), with 5- and 10-year OS to 37.2% and 24.6%, respectively. Median CSS was 20 years (95% CI 15.8-24.1) for all intestinal STS compared to 5.8 years (95% CI 4.8-6.9) for non-GIST STS. In multivariate analysis, rectum location (HR=0.78; 95% CI 0.68-0.89), Asian and Pacific Islander race (HR 0.83, 95% CI 0.73-0.94), age>50 years (HR=2.18; 95% CI 1.97-2.42), male gender (HR 1.2; 95% CI 1.12-1.30), stage (regional HR1.51, 95% CI 1.37-1.68; distant HR 2.74, 95% CI 2.50-3.02), grade (moderate differentiated HR 1.24, 95% CI 1.04-1.48; poorly differentiated HR 2.20, 95% CI 1.82-2.66; undifferentiated HR 2.45, 95% CI 2.05-2.93), histology (liposarcoma HR=1.96, 95% CI 1.36-2.83; myomatous sarcoma HR=2.18, 95% CI 2.00-2.38), and treatment method are prognostic factors for survival. As for treatment, 96.2% of patients did not receive radiation therapy or the treatment was unknown. The combination of surgery and chemotherapy yielded better survival benefit than either alone (HR=1.28; 95% CI 1.16-1.42) or no treatment (HR=2.46; 95% CI 2.09-2.90). After excluding GIST, race and histology were no longer significantly different in terms of survival.

Conclusion: Intestinal STS accounts for 3.45% of all STS, with the incidence highest among age>50 years old, male and white race. Age >50, male, liposarcoma or myomatous sarcoma, advanced stage, and poor differentiation are poor prognostic factors, while Asian or Pacific Islander race and chemotherapy combined with surgery are associated with better outcomes.

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P-158 Clinical impact of oral intake in third-line treatment for advanced gastric cancer

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Background: Trifluridine/tipiracil, an oral drug, was approved in Japan for patients with advanced gastric cancer (AGC) according to the TAGS trial. Insufficient oral intake (INSUF) is one of the most common complications. We evaluated the clinical characteristics and impact of oral intake during third-line chemotherapy.

Methods: We retrospectively evaluated data of patients with AGC receiving third-line chemotherapy among the patients who received first-line chemotherapy from January 2012 to December 2018 at a single institution. We defined "INSUF" as requiring daily intravenous fluids or hyperalimentation, and "improvement of oral intake (IMP)" as no such requirement for >1 week. Exacerbation (EXA) was defined as a change from "sufficient oral intake (SUF)" to INSUF.

Results: The numbers of patients receiving first-line chemotherapy, second-line chemotherapy, and third-line chemotherapy were 589, 495, and 298, respectively. Among the 298 patients receiving third-line chemotherapy, 39 (13%) and 259 (87%) patients had INSUF and SUF, respectively, before starting third-line chemotherapy. Differences in the patient characteristics such as ECOG PS 2 (64% vs. 12%; p< 0.001), previous palliative surgery (26% vs. 10%; p=0.013), liver metastasis (18% vs. 36%; p=0.029), peritoneal metastasis (77% vs. 47%; p=0.001), moderate or severe ascites (62% vs. 28%; p< 0.001), median neutrophil-to-lymphocyte ratio (NLR, 4.66 vs. 2.78; p=0.001), and median serum sodium (Na, 136 vs. 140 mmol/L; p< 0.001), were statistically significant between the INSUF and SUF group, respectively. Irinotecan use was significantly different between INSUF and SUF groups (15% vs. 42%, p=0.002), while with nivolumab use, there was no difference (36% vs. 31%; p=0.607). The causes of INSUF were peritoneal metastases (79%), cachexia (15%), and primary complications (5%). The median follow-up time was 19 months. INSUF patients had poorer PFS (1.1 vs. 2.0 months; Hazard ratio [HR], 1.75; 95% confidence index [95% CI], 1.24-2.48; p< 0.001) and had significantly poorer OS (1.9 vs. 7.0 months; HR, 3.34; 95%CI, 2.33-4.80; p< 0.001) than SUF patients. At the end of third line chemotherapy, 107 (37%) and 179 (63%) patients had INSUF and SUF, respectively. Among these INSUF patients, only 2 patients (5%) achieved IMP (nivolumab 1 patient; irinotecan 1 patient). In SUF patients, factors correlating with EXA were pathological type (intestinal vs. diffuse type; odds ratio [OR], 2.46; p=0.041), NLR (< 2.5 vs. ≥2.5; OR, 2.58; p=0.021), and serum Na levels (≥140 vs. < 140; OR, 2.26; p=0.027). Subsequent chemotherapy was administered to 13 patients (12%) and 118 patients (66%) of the INSUF and SUF groups. The patients with SUF in third-line chemotherapy was only 20% compared to that in first-line chemotherapy.

Conclusion: INSUF at the start of third-line chemotherapy was found to be a poor prognostic factor. At the end of third-line chemotherapy, INSUF patients increased from 13% to 36%. Thus, for effective use of oral drugs, we need to adapt late line chemotherapy regimens carefully, paying particular attention to patients with diffuse-type histology, high NLR, and hyponatremia.

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P-159 First-in-human phase 1 dose-escalating study protocol of pressurized intraperitoneal aerosol chemotherapy with paclitaxel in peritoneal carcinomatosis (PIPAC2 study)

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Background: Pressurized intra-peritoneal aerosol chemotherapy (PIPAC) is a relatively novel laparoscopic intraperitoneal chemotherapy delivery technique, with advantages such as the homogeneous distribution of aerosol and deeper tissue penetration. Thus far, PIPAC paclitaxel has not been administered in humans. However, intra-peritoneal paclitaxel administration has shown promising results in selected patients. We aim to determine the dose-related safety profile and tolerability of PIPAC paclitaxel using an evidence-based approach. The secondary aims are to evaluate the clinic-pathologic response and to identify the pharmacokinetic profile of PIPAC paclitaxel.

Methods: This is a phase I 3+3 dose-escalation study for gastric and gynaecological patients with predominant peritoneal metastasis. Safety is assessed according to Clavien-Dindo Classification and National Cancer Institute — Common Terminology Criteria for Adverse Events (version 4.0). Clinicopathologic response is assessed using the Peritoneal Regression Grading Score, Peritoneal Cancer Index and Response Evaluation Criteria In Solid Tumour criteria (version 1.1). Pharmacokinetic analysis is performed using Inductively Coupled Plasma-Mass Spectrometry assay.

Results: Recruitment for this study is planned to begin in May 2020, starting at the dose of 15mg/m^2. Subsequent dose cohorts are planned at 30mg/m^2, 45mg/m^2 and 60mg/m^2. This is based on a pre-clinical study in swine by our group, which showed hematologic toxicity at 60mg/m^2 but was well tolerated at 30mg/m^2 and 15mg/m^2.

Conclusion: This phase I study can provide a scientific basis to identify the recommended phase II dose for PIPAC paclitaxel such that the benefits of this promising intraperitoneal chemotherapy delivery technique can be further evaluated.

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P-160 A phase II study of resection followed capecitabine plus oxaliplatin for liver metastasis of colorectal cancer (REX study): Safety analysis

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Background: Surgical resection has been accepted as the standard therapy for colorectal cancer liver metastases (CRLM), however, high recurrence incidence even after curative resection remains an unsolved problem. There is no established adjuvant chemotherapy for CRLM, although the efficacy of several adjuvant treatments for stage III colorectal cancer has been confirmed. Capecitabine plus oxaliplatin (CapeOx) is one of the standard therapies for stage III colorectal cancer in the adjuvant setting. We conducted this phase II trial to evaluate the safety and efficacy of adjuvant CapeOx for CRLM.

Methods: Patients (pts) undergoing curative resection of CRLM were eligible for this study. Capecitabine 1,000mg/m^2 was given orally twice daily for 14 days followed by a 7-days rest; oxaliplatin 130mg/m^2 on day 1 was given by intravenous infusion. CapeOx was performed for up to 8 cycles. The primary endpoint was 3-year relapse-free survival (RFS), while secondary endpoints were overall survival (OS), relative dose intensity and safety.

Results: This study was closed prematurely due to poor accrual. In total, 27 patients were enrolled from 9 institutions in fifty-four months. As two patients were excluded from this analysis because of their condition worsening, 25 patients were evaluated. Median age was 64, male/female; 15/10, ECOG PS 0/1/2; 23/1/1, sidedness right/left; 8/17, tub1/tub2; 12/13, number of metastases 1～3/ 4～; 17/8. The completion rate of protocol treatment was 64%. The reasons for discontinuation were adverse events (28%) and recurrence of cancer (8%). The most frequently reported grade 3-4 adverse events were neutropenia (20%), sensory neuropathy (12%) and leucopenia (8%). One treatment-related death was observed because of DIC.

Conclusion: Our data suggested that capecitabine plus oxaliplatin for adjuvant chemotherapy after hepatectomy in patients with colorectal cancer is tolerable. The analysis of efficacy is awaited.

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Disclosure: The presenting author has declared no conflicts of interest.

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P-161 Efficacy of third-line anti-EGFR-based treatment versus regorafenib/TAS-102 (R/T) according to primary tumor site in RAS/BRAF wild-type metastatic colorectal cancer patients

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Background: Right(R)- and left(L)-sided metastatic colorectal cancers (mCRCs) exhibit different clinical and molecular features. Several retrospective analyses showed that the survival benefit of anti-EGFR-based treatment (tx) is limited to RAS/BRAF wild-type (wt) L-sided mCRC pts, which a larger effect in the first-line setting. Few data are available concerning the anti-EGFR efficacy according to primary tumor site in third line. In particular, a retrospective analysis of the phase III study 20020408 comparing panitumumab vs BSC in third line, showed a significantly higher PFS (5.5 vs. 1.6 months; HR, 0.31, $p < 0.0001$) and RR (24% vs. 0%) for panitumumab tx vs BSC in RAS wt L-sided mCRC pts. No difference was observed in R-sided pts both in terms of PFS and RR (RR=0% in both arms).

Methods: Pts affected by RAS/BRAF wt mCRC treated with third-line anti-EGFR-based tx or R/T were retrospectively collected. The objective of the analysis was to compare tx activity and efficacy according to tumor site. Primary endpoints were OS and PFS; secondary endpoint was RR.

Results: A total of 76 RAS/BRAF wt mCRC pts, treated with third-line anti-EGFR-based tx or R/T, were enrolled. Of those, 19 (25%) pts had R-sided tumor (9 pts received anti-EGFR tx and 10 pts received R/T) and 57 (75%) pts had L-sided tumor (30 pts received anti-EGFR tx and 27 pts received R/T). A significant PFS and OS benefit in favor of anti-EGFR tx vs R/T (PFS: 7.3 vs. 3.6 months, HR=0.47, 95%CI 0.26-0.85, p=0.0028; OS: 15.2 vs 11.0 months, HR=0.58, 95%CI 0.31-1.08, p=0.0428) was observed in L-sided pts. No difference in PFS and OS between anti-EGFR and R/T was observed in pts with R-sided tumor (PFS: 3.5 vs. 3.8 months, HR=1.4, 95%CI 0.53-3.75, p=0.49; OS: 9.3 vs 9.2 months, HR=0.83, 95%CI 0.30-2.26, p=0.696). RR was significantly higher in L-sided pts treated with anti-EGFR vs R/T (43% vs 0%; $p < 0.0001$), while no difference was shown in R-sided pts (anti-EGFR RR=11% vs R/T RR= 10%; p=0.99). At the multivariate analysis, tx regimen was independently associated with PFS in L-sided pts, but not in R-sided pts.

Conclusion: Our study confirmed the results deriving from the retrospective analysis of the phase III study 20020408. Our results demonstrated a different benefit from third-line anti-EGFR tx according to primary tumor site, confirming the role of L-sided tumor in predicting benefit from third-line anti-EGFR vs R/T, while no difference was observed in R-sided tumors.

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P-162 Perioperative capecitabine-oxaliplatin chemotherapy in resectable gastric cancer

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Background: Perioperative chemotherapy with 5-fluorouracil and platinum-based regimen with or without docetaxel (FLOT) or epirubicin (ECF) improves outcome in resectable gastroesophageal junction and gastric adenocarcinoma. Additional epirubicin does not seem to show advantages. The aim of this retrospective study was to evaluate the safety and efficacy of perioperative chemotherapy with a CAPOX-based regimen.

Methods: Patients with resectable gastric or gastroesophageal adenocarcinoma with a clinical stage higher than cT2, or nodal positive disease, or both without evidence of metastatic disease, were enrolled to receive 3 cycles of a pre-operative and 03 cycles of post-operative CAPOX-based regimen. We assessed disease-free survival, overall survival, surgical outcomes, radical (R0) resections rate, pathological tumor response, and toxicity.

Results: We enrolled 15 patients from January 2014 to December 2015. Median age was 52 years [19-76]. All patients completed the 3 planned pre-operative cycles and 11 patients (73%) started post-operative chemotherapy (7 completed the 3 post-operative allocated cycles). 13 (87%) patients had surgical resection. 2 (13%) patients achieved a pathological complete regression. 5 patients had at least one grade 3/4 toxicity. The median disease-free survival and overall survival was 43 and 48 months.

Conclusion: Patients who received the CAPOX-based perioperative regimen showed favorable survival. CAPOX might represent an option for patients eligible for perioperative chemotherapy. A prospective randomized study is ongoing to confirm these results.

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P-163 Systemic chemotherapy for previously treated metastatic small bowel adenocarcinoma

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Background: Metastatic small bowel adenocarcinoma (mSBA) is a rare condition with a poor prognosis. Enough data are not available on second-line chemotherapy (SLC) for mSBA. The aim of this study was to explore the efficacy and safety of SLC for mSBA patients.

Methods: We retrospectively reviewed the clinical characteristics of 27 patients with mSBA who received SLC or best supportive care (BSC) after progression on first-line chemotherapy from January 2011 to October 2019 at a single institution. We evaluated efficacy outcomes, including objective response rate (ORR), disease control rate (DCR), progression-free survival (PFS), and overall survival (OS). The treatment-related adverse events (TRAEs) were assessed according to CTCAE version 5.0. The PFS and OS were estimated from the disease progression date of the first-line chemotherapy using the Kaplan-Meier method, and Cox models were applied for univariate analyses.

Results: Of the 27 patients, 21 patients received SLC and 6 patients received BSC. The patient characteristics were as follows: median age (range), 60 (36—83) years; male/female, 16/11; Eastern Cooperative Oncology Group performance status (PS) (0/1/$\geq$2), 7/15/5; primary tumor location (duodenum/jejunum or ileum), 13/14; resection of primary tumor (yes/no), 13/14; MSI-High/MSS/unknown, 1/8/18; number of metastatic sites (1 or 2/$\geq$3), 18/9; ascites (yes/no), 13/14; neutrophil-to-lymphocyte ratio (NLR) ($\leq$4/$>$4), 17/10; Glasgow prognostic score (GPS) (0/1 or 2), 16/11; first-line chemotherapy regimens (fluoropyrimidines plus platinum/taxane-based), 26/1; and SLC regimens (irinotecan-based/taxane-based/others), 14/5/2. The proportion of patients with poor PS (67% vs. 4.8%), presence of ascites (67% vs. 43%), past history of primary tumor resection (63% vs. 47%), high NLR (67% vs. 29%), and high GPS (67% vs. 33%) was significantly higher in the BSC group than in the SLC group. The SLC was discontinued in 18 patients (86%), and the reasons for discontinuation were disease progression in 15 patients, unacceptable adverse events in 2 patients, and patient refusal in 1 patient. In the BSC group, the reasons for receiving BSC were worsening of general condition due to disease progression in 3 patients, patient refusal in 2 patients, and infectious disease in 1 patient. During the median follow-up time of 20.4 months, the median OS (mOS) in the whole population was 9.4 months. The patients in the SLC group had obviously better OS than those in the BSC group [Hazard ratio (HR), 0.11; 95% confidence index (95% CI), 0.02-0.52; mOS, 15.6 vs. 3.3 months; $p < 0.001$]. ORR, DCR, and median PFS of the SLC group were 5.0%, 73%, and 5.0 months, respectively. The mOS of the patients who underwent irinotecan-based chemotherapy was longer than that of taxane-based chemotherapy (HR, 0.21; 95% CI, 0.06-0.78; mOS, 12.6 vs. 5.4 months; $p = 0.020$). The most common TRAEs of grade 3 or 4 in the SLC group were neutropenia (43%), anemia (19%), anorexia (10%), and febrile neutropenia (5%). There was no treatment-related death, and no patients died within 30 days after the start of SLC.

Conclusion: The SLC for mSBA demonstrated clinical activity and had acceptable toxicities. The results of this study support further clinical trial investigation.

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P-164 The role of response as a predictor of improved outcome in advanced pancreatic cancer patients treated with first-line gemcitabine plus nab-paclitaxel

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Background: Gemcitabine plus nab-paclitaxel (GemNab) is one of the first-line standard treatments (tx) of advanced pancreatic cancer (APC). To date, no predictive factors, both clinical and molecular, of benefit from this regimen exist. Two retrospective studies showed that early tumor shrinkage (ETS) can predict an improved outcome in APC pts receiving a first-line tx with FOLFIRINOX or GemNab. However, data regarding GemNab, limited to a small population of only 57 pts, seem to not confirm the association of ETS with a better outcome. Hence, we retrospectively analysed an homogeneous population of APC treated with first-line GemNab at our Institution, investigating the impact of several clinical factors, including response and ETS.

Methods: APC pts receiving a first-line tx with GemNab were included in the analysis. The association of RECIST response and ETS with PFS and OS was evaluated. The following variables were collected: gender; age ($>$ vs $\leq$ 55 years and $\geq$ vs 1); m sites (liver, peritoneum, lung, nodes); number of tx lines (1 vs $>$1). Univariate and multivariate analyses for PFS and OS were performed.

Results: A total of 184 APC pts receiving first-line GemNab at our Institution from February 2014 to May 2019 were included in the analysis. RR and ETS were assessed in 174 and 168 pts, respectively. RR was 30%, disease control rate (DCR) 63% and ETS was 24%. Responders had a significantly better PFS (12.5 vs 5.7 months, p 1 were also independently associated with better OS.

Conclusion: Despite its retrospective nature, this is one of the largest series of APC pts treated with first-line GemNab investigating the role of RECIST response and ETS in predicting outcome. On the basis of our results, RECIST response may be considered a positive prognostic factor, whereas ETS may not. In conclusion, achieving tumor shrinkage, not necessarily early, significantly delays PC progression and prolongs survival in pts treated with first-line GemNab.

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P-165 Paclitaxel-based intraperitoneal chemotherapy for gastric and pancreatic cancer with peritoneal metastases achieves higher conversion surgery rate and longer survival

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Background: Peritoneal metastases (PM) represent one of the most refractory disease states. It frequently develops in patients (pts) with gastric (GC) or pancreatic (PC) cancer, significantly impacting their prognosis. Many types of systematic chemotherapies have been evaluated for PC but the results were not satisfactory. Recently, the use of intraperitoneal paclitaxel (ipPTX) plus systemic chemotherapy for GC with PM has shown promising clinical results, especially in pts who underwent conversion surgery after the disappearance of PM due to ipPTX (Ishigami H, et al. J. Clin Oncol. 2018). We have studied ipPTX for GC and PC with PM since 2012. In this analysis, we focus on cases resulting in successful conversion surgery.

Methods: 142 pts with GC and 34 pts with PC with PM have been treated with ipPTX from February 2012 to December 2019. Systemic chemotherapies were selected from standard regimens for GC or PC, such as DCS (docetaxel/CDDP/S-1), SP (S-1/CDDP), or FOLFORINOX, gemcitabine/nab-paclitaxel, depending on the patient's condition. IpPTX was administered at 20mg/m^2 weekly, 2-weeks or 3-weeks in a row with 1-week rest, according to the schedule of systemic regimens. Patients whose metastases were limited to peritoneum became candidates for conversion surgery.

Results: Of the 46 candidates in GC and 15 in PC, 25 and 6 cases, respectively, achieved conversion surgery after confirmed complete disappearance of PM. Progression-free survival and overall survival were 20.9 months and 47.4 months in GC, and 21.8 months and not reached in PC.

Conclusion: Our retrospective analysis showed that the combination of ipPTX with systemic chemotherapy for both GC and PC with PM increases the probability of achieving conversion surgery, which in turn provides significantly better survival benefits than conventional chemotherapy.

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P-166 Baseline radiomics features in metastatic colorectal cancer: Correlation with metastatic site and clinical-pathological characteristics

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Background: Radiomics is an emerging field of research based on the extraction of a large amount of features from biomedical images and on computed analysis algorithms of tumour architecture. Few data regarding metastatic colorectal cancer (mCRC) are available. In particular, no correlation of baseline radiomics features (RF) both with metastatic (m) sites and clinical-pathological characteristics has been investigated so far.

Methods: Baseline chest-abdomen CT scans of mCRC patients (pts) were retrospectively analysed. RF were extracted from regions of interest (ROI) delineated on CT scan from each m site, including primary tumor, when on-site. The association of specific F and disease site (liver, lung, nodes, peritoneum and on-site primary tumor) was investigated. Sites similarity was assessed with Principal Component Analysis, an unsupervised learning technique to identify patterns and clusters. Then RFs were tested individually for correlation with clinical-pathological covariates of interest (gender, CEA level, synchronous disease, RAS/BRAF status, mucinous histology, grading, number of m site, primary tumor site). Wilcoxon-Mann-Whitney test was used for this purpose (significance level set at 0.05).

Results: After RF extraction from the different ROIs, the dataset was composed of 433 observations of 236 variables. Observations referred to the number (N) of pts = 89 and the N of ROIs = 18. RF classes were divided in statistical F (grey-level histogram) (N of F=10); morphological F (N=14); texture F GLCM (grey level co-occurrence matrix) (N=100); texture F GLRLM (grey level run length matrix) (N=66); texture F GLSZM (grey level size zone matrix) (N=32). Regarding the association of RF with m sites, an homogenous distribution with liver, nodes, peritoneum and primary tumor was detected, while lung metastases showed a different pattern for all the RF classes. A significant correlation of specific RF with clinical-pathologic characteristics was shown, in particular with gender, CEA level, synchronous disease, mucinous histology, RAS/BRAF status.

Conclusion: Despite its retrospective nature and the limited number of pts, this is the first experience demonstrating I) a different pattern of RF for lung m versus a homogeneous RF distribution for the other m sites; and II) a significant association of specific RF with few clinical-pathologic characteristics. Our results, if confirmed in a prospective validation set, may represent a hypothesis generator regarding the different behaviour of lung metastases and a possible R signature able to identify different prognostic subgroups of pts.

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P-167 Impact of testosterone on sexual function in women with rectal cancer: A prospective, longitudinal, cohort study

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Background: Women with rectal cancer planned for surgery with or without preoperative (chemo)radiotherapy are at risk for impaired sexual function and a decrease in sex hormone levels. It is unclear to what extent testosterone levels are important for sexual function in women with rectal cancer. The study aim was to investigate if the levels of testosterone were associated with sexual function in a cohort of female rectal cancer patients.

Methods: A total of 142 women with rectal cancer stage I—III were included at four Swedish referral centres. The questionnaire Female Sexual Function Index (FSFI) covers six domains of sexual function, each with a maximum domain score of six. The total FSFI score ranges from two to 36. The FSFI was completed and blood samples were collected at baseline and twice during two years follow-up. The serum-level of testosterone was analysed and tested for association with sexual function in regression analysis. In the longitudinal regression model, adjustments were made for age, psychological well-being, and partner.

Results: Longitudinal regression analysis showed an association between one unit higher level of testosterone and an increase in FSFI total score of 5.59 (95% CI 2.48 to 8.69; P< 0.001). Equally, testosterone was associated with the FSFI domain scores of desire (0.54 points; P< 0.001), arousal (0.81 points; P=0.002), lubrication (1.30 points; P< 0.001), orgasm (1.24 points; P< 0.001), and pain (1.18 points; P=0.004). The association with satisfaction did not reach statistical significance (0.40 points; P=0.149). Adjustments for confounders did not significantly change the coefficients from the unadjusted analyses.

Conclusion: The level of testosterone was associated with female sexual function in the present study. The results indicate that testosterone plays a role in several aspects of sexual function in women with rectal cancer. Future studies to evaluate testosterone substitution therapy for women after rectal cancer treatment may be of interest.

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P-168 Second-line, anti-VEGF based after first-line, anti-EGFR based treatment in RAS wild-type metastatic colorectal cancer: The multicenter, retrospective, real-life SLAVE study

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Background: The optimal antiangiogenic strategy as second-line treatment in RAS wild-type (WT) metastatic colorectal cancer (mCRC) treated with anti-EGFR based first-line treatment is still debated.

Methods: This multicenter, retrospective study aimed to compare clinical outcomes of activity (ORR), efficacy (PFS, combined I and II line PFS [PFS1-PFS2], OS) and safety of WT mCRC patients treated with second-line bevacizumab or aflibercept-based therapy (Bev-CT and Afli-CT, respectively), after a first-line panitumumab or cetuximab-based therapy in a "real-life" setting. Clinical data of patients from 14 Italian hospitals were retrospectively collected.

Results: From February 2011 to October 2019, 277 consecutive mCRC patients were treated with Bev-CT (82.3%) or Afli-CT (17.7%). Median age was 64.5 years (range: 29-84). Male/female ratio was 168/109; ECOG-PS 0/1/2 ratio was 147/116/14; right/left sidedness ratio was 73/204; number of metastatic sites was 1 in 93 (33.6%) and 2 or more in 184 (66.4%) patients, respectively; primary tumor was resected in 204 (73.6%) patients; BRAF status was WT, mutated (V600E-not V600E) and not evaluable in 240, 13 and 24 patients, respectively. All patients were evaluable for activity and efficacy analysis. At a median follow-up of 43.2 months (95%CI: 39.8-51.7), according to Beva-CT and Afli-CT, median PFS was 7.1 (95%CI: 6.4 — 8.5) and 5.6 (95%CI: 4.1 — 7.8) months (HR= 1.39 [95%CI: 0.95-1.89] p=0.09), respectively; median OS was 16.2 (95%CI: 15.3 — 18.1) and 12.7 (95%CI: 8.8 — 17.5) months (HR= 1.31 [95%CI: 0.89-1.92] p=0.16), respectively; median PFS1-PFS2 was 21.2 (95%CI: 18.5 — 23.5) and 21.4 (95%CI: 14.5 — 25.0) months (HR= 0.99 [95%CI: 0.70-1.40] p=0.98), respectively. At univariate analysis only, ECOG-PS (≥ 2 vs 0-1) and number of metastatic sites (≥ 2 vs 1) were predictors for shorter PFS (HR= 2.46 [95%CI: 1.35—4.43]; p=0.0025) (HR= 1.68 [95%CI: 1.27—2.21] p=0.0002) and shorter OS (HR= 4.5 [95% CI: 2.5—8.1]; p< 0.0001) (HR= 2.1 [95%CI: 1.6—3.0] p=0.0002). ORR was 45.2% (95% CI: 36.8—54.8) for Bev-CT and 30.6% (95%CI: 17.1—50.5) for Afli-CT, with no statistically significant differences. The incidence of G1-G2 and G3-G4 class-specific (hypertension, fistules, perforation, proteinuria, bleeding, ischemia) adverse events (AEs)

was 23.7% and 7.5% for Bev-CT and 32.7% and 26.5% for Afli-CT, respectively. The incidence of G1-G2 and G3-G4 ematologic AEs was 36.4% and 4.4% for Bev-CT and 59.2% and 10.2% for Afli-CT, respectively. The incidence of G1-G2 and G3-G4 non class-specific and non-ematologic AEs was 36.4% and 4.4% for Bev-CT and 59.2% and 10.2% for Afli-CT, respectively.

Conclusion: This study shows no differences in efficacy and activity between Bev-CT and Afli-CT, with a slightly higher incidence of class-specific, hematologic and non-class-specific, non-hematologic AEs for Afli-CT compared to Bev-CT. Further analyses with larger sample size and a prospective design are certainly needed to better define and personalize the antiangiogenic strategy as second-line treatment in WT mCRC.

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P-169 A first-in-human phase Ia/b, open-label, multicentre, dose-escalation study of BI 905711 in patients with advanced gastrointestinal cancers

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Background: Activation of the tumour necrosis factor-related apoptosis-inducing ligand receptor 2 (TRAILR2) induces apoptosis via caspase activation. Hence, targeting TRAILR2 is an attractive therapeutic strategy; however, early trials of TRAILR2 agonists resulted, in some cases, in severe hepatotoxicity that may have been due to TRAILR2 activation on hepatocytes. Cadherin 17 (CDH17), a membrane protein highly expressed in gastrointestinal (GI) cancers, is not expressed in normal hepatic cells. Thus, the hepatotoxicity of prior TRAILR2 agonists may be avoided through cross-linking with CDH17. BI 905711 is a tetravalent bispecific antibody targeting both TRAILR2 and CDH17 that demonstrated a potency shift of ~1000 fold compared with previously described TRAILR2-binding agents. In pre-clinical assays, BI 905711 induced apoptosis in CDH17-positive tumour cells in vitro, impaired tumour growth in patient-derived colorectal cancer (CRC) xenografts, and was not associated with hepatic toxicity (Garcia-Martinez J-M. AACR 2019, ENA 2018).

Trial design: This is an international, phase Ia/Ib, first-in-human trial of BI 905711 in patients with treatment-refractory GI cancers (NCT04137289). Eligibility includes histologically-confirmed unresectable/metastatic CRC, gastric, oesophageal, pancreatic adenocarcinoma or cholangiocarcinoma progressing on standard of care therapies; adequate hepatic, renal and bone marrow functions; age ≥18 years, ECOG PS ≤1; and for phase Ib only, CRC with ≥1 lesion site evaluable per RECIST v1.1. The starting dose of BI 905711 is 0.02 mg/kg every 14 days intravenously. Treatment will continue until disease progression or unacceptable toxicities. CRC patients will be recruited as mandatory cohorts in phase Ia that will include 1 patient at each of the 2 lowest dose levels (0.02/0.06 mg/kg) and 4 patients at each subsequent dose level (0.2/0.6/1.2/2.4/3.6/4.8 mg/kg). Dose escalation will proceed sequentially assuming no dose-limiting toxicities (DLTs) in the first 28 days of treatment. In parallel to the dose escalation in CRC patients, up to 4 patients with non-CRC GI cancers may be included at the dose level below that of the CRC cohort. In phase Ia, a Bayesian logistic regression model will be applied to determine the next dose levels in the CRC and non-CRC cohorts, and evaluate the maximum tolerated dose (MTD). In addition, a dose range will be selected based on efficacy signals. In phase Ib, patients with CRC will be randomised into up to four dose cohorts of up to 20 patients each in a 2-stage design (10 patients at stage 1) to define the recommended phase II dose. If an objective response (OR) is observed in a particular tumour type in phase Ia, the dose cohort will be increased to up to 10 patients with the same tumour type. In phase Ia, the MTD (primary endpoint) will be determined based on the proportion of patients with DLTs as assessed by CTCAE v.5.0. Secondary endpoints include pharmacokinetic parameters and OR in patients with measurable disease. For phase Ib, the primary endpoint is OR, and secondary endpoints include tumour shrinkage, duration of response, and progression-free survival. CDH17 expression (immunohistochemistry) and other biomarkers will also be evaluated.

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P-170 Understanding patient experience in hepatocellular carcinoma: A qualitative patient interview study

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Background: Patients with hepatocellular carcinoma (HCC) have both disease- and treatment-related increased symptom burden and decreased health-related quality of life (HRQoL). The aim of this study was to obtain a detailed understanding of the patient experience of HCC-related signs/symptoms and impacts on daily functioning and HRQoL through qualitative interviews, to guide fit-for-purpose patient-centred outcome measurement in medical product development.

Methods: Patients diagnosed with HCC (Barcelona Clinic Liver Cancer [BCLC] Stage A, B or C) participated in qualitative concept elicitation interviews (each lasting 75—90 minutes), conducted using a semi-structured interview guide with open-ended and prompted questions, over five interview waves. To guide the patient interviews, the signs/symptoms and impacts of HCC were explored by targeted literature searches, review of HCC patient blogs/forums and interviews with five oncologists. Patient interviews were transcribed and coded using qualitative research software. A sign/symptom or impact was defined as being 'salient' if it was mentioned by ≥ 50% of patients, with a mean disturbance rating of ≥ 5 (on a 0—10 scale). A conceptual model focusing on HCC-related signs/symptoms and impacts was developed. Mapping of salient concepts to the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) and its disease-specific module HCC18 was performed to help inform patient-centred outcome measurement in medical product development across various stages of HCC.

Results: Literature searches identified 57 concepts related to signs/symptoms and impacts of HCC. Patient blogs/forums confirmed the literature review results but did not contribute additional concepts. Complementary interviews with oncologists identified five additional concepts related to HCC signs/symptoms. Interviews with 25 patients with HCC (68% men; median age: 63 years [range: 44—79 years]; 12% BCLC stage A; 32% stage B; and 56% stage C) identified 73 concepts, comprising 54 signs/symptoms and 19 impacts. Concept saturation was reached by the fifth and third of five interview waves for signs/symptoms and impacts, respectively. Salient concepts for HCC from the patient interviews included 12 signs/symptoms (lack of appetite/feeling of fullness; weight loss; fatigue/lack of energy; muscle/strength loss; diarrhoea; nausea/queasiness; vomiting; abdominal pain; difficulty concentrating; dizziness/vertigo; dry mouth; and shortness of breath) and eight impacts (disturbed sleep; emotional impacts; impact on family/friends; impact on social life; frequent bed rest/naps; impact on instrumental activities of daily living; difficulty performing strenuous activities/exercise; and decrease in overall physical activity). Although patient numbers per disease stage were small, the interview data suggested some differences in patient experiences across various stages of HCC. The EORTC QLQ-C30 and HCC18 captured relevant signs/symptoms and impacts associated with patient experience in HCC.

Conclusion: Patients with HCC reported a range of signs/symptoms and impacts that negatively affect daily functioning and quality of life. The interview findings highlight the importance of obtaining information on the patient experience directly from patients. Including patient-reported outcome measures such as the EORTC QLQ-C30 and HCC18 in HCC medical product development can provide meaningful patient perspectives, complementing traditional efficacy and safety outcome measures.

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P-171 Lenvatinib in patients with unresectable hepatocellular carcinoma who do not meet REFLECT trial inclusion criteria

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Background: The phase 3 clinical trial of the novel multikinase inhibitor lenvatinib for patients with advanced HCC (REFLECT trial) showed that its overall survival (OS) is non-inferior to and the progression-free survival (PFS) is significantly longer than that of sorafenib. However, data on the safety and efficacy of lenvatinib for patients with unresectable HCC who did not meet the REFLECT inclusion criteria are limited. In the REFLECT trial, patients were excluded if they had history of multikinase inhibitor treatment, had HCC involving ≥50% of the liver, main portal vein invasion, Child-Pugh grade B, platelet count 9 /l, or obvious bile duct invasion; thus, the efficacy and safety of lenvatinib for such patients have not been clarified. Hence, in this study, we aimed

to evaluate the tolerability, objective response rate (ORR), and PFS of lenvatinib for patients with unresectable HCC, specifically those who did not meet the REFLECT inclusion criteria.

Methods: In this multicenter, retrospective study, patients with unresectable HCC treated with lenvatinib between 2018 and 2019 who had adequate clinical data were included. Objective response rate, progression-free survival, and safety were evaluated according to meeting or not meeting the REFLECT inclusion criteria and according to the exclusion criteria of the REFLECT trial.

Results: Of the 105 patients included, 61% (64/105) did not meet the REFLECT inclusion criteria. Safety, ORR, and median PFS of lenvatinib were similar between the patients who did and those who did not meet the criteria. Among the patients who did not meet the criteria, 28, 27, 14, 6, 7, and 5 had a history of tyrosine kinase inhibitor (TKI) treatment, Child-Pugh score B, HCC in $\geq$50% of the liver, reduced platelet count, bile duct invasion, and main portal vein invasion, respectively. Although treatment outcome was not significantly different, patients with TKI treatment history and bile duct invasion tended to have longer median PFS and/or favorable ORR, whereas those with reduced platelet count and main portal vein invasion tended to have shorter median PFS.

Conclusion: Lenvatinib was effective for patients who did not meet the REFLECT inclusion criteria. However, the treatment outcome may vary according to several factors, such as history of TKI treatment, tumor invasion, and platelet count.

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P-172 Prognostic factors in metastatic gastric cancer patients

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Background: Metastatic gastric cancer is associated with poor prognosis with a median overall survival (OS) of 9–11 months, and nearly half of patients have advanced disease at diagnosis. Some prognostic models were proposed in these patients including baseline characteristics. The objective of this study was to characterize metastatic gastric cancer population and to evaluate the prognostic factors.

Methods: Patients that started 1st line systemic therapy (ST) for metastatic gastric cancer between January/2015 and December/2019 in a single center were retrospectively analyzed. A clinicopathologic characterization and survival analysis were performed using Kaplan-Meier and Log Rank test. Cox regression was used to identify prognostic factors. Statistical significance 5% was considered.

Results: Fifty-five patients started ST with median age of 63 years (36-78), male sex (n=43; 78.2%), ECOG PS 0-1 (n=42; 76.4%), synchronous metastatic disease at diagnosis (n=35; 63.4%) and median disease-free survival of 19 months (1-111) in metachronous disease. Most patients had tumour localized in antrum and pylorus (n=26; 47.3%) and intestinal histology (n=30; 54.5%). Eighteen patients (32.7%) had history of perioperative/adjuvant chemotherapy. Peritoneal carcinomatosis was the most frequent site of metastatic disease (n=26; 47.3%). Seventeen patients (30.9%) had $\geq$ 2 sites of metastatic disease. HER2 was positive in 5 patients (9.1%). Ca19-9 was $\geq$ 37 U/mL in 54.5% (n=30) and CEA $\geq$ 5 ng/mL in 47.3% (n=26). Albumin $<$ 3,5 g/dL was present in 23.6% (n=13). Neutrophil to lymphocyte ratio (NLR) $\geq$ 5 in 34.5% (n=19) and prognostic nutritional index (PNI) $\geq$ 50 in 21.8% (n=12). Body mass index (BMI) was $<$ 5, p=0.009. Multivariate analysis (synchronous, previous chemotherapy history and NLR) revealed that NLR $\geq$ 5 was associated with a poor OS (HR 2.28; 95% CI 1.15-4.52; p=0.019). There were no statistically significant differences in OS taking account sex, age, ECOG PS, tumor location, histology, peritoneal carcinomatosis, number of sites of metastatic disease, Ca19-9, CEA, albumin, PNI and BMI.

Conclusion: The outcomes verified in our population were similar to those previously published. Metachronous metastatic disease, previous perioperative/adjuvant chemotherapy and NLR $\geq$ 5 were associated with poor outcomes and high NLR was an independent prognostic factor for poor OS in our population.

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P-173 The role of maintenance therapy in the first and second lines of treatment of metastatic colorectal cancer

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Background: The first and second lines of CT is decisive in the treatment of colorectal cancer. Choosing the right one allows you to increase PFS and improve long-term results. Surgical treatment and maintenance therapy (MT) increase PFS and OS, as they can be prescribed at any stage of treatment.

Methods: The analysis included 192 patients diagnosed with metastatic colorectal cancer (mCRC) who received treatment between 2014 and 2019. The average age of the patients was 62 years. At the beginning of treatment, the overall condition of all patients was ECOG1. Primary mCRC had 129 (67%) patients. In 63 (33%) patients, locally advanced disease was first diagnosed, which were included in the study after progression. PFS and OS for all patients were calculated from the start of the 1st line. Localization of the primary tumor in 42 (22%) patients was on the right side of the colon and on the left side in 149 (78%) and 1 patient did not show primary tumor. Among the patients with primary metastatic disease, 100 (52%) had isolated metastases, while the remaining 92 (48%) had 2 or more localizations. Different types of surgical treatment of metastases in the liver occurred in 41 (21%) patients. 119 patients never received MT (with any number of lines) and made a comparison group (A). 73 patients received MT in at least one of the CT lines (B). 12 patients received MT in the 1st and 2nd CT (C). These groups were homogeneous in terms of gender, age, ECOG, accessibility of surgical treatment of distant metastasis, mutational status of the tumor, and accessibility of biotherapy. Evaluation of the effect was performed using RECIST criteria, at intervals of 3 months or the appearance of clinical symptoms of progression. The treatment was carried out before the progression. At the time of analysis, 94 patients are alive and continue to receive treatment.

Results: We compared in all three groups:

In group A: OS - 12.2 months, PFS 1-line CT - 9.3 months, PFS 2-line CT - 4.4 months

In group B: OS - 24.6 months, PFS 1-line CT - 13.6 months, PFS 2-line CT - 9.1 months

In group C: OS - 37.3 months, PFS 1-line CT - 14.2 months, PFS 2-line CT - 9.1 months

Conclusion: Increase of PFS and OS in patients who received MT at least at one of the stages of treatment, and continues to increase in patients receiving MT in the first two lines CT. Thus, MT is a necessary component of the treatment of mCRC.

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P-174 When to do PET-CT and diagnostic laparoscopy in gall bladder cancer? A prospective study to assess the role of PET-CT and diagnostic laparoscopy in the staging of gall bladder cancer

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Background: Gall bladder cancer (GBC) is the most common malignancy of the biliary tract. Preoperative staging is the most important tool in deciding the management protocol of the patients. Though PET-CT and diagnostic laparoscopy (DL) have been increasingly performed, the exact role of each modality in the staging of GBC patients is not clear. In the present study, we evaluated the utility of PET-CT and DL in the staging of GBC patients in the same study population.

Methods: This prospective study was conducted in the Department of Surgical Oncology, at AIIMS, New Delhi over a period of 1 year (August 2018 to September 2019) in 67 patients. The patients diagnosed with GBC or suspicious of GBC, deemed operable in CECT, were included in the study. PET-CT was done in all the patients and those patients who deemed operable in PET-CT were subjected to DL. The patients in whom DL did not detect any metastatic disease (omental and peritoneal deposits) were subjected to laparotomy and the results were evaluated for staging of GBC.

Results: Among the total of 67 patients (CECT-wise operable), PET detected inoperability in 6 (8.96%) patients (peritoneal 3, peritoneal and para-aortic nodes 2 and omental metastasis in 1). Among the 61 patients in whom PET-CT showed operability,

21 (34.4%) patients were found to be surgically inoperable either due to metastasis or local unresectability after laparotomy. If CECT was considered as a sole diagnostic modality, 27 (40.3%) patients would have been surgically inoperable. Among those patients who were deemed operable by PET-CT, DL detected inoperability in 9 patients (14.7%) (peritoneal 8, omental 6, and liver 3). Laparotomy was performed in the DL-wise operable patients (N=52) and 12 (23.08%) patients were found to be inoperable due to local invasion. Hence the FNR of CECT, PET-CT, and DL in detecting the inoperability was 40.3%,34.4%, and 23.1%, respectively. Out of the 27 patients who were surgically inoperable, DL detected inoperability and futile laparotomies were avoided in 9 patients. The actual rate would have further increased to 15/27(55.5%) if the PET-CT detected metastasis (6 patients) were subjected to DL. On univariate analysis, size of the GB mass in CECT significantly correlated with PET-CT detected inoperability (p value = 0.006; Odds ratio 1.64; CI 1.09 to 2.47). The sensitivity, specificity, PPV and NPV of CECT and PET-CT in detecting the lymph node involvement in operable GBC patients were 14.3%, 82.2%, 11.1%, 86% and 57.1%, 79.1%, 30.8%, 86.1%, respectively.

Conclusion: Diagnostic laparoscopy obviated futile laparotomies by more than half (55.5%) of unresectable patients and 22.38% in overall patients. Hence DL should be performed in all the operable GBC patients before surgery. PET-CT can be selectively done in patients with larger GB masses in CECT (>1cm). Though PET-CT is more sensitive compared to CECT, both are not an accurate modality in detecting the lymph node involvement in the case of GBC.

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P-175 Total neoadjuvant treatment versus standard therapy (neoadjuvant radiochemotherapy and adjuvant chemotherapy) of rectal cancer with high-risk factors for local or systemic recurrence

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Background: Standard therapy (neoadjuvant radiochemotherapy, surgery, adjuvant chemotherapy) of locally advanced rectal cancer (LARC) achieves excellent local control. However, survival is poor due to distant metastases, which are the leading cause of death in these patients. In recent years the concept of total neoadjuvant treatment (TNT) has been developed, where systemic chemotherapy, mainly affecting micrometastasis, is introduced prior to surgery, in conjuction with radiochemotherapy.

Methods: In a retrospective study, we compared patients with LARC at increased risk for failure who were treated with standard therapy or TNT. Patients at high risk for local or distant failure had one of the following factors: T4, N2, positive mesorectal fascia, presence of extramural vascular invasion, or presence of lateral lymph node. TNT consisted of 4 cycles of induction chemotherapy with CAPOX/FOLFOX, radiochemotherapy with capecitabine and 2 cycles of consolidation chemotherapy with CAPOX/FOLFOX prior to surgery. The primary endpoint was pathological complete response (pCR).

Results: 72 patients were treated with standard therapy and 89 patients had TNT. Groups were matched by gender, clinical disease stage, performance status and tumor location from anal verge. They differed significantly by age and in proportion of high-risk factors for failure, but these characteristics alone did not significantly influence the primary endpoint. Compared to standard therapy, TNT resulted in higher proportion of pCR (23% vs. 7%; p 0.01), lower NAR prognostic score (median 8.42 vs. 14.98; $p < 0.05$), higher T- and N-downstaging (70% and 94% vs. 51% and 86%), shorter time to stoma closure (average 30 vs. 32 weeks; $p < 0.05$), higher compliance to chemotherapy (all cycles completed 65% vs. 50%), lower rate of acute toxicities grade ≥ 3 during chemotherapy (3% vs. 20%) and perioperative period (7% vs. 11%). Rates of R0 resections (95% vs. 93%) and acute toxicity during radiochemotherapy were comparable between the two groups. The pCR rate in patients treated with TNT was significantly higher when intensity-modulated radiotherapy (IMRT, VMAT) was used rather than 3D conformal radiotherapy (32% vs. 9%; $p < 0.05$).

Conclusion: In patients with LARC with high-risk factors for failure, TNT was found to be more effective compared to standard therapy in terms of pCR and prognostic NAR score.

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P-176 Epidemiology and clinical outcomes of patients with pancreatic tumors discussed in tumor board

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Background: Tumor Boards (TB) are multidisciplinary meetings that direct the management of treatment of highly complex diseases such as pancreatic cancer. The benefits of TB suggest an increase in the survival rate, better use of resources from medical practice, promotion of educational opportunities, adequate statistical classification and, consequently, better precision of the therapeutic plan. The recommended decisions in TB should be followed up to identify which obstacles reflect on unfulfilled conducts and can assist in interventions that improve the patient's clinical outcome. Therefore, the objective of this study is to evaluate whether the decision to conduct was made in pancreatic tumors, the status of patients after 90 days of discussion on TB and to analyze the reasons why the conduct was not performed.

Methods: We conducted a retrospective, quantitative study, consisting of cases of patients diagnosed with malignant neoplasm of the pancreas and other diseases of the pancreas, discussed in the tumor board meetings from September 2017 to September 2019. Information from the electronic medical record was collected and analyzed including epidemiological data of the patients, whether the TB conduct was performed, the reason for not conducting it, survival 90 days after TB decision, and date of death or last follow-up. Categorical variables were presented as a percentage and compared with the chi-square test. They were presented as means and interquartile ranges. Multivariate logistic regression was performed to identify factors associated with failure to conduct the tumor board.

Results: 111 cases discussed in tumor board were analyzed, with 95 patients, 50 (52.6%) of whom were male, 86 (90.5%) diagnosed with cancer, 60 (63.2%) were ECOG 0 at the time of the discussion and without metastasis; there were 68 (71.6%). The age of the patients discussed ranged from 17 to 88 years. After 90 days of the tumor board meeting, 83 patients (87.37%) remained alive, 9 patients (9.47%) died and 3 (3.16%) were lost to follow-up. The management of the tumor board was performed in 99 (89.2%) of the cases and in 12 (10.8%) cases, the procedure was not performed. The decision of the tumor board was objective and answered the question of 105 case (95%). The reasons for not conducting the conduct were: 25% (3) due to loss of follow-up, 8.33% (1) due to patient refusal and 66.67% (8) due to clinical worsening. Of these cases, local treatments were proposed in 7 (58.33%), systemic treatment in 5 (41.67%). In the data analysis, the cases with metastases had less execution of the tumor board ($p = 0.006$).

Conclusion: The study concluded that the management of the tumor condition is performed in most cases of pancreatic tumors, after a meeting of the tumor condition 87.37%, if found alive and the most evident reason for the fact that clinical examination of patients.

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P-177 Overall survival of patients with left-sided metastatic colorectal cancer in real life: Experience from University Hospital for Tumors in Zagreb, Croatia

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Background: According to 2016 Eurostat cancer statistics, Croatia has the second-highest standardised death rate for colorectal cancer (CRC) among the EU Member States. In light of that fact, we tried to analyse the reasons behind this bad result in our cohort of patients. Available real-world data suggest that median OS of patients with left-sided mCRC is 22 to 25 months. Overall, around 750 patients are treated each year due to mCRC in Croatia. Of that, 70-75% are left-sided tumors. We present survival results of patients treated for left-sided mCRC in our institution.

Methods: We conducted retrospective analysis on a consecutive sample of all patients who started their treatment with chemotherapy dublet +/- biological agent between January 1st, 2016 and December 31st, 2017. OS was calculated from the start of induction therapy to the death of the patient. Kaplan-Meier curves were used to estimate median survival and survival rates.

Results: A total of 112 patients were analysed. Median age was 62 (39-85), 60% of patients were men and 40% women. At the time of diagnosis, as much as 60% of patients were metastatic and 60% of patients had more than one metastatic site. Chemotherapy without a biological agent was used in 25% of patients. An irinotecan-based induction chemotherapy regimen was used in 81% of patients. Among patients with biological therapy, 66% received bevacizumab and 34% received an anti-EGFR drug. When analysing two-year follow-up outcomes, the median PFS for 1st-line treatment was 11 months; 38% of patients who received 2nd-line treatment had a median PFS of 5 months and only 5% of those who received 3rd-line treatment had a

median PFS of 5 months. Two-year OS rate was 50%. More than a quarter of patients are still on therapy (27%) and median duration of treatment is 32.5 months.

Conclusion: To best of our knowledge, this is the first report of overall survival data of patients with mCRC in Croatia to date. The negative trend in OS could be partly determined by late diagnosis and the fact that as much as 60% of patients were high-risk patients with initially metastatic disease and high tumor burden. This suggests that perhaps more effort should be made to diagnose the disease in an earlier stage. The lack of multidisciplinarity in our institution probably has a major impact on our results.

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P-178 Prognostic impact of immune-related adverse events with nivolumab or pembrolizumab monotherapy in patients with advanced gastric cancer: A multicenter retrospective analysis

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Background: Nivolumab was established as one of the standard treatments for previously treated advanced gastric cancer (AGC) and pembrolizumab was recommended to microsatellite instability-high (MSI-H) solid tumor. Recent studies have shown that immune-related adverse events (irAEs) caused by immune checkpoint inhibitors were associated with clinical benefit in patients with melanoma and lung cancer. In AGC patients, there have been few reports about the correlation between irAEs and the efficacy of immune checkpoint inhibitors. The aim of this study was to evaluate the frequency of irAEs with immune checkpoint inhibitors (nivolumab or pembrolizumab) and the correlation between irAEs and efficacy in AGC patients treated with immune checkpoint inhibitors.

Methods: We performed a multicenter retrospective analysis, which included 108 patients with AGC who received nivolumab or pembrolizumab monotherapy between October 2017 and February 2020. The frequency of irAEs and its treatment outcome (response rate, progression-free survival (PFS) and overall survival (OS)) were evaluated. We divided the patients into two groups based on the occurrence of irAEs; those with irAEs (irAEs group) or those without (non-irAEs group) and performed 6-week landmark analysis including only patients manifesting disease control or those who were alive at 42 days after initiation of immune checkpoint inhibitors treatment for PFS (n=51) or OS (n=86) to evaluate the association of irAEs with survival considering lead-time bias.

Results: The characteristics of 108 patients in this analysis were as follows: median age (range), 68 (36-87); male/female, 68/40; ECOG PS 0-1/≥2, 68/40; number of metastatic sites 1/≥2, 41/67; treatment line 3/≥4, 78/30; MSI (n=15) stable/high 13/2. Median treatment cycle of immune checkpoint inhibitors treatment was 3 (range 1-41). The overall response in 79 patients with target lesions was 5.0% (4/79), the disease control rate was 31.6% (25/79) and the median PFS and OS were 1.3 months (95%CI, 0.3-7.4) and 3.6months (95%CI, 0.6-21.6), respectively. IrAEs were observed in 13 patients (12.0%), including grade 4 pneumonitis, grade 2 or 3 adrenal insufficiency, and grade 2 hypothyroidism, encephalitis, colitis/diarrhea, and immune thrombocytopenia. The most frequent irAEs was hypothyroidism (n=4). Median time to onset of irAEs was 1.2 (range 0.2-10.5) months. Four patients were treated with systemic corticosteroid therapy, and 11 patients were relieved, but two patients were treatment related death including pneumonitis and myocarditis. Six patients received Nivolumab retreatment. In 6-week landmark analysis, the median PFS and OS were 7.3 months (95%CI, 3.0-17.2) and 12.2 months (95% CI, 5.2-28.4) in irAEs groups, and 2.5 months (95%CI, 1.0-5.9) and 3.9 months (95%CI, 1.8-9.8) in the non-irAEs group, respectively. There was a significant difference in the PFS (p=0.004) and OS (p=0.03). In addition, 4-week and 8-week landmark analyses were performed. Similarly, the irAEs group showed significantly longer OS and PFS than the non-irAEs group.

Conclusion: Nivolumab or pembrolizumab was effective and well-tolerated even in clinical practice. Development of irAEs was associated with survival outcome with immune checkpoint inhibitors treatment in patients with AGC.

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P-179 The screening and consensus based on practices and evidence (SCOPE) survey: Results of a real-world survey on metastatic colorectal practice patterns

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Background: The SCOPE project was undertaken to gather insights on current clinical practices for patients with pretreated metastatic colorectal cancer (mCRC) across different countries. The aim was to better understand medical and social factors influencing practice patterns, identify drivers for treatment choices, and describe any geographic disparities.

Methods: The survey was developed by an expert panel of gastrointestinal oncologists from different countries. It analyzed general practice patterns and treatment decisions in different third- and fourth-line patient scenarios. Participants had to routinely manage patients with mCRC. Data were collected at in-person meetings.

Results: As of 17/01/2020, 706 caregivers from 12 countries had participated, including healthcare practitioners, pharmacists, and nurses. The final analysis included only participants who provided input on patient treatment scenarios (n=629). The majority were medical oncologists (72%), practiced in university hospitals (43%), saw 10—19 patients/month (27%), and were 35—55 years old (53%). Systematic KRAS and NRAS testing was undertaken by 90% of participants; 80% requested BRAF tests, except Central/Eastern Europe, where 69% requested testing. MSI and HER2 were not systematically tested and there was more regional variation. Treatment goals differed between the first and third lines. Prolongation of OS (44%) was the primary goal in the first line, while in the third line, quality of life (33%) was the primary goal, although participants also considered efficacy goals, such as prolonged OS (17%) and PFS (13%). The impact of tumor sidedness on first-line targeted therapy choice for patients with RAS wildtype varied widely across geographic regions; 70% of respondents in Central/Eastern Europe considered tumor sidedness, versus 46% in Western Europe. Most participants (89%) considered trifluridine-tipiracil an appropriate treatment choice for fit and active RAS/BRAF wild-type patients who had received first-line anti-EGFR and second-line anti-VEGF; this was driven by survival data and safety. For KRAS-mutated patients with comorbidities and previous tolerability issues, most participants (83%) did not consider oxaliplatin rechallenge a suitable third-line treatment, while trifluridine-tipiracil followed by regorafenib was considered the best treatment sequence by 50% of them. Generally, the preferred fourth-line treatment option after receiving trifluridine-tipiracil for KRAS-mutated patients with comorbidities and tolerability issues followed guideline recommendations, favoring regorafenib and clinical trial enrollment. Distance from hospital, ECOG, age, level of understanding of options and choices, and social activity levels tended to influence mode of administration choice (intravenous vs oral). Proximity to hospital, general condition, patients' treatment knowledge, age, and level of activity became more important in later lines of treatment; limited family support was mentioned by ≥30% of HCPs as the main driver for choosing only BSC in the fourth line.

Conclusion: The SCOPE project revealed that most countries systematically perform KRAS, NRAS, and BRAF testing. The impact of tumor sidedness on practice patterns varied widely, possibly due to drug availability and discrepancies between national guidelines. Trifluridine-tipiracil is considered an appropriate treatment in the third-line setting for patients with or without comorbidities. In later treatment lines, patient-centric factors have more influence on treatment decisions.

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P-180 Serum lipid levels and gastric cancer risk: A prospective case-control study

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Background: Serum lipid levels and its association with gastric cancer is controversial with inconsistent study results being reported. We aimed to further clarify the role of serum lipids level as a risk factor for gastric cancer risk.

Methods: A total of 434 consecutive patients pathologically diagnosed gastric cancer were prospectively enrolled between December 2013 to March 2017, and 3053 controls from Health Promotion Center who received health examination during the

same period were collected for this case-control study. All patients had measured laboratory data including total cholesterol, triglycerides, LDL cholesterol, HDL cholesterol, apolipoprotein B, and apolipoprotein A-I. A total of 434 consecutive patients pathologically diagnosed gastric cancer were prospectively enrolled between December 2013 to March 2017, and 3053 controls from Health Promotion Center who received health examination during the same period were collected for case-control. All patients had measured laboratory data including total cholesterol, triglycerides, LDL cholesterol, HDL cholesterol, apolipoprotein B, and apolipoprotein A-I.

Results: After adjusting for age and gender, lower HDL level (< 40 mg/dL, adjusted OR =1.629, 95% CI=1.252−2.119), higher LDL levels (LDL=100-129 mg/dL: adjusted OR=1.742; LDL=130-160: adjusted OR=1.857; LDL≥160: adjusted OR=1.663), and lower apolipoprotein A-I level (< 178 mg/dL, adjusted OR=1.795, 95% CI=1.190−2.710) were significantly associated with an increased risk of gastric cancer. After adjusting multivariate factors including age, gender, Helicobacter pylori infection, body mass index, smoking status, alcohol drinking status and family history of gastric cancer, higher LDL level (LDL=100-129 mg/dL: adjusted OR=1.655; LDL=130-160: adjusted OR=1.787) and lower apolipoprotein B (adjusted OR=1.381, 95% CI=1.034−1.848) were identified as significant factors for gastric cancer. In subgroup analysis of gastric cancer patients, triglyceride level was inversely correlated with advanced cancer stage and poor differentiation.

Conclusion: Low serum HDL level, high LDL level, low apolipoprotein A-I and lower apolipoprotein B level were significantly associated with increased risk of gastric cancer, and low triglyceride level was correlated with advanced cancer stage and poorer differentiation.

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P-181 Role of detection and quantification of plasma ctDNA RAS mutations by BEAMing digital PCR in patients with locally advanced and metastatic pancreatic cancer

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Background: Pancreatic ductal adenocarcinoma (PDAC) is associated with poor prognosis and high mortality worldwide. At the time of diagnosis 80% of cases are already locally advanced or metastatic. Despite the emergence of new therapies for the treatment of metastatic or locally advanced PDAC, reliable prognostic/predictive biomarkers are lacking. PDAC harbours mutations in the KRAS gene on exons 2 and 3, in 80-90% of patients. The aim of the present study was the detection and quantification of RAS mutations in the ct DNA (circulating tumour DNA) of patients with inoperable PDAC by BEAMing digital polymerase chain reaction (PCR) in order to (a) evaluate the correlation with tissue RAS mutation status in the tumour, (b) study the baseline prognostic significance, and (c) study the predictive significance of ctDNA RAS mutation kinetics for the prediction of response to systemic/neo-adjuvant therapy, in correlation with Ca 19-9 serum tumor marker and the CT scans response.

Methods: The plasma samples were collected at two time points, the first one at diagnosis, before chemotherapy and the second one 4-6 weeks later. BEAMing digital PCR technique (KRAS/NRAS profiling-Digital PCR-OncoBEAMTM RAS CRC kit-Sysmex Inostics) is characterized by high sensitivity and allows the quantification of plasma mutant alleles. The technique consists of 4 steps: pre-amplification, emulsion PCR, hybridization and flow cytometry. The determination of tissue KRAS profiling was performed by allele-specific RT-PCR (Cobas KRAS mutation test).

Results: Plasma samples from 23 patients were used for cell-free DNA (cfDNA) purification and cfDNA was further analyzed for 34 mutations in the KRAS and NRAS genes(exons 2,3,4) by BEAMing digital PCR. In 13 patients mutation was detected in exon 2 codon12 of KRAS gene (KR2-12), in 2 patients mutation was detected in KR2_12 and additionally, in exon 3 codon 61 of the NRAS gene (NR3_61) in one of them and in exon 2 codon 12 of NRAS in another patient. Tissue and plasma samples were analyzed for KRAS mutation for 11 patients. The concordance between plasma and tissue-based detection of KRAS mutations was high (9 out of 11 patients). In addition, 32 plasma samples from 16 patients have been analyzed for ctDNA RAS mutations. MAF values vary between 0,001-27,932% (MAF=RAS mutant alleles/RAS mutant+RAS wild-type alleles). Patient RAS Mutant allele fraction value (%) changed between the two time points (baseline and 4-6 weeks after). he number of mutant beads seems to have a prognostic role, as patients with a significantly high number of mutant beads tended to have a poor prognosis. At this point, MAF change has no significant correlation with CA19-9 change at the time points under study.

Conclusion: This work highlighted the potential role of liquid biopsies in the management of PDAC and, more specifically, yielded preliminary data on the role of RAS ctDNA profiling as a predictive and prognostic marker. Kinetics of the RAS mutational load during therapy and its prognostic or predictive value will be analyzed with further cohort expansion.

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P-182 Understanding biliary tumours: Survival outcomes and prognostic factors in a single center

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Background: Biliary tumours are a rare group of neoplasms, comprising

Methods: A descriptive retrospective analysis of all patients diagnosed with biliary tumours from 2013 to 2018 at our center was performed. Demographic, pathological, biochemical and survival data were reviewed. Statistical analysis was performed using SPPSS statistical software (V.25).

Results: 60 patients (pts) with a median age of 75 (IQR=53-97) years and median ECOG of 2 (IQR=0-4) at diagnosis, subdivided into 32(53%) men and 28(47%) women. Of these, 18 (30%) were diagnosed as GBC and 42 (70%) were cholangiocarcinomas; 12 (20%) iCC, 14 (23%) pCC and 16 (27%) dCC. At presentation, 2 (5%) were cholangiocarcinoma stage I, 4 (9%) stage II, 6 (14%) stage III and 30 (71%) stage IV. 5 (28%) were gallbladder adenocarcinomas stage I, 4 (22%) stage II and 9 (50%) stage IV. 27 (45%) cholangiocarcinomas and 9 (50%) GBC presented with hyperbilirubinemia with a median value of total bilirubin of 7 (IQR=1-21) mg/dL and 4 (IQR=1-14) mg/dL, respectively. Biliary stenting was performed in 25 (60%) for cholangiocarcinoma and in 6 (33%) for GBC. Regarding management, 29 (48%) pts received systemic chemotherapy, with adjuvant intent in 11 (37%) and palliative intent in 18 (72%) pts. The first-line regimen was gemcitabine plus platinum in 21 (72%) pts and gemcitabine plus capecitabine in 8 (32%) pts. Due to progression, 18 (78%) pts discontinued treatment. A total of 48 (80%) deaths occured, 25 (52%) in the cholangiocarcinoma group and 13(72%) in the GBC group. OS was 7 (IQR=1-83) months for cholangiocarcinoma and 11 (IQR=2-53) months for GBC. Stratifying by performance status, OS was 11 (IQR=1-26) months for ECOG 1 and 12 (IQR=1-35) months for ECOG 2 (p=0,013). Regarding location, OS was 3 (IQR=1-6) months for iCC, 7 (IQR=4-11) months for pCC, 7 (IQR=2-11) months for dCC and 11 (IQR=8-14) months for GBC (p=0,152). Concerning levels of bilirubin, OS was 9 (IQR=6-12) months for pts with hyperbilirubinemia and 3 (IQR=1-15) months for normal values (p=0,357). Pts needing biliary stenting had an OS of 7 (IQR=4-9) months comparing to an OS of 11 (IQR=5-17) months for the non-stenting group (p=0,018).

Conclusion: Despite the small population included, demographic, pathological, management and survival characteristics agreed with existing scientific evidence. Few studies managed to establish strong prognostic factors for biliary tumours. Our results validate performance status, bilirubin levels at presentation and need for biliary stenting as prognostic factors. Regarding hyperbilirubinemia, existing literature diverges as to whether it is a predictor of increased or decrease OS. This diverging evidence reinforces the need for multicentric collaborative studies in order to build stronger predictive models for this rare but lethal group of cancers.

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P-183 Inflammatory response prediction of systemic therapy outcome in metastatic colorectal cancer

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Background: Colorectal cancer (CRC) is a common cancer, both nationally and globally. Platelets had a proinflammatory action, recruiting neutrophils and macrophages, driving vessel-wall inflammation, and influencing lymphocyte function, NK cells, and B cells. Sizeable changes in the number and ratio of peripheral immune cells, including monocytes, lymphocytes, neutrophils, platelets, and tumor-educated platelets, have been observed, with both favorable and unfavorable consequences in solid tumors. Little is written about the predictive value of these inflammatory response changes for the metastatic colorectal cancer (MCRC) treatment outcome and their clinical

application. The objective of this study was to assess the prediction of peripheral inflammatory response indicators for the first-line systemic treatment response rate (RR) and progression-free survival (PFS) in MCRC.

Methods: A retrospective chart review at Princess Norah Oncology Center (PNOC) included histopathology-proven MCRC from January 2013 to December 2018. Younger patients (< 18 years), and cranial and immeasurable metastases were excluded. RR was assessed by the chi-square/Fisher-exact and Mann-Whitney tests, whereas PFS was assessed by the Kaplan-Meier survival curve. Peripheral blood Pre-cycle 1 and Cycle 3 counts were checked for neutrophils (N), lymphocytes (L), monocytes (M), platelets (P), and ratios (R) of N/L (NLR), M/L (MLR), P/L (PLR), and mean platelet volume (MPV). The counts were classified as high, low, or normal, as per standard laboratory values.

Results: Of 337 identified cases, 102 cases were analyzed. The median age of the cases was 58 years, 52.9% were male, and 82.4% had a left-side primary tumor location. In all, 53% received chemotherapy (FOLFOX, CAPOX or FOLFIRI) with targeted agents, and 47% were treated with chemotherapy alone. The peripheral blood cell count for N, L, M, P, and MPV, Pre-cycle 1 and Cycle 3, were not predictive of RR; however, prior to Cycle 1 and Cycle 3, PFS was better for normal platelet count vs high count (P = .009 and P = .038 respectively). A low PLR was associated with a better PFS than high PLR values (P = .036 and P = .029, respectively). Prior to Cycle 1, PFS was significantly higher with low vs high NLR (P = .038). There was no prediction for MLR.

Conclusion: Platelet peripheral blood count, PLR, and NLR could be predictors of systemic therapy outcomes in MCRC. Having a high platelet count prior to MCRC systemic therapy might be a biomarker for antiplatelet agent benefits and warrants investigation in clinical trials.

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P-184 A phase 2 trial of trastuzumab deruxtecan (T-DXd, DS-8201) in patients with HER2-positive, unresectable or metastatic gastric or gastroesophageal junction adenocarcinoma

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Background: Despite attempts, no HER2-directed therapies have been approved for gastric or gastroesophageal junction (GEJ) cancer after disease progression on trastuzumab. Trastuzumab deruxtecan (T-DXd, DS-8201) is a novel HER2-targeted antibody-drug conjugate composed of a humanized monoclonal antibody specifically targeting HER2, a cleavable tetrapeptide-based linker (drug-to-antibody ratio of ≈8), and a potent topoisomerase I inhibitor payload. In a phase 1 study, T-DXd (5.4 or 6.4 mg/kg) showed promising antitumor activity in a variety of tumor types, including a confirmed objective response rate (ORR) of 43% among patients with extensively pretreated HER2-positive gastric cancer (Shitara et al. Lancet Oncol. 2019;20(6):827-836). Here we describe the phase 2 trial evaluating the efficacy and safety of T-DXd in patients with HER2-positive gastric/GEJ cancer previously treated with trastuzumab (NCT04014075).

Trial design: This is a single-arm, open-label, multicenter, phase 2 study in patients with centrally confirmed, HER2-positive (immunohistochemistry [IHC] 3+ or IHC 2+/in situ hybridization positive), unresectable or metastatic gastric/GEJ cancer that progressed on or after first-line therapy with a trastuzumab-containing regimen. HER2 status will be confirmed by a fresh biopsy before enrollment. Patients are excluded if they received anticancer therapy after a first-line trastuzumab-containing regimen. The study began in August 2019 and will recruit ≈ 72 patients from 25 to 30 sites in North America and Europe. T-DXd at 6.4 mg/kg will be administered intravenously once every 3 weeks until disease progression. The primary efficacy endpoint is confirmed ORR by independent central review (ICR) using RECIST v1.1 criteria. Secondary endpoints include duration of response and progression-free survival by ICR and investigator assessment, ORR by investigator assessment, and overall survival. Additional endpoints include safety, disease control rate, and pharmacokinetic analyses. Health-related quality of life will also be measured. This abstract was accepted and previously presented at the 2020 Gastrointestinal Cancers Symposium. Additional sites have been opened in North America and Europe.

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P-185 Dietary factors in gastrointestinal cancers: A hospital-based case-control study

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Background: Cancer is the sixth leading cause of death worldwide. However, thirty-five percent of all cancer deaths may be preventable by alterations in diet. Relationship between diet and cancer has for long been an intriguing research domain but even within the hospital and population-based cancer registry networks, such relationships have only been minimally investigated due to problems with measurement of diet, long latent periods between diet and development of cancers, and complex natural history of the disease itself.

Methods: A case-control study, comprised of 171 cases, 151 healthy controls, and 167 hospital controls, was conducted in Regional Cancer Centre, Jammu under the Hospital-Based Cancer Registry project to evaluate the relationship between diet and selected GI cancers (oesophageal, stomach and colorectal) using a food frequency questionnaire method.

Results: The individual analysis of food groups showed 2-3 times increased risk of gastrointestinal cancers with hot and salted tea. Alcohol consumption [OR 2.30(1.32-4)] and smoking [OR (2.77(1.77-4.33)] emerged as risk factors when comparisons were made with healthy controls among in whom freshly prepared food had a significant protective effect [OR 0.57(0.37-0.88)]. Sweet tea showed a protective effect both in hospital and healthy controls (OR 0.33 and 0.26, respectively). Intake of NSAIDS and other medications was also associated with a significantly higher risk of GI cancers (3-4 times). Consumption of dietary fibres from cereals (wheat, pulses, and rice) showed a reduced risk of gastrointestinal cancers which were significant in the case of wheat and pulses but insignificant in the case of rice. Consumption of non-vegetarian food was higher among cases across all the various non-vegetarian food groups. Consumption of green—leafy vegetables, non-green leafy vegetables, raw vegetables, and fruit showed significant protective effect ranging from 20-80% while the intake of non-vegetarian foods showed significantly higher odds of GI cancers in both hospital and healthy controls (OR ranging from 2.37- 13.4). The odds of patients with GI cancer having consumed chutneys, fruit and vegetable pickles were significantly higher in comparison to healthy controls (OR 2.06, 1.97 and 3.61 respectively) while consumption of dairy products showed some protective effect. Low and medium intake of mixed spices inclusive of curcumin indicated protection from GI cancers (OR 0.13, 0.39, respectively) while intake of red chilies was associated with 2-30 times significantly higher odds of GI cancers.

Conclusion: We have been able to generate evidence of a relationship between certain locally consumed food items and cancers, in spite of the existence of potential confounding variables that were beyond our control. With these results, we intend to further refine the tools used in this study and plan more extensive and robust studies within the ambit of the Hospital-Based Registry Project in GMC Jammu. We also intend to use this understanding to plan IEC activities for the local population and share our understanding with other stakeholders in the state for policy planning in the context of the expansion of Cancer Control activities in Jammu and Kashmir.

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P-186 Introduction of DYPD screening and its impact on treatment decisions: One centre's experience

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Background: Fluorouracil (5FU) forms the backbone of treatment for colorectal cancer (CRC). Dehydropyrimidine-dehydrogenase (DPD) breakdowns 5FU into inactive metabolites. Patients with genetic polymorphisms in the DYPD gene are at risk of DPD deficiency and subsequent severe toxicity. There are a number of commercially available tests for DPD deficiency but these are not standardly used in the UK. We introduced routine screening for DPD deficiency in Sheffield and present our results.

Methods: From December 2018 to Feb 2020 all new patients with CRC were offered DYPD testing. For 3 months we used multi-parametric testing (Biomnis) phenotyping and genotyping but switched to a genotyping only method (Oxford Biomarkers) due to practicalities. We reviewed the outcomes of patients with DPD deficiency using case notes, chemotherapy prescribing software and online results system to collect details of toxicities. These results were entered onto an excel spreadsheet with both quantitative and qualitative information gathered.

Results: Over 14 months we tested 506 patients. During the first 3 months, 3/55 were found to have abnormal phenotyping suggestive of DPD deficiency. 11/451 tested with the Oxford biomarkers had a DYPD polymorphism. 10/11 had one of the 4 most common variants (5 = rs67376798, 5= rs3918290) and one rare variant was found

(257C>T; Pro86Leu. T). In total 14/506 (2.7%) patients had some form of DPD deficiency. 8/14 patients went on to have 5FU-based chemotherapy. Five opted against treatment and one patient was found to have an alternative diagnosis and treated with non-5FU-based chemotherapy. Both commercial testing kits give recommendations for treatment dosing. Of the 8 we treated: one received the recommended reduced dose, 5 commenced at a lower dose (due to safety concerns) and 2 patients received higher than the recommended dose (due to result not being available before treatment started). One of these 2 patients, was de-escalated to the recommended dose. The other had retrospective testing at representation with metastases; she had previously received 1 cycle of adjuvant treatment at 100% of the dose (before routine testing), developed significant toxicity and stopped after cycle 1. 5/8 (62%) patients who received 5FU-based chemotherapy experienced grade 3 toxicities leading to cessation of 5FU-based chemo in 4/5 of the cases. The most common toxicities were: diarrhoea (5 patients — 1 grade 3 toxicity), nausea (5 patients — no grade 3 toxicities), fatigue (4 patients — all grade 1) and mucositis (3 patients — 1 grade 3 toxicity).

Conclusion: Treatment decisions in colorectal oncology are often complex and it is clear that the presence of DPD deficiency adds further complexity to these situations. Patients with DPD deficiency can experience severe side effects when treated with fluoropyrimidines and clinicians fear harming patients. Decisions based on results showing DPD deficiency varied widely in our centre and we clearly need structured guidelines on how these results should influence our treatment decisions so as not to harm patients, but also to not exclude patients from potentially beneficial treatments.

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P-187 Impact on survival of local complications in pancreatic cancer: Experience at the Ramón y Cajal University Hospital (HURyC)

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Background: Pancreatic cancer (PC) has a high mortality rate, even in operated patients, with a 5-year survival of 30% without lymph node disease and 10% with it. Approximately, 55% of patients present with jaundice, which can increase to up to 70% in PC located in the head of the pancreas.

Methods: We present a retrospective study of 171 patients diagnosed with PC between 2014 and 2018 at HURyC. Data were collected from patients who started with metastatic or unresectable locally advanced disease, studying the incidence, management and time of onset of biliary tract obstructions, cholangitis and duodenal obstructions at diagnosis and during the first line (1L) treatment. We evaluated if progression-free survival (PFS) and overall survival (OS) are affected by the presence of any of these complications. In addition, we evaluated if the time between diagnosis until the start of 1L and the time the patient remains admitted (both globally and during the 1L) impacts on survival.

Results: The median age was 71 years (30-91) and 124 patients (72.51%) were metastatic at diagnosis. The incidence of complications was 68.42% (117), and 81 occurred at diagnosis (47.37%). Of the patients who received 1L treatment (142, 83.04%), 96 presented some complication (67.61%). There were 90 biliary complications (52.63%), with endoscopic retrograde cholangiopancreatography being the most used method (55, 60.44%); and 29 duodenal obstructions (17.16%). There was no difference in PFS between patients who presented with complications and those who did not (Hazard ratio (HR) 0.82, 95% CI 0.6-1.12, p=0.21). There were no differences in OS between initiating the treatment more than 30 days from the diagnosis compared with initiating it before (HR 0.73, 95% CI 0.51-1.06, p=0.096), nor in PFS (HR 0.9, 95% CI 0.63-1.29, p=0.58). There was no detriment in PFS in patients admitted during the 1L compared with those who were not; HR 0.84, 95% CI 0.58-1.2, p=0.34 for income during 30 days or less and HR 1.62, 95% CI 0.86-3.07, p=0.051 for income more than 30 days. Those patients never admitted had similar OS than those admitted between 1 and 45 days (HR 0.62, 95% CI 0.31-1.22, p=0.17) and those admitted for more than 45 days (HR 0.95, 95% CI 0.45-2, p=0.9). However, those patients who were admitted less than 45 days had worse OS than those admitted for more than 45 days (HR 0.65, 95% CI 0.44-0.97, p=0.033).

Conclusion: Local complications in PC are frequent and often the first symptom of the disease, but do not seem to impact on patient survival. Timing to start the treatment, 30 days or less, does not impact on OS. Being admitted during 1L does not reduce PFS, regardless of whether the time was greater or less than 30 days (probably biased by only having 11 patients with prolonged income). Interestingly, those patients with prolonged admissions during the evolution of the disease had similar OS than those who had never entered and better OS than those with admissions less than 45 days. This may suggest that patients enter more times because they live longer, and not the other way around.

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P-188 Safety and efficacy of first-line gemcitabine plus nab-paclitaxel for elderly metastatic pancreatic cancer patients

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Background: Pancreatic cancer (PC) is a disease of the elderly since the average age at diagnosis is 71 years. Gemcitabine plus nab-paclitaxel (Gem-Nab) is a standard first-line treatment for metastatic pancreatic cancer (mPC), but few data about the safety and efficacy of this regimen are available for the elderly population, which is often underrepresented in randomized clinical trials.

Methods: We retrospectively collected data from 156 PC patients aged ≥65 years treated with Gem-Nab at 4 Italian Institutions. Patients were stratified according to age: <70 (group 1) and ≥70 (group 2) years. The primary endpoint was the evaluation of the rates of treatment-related adverse events as well as the assessment of the activity and efficacy of Gem-Nab in the two age groups. Toxicity was graded according to CTCAE version 4.0. Activity was evaluated according to RECIST version 1.1. Estimations of time-to-event curves were generated by the Kaplan-Meier method. Chi-square test was used to compare incidence of toxicities and their grades between the two age groups. Correlations between baseline characteristics with both progression-free (PFS) and overall (OS) survival were also performed and a multivariate analysis was carried out using a stepwise Cox proportional hazards regression model.

Results: Median age was 71 years (range: 65-87), with 65 patients in group 1 and 91 in group 2. After a median follow-up of 26.5 months, patients in the two groups received a median of 4 and 5 cycles of treatment, respectively. In the entire cohort, hematologic toxicities occurred as follows: anemia (84.2%; grade 3-4: 12.6%), neutropenia (73.6%; grade 3-4: 41.4%) and thrombocytopenia (53.9%; grade 3-4: 2.6%). Most common non-hematologic events were neurotoxicity (49.3%; grade 3-4: 7.2%), nausea (44.1%; grade 3-4: 2.0%) and diarrhea (43.4%; grade 3-4: 3.3%). When the two age groups were compared, a significantly higher rate of grade 3-4 diarrhea (7.9% vs. 0%; p=0.02) and all grade neurotoxicity (61.9% vs. 40.4%; p=0.02) was reported in younger patients, possibly reflecting the higher median dose intensity of nab-paclitaxel received in group 1 (86.7 vs. 78.1 mg/sqm/week; p=0.04). Median PFS and OS were 6.2 (95% CI: 5.5-7.1) and 10.8 (95% CI: 8.9-11.8) months, respectively, in the whole population. Neither PFS (HR 1.16, 95% CI: 0.82-1.63; p=0.41) nor OS (HR 1.00, 95% CI: 0.69-1.46; p=0.99) differed between group 1 and 2. Partial response was achieved in 40 patients (25.6%, 95% CI: 18.7%-32.6%); response rate was similar in the two analyzed age groups (20.0% vs. 29.7%, respectively; p=0.12). At multivariate analysis, only baseline CA19.9 was confirmed as an independent predictor of OS, whereas the starting dose of Gem-Nab did not significantly influence PFS and OS.

Conclusion: Gem-Nab is safe and effective in geriatric patients with mPC. Dose modifications in patients aged ≥70 years may be required to optimize the benefit-to-risk ratio of the combination. However, dose adjustments do not seem to affect overall treatment efficacy. Validation of these findings in prospective, dedicated studies is warranted.

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P-189 Role of radiomics in clinical prognostication and prediction of survival among a cohort of metastatic intrahepatic cholangiocarcinoma

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Background: Cholangiocarcinoma is the second most belligerent primary tumor of the liver after hepatocellular carcinoma (HCC). The promising field of radiomics has offered substantial potential in prognosis evaluation and prediction of treatment response.

Methods: A predictive model was developed from a training cohort comprising 36 intrahepatic cholangiocarcinoma (IHCC) patients diagnosed between January 2010 and June 2014, from a single institutional retrospective database of patients confirmed histopathologically as IHCC and presenting as mass forming IHCC on radiological imaging. As per NCCN guidelines these patients received upfront gemcitabine-based chemotherapy. All patients underwent computed tomography (CT) examination protocol in a dual-energy 128 slice CT scanner and feature extraction was done using late arterial-phase image of contrast-enhanced CT images. One radiologist having 6 years of experience manually drew the region of interest on the tumor for purposes of segmentation and textural analysis. The segmented tumor was validated independently by two radiologists having 30 years of experience each. A total of 851 radiomics features were extracted from the available imaging using slicer 3D software and Pyradiomics. Feature selection (20 for response assessment and 21 for predicting overall survival [OS]) was done by taking the union of the features which had Pearson correlation $>$0.6. Models were trained to predict the response using leave one out cross-validation and different algorithms. Combined with clinical characteristics (serum biomarkers of CEA, AFP and CA 19-9) a radiomics nomogram was developed to discriminate responders and non-responders and to predict the OS.

Results: Using radiomics features alone and nearest shrunken centroids (pam) model in prediction of response we were able to achieve an accuracy of 81%, Kappa score(0.60) and the area under the curve (AUC) was 0.79. Using the bagged CART (tree bag) k to determine OS, we found the mean absolute error (MAE) was 103 days where MAE using the mean value of OS (358 days) was 184 days.

Conclusion: This study was an effort to bridge the unmet need for translational predictive biomarkers in IHCC patients based on prognostic value. This was the first study done to use radiomics features to serve as tools for deciphering prognostication and predicting recurrence in metastatic IHCC.

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P-190 A retrospective study of regorafenib versus trifluridine/tipiracil efficacy in chemorefractory metastatic colorectal cancer patients: Multi-institution real-life clinical data

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Background: Colorectal cancer (CRC) is a leading cause of cancer-related death worldwide. Over the last two decades, median overall survival (OS) for patients with metastatic CRC (mCRC) has increased to roughly 30 months due to the improvements in the number and efficacy of systemic therapies. Recently, two novel drugs have been approved for the treatment of chemorefractory mCRC patients such as regorafenib and trifluridine/tipiracil (TAS-102). However, despite their clinical approval, it still remains unclear which of these two drugs should be used first because of a lack of head-to-head randomized trials.

Methods: We have compared retrospectively the safety and efficacy between regorafenib and Tas-102 in patients with mCRC refractory to standard therapies who had access to both drugs in three different institutions between January 2018 to February 2020, in a clinical practice setting. The progression-free survival (PFS) and overall survival (OS) were compared using a log-rank test with 95% confidence intervals (95% CIs).

Results: One hundred and twenty-two patients with mCRC treated with regorafenib or TAS102, in a clinical practice setting, after failure of standard therapies including fluoropyrimidine, oxaliplatin, irinotecan, anti-VEGF therapy and anti-EGFR agents in RAS wild type were included in the analysis. In particular, 63 patients were treated for the first time (primary treatment) with regorafenib whereas 59 patients were treated with TAS-102. Of these patients, 53 switched to crossover treatment. In particular, 23 went on to receive TAS-102 and 30 went on to receive regorafenib as secondary treatment. Baseline demographic and disease characteristics were well balanced between the two groups in terms of the primary treatment. No patient had a complete response (CR) or partial response (PR). The median OS1 was 6.8 months for regorafenib and 8.4 months for TAS-102 and the corresponding values after crossover, defined as OS2, were 4.5 and 5.1 months, respectively. Median PFS1 defined as the interval from the first administration of the primary treatment to the first radiological progression or death from any cause, whichever come first, was 2.6 months for regorafenib and 3.1 months for TAS-102. However, median PFS2 defined as the interval from the initiation of secondary treatment to secondary progression, for those who had undertaken crossover treatments after first progression was 2.0 months for regorafenib and 2.6 months for TAS-102. No unexpected adverse events (AEs) were found compared with previously reported data. Moreover, AEs were tolerable even after the crossover.

Conclusion: No significant difference between regorafenib and TAS-102 sequence treatments was observed in patients with mCRC. Further analyses are ongoing to potentially identify a biomarker or a clinical sub-group to distinguish the two drugs.

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P-191 Optimal age to start screening for colorectal cancer in average-risk adults: 50 or 45 years old?

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Background: According to current international colorectal cancer (CRC) screening guidelines, regular screening for CRC should start at 50 years of age in average-risk adults. Recent epidemiological data show constantly increasing incidence of CRC in patients of younger age, which led the American Cancer Society to issue a guideline suggesting that regular screening for colorectal cancer should start at 45 years of age (American Cancer Society, qualified recommendation). The aim of the study was to compare the screening colonoscopy findings in 3 different age groups (40-44, 45-49, 50-54 years) in a Greek referral centre.

Methods: We retrospectively studied people of 40 to 54 years old who underwent colonoscopy screening with high definition endoscopes during the last 2 years in the Endoscopy Unit of the Gastroenterology Department. High-risk patients were excluded (polyposis syndrome, positive family history for colon cancer, inflammatory bowel disease), as well as symptomatic patients (with the exception of irritable bowel syndrome symptoms) and those with inadequate bowel preparation. Sex, age, endoscopic findings (cancer, advanced adenomas, any adenomas, serrated polyps, localization) and bowel preparation (Boston Bowel Preparation Scale) were registered.

Results: From November 2016 to December 2019 a total of 411 patients (282 female) were assessed: 40 patients aged 40-44, 110 patients aged 45-49, and 261 patients aged 50-54. The bowel preparation was characterized as excellent in 63.3% of the patients, average in 5,1% and good in the remaining. The overall adenoma detection percentage was 18.6% for men and 6.5% for women. No cancers were reported. The percentage of findings for every age group respectively were for advanced adenomas 0%, 6.5% and 1.9%, for any adenomas 2.5%, 13% and 10.4%, for serrated polyps 0%, 1.9% and 2.7% and for isolated right colon adenomas 0%, 23.1% and 33.3%. No significant statistical difference was found in the comparison between age groups. Logistic regression analysis showed that adenomas were 3.3 times more frequent in male patients.

Conclusion: No statistically significant differences were detected, especially between age groups 45-49 and 50-54 years. Notably, there was a very low percentage of findings in the age group 40-44 years. Interestingly female patients were more prone to undergo screening colonoscopy, while they presented with a 70% lower probability of finding adenomas compared to male patients. The topic of starting regular screening colonoscopy at 45 years of age remains under discussion.

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P-192 ART SCORE in determining the feasibility of TACE in hepatocarcinoma

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Background: Hepatocarcinoma is the sixth most common cancer worldwide, but it is considered the second most lethal cancer; only supplanted by lung cancer. The most used prognostic tool in hepatocarcinoma is the Barcelona Clinic Liver Cancer (BCLC) which divides patients considering the tumor size, liver function, performance status, and venous involvement. BCLC A and B patients could be submitted to transarterial chemoembolization (TACE) but the number of procedures acceptable is not known.

Methods: We studied 76 patients treated in an oncologic center from January 1993 until December 2019, with the diagnosis of hepatocarcinoma, who had at least 1 treatment with TACE. The evaluation of the response was made by RECIST 1.1. Patients were divided into low ART Score (between 0-1.5) and high ART Score (higher than 2.5). The objective was to evaluate the applicability of Assessment for Retreatment with TACE (ART Score) to determine the number of procedures acceptable for a patient with hepatocarcinoma.

Results: A total of 76 patients were included: 92.1% were males, with a median age at diagnosis of 70 years old (min 39, max 88). The main etiologic factor was alcohol. The tumor was unifocal in 58% of the patients; 82% of the patients were Child-Pugh A and 18% were Child-Pugh B. After the first TACE, 72% of the patients had a low ART Score and 28% had a high ART Score. The patients with lower scores who performed a second TACE obtained better PFS and OS compared to patients that did not perform TACE and patients with a higher score. The patients with lower scores who performed a third TACE obtained, once more, better PFS and OS. However, in this instance, patients with a high score who performed a TACE obtained a superior OS than patients who did not. When we analyzed the Art Score as survival predictor, we concluded that there is a tendency for statistical significance for lower scores being associated with a longer survival rate (HR: 0,6; IC 95% 0.3 — 1.0, p=0,06).

Conclusion: Low Art Score is associated with longer OS. A second TACE is beneficial in patients with low Art Score, and a third TACE is beneficial in all patients.

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P-193 Safety, tolerability, and efficacy of total neoadjuvant therapy for adult patients with locally advanced high-risk rectal adenocarcinoma: Retrospective real-world data from South India

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Background: The treatment of locally advanced rectal adenocarcinoma with preoperative long-course chemoradiation (LCCRT) followed by TME has been established as a standard by prior studies. However, improvements in survival have plateaued due to an inability to deliver the planned adjuvant therapy. Total neoadjuvant therapy (TNT) has been developed to address this issue, but better patient selection is required to identify those who derive the most benefit from TNT. This retrospective cohort study evaluated TNT among a population of high-risk rectal adenocarcinoma patients selected on the basis of poor pathological and radiological parameters in a resource-limited setting.

Methods: This retrospective, single-institution cohort study was done among adult (age> 16 years) patients with locally advanced non-metastatic rectal adenocarcinoma (LARC) treated at a referral hospital in Southern India from January 2018 to January 2019. LARC was defined as the presence of either T3-4 node-negative or node-positive, biopsy-proven adenocarcinoma with distal margin <15cm from the anal verge as determined by MRI. Patients were assigned to TNT protocol based on the presence of high-risk features, such as signet-ring cell histology, absence of circumferential resection margin(CRM), imaging features of vascular invasion(EMVI), pelvic sidewall/N2 disease. Patients who were assigned to TNT protocol were planned for six cycles of chemotherapy followed by LCCRT and surgery after a 12-week break. They were followed up to assess a) feasibility-measured as proportion who completed the planned treatment, b) safety-measured by treatment-related death, grade 3 or 4 adverse event (CTCAE version5), and c) efficacy-measured by the proportion of patients who achieved complete response; a composite of clinical and pathological complete response. PFS and OS data were collected with data censoring on 10 February 2020 for this analysis.

Results: Our cohort consisted of 59 relatively young (41.7±13.4 years) patients with multiple poor prognostic factors such as >T3 tumor size in 56 (94.9%), N2 nodes in 39 (66.1%), signet-ring cell histology in 17 (28.8%), low-rectal involvement in 31 (52.5%), absent CRM in 50 (84.7%), EMVI in 35 (59.3%)and lateral pelvic nodes in 20 (33.9%). Ten patients (16.9%) did not complete the treatment protocol with 3 (5%) not receiving radiotherapy due to disease progression on chemotherapy, 9 (15.2%) not undergoing surgery due to inoperable disease on pre-operative assessment and 1 (1.6%) death due to post-chemotherapy neutropenic sepsis. Thirty-six patients (61%) completed the planned 6 cycles of chemotherapy. The most commonly used regimen was FOLFOX in 45 patients (73%) with the remaining receiving CAPEOX (11.5%), FOLFIRINOX (8.2%) and 5FUFA (3.3%).Toxicities of grade 3 or higher were: diarrhea (32.2%), proctitis (23.7%), neutropenia (13.5%), thrombocytopenia (5%). Among the 41 patients who underwent surgery 4 (9.7%) had postoperative leak and 2 (4.8%) had postoperative sepsis. Mean postoperative hospital stay was 11±4 days. Complete response was seen in 27 patients (45.8 %) among whom seven had a complete clinical response and avoided surgery. The median duration of follow up was 20 months with mean PFS of 26 months and 22 months (P=0.25) for those with and without CR, respectively. The median PFS and OS durations were not achieved at the time of censoring.

Conclusion: TNT was feasible and effective in a population with high-risk rectal adenocarcinoma, producing high complete response rates with frequent and manageable toxicity, but one treatment-related death.

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P-194 The use of cytoreduction and HIPEC in the treatment of peritoneal carcinomatosis: The experience in Ramón y Cajal University Hospital

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Background: The use of surgical cytoreduction, combined or not with HIPEC, has been used as a locoregional approach to treat peritoneal carcinomatosis, with good outcomes in terms of overall survival, although the studies are very heterogeneous. However, the data of phase III trials published so far have not shown benefits in common outcomes such as overall survival (OS) or progression-free survival (PFS) rates. The aim of this study was to show our experience with this approach.

Methods: We conducted a retrospective descriptive study including all patients diagnosed with peritoneal carcinomatosis from intraabdominal primary tumors and treated with surgical cytoreduction plus HIPEC in our centre.

Results: A total of 41 patients were treated with cytoreduction and HIPEC between 2015 and 2019 in our centre were included. 20 (49%) patients had tumors from colorectal origin, 16 (39%) had mucinous neoplasms of the appendix, and 4 (10%) were from gastric origin. The most frequently used chemotherapy scheme was intraperitoneal oxaliplatin with intravenous 5-FU simultaneously administered. All our patients underwent complete resection, with a median PCI of 6 (range 0-35). 85% of the population developed post-surgical complications, with 65% of infections and 40% of hematological toxicity. 24% of patients with a complication required admission to the ICU and the mean time of hospital stay was 31 days (IQR 14-44 days). 44% and 54% of the patients received neoadjuvant or adjuvant treatment, respectively. 58% of the patients progressed, the peritoneum being the most frequent relapse site (45%). Of these patients, 29% underwent surgical resection of the relapse site. With a median follow up of 23 months, median overall survival of this population was 48 months. The median OS for the colorectal origin patients was 48 months, the gastric origin patients had a 6 median OS, while median OS has not been reached in patients with mucinous neoplasms of the appendix. The median progression-free survival (PFS) of the total population was 13 months. In the colorectal group, the median PFS was 12 months, the gastric group was 1 month, while it has not been reached in the mucinous neoplasms group.

Conclusion: The use of surgical cytoreduction and HIPEC is feasible in neoplasms with a good prognosis such as mucinous neoplasms of the appendix and colorectal adenocarcinomas, while in other tumors with poorer prognosis such as gastric tumors this approach should be adopted with caution.

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P-195 Treatment outcomes of trifluridine/tipiracil therapy in refractory metastatic colorectal cancer: A single-centre observational study

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Background: Treatment options for patients (pts) with metastatic colorectal cancer (mCRC) after progression to standard therapy are limited. Trifluridine/tipiracil (TAS-102) is an orally administered cytotoxic agent approved for the treatment of patients with refractory mCRC. Patients treated with TAS-102 derived a significant benefit in OS compared with placebo as demonstrated in two phase III trials (RESOURCE and TERRA). However, real-world data on the effectiveness of TAS-102 are sparse.

Methods: The aim of this observational study was to investigate the efficacy and safety of TAS-102. We included 72 pts (47 men, 25 women) who began treatment with TAS-102 between May 1st, 2018 and Dec 31st, 2019 in the University Hospital Centre Zagreb. Eligible pts had metastatic disease and were in good general condition (ECOG $\leq$1). Forty-three started irinotecan- and 29 pts oxaliplatin-based chemotherapy (CT) with a biological agent added according to RAS status in 53 pts. TAS-102 was introduced after progression to two standard treatment lines. Outcomes were measured as PFS in the 3rd line and overall duration of therapy (DoT). To further assess the potential influence of other variables, correlation with Spearman's rank test was used.

Results: PFS in the 3rd line was 2.4 months (95% CI 1.94-2.80) and DoT was 25.2 months (95% CI 21.59-34.64). DoT was signifantly correlated with PFS in the 3rd line (P=0.001) and no other significant correlation was found for age, performance status, RAS status, primary tumor sidedness, number of metastatic sites, liver metastases, CT, or biological agents received in the 2 previous treatment lines. The patients received a median of 3 cycles of TAS-102 and PFS rate at 12 weeks was 37.5%. One patient (1.4%) achieved a partial response and 14 (19.4%) achieved disease stabilization. Although there was a relatively high incidence of grade 1 and 2 neutropenia (38.9%), the incidence of grade 3 neutropenia (8.3%) was not high and only 1 case of febrile neutropenia was documented.

Conclusion: We aimed to investigate the outcomes and safety of TAS-102 treatment in a real-world setting. Our results, being comparable with previously reported studies, further demonstrate the clinical benefit of TAS-102 for refractory mCRC patients with manageable toxicities. Furthermore, the benefit was derived regardless of tumour characteristics or previous treatment received.

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P-196 CA 19-9 and CEA as markers of survival in rectal cancer

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Background: Carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9) are recognized biomarkers for disease monitoring in rectal cancer. The aim of the present study was to evaluate the value of pre-radiotherapy serum CA19-9 and CEA levels for the prediction of disease-specific survival (DSS) and overall survival (OS) in rectal cancer treated with curative intent.

Methods: A retrospective observational study of 268 patients with a diagnosis of rectal cancer treated with curative intent at the Department of Radiotherapy between 2013 to 2017 was conducted. The optimal CA19-9 cut-off values for the prediction of DSS and OS were identified by receiver operating characteristic (ROC) curve analysis according to the highest Youden index using MedCal software, version 19.1.7. The other data were analysed through IBM SPSS statistics software, version 26.0. Differences in DSS and OS rates stratified by CA19-9 and CEA levels were compared by using Kaplan–Meier and log-rank tests. Cox proportional hazards model was used to identify prognostic variables for DSS and OS.

Results: Patients were followed up for a mean time of 33 months (SD: 19.3), and the mean age at diagnosis was 63.9 years (SD: 11.96). According to ROC analysis, the optimal CA19-9 cut-off value for 5-year OS was 12 U/ml, with the highest Youden index (0.2545), a sensitivity of 54.90% and a specificity of 70.55% (area under the ROC curve [AUC], 0.652; 95% CI, 0.581-0.718; p= 0.001). The optimal CA19-9 cut-off value for 5-year DSS was 12, with the highest Youden index (0.3006), a sensitivity of 60% and a specificity of 70.06% (AUC, 0.685; 95% CI, 0.615-0.749; p= 0.0002). Thus, patients were divided into the high-CA19-9 group (n=71, 26.5%) and the low-CA19-9 group (n=126, 47%) based on the CA19-9 cut-off value of 12 U/ml. According to ROC analysis, the optimal CEA cut-off value for 5-year OS was 8.3 ng/ml, with the highest Youden index (0.1966), a sensitivity of 41.54% and a specificity of 78.12% (area under the ROC curve [AUC], 0.618; 95% CI, 0.555-0.677; p= 0.003). The optimal CEA cut-off value for 5-year DSS was 8.3 ng/ml, with the highest Youden index (0.1543), a sensitivity of 39.22% and a specificity of 76.21% (AUC, 0.587; 95% CI, 0.524-0.648; p= 0.049). Thus, patients were divided into the high-CEA group (n=69, 25.7%) and the low-CEA group (n=188, 70.1%) based on the CEA cut-off value of 8.3 ng/ml. The univariate analysis revealed that high CA19-9 level (p=0.001) and high CEA level (p=0.007), were the significant negative predictors of DSS. In OS, high CA19-9 level (p=0.002) and high CEA level (p=0.001), were the significant negative predictors. Multivariate analyses revealed that CA19-9 was an independent factor associated with DSS (hazard ratio [HR], 2.108; 95% CI, 1.040-4.273; p=0.039).

Conclusion: The results of this study showed that high levels of pre-radiotherapy serum CA19-9 (>12 U/ml) indicated a worse DSS for rectal cancer treated with curative intent.

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P-197 The prognostic role of body mass index on survival of non-metastatic colorectal cancer patients

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Background: The prognostic role of body mass index (BMI) in patients with colorectal cancer is not established clearly. This study aimed to determine the relationship between pre-treatment BMI and long-term outcomes in patients with colorectal cancer.

Methods: In this retrospective cohort of 1550 colorectal cancer patients from Omid and Emam Reza Hospitals of Mashhad, Iran, between 2002 and 2020, 920 patients with non-metastatic disease were identified. Multivariable logistic regression and Cox proportional hazard regressions were used to examine the difference in clinicopathologic and survival characteristics between BMI categories at presentation. The BMI ranges were then used to determine the different weight groups: underweight (BMI is less than 18.5); normal weight (BMI is 18.5 to 24.9); overweight (BMI is 25 to 29.9); and obese (BMI is 30 or more).

Results: Among 920 patients included in the study, there were 38.91% normal weight, 26.19% underweight, and 34.9% overweight/obese. With all stages combined together, the mean overall survival for underweight, normal weight, and overweight/obese patients was 108.2 $\pm$ 7.0, 124.0 $\pm$ 6.2, and 130.9 $\pm$ 4.5, respectively (P = .2) and the mean disease-free survival was 97.0 $\pm$ 6.5, 110.0 $\pm$ 5.6, and 113.7 $\pm$ 5.0, respectively (P = .3). There was a trend that overweight patients had better overall (HR = 1.14, P = .367) and disease-free survival than the underweight group (HR = 1.10, P = .883).

Conclusion: This was a large-scale, population-based study that provides data from real-world evidence outside of clinical trials, which is the main strength of the present study. However, the retrospective approach and possible biases due to the nature of these studies is the main limitation of the present study. Moreover, we only assessed the outcomes based on BMI of patients at their initial consultation visit; therefore, we could not predict how changes in BMI may influence the prognosis of patients. In conclusion, this study showed that there is no significant relationship between BMI and long-term outcomes in patients with colorectal cancer. However, there was a trend that overweight patients had better overall and disease-free survival than the underweight group, which may be the subject of future studies.

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P-198 The AST/ALT ratio predicts clinical outcome in pancreatic cancer patients treated with capecitabine and gemcitabine: A single institution experience in the west of Algeria

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Background: Combination chemotherapy with gemcitabine and capecitabine represents a valuable treatment option for patients with advanced pancreatic ductal adenocarcinoma (PDAC). However, biomarkers for disease outcome and treatment response are scarce. The serum transaminases AST and ALT are routinely measured laboratory markers in clinical practice for assessing liver function. Recently, studies have demonstrated that a high AST/ALT ratio is a marker of poor prognosis in cancer

patients. In the present study, we investigated the ratio (AST/ALT) for predicting treatment response and disease outcome in advanced PDAC patients treated with capecitabine and gemcitabine.

Methods: A retrospective analysis was performed at a single Algerian center between 2019 and 2020. A total of 41 patients treated with capecitabine and gemcitabine with available AST/ALT ratios measured on the day of treatment start were included in the analysis.

Results: After a median follow-up of 12 months, disease outcomes were significantly worse in patients with an elevated AST/ALT ratio defined by an empirical cut-off at the 75th percentile (> 1.23 units). In multivariable analysis, the prognostic association between a doubling of the AST/ALT ratio was associated with a 1.4-fold relative increase in the risk of progression or death (HR = 1.38; 95% CI, 1.06-1.80; P = .017).

Conclusion: In the present study, the pretreatment serum AST/ALT ratio was significantly associated with PFS and response rate in advanced PDAC patients treated with gemcitabine/capecitabine. These results suggest that the AST/ALT ratio might represent a novel and inexpensive marker for individual risk assessment in the treatment of PDAC.

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P-199 The prognostic and therapeutic impact of microsatellite instability in stage II colon cancer: Medical Oncology Service CHU Hassan II Fes

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Background: Colon cancer stage II is a very heterogeneous group in terms of anatomopathological prognosis. The determination of MSI status is useful to discuss the indication of adjuvant chemotherapy for a patient operated on for colon cancer stage II with poor prognostic factors.

Methods: This is a retrospective study including patients with stage II colon cancer, managed within the Medical Oncology service, over the period from January 2015 to June 2019. The objective of our study was to describe the epidemiological, clinicopathological and prognostic aspects of stage II CRCs in the Fez region, and report our experience in their therapeutic management.

Results: Sixty-one cases were identified. The average age of the patients was 56.4 years [25-73], with a peak incidence between 40 and 50 years. A slight female predominance was noted with a sex ratio M/F of 0.94. The tumor location was on the right side in 29.7%, 54.04% on the left side, and 16.1% in the transverse colon. All of our patients received surgical treatment and 40.5% of patients underwent hemicolectomy. In our series the determination of MSI status was as follows: 43.3% of patients had MSI status, 56.7% had a stable phenotype. The other anatomopathological prognostic factors were as followed: the diagnosis was revealed by an acute occlusive syndrome or colon perforation in 23.5%, the number of lymph nodes examined was insufficient in 13.7% of cases. Histologically, the well-differentiated type was found in 59.4%, followed by moderately differentiated adenocarcinomas in 27.02% of the cases. Concerning the TNM classification, parietal invasion (pt4) was found in 19.6%, the presence of vascular emboli in 18.4% of the cases and 13.5% had a peri-nervous sheathing. 67.5% of the patients were eligible for adjuvant chemotherapy. The chemotherapy used was a combination of oxaliplatin and 5FU in 55.1 while capecitabine as monotherapy was prescribed in 16.2% of cases. The patients were followed until a median follow-up 57 months. Survival was prolonged in MSI patients overall survival (OS) and SSR relapse-free survival was 42.6 months, 14 months for MSI tumors and 38 months and 11.6 months for those with MSS status, respectively. Chemotherapy was relatively well tolerated hematologically and digestively. The acute toxicities observed were essentially of grade 1 or 2. They mainly consisted of vomiting and diarrhea in 25% of the cases, peripheral neuropathy in 21.5%, and neutropenia in 8.5%.

Conclusion: Patients with colon cancer Stage II MSI without high-risk factors for recurrence have an excellent prognosis and the indication for adjuvant chemotherapy does not seem to be justified. The MSI phenotype of colon tumors is a prognostic molecular marker giving patients an advantage of survival compared to those with a stable MSS phenotype.

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P-200 Bone metastases from colorectal cancer correlate with biological characteristics of primary tumors: A retrospective analysis from a single institution

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Background: Bones are an uncommon site of metastases in colorectal cancer (CRC) patients. However, despite the high prevalence of metastatic CRC (mCRC) worldwide, biology of bone metastases (BM) remains unknown at present. Previous studies correlated the onset of BM to some clinicopathological features, including primary tumor site (rectum), tumor grade of differentiation (moderately or poorly differentiated) and male gender.

Methods: We retrospectively analyzed clinical data from mCRC patients treated at our Oncology Unit (2010-2019) to identify BM, focusing on clinical history (primary tumor site, RAS-BRAF mutational status, sites and number of metastases at baseline and during treatment), timing of onset of BM and overall survival (OS) from diagnosis of BM. The aim of our analysis was to find biological characteristics associated with the onset of BM in mCRC patients.

Results: 31 patients with BM from CRC have been analyzed, with a median age of 65 years and a male to female ratio of 2:1. Primary tumors were more frequently localized in the rectum (42%) and left colon (45%); all primary tumors were moderately/poorly differentiated and 20 (64%) were RAS mutant (mainly KRAS exon 2). No BRAF mutations were found. The spine was the main site of metastases (71%), followed by ribs (19%) and pelvis (13%). Median OS from diagnosis of BM was 6.7 months (range: 0.5 – 66.3), whilst time interval from diagnosis of CRC to onset of BM was 47 months (range: 0 – 191.5). Bones were the first metastatic site in 7 (23%) patients, and, interestingly, all of them had RAS mutant primary tumors. All 11 patients with RAS wild-type primary tumors have developed BM after progression to anti-EGFR therapies, and, of note, in 3 of them, mutation or amplification of KRAS gene was found in liquid biopsies performed at the time of diagnosis of bone metastases.

Conclusion: Our data suggest that BM from CRC has a distinct biological behavior, being more frequent in moderately/poorly differentiated, RAS mutant and left-sided/rectum adenocarcinomas, especially as the first metastatic site, or in patients who developed resistance to anti-EGFR therapies. Since this is a retrospective analysis of 31 patients, a larger population should be analyzed to confirm our hypothesis.

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P-201 Neoadjuvant hypofractionated intensity-modulated radiotherapy with a simultaneous integrated boost combined with capecitabine in locally advanced rectal cancer

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Background: Neoadjuvant chemoradiotherapy followed by total mesorectal excision is the standard treatment in locally advanced rectal cancer (LARC) (stages II T3/T4N0 y III T N1/N2). It aims at reducing the risk of distant recurrence while pelvic radiotherapy focuses on the prevention of local recurrence. The use of advanced techniques such as Intensity-Modulated Radiotherapy (IMRT) based on multileaf collimator (MLC) allows higher doses to be delivered to the tumor volume, taking into account the tolerance dose in the organs at risk. Our objectives were to report on early and late toxicity, evaluate complete pathological response (pCR) and reduce standard treatment time while maintaining clinical results.

Methods: Between April 2016 and December 2019, 112 patients with LARC, mean age 64 years, treated with neoadjuvant hypofractioned modulated intensity radiotherapy (IMRT) with simultaneous integrated boost (SIB), concomitant to capecitabine were retrospectively analyzed. The treatment dose was SIB 54 Gy (EQD2 57.1 Gy) and ganglion subsites 48 Gy (EQD2 49.6 Gy) in 20 daily fractions, utilizing volumetric arc therapy, a 10-MV photon beam and Linac Novalis IGRT-ExaTrac accelerator. Pelvic ganglion subsites were contoured according to RTOG (Radiation Therapy Oncology Group) criteria. OARs were drawn: small intestine, colon, bladder, femoral heads, erectile tissues, gynecological, gluteal skin, gluteus maximus and pelvic bones. The treatment planning was done in Eclipse V15.6. Early (≤3 m) and late (>3 m) toxicities grades were classified according to the CTCAE V.5.0.

Results: Of 112 LARC patients (48 women/64 men), mean follow up 16.6 m, 96% were histology adenocarcinoma, most frequent location: lower rectum level (48%), and

predominant stage according to AJCC IIA (34.8%). Early toxicity (112 pts): enteritis G1 49%, G2 27.7%, G3 4.5%; rectitis G1 51.8%, G2 29.5%, G3 0.9%; epidermitis G1 49.8%, G2 16.1%; abdominal pain 50%; proctorrhagia 52%; and dysuria in 30% of patients. Thirteen of 112 pts (11.6%) had treatment interruption, which was associated to toxicity in 6 pts. Late Toxicity (104 pts): enteritis G1 24%, G2 4.8%; rectitis G1 28.8%, G2 5.8%; anal incontinence 9.6%; dysuria 2.9%; proctorrhagia 13% of patients. Late toxicity was not reported in 51 pts (49.1%). Kaplan-Meier overall survival at 12 and 18 months was 92% and 85%, respectively. Of the 112 pts, 74 (66%) underwent surgery and 43/74 (46%) presented pCR. The anal sphincter was preserved in 46 (62%) of the operated patients. Mean time from completion of neoadjuvant until surgery was 4.1 [1,1-18] months. In 19 non-operated patients only biopsy was performed, and 15/19 (79%) got a negative result for malignancy. Average time from completion of neoadjuvant until biopsy was 5.3 [0.8-15.02] months.

Conclusion: Despite of the low mean follow-up, we suggest that IMRT with SIB concomitant to capecitabine is a safe option and effective, in terms of pCR for patients with LARC. The low acute toxicity without G3 or higher late toxicity at the last control, are encouraging to reduce the total treatment time from 5-6 weeks to 4 weeks, without increasing toxicity.

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P-202 Demographics and clinical characteristics of metastatic colorectal cancer patients treated with a biosimilar to bevacizumab

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Background: Bevacizumab-awwb, a biosimilar to bevacizumab, is the first therapeutic biosimilar to receive FDA approval for the treatment of metastatic colorectal cancer (mCRC) with intravenous 5-FU-based chemotherapy for first-line or second-line treatment, as well as for use in treatment regimens for first-line non-squamous non-small cell lung cancer, recurrent glioblastoma, metastatic renal cell carcinoma, and metastatic cervical cancer. The present real-world study evaluates initial experience with bevacizumab-awwb (launched 07/19/2019) in a post-approval community oncology setting.

Methods: This retrospective analysis identified patients with an mCRC diagnosis who initiated treatment with bevacizumab-awwb as first- or later-line treatment within existing medical records. Eligibility criteria included treatment with bevacizumab-awwb in any line following diagnosis of mCRC, patient age $\geq$18 years (y), and known Eastern Cooperative Oncology Group (ECOG) performance status score of 0-2 at mCRC diagnosis, or not indicated to have an ECOG score of $\geq$3. Patients were identified from the Concerto Health AI Definitive Oncology Dataset (a consolidated EMR database of CancerLinQ and Vector Oncology), representing geographically diverse practice locations within the US. The source practices are primarily community oncology practices, including rural and urban centers and members of different group purchasing organizations. Descriptive statistics were used to evaluate patient characteristics.

Results: Among patients who received bevacizumab-awwb, a total of 69 were eligible for the current analysis. Median age was 65.1 y at mCRC diagnosis and 55.1% (n=38) of patients were male. The majority of patients were White (66.7%, n=46) or African American (21.7%, n=15), and most had private insurance (78.3%, n=54). Two-thirds of patients (66.7%, n=46) were stage IV at diagnosis and 94.2% (n=65) of patients had adenocarcinoma histology. First use of bevacizumab-awwb in mCRC occurred within 20 days of product launch. Additionally, 75.4% (n=52) of patients had previously received brand bevacizumab. Over half of patients (52.2%, n=36) received bevacizumab-awwb in the second line. Most patients had ECOG score of 0 (34.8%, n=24) or 1 (30.4%, n=21). Most patients underwent biomarker testing (NRAS: 55.1%, n=38; KRAS: 66.7%, n=46; BRAF: 58.0%, n=40; MSI: 58.0%, n=40; MMR: 63.8%, n=44). The majority of NRAS-tested patients (92.1%, n=35) had negative NRAS status; 52.2% (n=24) of KRAS-tested patients had positive KRAS status, while 45.7% (n=21) had negative KRAS status. A majority of BRAF-tested patients (85.0%, n=34) had negative BRAF status; 90.0% (n=36) of MSI-tested patients had MSI stable (negative) status, while 5.0% (n=2) had MSI high (positive) status. Proportions of MMR tested patients with MMR proficiency vs. deficiency were 95.5% (n=42) vs. 4.5% (n=2).

Conclusion: This is the first study to report on the uptake and utilization of biosimilar bevacizumab in the real world. Results of this study depict the demographic and clinical characteristics of mCRC patients who received bevacizumab-awwb in a community oncology setting within the first few months of product launch. Uptake and utilization of bevacizumab-awwb will continue to be monitored for longer-term follow-up information.

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P-203 Restaging rectal cancer after neoadjuvant chemoradiation therapy: Is magnetic resonance imaging accurate enough?

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Background: Magnetic resonance imaging (MRI) is the gold standard for evaluating the extent of the disease in treatment-naïve rectal cancer patients. However, the role of MRI for restaging after neoadjuvant chemoradiation therapy (NACRT) is controversial. Retrospective data raised questions as to whether radical surgery could be avoided in patients with complete clinical response (cCR) by clinical examination, MRI and endoscopic evaluation. A major setback with MRI is its difficulty to differentiate small areas of residual tumor from fibrosis, and the tendency to overestimate the presence of tumor. We aim to evaluate the accuracy of MRI for restaging rectal cancer after NACRT compared with surgical restaging.

Methods: A retrospective single-center analysis of clinical stage II (T3-4N0) and III (T1-4N1-2) rectal cancer patients treated with NACRT followed by surgery from 2016 to 2018 was performed. Restaging MRI was performed before surgery if no contraindication was present. Concordance degree was assessed by Kendall's concordance coefficient test.

Results: In total, 137 patients were analyzed. Median age was 65 years (y) [interval 35-83], 56% were male, 66% had an ECOG performance status of 0 and 34% 1. The tumor was localized to the upper third of the rectum (10-15cm) in 37%, medium rectum (5-10cm) in 42% and lower third (< 0.001).

Conclusion: In our cohort of rectal cancer patients, MRI restaging could not accurately determine pathologic restaging. Overstaging was more frequent, especially regarding pathologic T, with fairer results in N restaging. The use of MRI to evaluate cCR and decide for a nonoperative approach is a controversial issue and prospective randomized trials are needed.

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P-204 C60 fullerene inhibits hepatocellular carcinoma development and metastasis: In vitro and in vivo studies

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Background: Hepatocellular carcinoma (HCC) has an extremely unfavorable prognosis and lack of effective medication therapy. The excessive production of reactive oxygen species is the main cause of its initiation and progression, therefore the use of antioxidants could be a promising treatment. Biocompatible pristine C 60 fullerenes are powerful antioxidants, non-toxic and able to be accumulated in the liver. Therefore, their effects on HepG2 cells and liver state on rat HCC models were aimed to be discovered.

Methods: HepG2 cells were incubated with pristine C 60 fullerene aqueous colloid solution (C 60 FAS; 0.15 mg/ml, diameter of nanoaggregates 1.2-100 nm); IC 50, cells redox state (malonic dialdehyde (MDA), protein carbonyls (PC), superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GP), glutathione-S-transferase (GST), reduced glutathione (GSH)), lactate dehydrogenase (LDH) and glucose-6-phosphate dehydrogenase (G6PD) activities, pan-cytokeratin, vimentin and p53 expression were assessed. HCC was initiated in male Wistar rats by N-diethylnitrosamine (200 mg/kg) injection with subsequent tumor promotion by CCl 4 (0.1 ml/100g) injections twice/week continuously. C 60 FAS was administered daily (0.25 mg/kg) starting in 15 weeks (confirmed liver cirrhosis) for 7 weeks. Liver injury was assessed according to 13-point score, Ischak score (fibrotic alterations), serum and redox markers. Median survival was estimated (in 53 weeks) and pancreatic metastasis if any were recorded.

Results: HepG2 studies demonstrated C 60 FAS IC 50 =108.2 μmol and inhibition of G6PD in a dose-dependent manner (down to fully blocking) with simultaneous LDH activity increase (up to 63%). HepG2 redox state was altered: SOD increase (up to 93%) and PC decrease (down to 95%) manifested the redox state recovery, but CAT, GST, GP and GSH downregulation (by 22-46%) and MDA elevation (up to 6.5 times) indicated the oxidative stress. C 60 FAS enhanced p53 expression and diminished vimentin and pan-cytoceratin one. Applying to HCC-animals, C 60 FAS improved their

survival similar to 5FU (31[35;30] and 30[32;7] weeks, respectively, compared to 17 [23;3] weeks). No atypical cells were observed in pancreas at the 22 nd and 53 rd week in C 60 FAS group but well-developed metastasis at the 53 rd week in 5FU group, whereas non-treated animals demonstrated neoplastic cells aggregates and well-developed tumors at the 22 nd week and massive metastasis at 53 rd one. Livers of HCC-rats demonstrated well-developed tumors (10[10;11] points) and established cirrhosis (5[5;5] points). Bilirubin, ALT, AST, GGT and all liver redox markers were elevated by 1,7-7,7 times, suggesting liver injury and oxidative stress. C 60 FAS attenuated liver injury (down to 7[5;10], no tumors) and fibrosis (down to 3.3 [2.3;3.9]), decreased liver enzymes (by 12-15% down to control) and normalized bilirubin and redox markers as well. 5FU was less effective: liver damage score corresponded to 10[5;12] (small single tumors) and fibrotic score – to 3[2.25;3.38], liver enzymes remained elevated, bilirubin decreased by 40% but remained higher than that of controls. Redox markers were also leveled.

Conclusion: C 60 FAS inhibits HepG2 cell growth and HCC development and metastasis, and improved animal survival. C 60 cytostatic action might be realized through enhancing p53 and blocking G6PD. Despite that C 60 affects HepG2 redox state it could improve that in malignant liver in vivo and normalizes liver serum markers as well. Thus, C 60 FAS could be considered as potential anti-HCC therapeutic.

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P-205 Could chemotherapy still be useful in hepatocarcinoma? Experience at a single institution in Lima, Peru

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Background: Hepatic cancer is a major health problem in the world, with almost one million people affected the last year. With oral multikinase inhibitors (TKI) and checkpoint inhibitors as first-line therapy for advanced diseases and without any chemotherapy protocol accepted as part of treatment in the principal international guidelines. In our institution, we recently gained access to TKIs, but until last year we only could treat patients diagnosed with hepatocarcinoma with chemotherapy. This study evaluated the survival rates from chemotherapy considering the lack of accessibility to TKIs in our country.

Methods: We reviewed the medical records from patients with hepatocarcinoma diagnosed between January 2011 and December 2017. In this descriptive analysis, we found 82 patients who received at least one line of chemotherapy at the Instituto Nacional de Enfermedades Neoplásicas in Lima-Perú.

Results: The median age was 39 years old (16-95), 26 patients were female (31.7%) and 56 male patients (68.3%). 58.5% (48) patients had hepatitis related to the disease, and received antiretroviral treatment, with 96% less death risk compared with patients without hepatitis. 53 patients (64.6%) received 1 type of chemotherapy. The median of follow up for overall survival was 10 months. The overall survival for 12, 36 and 60 months was 39.6%, 17%, and 14.6%, respectively. For progression-free survival, the median of follow up was 5 months. Considering the first line of treatment, 58.5% received 5-FU-based chemotherapy, 30,5% received Adriamicyn and 9.8% gemcitabine-based chemotherapy without statistical differences in progression-free survival.

Conclusion: We could identify that some of our patients with advanced or metastatic hepatocarcinoma could achieve unexpected overall survival and progression-free survival rates, with a median of 10 months of overall survival and 5 months for progression-free survival. We need future studies evaluating molecular features in our patients that could explain these results and may increase the possibilities of enlarging treatment.

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P-206 Prognosis of patients presenting as carcinoma of unknown primary and effectiveness of acute oncology service: A single institution experience

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Background: Carcinoma of unknown primary represents a heterogeneous group of patients who would often present in the acute setting with advanced cancer and in a poor state of general health, and as such, carries a poor prognosis. In 2010, the National Institute of Health and Clinical Excellence produced a guidance document mandating all acute trusts to formulate an acute oncology service and a CUP MDT to systematically assess and manage these patients for optimal outcomes.

Methods: Consecutive patients discussed in the MUO/CUP MDT as part of the UGI cancer MDT at HUTH NHS Trust between September 2018 and October 2019 were identified from the Somerset cancer database for these analyses. The demographic and clinical details were identified from the electronic patient records. Local ethics approvals were obtained prior to data collection and analysis. Data were collected in an Excel database and statistical analyses were performed within Excel and SPSS software.

Results: A total of 110 patients were identified during this period, including 60 women and 50 men. Age ranged from 25-94 years. Overall, 47 referrals were from acute medical wards, 12 patients were directly referred to the MDT by GP, and 21 referrals came from other site-specific MDTs. Of 47 patients, 45 were referred to the AOS within 7 days of admission, and all 45 patients were reviewed within 3 days of referral. In all, 43 patients had a WHO PS of 0-1. A total of 20 patients had solitary organ involvement, 13 had 2 organs involved (oligo/pauci metastases), and the rest had multiple organ involvement. Imaging identified a primary site in 12 patients; imaging, histology, and immunohistochemistry suggested benign disease in 16 patients; 35 patients had a primary site suggested on immunohistochemistry; and 47 patients had a diagnosis of CUP. Overall, 33 patients had adeno/poorly differentiated carcinoma with immunohistochemistry suggestive of OG/HPB origin and 12 had hematological malignancies. Of patients with solitary organ/site involvement, 12 had radical therapy, 38 had palliative chemo or radiotherapy or both, and 60 patients had supportive care alone. Of the 47 CUP patients, 32 had supportive care, 14 had palliative oncological interventions, and 1 had radical therapy. The median OS of treated CUP patients was 10.7 months (95% CI, 6.4-15.1), and for untreated patients, 1.24 months (95% CI, 0.8-1.7). Patients who had a primary site identified and treated accordingly had a mean OS of 15.43 months (95% CI, 12.6-18.3).

Conclusion: Our data show that it is vitally important to assess patients with MUO/CUP at an early stage, and to identify patients who will not benefit from any therapy and should be offered appropriate supportive and end-of-life care. It is also important to identify patients with good PS and offer appropriate oncological interventions, as the prognosis for such CUP patients is comparable with patients with metastatic disease from known primary sites. Hence, a dedicated CUP/AO service is a cost-effective and efficient way of managing these patients.

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P-207 Impact of renal function on CAPOX / FOLFOX adjuvant chemotherapy in colon cancer

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Background: Results from the IDEA collaboration study indicated that the efficacy of CAPOX was better than that of FOLFOX as adjuvant chemotherapy in patients with stage III colon cancer. Although dose adjustment of capecitabine was required depending on renal function, the results from this study did not mention renal function. Here, we investigated the impact of renal function on CAPOX and FOLFOX adjuvant chemotherapy in colon cancer.

Methods: We retrospectively reviewed the medical records of patients with stage III colon cancer who received adjuvant CAPOX/FOLFOX following R0 resection in our hospital between January 2011 and December 2018. Patients were divided into 3 groups based on creatinine clearance (Ccr) calculated by the Cockcroft-Gault equation: Ccr $\geq$ 80 ml/min were included in Group A, Ccr 50-80 ml/min were included in Group B, and Ccr 30-50 ml/min were included in Group C. We compared the relative dose intensity (RDI), 3-year disease-free survival (3y-DFS) and 5-year overall survival (5y-OS) between patients who received CAPOX and FOLFOX in each group. Furthermore, we compared 3y-DFS between patients who received CAPOX and FOLFOX by tumor stage in Group A and Group B (the number of patients in Group C was too small to compare).

Results: A total of 91 patients were analyzed. Patients who received CAPOX and FOLFOX were 51 and 40, respectively. Median age was 63 and 65 years, males accounted for 55% and 54%, 61% and 48% were low-risk stage (T1-3, N1 tumor), and 39% and 52% were high-risk stage (T4, N2 tumor), respectively. Patients who received CAPOX/FOLFOX were 20 (39%)/15 (37%) in Group A, 29 (57%)/21 (53%) in Group B, and 2 (4%)/4 (10%) in Group C, respectively. In Group A, the RDI of capecitabine/oxaliplatine and fluorouracil/oxaliplatin was 76.8%/80.6%, and 70.1%/69.4%, respectively. The 3y-DFS and 5y-OS rates for CAPOX/FOLFOX were 75%/100% (p=0.022), and 94.4%/93.3% (p=0.803), respectively. In Group B, the RDI of capecitabine/oxaliplatine and fluorouracil/oxaliplatin was 80%/84.7%, and 78.5%/79.5%, respectively. The 3y-DFS and 5y-OS rates for CAPOX/FOLFOX were 72.4%/61.9%

(p=0.576), and 95.7%/76.2% (p=0.025), respectively. In Group C, the RDI of capecitabine/oxaliplatine and fluorouracil/oxaliplatin was 87.1%/65.8%, and 87.3%/81.6%, respectively. The 3y-DFS and 5y-OS rates for CAPOX/FOLFOX were 0%/50% (p=0.774), and 50%/100% (p=0.090), respectively. In patients with low-risk tumors, the 3y-DFS rates of CAPOX/FOLFOX in Group A and Group B was 100%/100%, and 73.3%/80% (p=0.821), respectively. In patients with high-risk tumors, the 3y-DFS rates of CAPOX/FOLFOX in Group A and Group B was 58.3%/100% (p=0.025), and 57.1%/40% (p=0.675), respectively.

Conclusion: CAPOX was poorer than FOLFOX regarding DFS and OS in patients with poor renal function. However, CAPOX tended to be better than FOLFOX in patients with Ccr of 50-80 ml/min. In patients with Ccr $\geq$ 80 ml/min, FOLFOX was significantly associated with better DFS than CAPOX, especially in high-risk tumors. This may indicate that the prescribed dose of capecitabine was not sufficient for the patients with good renal function.

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P-208 Is there a role for adjuvant chemotherapy in ypN0 disease rectal cancer patients?

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Background: Several studies attempted to identify prognostic factors to predict long-term outcomes and support adjuvant chemotherapy (ACh) after neoadjuvant chemoradiation (NACRT) in rectal cancer. Currently, there is no definitive evidence that ACh is able to improve disease-free survival (DFS). We aimed to evaluate the impact of ACh in DFS in pathological node-negative (ypN0) rectal cancer patients.

Methods: We conducted a retrospective single-center analysis of stage II and III rectal cancer patients treated with NACRT followed by surgery from 2016 to 2018 who achieved ypN0. We defined DFS as the time from surgery until disease recurrence/distant metastases. Analysis at 3 years (y) was performed.

Results: In total, 119 ypN0 patients were analyzed. Median age was 66y [interval 35-83], 59% were male, 66% had an ECOG PS of 0 and 34% 1. The tumor was localized to the upper-third of the rectum in 37%, medium in 42% and lower-third in 21%. Adenocarcinoma histology was well differentiated in 80%, moderately in 17% and poorly in 3%. Stage III disease was observed in 84% and stage II in 16%. All patients underwent NACRT (84% 5-fluorouracil infusion and 16% capecitabine for 5 weeks (w)). Long-course radiotherapy was administered in all patients. Pre-treatment CEA was elevated in 24%. Median time between NA treatment completion and surgery was 12w [5-19]. In 68% of patients, $\geq$12 lymph nodes were surgically resected. Pathologic complete response (pCR) was achieved in 45%, a tumor regression score was 1 in 8%, 2 in 45% and 3 in 2%. In total, 63% underwent ACh (87% 5-fluorouracil infusion and 13% capecitabine). Median follow-up was 32 months. Disease recurrence was detected in 13%. Those who underwent ACh were younger (median 64y vs median 70y, p=0.005), surgically removed more lymph nodes ($\geq$12 47% vs 27%, p=0.02), had more ECOG PS 0 (76% vs 50%, p=0.004), more moderately/poorly-differentiated histology (24% vs 14%, p=0.03) and less pCR (33% vs 64%, p=0.001). Patients who underwent ACh had a DFS at 3y of 85% vs 74% in the surveillance group (p=0.501). In univariate analysis, ACh did not impact on DFS at 3y along with ECOG PS, gender, histology, NACRT regimen, MRI restaging, time between NACRT completion and surgery, removed lymph nodes, pathologic T status, and pCR. Patients >65y (p=0.04), elevated pre-treatment CEA (p< 0.001), and pathologic regression score of 3 (p=0.008) negatively impacted on DFS at 3y. In multivariate analysis, only elevated pre-treatment CEA (HR 12.9 [CI 95% 4.0-41.8], p< 0.001) and pathologic regression score 3 (HR 8.8 [CI 95% 1.6-48.7], p=0.013) had a negative impact in DFS at 3y.

Conclusion: In our cohort of ypN0 patients, there was no impact from ACh in DFS at 3y, regardless of ypT status. Although pCR is a parameter for treatment success, our study suggests no impact on relapse. In this cohort, elevated pre-treatment CEA and pathological NACRT non-response increased the risk of recurrence, perhaps identifying a high-risk group of patients.

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P-209 Multicenter real life experience of biological agents in patients with metastatic colorectal cancer

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Background: To investigate therapeutic approaches and the effect of waiting time for molecular test results in clinical daily practice on the treatment decision in patients with metastatic colorectal cancer (mCRC).

Methods: As of January 2018, the first 25 patients admitted to each institution participating in the study and with at least 3 months follow-up were included in the study. Data of 282 patients from 11 centers were analyzed retrospectively.

Results: Fifty-eight percent (n = 164) of the patients included in the study were male and 42% (n = 118) were female. The median age of patients at the time of metastasis was 60 (16-90 years). Seventy-five percent of the patients were metastatic at diagnosis, and 25.0% developed metastases afterwards. Localization was specified in 269 patients; 73.2%, 23.0% and 3.7% in the left colon, right colon and transverse colon, respectively. While the frequency of RAS wild-type in patients was 49.3%, the frequency of BRAF mutation was 3.5% and MSI-High in 3.5% of the patients. Regardless of treatment regimen, 53.5% of the patients received chemotherapy + anti-VEGF, 35.3% received chemotherapy + anti-EGFR therapy and 11.2% received chemotherapy alone. Of the patients with right colon tumors; 78.5% received chemotherapy + anti-VEGF, 14.3% chemotherapy + anti-EGFR, and 7.2% chemotherapy alone. The frequency in patients with left colon tumor was 45.9%, 42.6% and 11.5%, respectively. In RAS wild-type patients with left tumors, median PFS was 10.8, 13.8 and 6.9 months in patients treated with chemotherapy + anti-VEGF, chemotherapy + anti-EGFR, and chemotherapy alone, respectively (P = 0.119). While 80.2% of patients with RAS wild-type and left colon tumor received chemotherapy + anti-EGFR, 14.3% received chemotherapy + anti-VEGF, and 5.5% chemotherapy alone. In patients with RAS wild-type and right colon tumor, the frequency of chemotherapy + anti-EGFR was 33.3% and chemotherapy + anti-VEGF was 66.7%. The median time to the start of biological therapy was 14 days.

In 15.2 % of patients, the time to start biological treatment was longer than 30 days, and 15.6% of the patients had not received any biological treatment.

Conclusion: Biological therapy was started in the first 30 days in 69.1% of the patients. Since biological treatment was added to chemotherapy at the second cycle of treatment in the vast majority of patients, we did not observe PFS differences between groups according to the timing of biological treatment.

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P-210 The outcomes and toxicity of FOLFIRINOX treatment in a cohort of patients with incurable pancreatic cancer treated in a single centre in Northern Ireland

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Background: The ACCORD 11 trial demonstrated the superiority of FOLFIRINOX over Gemcitabine monotherapy in patients with metastatic pancreatic cancer, with minimal co-morbidities and an ECOG performance status of 0 or 1. This regimen also has increased toxicity, particularly neutropenia and diarrhoea. We report the outcomes and toxicity of FOLFIRINOX treatment in a 'real world' cohort of sequential patients with incurable pancreatic cancer treated in a single centre.

Methods: Patients who received FOLFIRINOX (Irinotecan 180mg/m^2, Oxaliplatin 80mg/m^2, Folinic acid 200mg/m^2 and 5FU infusion 2400mg/m^2 over 46 hours) for advanced pancreatic cancer between 2010 and 2019 in the Northern Ireland Cancer Centre, were identified from the oncology information system. GCSF prophylaxis was not routinely used. Data was extracted from standard electronic patient records and the ARIA prescribing system. Information on the patient's treatment toxicity profile, dose interruptions, cycles of FOLFIRINOX received, response to treatment and admissions to hospital were collected during this period. Survival was calculated using the Kaplan Meier method using Statplus software.

Results: Seventy-seven patients who had received FOLFIRINOX chemotherapy between January 2010 and December 2019 for pancreatic cancer were reviewed. Forty of these patients had locally-advanced pancreatic cancer and thirty-seven patients had metastatic disease. There were 45 males and 32 females, and the median age was 61. 53/77 (69%) were ECOG performance status 0 and 24/77 (31%) were ECOG PS 1. 57 patients (74%) experienced at least one grade three/four toxicity with 37% of

patients having had one grade three/four toxicity, 21% had two, 28% had three, 11% had four and 3% had five. The most common grade 3/4 toxicity was neutropenia (65% of patients experienced this). 55/77 patients had a dose reduction and 33% had more than one dose modification.

65% of patients had at least one hospital admission during treatment (50/77), and 38% of patients having more than one admission (19/50). The median length of hospital stay was five days and the longest length of hospital stay was forty-two days. 81% (63/77) had at least one cycle of chemotherapy deferred with 47.5% (30/63) of these patients having one cycle deferred, 16% (10/63) having two cycles deferred, 24% having three/four deferrals (15/63) and 12.5% having five/six deferrals (8/63). The median number of cycles received was ten.

The disease control rate (CR/PR and SD) was 70% (54/77) and one patient had a CR. 12% of patients had radiological PD as best response and 18% progressed clinically or wished to discontinue chemotherapy prior to first planned interval CT scan. The median OS for the metastatic pancreatic patient group was 10.0 months (95% CI 8.2 - 13.3 months) and the median OS for the locally —advanced pancreatic patient group was 12 months (95% CI 9.9 — 15.5 months).

Conclusion: This study demonstrates the 'real life' activity of FOLFIRINOX approaches that were observed in the ACCORD 11 trial in incurable pancreatic cancer. Given the high toxicity rates and incidence of hospital admissions, we recommend the use of the modified FOLFIRINOX regimen (irinotecan 150mg/m^2) in patients receiving palliative treatment with this regimen for pancreatic cancer.

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P-211 Prognostic value of interleukin-6 in colon cancer patients: A prospective study in 60 Tunisian patients

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Background: Interleukin-6 (IL-6) is a pro-inflammatory cytokine that has been reported to have an important role in cancer development and progression. High serum levels of IL-6 have also suggested poor prognosis in a variety of cancers such as multiple myeloma, ovarian cancer, prostate cancer and colon cancer. The aim of this study was to assess the prognostic value of serum levels of IL-6 in Tunisian patients with colon cancer.

Methods: We conducted a research on a cohort of 60 patients with colon cancer. Blood samples were collected to measure circulating levels of IL-6 with a solid-phase technique using chemiluminescence enzyme immunoassay (Immulite 1000, Simens, USA). We followed patients for a mean time of 30 months. We analyzed data with SPSS 21th version.

Results: Mean age of the patients at diagnosis was 57 ± 13 years old. Male/female ratio was 1.5. Forty percent of the patients had metastatic disease at diagnosis, 36% had stage III, 22% had stage II and 2% had stage I disease.

Serum levels of IL-6 were higher in metastatic patients (25 ±26 pg/ml vs 8 ±9 pg/ml in non-metastatic patients, p-value= 0.003). Patients with node involvement had also higher levels of IL-6 than those with negative nodes (18 ± 23 pg/ml versus 9±8 pg/ml, p=0.04).

Patients with T4 tumors had higher levels of IL-6 but the difference was not statistically different (16 ±17pg/ml versus 14± 22pg/ml,p=0.6).

Patients with mutant RAS gene had also higher levels of IL-6 (20± 5 pg/ml versus 18 ±7 pg/ml in patients with wild type RAS tumors), but the difference was not statistically significant (p=0.8).

We did not find a statistical difference in IL-6 levels according to gender nor to patients' ages.

Survival analysis using Cox regression model indicated that, after a mean follow-up of 30 months, patients with high levels of IL-6 had a higher risk of death of 5% (95%CI: 2 — 6.3%) compared to patients with low IL-6 levels (p=0.001).

Conclusion: Our findings highlight the prognostic value of serum levels of IL-6 in patients with colon cancer. Patients with stage III and IV disease had significantly higher levels of IL-6. More studies investigating the role of this biomarker as a targeted therapy should be conducted in this subgroup of patients. This may represent an additional therapeutic option especially for metastatic patients.

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P-212 Factors affecting median PFS in patients with advanced, non-resectable well differentiated pancreatic neuroendocrine tumors treated initially with octreotide LAR - real world data

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Background: Somatostatin analogues (SSA) are widely used in the treatment of patients with functioning and non-functioning well-differentiated neuroendocrine tumors (NET). The antiproliferative activity of SSA in NETs has been confirmed in two randomized placebo-controlled trials. The PROMID trial was the study assessing the effect of octreotide LAR on the control of tumor growth in patients with metastatic, well-differentiated mostly G1 midgut NETs, but not pancreatic NET. The Clarinet trial evaluated the effect of another analogue of SST - lanreotide autogel (AG) 120mg sc in patients with metastatic, well- or moderately differentiated, non-functional enteropancreatic NETs including also pancreatic NET G1/G2 (Ki-67 index < 10%), nonfunctioning, SSTR-positive There are only a few retrospectives study evaluated the efficacy of octreotide LAR 30mg in pan NET.

Methods: Retrospectively analyzed 57 patients with pancreatic NETG1/G2, treated as the first line with Octreotide LAR 30mg with overexpression of SST receptors, seen in somatostatin receptor imaging (SRI): WB-SPECT/CT utilized 99mTc-[HYNIC, Tyr3] octreotide [TOC] (Tektrotyd®, National Centre for Nuclear Research-Polatom, Poland) or PET/CT with 68Ga DOTATATE. The patients were assessed for clinical responses by physical examination every 4 weeks and by completing a self-assessment questionnaire (EORTC, QLQ-C30, and GI-NET21) before and then every 3 months. The evaluation of objective response in each case was utilized by multiphase structural imaging (CT/MRI), based on RECIST 1.0 performed at 3 months after the start of therapy and then 6 months intervals during the first 2 years of follow-up, after that annually. The primary objective of the study was to investigate the efficacy of Sandostatin LAR 30mg im every 28 days based on median PFS. Furthermore, the analysis of PFS using parameters that might influence the response to SSA was investigated using the Kaplan—Meier estimator. Parameters such as age, gender, sporadic vs. genetics, proliferation index (as measured by MIB1/Ki-67 staining), locally advanced, or metastatic, PS WHO, prior pancreatic surgery with intention to treat (ITT), secretory or non-functional tumors, liver involvement (bulky or non-bulky disease), bone metastases, and elevation of Chromogranin A (CgA) at the baseline more or less than 5 times upper level were considered.

Results: Initially, 36 of 57 patients had liver involvement. NETG1 22 (38.6%), G2 35 (61.4%). There were 40 (70%) subjects with sporadic NET and 17 (30%) with MEN1 (15) and VHL (2). Functioning tumours were diagnosed in 15 (26.3%). Median PFS 14.4 months (6.0-38.4 95%CI). Significant differences in PFS noted between sporadic vs. genetics (p=0.01), NETG1 vs. NETG2 in sporadic (p=0.02), also clinical-stage CS I-III vs. IV; (p< 0.001). In univariate analysis the PS WHO2, NETG2, sporadic subgroup, CS IV, liver involvement ≥25% significantly increased risk of progression. In the multivariable model G1 vs. G2, (HR: 6.93; p=0.018) and CS I-III vs. CS IV, HR: 3.11; p=0.04) were independent factors of decrease PFS.

Conclusion: Octreotide LAR shows his antiproliferative activity in pNET. Prolongate PFS was found in G1, but no bulky liver disease; in cases with a genetic mutation, compared to sporadic pNET. The favorable PFS was noted in those with initial PS WHO 0 and those with only locally advanced disease.

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P-213 Role of reactive oxygen species, IL-6 and KRAS mutation in rectal adenocarcinoma

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Background: Colorectal cancer is the fourth most commonly diagnosed cancer. KRAS mutation is a well-established biomarker in targeted therapy of this pathology. Therefore, this study aimed to establish a relationship between reactive oxygen species (ROS), IL-6 and KRAS mutation in the context of carcinogenesis in rectal cancer.

Methods: Thirty-two patients diagnosed with metastatic rectal adenocarcinoma who underwent systemic therapy were included in the study. Two blood samples were obtained in dynamics during treatment (at the beginning and at restaging) to determine serum levels of the biochemical parameters of the oxidative stress (malondialdehyde, ceruloplasmin) and IL-6. KRAS mutation testing was performed as part of a next-generation sequencing panel. Patients who had a partial or complete response were deemed treatment responders and the others were deemed resistant.

Results: Increased values of IL-6 from the beginning of treatment were associated with a high tumor burden (mean value 42.19 pg/mL vs. normal range 0-12.7 pg/mL) and decreased until the end of it (mean value 40.13 pg/mL). The significant oxidative stress generated by rectal cancer cells was sustained by the increased mean value of malondialdehyde (10.8 µmol/100 ml vs. normal limit 2 µmol/100 ml) and ceruloplasmin (124 UI vs. normal range 80-120 UI) measured at the beginning of the treatment. The mean value of the last evaluation of IL-6, malondialdehyde, and ceruloplasmin showed significant differences between treatment responders versus those with resistance ($p< 0.05$). Regarding the second determination, there was an important relationship between IL-6 and both malondialdehyde (Pearson correlation coefficient=0.702, $p< 0.01$) and ceruloplasmin (Pearson correlation coefficient=0.678, $p< 0.01$). KRAS mutation was detected in 37.5% of the patients and its wild-type status correlated with malondialdehyde and IL-6 (Pearson correlation coefficient=0.515, respectively 0.498, $p=0.01$).

Conclusion: There is a strong and statistically significant correlation between malondialdehyde, ceruloplasmin, IL-6, and KRAS mutation status. ROS and IL-6 act as signaling molecules and potential target molecules in rectal cancer.

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P-214 A single-centre experience of adjuvant oxaliplatin based chemotherapy in elderly stage II-III colorectal cancer patients

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Background: The MOSAIC trial showed the benefit of adding oxaliplatin to fluorouracil plus leucovorin with a 78.2% 3-year survival, however, patients > 75 years old were not included. The SCOT trial found that 3 months of treatment with oxaliplatin-containing chemotherapy was not inferior to 6 months, with a 3-year disease free survival of 76.6% and 77.1% respectively. There is a paucity of published data for adjuvant doublet chemotherapy within elderly (>70 years old) colorectal patients. We aimed to assess whether 3 months of adjuvant doublet chemotherapy in elderly patients with stage II-III colorectal cancer is tolerated.

Methods: Retrospective data was collected on all patients > 70 years old receiving adjuvant chemotherapy for stage II and III colorectal cancer at a single centre between Jan 2014 and Dec 2017.

Results: 108 patients were identified, 63 receiving doublet chemotherapy (FOLFOX and CAPOX) and 45 receiving single-agent chemotherapy (Capecitabine or modified de Gramont). The median age was 74 (70-84) and 78 (73-89) in the doublet and single chemotherapy group respectively. Overall, 60% of patients were male and had ECOG performance status 0-2. At time of data analysis 95 patients had at least 36 months follow up. 60% of patients commenced on doublet chemotherapy completed at least 3 months of treatment. A further 20% completed 3 months of treatment once switched to single-agent chemotherapy. 14% of patients experienced dose delays and 54% had at least one drug dose reduced. Compared with the single-agent chemotherapy cohort, 27% experienced dose delays, 20% received dose reductions during treatment and 82% completed at least 3 months of treatment. 24% of patients receiving doublet chemotherapy were admitted to the hospital within 30 days of chemotherapy, compared to 11% in the single-agent group. The most common side effects leading to hospitalization were infection (6%) (6 patients, only one of which was neutropenic), diarrhoea (4%), thrombosis (3%) or secondary to needing blood products (2%). One patient (2%) died due to a cerebrovascular event. The 3-year disease-free survival was 89% in the doublet chemotherapy group, which includes patients who switched to single-agent part-way through treatment and 79% in the single-agent chemotherapy group.

Conclusion: Adjuvant chemotherapy with FOLFOX or CAPOX is feasible in selected fit elderly patients with excellent 3-year disease-free survival. However, care is required as there is a high risk of hospital admission due to toxicity. Single-agent capecitabine should be discussed and considered as an alternative.

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P-215 phase 2 HEPANOVA study of tumor treating fields (TTFields, 150 kHz) concomitant with sorafenib in advanced hepatocellular carcinoma (HCC): Interim safety analysis

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Background: Tumor Treating Fields (TTFields) is an anti-mitotic, regional treatment modality, utilizing low intensity alternating electric fields delivered non-invasively to the tumor using a portable medical device. TTFields, which are FDA-approved for the treatment of glioblastoma and malignant pleural mesothelioma, is being investigated in several tumor types including hepatocellular carcinoma (HCC). Most HCC patients are not amenable to curative therapies and are treated with systemic chemotherapy following the failure of local treatment options. Sorafenib, an oral multikinase inhibitor, is approved for patients with advanced HCC; however, survival benefit is limited. The effectiveness and safety of TTFields 150 hKz alone and in combination with sorafenib has been demonstrated in HCC preclinical models. The HEPANOVA phase II trial (NCT03606590) is a prospective, single-arm study investigating the safety and efficacy of TTFields as a treatment option for advanced HCC concomitant with sorafenib in 25 patients. We present the interim safety data on the HEPANOVA trial.

Methods: Incidence and severity of adverse events of the first nine patients who have been enrolled in the HEPANOVA phase II trial were analyzed based on the MedDRA body system (system organ class) and preferred terms.

Results: The median age was 70 (range 63-85), all the patients were male, 3 (33.3%) patients had an ECOG score of 0. The median number of prior treatments was 2 (0-6) and median time from diagnosis was 9 (0-56) months. Five (55.6%) patients had Barcelona Clinic Liver Cancer (BCLC) stage B disease. The median treatment duration was 2 months for sorafenib and 3 months for TTFields. The total TTFields treatment duration for all nine patients was 29.1 months. Six (66.7%) patients had severe AEs (grade 3-4) and 3 (33.3%) had serious adverse events (SAE), none of which were related to TTFields. Mild-moderate skin toxicity was the only TTFields-related AE, which was reported in seven (78%) patients.

Conclusion: No unanticipated serious adverse device effects have been reported to date in the HEPANOVA study. The majority of AEs reported to date were expected and associated with the disease or sorafenib. The most common adverse event reported was the expected TTFields-related dermatitis. In summary, these results emphasize the tolerability and safety of TTFields (150 kHz) concomitant with sorafenib in the treatment of advanced hepatocellular carcinoma.

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P-216 Incidence and trends of biliary tract cancer in Girona: A population-based study from the Girona Cancer Registry (1994-2016)

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Background: Biliary tract cancer (BTC) is an aggressive, uncommon and highly fatal epithelial malignancy whose incidence rates are yet to be determined in most western countries. Challenges in the diagnosis and classification of these neoplasms have made it difficult to quantify its true incidence until now. In this study, we analysed BTC's incidence and trends between 1994 and 2016 in Girona.

Methods: Data were extracted from the population-based Girona Cancer Registry. BTC was identified by diagnostic codes from the World Health Organization's ICD-O-3 Third Edition coding system C22.1 (Intrahepatic bile duct, ICC), C23.9 (Gallbladder, GB), C24.0 (Extrahepatic bile duct, ECC), C24.1 (Ampulla of Vater, AV), C24.8 (Overlapping lesion of biliary tract) and C24.9 (Biliary tract, NOS). We analysed the data to assess long-term trends in the age-standardized incidence between 1994 and 2016, correcting for systematic coding errors. Non-epithelial and neuroendocrine tumors were excluded for incidence analysis. Age-adjusted incidence rates (ASRE) to the European standard population and world standard population (ASRW) were obtained. Trends were assessed using the estimated annual percentage of change (EAPC) of the ASRE13.

Results: We identified 1,102 BTC incident adult cases (>15y), 49.5% females and 50.5% males. Median age at diagnosis was 75y (R25-101). According to histology, 66% of cases were epithelial tumors, 1% neuroendocrine neoplasms, and 2 non-epithelial tumors were detected (1 Lymphoma, 1 sarcoma). The remaining 33% of cases had non-specified histology ("Neoplasm, malignant"). The most frequent subsite was ECC (26.2%), followed by GB (23.2%) and ICC (22.7). We found 143(12.9%) cases arising from AV, 3 overlapping tumors, and 160 cases (14.5%) were classified as biliary tract,

NOS. Analysis: For the selected study population (N=1,088; non-epithelial and neuroendocrine tumors excluded) crude rate (CR) cancer incidence was 7.32 cases per 100,000 inhabitants/year (7.43 men; 7.21 women). Regarding the ASR, results show an ASRE13 of 8.39 (95% CI 7.9; 8.9) and ASRW of 3.26(95% CI 3.0; 3.5). A slight non-statistically significant decrease in the incidence of BTC cases over the study period was observed, with an EAPC of -0.18 (95% CI -1.09-; 0.73) per year. We analyzed trends in the incidence of epithelial BTC histologically confirmed (n=722) and BTC with non-specified histology (n=366) separately, finding an opposite behavior in each group: an increase of confirmed cases overtime (up to a 28% total increase at the end of the study period) and a concurrent decrease in the number of non-specified histology cases.

Conclusion: Incidence rates of BTC in Girona are within the European average, and they have been stable in the last two decades. The study reflects a change in attitude towards BTC, leaving nihilism behind, shown by the decreasing proportion of non-histology confirmed cases overtime, the first step to personalized treatment. Survival and subgroup analysis is ongoing and merits further research.

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P-217 Value of liquid biopsy using high-affinity plasma DNA binding magnetic beads and qualitative real-time PCR for KRAS, NRAS and BRAF mutations in metastatic colorectal cancer patients

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Background: Detection sensitivity of real-time PCR for liquid biopsy has been reported to be about 0.1-0.5%. We evaluated the clinical utility of this technique in the management of metastatic colorectal cancer patients (mCRC) patients.

Methods: Plasma DNA-binding magnetic beads (MagCore® Plasma DNA Extraction Kit) and selective detections of exons 2, 3 and 4 of KRAS and NRAS and exon 15 of BRAF mutations, by qualitative Real-Time PCR, (EasyPGX®) were used to assess circulating tumor (ct)DNA at baseline in consecutive mCRC patients (from September 2018 to February 2020). ctDNA mutations were compared to tissue RAS/BRAF status and correlated with progression-free survival (PFS) of standard first-line chemotherapy (either FOLFIRI or FOLFOX or FOLFOXIRI plus bevacizumab for tissue mutated patients or panitumumab/cetuximab in wild type patients).

Results: Enrolled patients (n = 49, 16 female, 33 male) had a median age of 64 years (range 39-84 years). According to liquid biopsy, the prevalence of KRAS/NRAS (RAS) and BRAF mutation was 26.5% and 10.2%, respectively. As compared to tissue mutation status, 11 cases were RAS discordant: 4 patients wt in tissue and mutated in plasma (WTT/MUTP) and 7 patients mutated in tissue and wt in plasma (MUTT/WTP). ctDNA BRAF V600E mutation was found in 5 patients with a 100% concordance with tissue status. After a median follow up of 10 months (range 2 to 20 months), median (m) PFS in tissue + plasma RAS wild type patients (T+PWT), was 15.9 months (reference group). Among RAS mutated patients both in tissue and liquid biopsy (T+PMUT) mPFS was 8.2 months, with an HR for PFS of 5.45 (95% CI 1.75-16.92) compared to T+PWT population (p-value 0.0061). A long mPFS was observed among MUTT/WTP patients (24.4 months, difference not statistically significant as compared to T+PWT patients, p-value 0,07), probably because of an inferior tumor burden making the RAS mutation undetectable in ctDNA. mPFS in WTT/MUTP patients was as short as 10.3 months, similar to that of T+PMUT patients (p-value 0.2520), indicating the remarkable informative value of liquid biopsy (more aggressive tumor behavior due to the acquisition of ras mutation during disease progression). Patients with V6005 BRAF mutation had the worst prognosis: median PFS, 2.5 months, HR 13.67 (95% CI 3.61-51.7) as compared to T+PWT, p-value < 0.0001.

Conclusion: Liquid biopsy for RAS and BRAF mutations using available kits of real-time PCR is feasible in clinical practice and was associated with a more informative prognostic value than tissue mutational status. A larger sample size is needed to confirm the results. The value of longitudinal ctDNA assessment during standard first-line chemotherapy using this technique is underway.

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P-218 Prognostic value of mTOR expression and mismatch repair gene profile in advanced gastric and gastro-oesophygeal cancer

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Background: Gastric carcinoma remains the second most common cause of cancer-related deaths. Although the outcomes have recently improved, there are some patients who show rapid progression and resistance to chemotherapy. The PI3K/AKT/mTOR pathway is an important promoter of cell growth, metastasis, and resistance to chemotherapy. Recently the FDA approved pembrolizumab for the treatment of unresectable or metastatic microsatellite instability-high (MSI-H) or deficient mismatch repair (dMMR) gastric cancer in the second-line or subsequent setting. We aimed to assess the impact of mTOR expression and dMMR status on PFS, OS and tumor response in metastatic gastric and gastro-oesophygeal cancer patients.

Methods: This prospective study enrolled 76 denovo metastatic gastric and gastro-oesophygeal cancer patients recruited from the Oncology Center Mansoura University in Egypt with ages 31-70 years. Patients received first-line chemotherapy (fluorouracil and cisplatin). Pretreatment mTOR expression by IHC and also MMR status assessed by IHC staining to measure expression levels of proteins involved in DNA mismatch repair (ie, MLH1, MSH2, MSH6, PMS2) on formalin-fixed paraffin-embedded tumor tissues from primary or metastatic site was evaluated.

Results: 40 patients (52.6%) had gastro-esophageal junction tumors, 24 patients (31.6%) had fundus and body tumors, and 12 patients (15.8%) had antrum and pyloric tumors. mTOR expression was significantly present in gastro-esophageal junction tumors (68.2%) followed by fundus and body tumors (20.5%) then antrum and pyloric tumors (11.4%) with P=0.006. However dMMR was significantly present in fundus and body tumors (43.8%), followed by 37.5% in gastro-esophageal junction tumors and 18.8% in the antrum and pyloric tumors (P=0.003). Patients with high mTOR expression showed significantly poor response to chemotherapy (61.4% progressed disease versus 38.6% were responsive, P=0.04). Tumors with dMMR were also poor responders for treatment (66.7% progressed disease versus 33.3% were responders, P=0.06); most of these tumors were in the fundus and pylorus (59%). In this study, there were only 21 patients with low mTOR expression associated with proficient MMR; of them, nine patients showed complete response to first-line chemotherapy. Upon progression, only 15 patients received ramucirumab and paclitaxel (according to financial and insurance support); of them, ten patients (66.6%) showed stable disease and were highly expressing mTOR in concordance with dMMR in their pretreatment biopsies which may denote a crosstalk between mTOR and vascular endothelial growth factor (VEGF). High mTOR expression was associated with significantly shorter PFS (median, 10 months vs. 19 months; P=0.01) and significantly shorter OS (median, 23 months vs. 35 months; P=0.003). dMMR tumors were associated with shorter PFS (median, 12 months vs. 20 months; P=0.08) and significantly shorter OS (median, 20 months vs. 37 months; P=0.04).

Conclusion: This study further validates high mTOR and dMMR expression as poor prognostic biomarkers correlated with poor response, short PFS and OS. Therefore, they could be used for tailoring first or second lines of treatment in advanced and metastatic gastric or gastro-esophageal cancer in further studies. Tumors with high mTOR expression and dMMR could get more benefit from a combination of anti-VEGF with other targeted therapies, such as immune checkpoint inhibitors in first-line or upon progression as a second-line treatment.

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P-219 Clear cell variant of hepatocellular carcinoma (HCC-CC): A single-center observational study of an uncommon subtype

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Background: HCC-CC is the second most frequent subtype among rare pathological variants of HCC. Despite epidemiological, clinical, radiological and molecular peculiarities have been reported, neither dedicated treatment guidelines nor clinical trials are available for HCC-CC.

Methods: We retrospectively collected clinical and survival data from HCC-CC patients followed at our Institution from January 2015 to present. The primary aim of our study was to describe both patients' baseline characteristics and outcomes in terms of progression-free survival (PFS) and overall survival (OS) according to disease stage and type of treatment. Estimations of time-to-event curves were generated by the Kaplan-Meier method.

Results: Among 138 HCC patients, 73 (52.9%) had a histologically confirmed diagnosis and 18 (13.0%) belonged to the HCC-CC subtype and were therefore included in the present analysis. Of the 18 HCC-CC patients, 16 (88.9%) were males and 2 females (11.1%), with a mean age at diagnosis of 67 years (range: 53-79).

As for etiology, 9 (50.0%) cases recognized a dysmetabolic cause, 1 (5.5%) was HCV-related and 8 (44.5%) arose on healthy liver. All patients showed a preserved liver function (Child-Pugh A) at baseline. Regarding disease extension at diagnosis, 12 (66.7%) were in early stage (BCLC-A), 1 (5.5%) had intermediate (BCLC-B) and 5 (27.8%) advanced (BCLC-C) disease due to ECOG PS$\geq$1. Sixteen patients (88.9%) underwent surgery as first treatment, while 1 case received liver transplantation and 1 received transarterial chemoembolization (TACE). At first evidence of progression, 4 patients were offered additional locoregional treatments: TACE in 2 cases, transarterial radioembolization and microwave ablation 1 case each.

After a median interval of 9.1 months from initial curative-intent treatment, 10 (55.5%) patients progressed, 2 showing hepatic-only spread, 1 lung-only and and 7 $\geq$2 metastatic sites, i.e. liver (6), peritoneum (4), lung (2), skeletal, lymph nodes and skin (1 each).

A systemic first-line therapy was administered to 7 metastatic patients, 6 of which were followed at our center: 4 received sorafenib and 2 received experimental treatment with durvalumab (1 patient) or lenvatinib plus pembrolizumab/placebo (1 patient). Disease progression was reported as best radiological response in 66.7% of cases. Notably, despite a median first-line PFS of 2.76 months (95% CI 1.38-5.03), most patients received subsequent systemic therapies (50% second-line, 20% third-line) and 20% were considered for surgery (peritonectomy with hypertermic intraperitoneal chemotherapy), reaching a survival rate of 100% and 60% at 6-months and 1-year respectively.

Surgery was performed as only treatment in other 2 metastatic patients; of note, 1 of them underwent multiple excisions of extrahepatic localizations, reaching a 50.0 months survival at the time of analysis.

Conclusion: Our cohort of HCC-CC patients showed a predominantly non-viral etiology, a mainly early-stage at diagnosis with preserved liver function and a relatively favorable outcome even in metastatic patients, consistently with previously published data. Interestingly, we observed a poor efficacy of systemic treatment with tyrosine-kinase inhibitors, whereas surgery seemed to be effective even in the metastatic setting. Role of immune checkpoints inhibitors in HCC-CC should be further explored. Wider multicentric experiences are warranted to shed light on this not-so-rare HCC-subtype.

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P-220 Management of colorectal cancers: Improving clinical management of patients with MSI-high disease through education

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Background: The treatment of metastatic colorectal cancer is evolving with the development of biomarker-driven therapies including targeted therapy and immunotherapy. Immunotherapy offers a therapeutic option for patients with MSI-high disease. The goal of this study was to determine if participation in an educational activity can improve the knowledge and competency of oncologists on the application of checkpoint inhibitors in the treatment of metastatic colorectal cancer.

Methods: An online continuing medical education (CME)-certified interactive, text-based activity developed by Medscape Oncology and the Society for Immunotherapy of Cancer included 2 patient cases, which served as the foundation for interactive questions. The educational design included a "test, then teach" approach to elicit cognitive dissonance, with evidence-based feedback provided following each learner response. A repeated pairs pre-/post-assessment study with 3 case-based questions and 1 confidence question was employed. A chi-square test assessed differences in responses from pre- to post-assessment. P values .26 is extensive). The activity was launched online 12/18/18 and data were collected through 2/11/19.

Results: Effect for oncologists (n=60; $p < 0.0001$, V =.289). An average of 74% of oncologists correctly responded to pre-assessment questions, increasing to 95% post-assessment. 24% of oncologists reported greater confidence determining which patients with CRC are candidates for immune checkpoint inhibitor therapy. Significant improvements in knowledge were observed in the importance of testing for microsatellite instability (75% vs. 95%; $p = 0.0022$, V = .277). Significant improvements in competence were observed among oncologists in selecting the most appropriate regimen for patients with MSI-high in mCRC (72% vs. 95%; $p = 0.0005$, V = 0.31) and communicating with the interprofessional care team to ensure optimal coordination of care in patients with MSI-high in mCRC (75% vs. 95%; $p = 0.0022$, V = .280).

Conclusion: This online interactive, case-based, CME-certified educational activity resulted in significant gains in oncologist knowledge and competency in testing for microsatellite instability, selecting appropriate treatment for such patients, and communicating with the care team on immune-mediated adverse events. These results demonstrate the effectiveness of on-demand education in improving the translation of clinical knowledge into practice scenarios while improving clinician confidence.

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P-221 Clinical and pathological characteristics of patients with gastrointestinal neuroendocrine tumors in the United States

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Background: Neuroendocrine neoplasms (NEN) are rare tumors and vary from well-differentiated (low grade) neuroendocrine tumors (NETs) to undifferentiated (high grade) tumors, named as neuroendocrine carcinoma. This classification of NETs is based mainly on Ki67 proliferation index that grades NETs into low proliferative tumors (GI, GII) and high proliferative tumors (GIII). The aim of this study was to evaluate the clinicopathological characteristics of patients with GIT neuroendocrine tumors in the United States, diagnosed from 1990 till 2015.

Methods: This study was conducted using SEER Stat version 8.3.6. to analyse characteristics of patients with gastrointestinal neuroendocrine tumors. Data obtained from SEER 18 Regs Research Data Nov 2018, were statistically analysed using SPSS version 22.

Results: In the period from 1990 to 2015, 15951 cases were diagnosed as GIT NETs in the United States. The median age at diagnosis was 62.2 years. Males represented the vast majority of cases (n= 8434, 52.9%). The white race was the commonest among the cases (n= 12494, 78.3%). The incidence rate of GIT NETs was estimated to be 14.9 per 100,000 cases. The tumor was found to be the only primary malignancy diagnosed in most of the cases (n= 11858, 74.3%). Most patients had localized disease at the time of diagnosis, with surgery performed for the majority of them (n= 9076, 56.9%). Pancreas represented the commonest site for GIT NETs (n= 5588, 35%), with well-differentiated, GI NETs being the most common histology identified (n= 5549, 34.8%). The median survival was 26 months, with observed survival at 10 and 20 years of 21.6% and 11.2%, respectively. The relative survival at 10 and 20 years was 27.1% and 19%, respectively.

Conclusion: NETs are relatively uncommon tumors. Their incidence within the GIT is about 14.9 per 100,000 with slight male predominance. Well-differentiated tumors were the commonest subtype of GIT NETs. The vast majority of cases tended to present at an early stage with localized disease for whom, surgery was performed. The median survival was 26 months with relative survival at 10 and 20 years of 27% and 19%, respectively.

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P-222 Primary malignant tumors of the small intestine: Clinical and therapeutic aspects

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Background: Malignant tumors of the small intestine are uncommon, accounting for less than 2% of digestive tract cancer. However, it is the first etiology for endocrine tumors, lymphomas or stromal tumors. They are characterized by anatomopathological heterogeneity and non-specific symptomatology. This causes a diagnostic delay and a fairly severe prognosis.

Methods: This is a retrospective study that included patients with small intestine cancer who were treated in the Medical Oncology department from January 2015 to June 2019. The objective was to study the epidemiological, diagnostic and therapeutic and prognostic factors of small intestine cancer and to relate our experience in their therapeutic management.

Results: Forty-three cases were reported, with median age 58.2 years (37 to 86 years), with a male predominance (the sex ratio M/F of 1.3). 20,9 % of patients were diagnosed with complications such as acute occlusive syndrome or intestinal perforation. The tumor localization was 23.2% in the jejunum, 32.5% duodenal and 44.1% ileal. Histologically, adenocarcinoma was the most common type (51.2%) followed by neuroendocrine carcinoma (27.9% of cases) and stromal tumors (16.2% of cases). The majority of cases were diagnosed with advanced metastatic disease (55.8% of cases). The sites of metastasis were respectively the liver (30.4%), the lung (16.6%) bone and the peritoneum (8.3%). The treatment was surgical in 44.1% of cases and consisted of a segmental intestinal resection, followed by a terminally terminal anastomosis. Seventy-nine percent of patients were eligible for systemic treatment, of which 23.6%

were in the adjuvant setting and 55.8% in palliative cases. The chemotherapy protocol depended on the histological type and was dominated by the 5FU-oxaliplatin combination in carcinomas, while the stromal tumors received TKI. After a median follow-up of 52.7 months, the median progression-free survival was 11.2 months and the median overall survival was 16.8 months all histological types combined.

Conclusion: Malignant tumors of the small intestine pose diagnostic problems because of their scarcity and the absence of specific clinical signs. They are often operative discoveries in the event of an acute complication. The curative treatment is surgical resection regardless of the histological type. The prognosis remains reserved because of the late diagnosis of the tumor.

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P-223 Prognostic role of inflammatory biomarkers in patients with advanced pancreatic adenocarcinoma undergoing first-line chemotherapy

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Background: The aim of the current study was to examine the prognostic significance of inflammatory biomarkers in patients with locally advanced or metastatic pancreatic adenocarcinoma undergoing first-line chemotherapy with nab-paclitaxel and gemcitabine.

Methods: In the current cohort study data from 57 patients were retrospectively collected. All patients had histologically or cytologically confirmed pancreatic locally advanced or metastatic adenocarcinoma and were treated with first-line nab-paclitaxel and gemcitabine from July 2014 to February 2020. White cell (WBC), neutrophil (NEUT), lymphocyte (LYMPH), monocyte (MONO) and platelet (PLT) blood levels during the last two days before the start of the first cycle of chemotherapy were measured. Median neutrophil to lymphocyte ratio (NLR), median monocyte to lymphocyte ratio (MLR), median systemic inflammatory response index (SIRI=NEUT × MONO/LYMPH) and median platelet-to-lymphocyte ratio PLR were calculated.

Results: Median age was 67 years (range, 43-81), while 29 (50.9%) male and 28 (49.1%) female patients were included in the study. PS (ECOG) was zero in 32 (56.2%) patients, one in 21 (36.8%) and two in 4 (7.0%) patients. Forty seven (82.5%) patients had stage IV and 10 (17.5%) had stage III disease. After a median follow-up of 20.6 months (range, 1.1-37.3), 48 (84.2%) developed progressive disease and 41 (71.9%) died of disease. Median progression-free survival (PFS) was 5.1 months (95%CI, 3.6-6.6) and median overall survival (OS) was 9.9 months (95%CI, 6.2-13.6). Patients with stage III had median PFS 9.2 months (95%CI 3.0-15.4), while stage IV patients had median PFS 5.1 months (95%CI 3.3-6.9), with statistically significant difference (p=0.011). Increasing NLR levels were correlated with poorer PFS (HR 1.10, 95%CI 1.01-1.20,p=0.033) but not with OS (HR 1.07,95%CI 0.98-1.18,p=0.139). Cox proportional hazard models confirmed that higher NLR levels were independently associated with poorer PFS (HR 1.14, 95%CI 1.03-1.25, p=0.009) and poorer OS (HR 1.11, 95%CI 1.01-1.23,p=0.037). Also, PS ECOG 1-2 (compared to PS 0) showed independent prognostic significance for PFS (HR 2.51, 95%CI 1.34-4.69,p=0.004) and OS (HR 3.00, 95%CI 1.53-5.76, p=0.001). In contrast, tumor stage did not demonstrate independent prognostic significance. Exploratory analysis examined the prognostic significance of different NLR cutoffs (by increasing the NLR value by 0.5) for PFS and OS. The best cutoff was NLR $\geq$4 vs. $<$ 0.001) and longest median OS compared to the group with PS ECOG 1-2 and NLR $\geq$4 (14.0 vs. 8.2 vs. 5.7, respectively, p$<$ 0.001).

Conclusion: The present retrospective analysis revealed clinically meaningful subgroups with distinct prognoses according to inflammatory biomarkers and performance status, irrespective of tumor stage, in patients with advanced pancreatic adenocarcinoma treated with first-line nab-paclitaxel − gemcitabine.

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P-224 Improving the management of patients with pancreatic cancer: Education from treatment to adverse events and coordination of care

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Background: Patients with pancreatic cancer experience significant benefit from treatment but are often not offered aggressive, life-prolonging therapies based on the historically poor prognosis of metastatic disease. The goal of this study was to improve the competency of oncologists in making optimal treatment choices for patients with metastatic pancreatic cancer.

Methods: An online, interactive, text-based continuing medical education (CME)-certified activity was developed by Medscape Oncology. This activity included 2 patient cases, which served as the foundation for interactive questions. The educational design included a "test, then teach" approach to elicit cognitive dissonance, with evidence-based feedback provided, following each learner response. A repeated pairs pre-/post-assessment study design with 3 case-based questions and 1 confidence question was used. A chi-square test assessed differences from pre- to post-assessment. P values .26 is extensive). The activity was launched online 3/28/19 and data were collected through 5/9/19.

Results: Participation in education resulted in statistically significant improvements and an extensive educational effect for oncologists (n=167; p $<$ 0.0001, V =.416). Oncologists on average responded correctly to pre-assessment questions 48% of the time, increasing to 87% post-assessment. 17% of oncologists had a measurable increase in confidence in their ability to select appropriate treatment regimens for patients with locally advanced or metastatic pancreatic cancer, based on disease- and patient-specific characteristics. Significant improvements in competency were observed in: selection of appropriate treatment regimens for patients with locally advanced or metastatic pancreatic cancer, based on disease- and patient-specific characteristics (e.g., performance status) (31% vs. 78%; p $<$ 0.0001, V = .475 and 39% vs. 87%; p $<$ 0.0001; V = .502) and coordinating care across the multidisciplinary team (73% vs. 95%; p $<$ 0.0001; V = .292).

Conclusion: This online, interactive, case-based, CME-certified educational activity resulted in significant gains in oncologist competency in selecting optimal therapy for patients with pancreatic cancer and coordinating care across the multidisciplinary teams. These results demonstrate the effectiveness of on-demand education in improving the translation of clinical knowledge into practice scenarios while improving clinician confidence.

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P-225 KRAS codon 12 and 13 mutations in metastatic colorectal cancer: Predictive marker in first-line bevacizumab-based chemotherapy

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Background: The three human RAS genes (KRAS, NRAS, and HRAS) are the most frequently mutated oncogenes and present in 45% of patients with colorectal cancer, being known as an early event in tumorigenesis. Most KRAS mutations (90%) occur in codons 12 and 13 of exon 2. However, the role of different KRAS mutations and its prognostic value remains controversial, with few studies showing a worse progression-free survival and overall survival with codon 12 KRAS mutation. The aim of our study was to evaluate KRAS codon mutation (codon 12 and 13) as a predictive marker of first-line bevacizumab-based chemotherapy response.

Methods: Retrospective single-center analysis of metastatic colorectal cancer patients with KRAS/NRAS mutations treated with first-line bevacizumab-based chemotherapy (fluorouracil plus irinotecan or oxaliplatin) between 2015 and 2019. Statistical univariate and multivariate analysis (Kaplan-Meier and Cox Regression) was performed using SPSS software version 23.

Results: From the 64 patients treated with bevacizumab, only 43 patients received bevacizumab in first-line chemotherapy. Henceforward we analyzed 43 patients, 60,5% were male individuals (n=26), with a median age at diagnosis of 65 years (36-77 years). 81,4% of patients showed an ECOG Performance Status (PS) 0 (n=35). 65,1% (n=28) of patients presented stage IV at diagnosis, with 41.5% (n=17) having extrahepatic metastasis. Regarding RAS mutational status, 46,5% of patients had a mutation in codon 12 (n=20), 48,8% in codon 13 (n=21), 2,3% (n=1) in codon 61 and NRAS mutation (n=1). With a median follow-up of 21 months (2 - 83 months), first-line palliative chemotherapy was prescribed with a median of 10 cycles (2-31 cycles) of bevacizumab in patients with KRAS mutation in codon 12 or codon 13. Adverse events CTCAE v4.0 grade ^{3} 3 occurred in 26,8% of patients (n=11). Median progression-free survival (PFS) was 11 months, patients with codon 12 mutation had a PFS of 7 months (1-30) versus 11 months (2-32) in patients with codon 13 mutation, without statistical

significance (HR 0,62, CI 95% :0,3-1,4, p =0,231). On a multivariate analysis concerning gender, synchronous metastasis, extrahepatic metastasis, and KRAS codon mutation, there were no statistically significant differences concerning PFS.

Conclusion: This small retrospective study shows a positive trend in progression-free survival of first-line bevacizumab-based chemotherapy patients with KRAS mutation in codon 13 versus codon 12. However larger studies are needed to enforce the reported findings, as well as to access the predictive value of KRAS mutations relating to other codons.

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P-226 Analysis of Hispanic Latino American patients with colorectal cancer, clinical features and laterality as a prognosis factor of overall survival

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Background: Colorrectal cancer (CCR) is one of the leading causes of death in the world. The laterality of the primary tumor has been divided in right-sided colon, and left-sided colon showing promising results in terms of overall survival regarding right side colon, nevertheless few information exists regarding Hispanic Latino American population. The objective was to evaluate the impact of the laterality on the overall survival of Mexican patients diagnosed metastatic colorectal adenocarcinoma treated at the National Cancer Institute.

Methods: Retrospective and observational study. Included patients with metastatic CCR treated with chemotherapy and monoclonal antibodies (anti-VEGF and anti-EGFR) in a period from 2010 to 2018. Descriptive and inferential statistics, Xi2; Kaplan-Meier, Log Rank and Cox-Regression for overall survival (OS) and factor analysis between the groups, p< 0.05 bilateral statistical significance.

Results: Were included 654 patients with metastatic CCR, men (n=634) and women (n=290) with median age of 56.3 years for both gender. The population was divided in 3 groups left-sided (n=177), right-sided (n= 135), and rectum (n= 342). From the total, 70% received treatment with chemotherapy +/- monoclonal antibodies. Chemotherapy included FOLFOX (n=195), XelOx (n=220), and Folfiri (n=26) and fluoropirimidines (n= 35). Monoclonal antibodies were received for the 31%, 34% and 30% of the right-sided, left-sided and rectum group respectively.

Xi2 test showed statistical significance between KRAS determination (0.036), metastatic sites (0.001) and chemotherapy treatment (0.040).

Overall Survival (OS) analysis showed statistical differences according laterality with median OS of 20 months for right-sided colon, 36 months for left-sided and 31 months for rectum (p=0.002;HR:1.76 IC-95% 1.24—2.51). A sub-analysis was performed including only patients treated with chemotherapy, and comparing laterality showed a median OS of 18 months for right-sided, 33 months for left-sided colon and 28 months for rectum (p=0.003;HR:1.7 IC-95% 1.13—2.59). On the other hand, patients treated with chemotherapy + monoclonal antibodies showed a median OS of 24 months for right-sided colon and 46 months for left-sided colon and rectum (p=0.001 HR: 1.85 IC 95% 1.04 — 3.65).

Response Rate. Regarding the type of monoclonal antibody and laterality, the Objective Rate Response (ORR) was 54% for right-sided colon (treated with anti-VEGF), 80% left-sided colon, and 66% for rectum (both treated with anti-EFGR).

Conclusion: This is the first registry of Hispanic Latino American patients with mCRC that presents an analysis of the clinical characteristics of these patients and analyzes the impact of laterality as a predictive factor of overall survival, as well as the response rate of patients treated with chemotherapy +/- monoclonal antibodies.

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P-227 Prognostic and predictive factors of platinum-based chemotherapy in gastroenteropancreatic neuroendocrine neoplasms G3

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Background: Data on gastroenteropancreatic neuroendocrine neoplasms (NEN) G3 (well-differentiated neuroendocrine tumors (NET G3) and neuroendocrine carcinoma (NEC) are limited. NET G3 are highly heterogeneous tumors, containing tumors that are both well and poorly differentiated. The assumption was reflected in the current 2019 WHO classification.

Methods: Patients were identified from hospital databases between 2016 and 2019 with the diagnosis of NEN G3 confirmed by synaptophysin (Syn) and/or chromogranin A (CgA) positivity, GEP primary or unknown primary, Ki-67 index >20% or poorly differentiated morphology. Mixed tumors (MANEC) were included. Response to chemotherapy was analyzed according to the following criteria: start and end date of chemotherapy, best response (local radiological review based on RECIST 1.0), progression-free survival (PFS) and overall survival (OS) using Kaplan—Meier analysis and comparisons were performed using the log-rank test. A p-value of < 0.05 was considered statistically significant. Cox proportional hazard models were developed using relevant clinicopathologic variables to determine the association of each parameter with PFS and OS. All statistical analyses were performed using the (Statistica ver. 13.1) (StatSoft, Poland).

Results: Two hundred twenty-one patients were analyzed (27 NET G3, 14 MANEC, and 180 NEC). The mean age of patients was 64.1±9.1 years. Women to men ratio was 1:1.8. Tumor origin included gastric (20%), duodenum and Vateri Ampullae (11%), pancreas (32%), ileum (12%) and colon-rectum (39,9%). The primary tumor was resected in 80 (36%) patients. Metastatic disease was evident at diagnosis in 90% (liver metastases: 69%). The median time of follow-up of those patients alive was 14.5 (range 1.1—124.7) months. Median Ki-67 index was 70% (30% in NET G3, 60% in MANEC and 80% in NEC; P 25%), Ki-67 index, platelet count, lactate dehydrogenase, and primary tumor location were prognostic for response and survival. Patients were significantly younger in the NET G3 cohort (P=0.001) and were significantly more likely to have a functional tumor compared to NEC (P=0.003). Primary localization was more often in the pancreas (65%) for NET G3, while colorectal NEC was more common than colorectal NET G3. Multivariate analyses identified performance status as the strongest prognostic factor in the NEC cohort. A Ki-67 threshold of 50% was predictive for response to first-line platinum-based chemotherapy. Tumors with a Ki-67 index < 50% were much less responsive to platinum-based chemotherapy (response rate, 10% vs 48%), but the patients with those tumors had a significantly longer survival compared with the patients who had higher Ki-67 levels.

Conclusion: In conclusion, NET G3 and NEC are characterized by significant differences in Ki-67 index and outcomes. While platinum-based chemotherapy is effective in NEC, it seems to have limited value in NET G3.

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P-228 SGNLVA-005: Open-label, phase 2 study of ladiratuzumab vedotin (LV) for aerodigestive tract malignancies

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Background: LIV-1 is a transmembrane protein with putative zinc transporter and metalloproteinase activity. It has been linked to the epithelial-to-mesenchymal transition that leads to malignant progression and metastasis. SGN-LIV1A, or ladiratuzumab vedotin (LV), is a novel investigational humanized IgG1 antibody-drug conjugate (ADC) directed against LIV-1. LV mediates delivery of monomethyl auristatin E (MMAE), which drives antitumor activity through cytotoxic cell killing and induces immunogenic cell death. In a phase 1 study, LV was well tolerated with manageable toxicities and showed antitumor activity in heavily pretreated patients with metastatic breast cancer (Modi et al 2017). The current study is evaluating the efficacy of LV in other advanced solid tumors with various LIV-1 expression, including advanced upper aerodigestive tract malignancies (esophageal squamous cell carcinoma, gastric and gastroesophageal junction [GEJ] adenocarcinoma), small cell lung cancer (SCLC), non-small cell lung cancer squamous and nonsquamous, and head and neck squamous cell carcinoma.

Trial design: SGNLVA-005 (NCT04032704) is an open-label, phase 2 study evaluating LV monotherapy for patients with advanced solid tumors. Up to approximately 30 previously treated patients with unresectable locally advanced or metastatic disease (for SCLC, extensive-stage disease) will be enrolled in each cohort. Patients must have measurable disease per RECIST v1.1, an Eastern Cooperative Oncology Group (ECOG) score of 0 or 1, and adequate organ function. Patients in the gastric and GEJ adenocarcinoma and esophageal squamous cell carcinoma cohorts must have received and progressed during or after no more than 1 prior line of platinum-based cytotoxic chemotherapy. Patients in the gastric and GEJ adenocarcinoma cohort may have received prior anti-programmed cell death-(ligand) 1 (anti-PD[L]1) therapy unless contraindicated. Patients are not preselected based on tumor LIV-1 expression, but their tumor samples will be analyzed for correlation between LIV-1 expression and response. Safety and efficacy will be monitored

throughout the study. Study objectives include objective response rate (primary); safety and tolerability, disease control rate, duration of response, progression-free and overall survival, and pharmacokinetics and immunogenicity (all secondary); and pharmacodynamics. Study accrual is ongoing in North America. Patients will also be enrolled in the UK, EU, Australia, and Asia.

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P-229 Elderly population do benefit from adjuvant chemotherapy in gastric cancer: Experience in a single institution

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Background: Gastric cancer in Peru represents the 4th most common cause of cancer and the second most deadly. In elderly people, defined as people 65 years old or more, it is one of the most frequent malignant diseases and the age-adjusted mortality rate was reported to increase with age. Adjuvant chemotherapy showed survival benefit compared to surgery alone. Because of comorbidities or age-related toxicities, some oncologists hesitate to recommend elderly patients receive additional adjuvant chemotherapy. We wanted to evaluate the benefit of adjuvant chemotherapy vs surgery alone in this population.

Methods: This is a single-centre, retrospective study. We analyzed 110 nonclinical stage IV gastric cancer medical records of patients older than 65 years old at the Instituto Nacional de Enfermedades Neoplásicas in Lima-Perú between 2013 and 2016, comparing those who were treated just with surgery versus those who received adjuvant chemotherapy.

Results: From 110 medical records, 54.9% of patients were treated only with surgery and 45.1% of patients received adjuvant chemotherapy. The median age was 72 years old (65-89). The median age in the surgery group was 75 (65-89) and in the adjuvant group it was 70 (65-81). 43.7% were female and 56.3% male. 66.2% of patients had any grade of anemia vs 33.8% of patients had normal hemoglobin. Regarding histological features, 57.7% were intestinal subtype, 28.2% were diffuse, and 14.1% were mixed. 81.8% had lymphovascular infiltration vs 18.3% who did not. 46.5% were histological grade 3 and 53.3% were less than grade 3. Regarding clinical stage, 23.9% were stage III and 76.1% were stage II. Lymph nodes infiltration was pN0-1 36.6%, pN2 38% and pN3 25.4%. The disease-free survival (DFS) to 36 months was 52.6% for patients with surgery vs 75% for patients with adjuvant chemotherapy and DFS to 60 months was 49.3% vs 67.8%, respectively, with p=0.058. The overall survival (OS) to 36 months was 53.8% for surgery vs 81.3% for adjuvant chemotherapy and OS to 60 months was 50.9% vs 70.3% respectively, with p=0.039.

Conclusion: There were no features differences between patients who were treated with surgery alone compared with those who received both surgery and adjuvant chemotherapy but we could see benefit in patients who received adjuvant chemotherapy, in all sub-groups; more so in patients who had pN3 or clinical stage III disease in terms of both disease-free survival and overall survival. There are studies comparing the effectiveness of chemotherapy between elderly and nonelderly patients but there are poor data regarding only elderly patients. We need to improve our data and pursue deeper analysis with a bigger population to understand the real importance of adjuvant chemotherapy in this population.

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P-230 Intensifying peri-operative chemotherapy with radiotherapy in resectable gastro-esophageal junction (GEJ) and stomach cancer patients: Initial results of a prospective trial at a tertiary cancer care centre

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Background: Different strategies have been proposed to improve outcomes of potentially resectable carcinoma GEJ and stomach patients, however the best sequence remains unclear. Various strategies have been proposed to improve pathological complete response rates (pCR) in the neoadjuvant setting. In this sense we conducted a prospective pilot study wherein we intensified pre-operative treatment with neo-adjuvant chemo-radiotherapy (NACTRT) and present initial results in the context of compliance, toxicity and outcomes.

Methods: Between 2017-2018, 28 patients of carcinoma stomach and GEJ adenocarcinoma after discussion in multidisciplinary tumor board, deemed resectable based on baseline CECT scan (abdomen+pelvis) were enrolled for neo-adjuvant chemo-radiotherapy protocol. Staging laproscopy was not required to be included in the protocol. This protocol was approved by Institute's ethical committee. Treatment comprised of two cycles neo-adjuvant chemotherapy with inj. Cisplatin (dose @60mg/m^2 day 1) and oral capecitabine (dose @ 625mg/m^2 bid day 1-21) followed by radiotherapy (EBRT) 45Gy/25# along with concurrent oral capecitabine (dose @ 850mg/m^2 bid day 1-5 on RT days only). Post EBRT a diagnostic CECT (abdomen and pelvis) was done to assess response and to rule out any asymptomatic progression. Those deemed fit were taken up for surgery following which patient received further adjuvant chemotherapy for another 3 cycles. Demographic, disease, treatment and toxicity data were summarized as crude percentages. Overall survival (OS) was calculated from the date of biopsy to death due to any cause using Kaplan Meier curves for all patients recruited i.e. intention to treat (ITT) population. All p less than 0.05 were considered statistically significant. The cut-off date for all time-to event analyses was 1st September 2019.

Results: The median age was 56 years (20-73) with male predominance in 85%. 1/3rd of the patient had >10% weight loss of the usual body weight in the preceding 6 months. 54% (n=15) patients had siewert type II/III disease. Majority were T3 82% (n=23) and T4 18% (n=5) and node positive 83% (n=24). 90% (n =25) of the patients completed the planned NACT without dose reduction. 2/3rd (n=18/28) patients received NACTRT while <50% (n=12) patients underwent surgery. The major reason for drop outs between subsequent treatments was tumor progression (35%, n =10) both before (n=5) and after (n=5) NACTRT. Among those who underwent radical surgery (39%; 11/28), primary tumor and nodal disease down staging was observed in nearly all patients with 25% (n=3) achieving pCR. Chemotherapy was well tolerated with less 10% patients had grade 3 or 4 hematologic toxicity while <5% patients had diarrhea or vomiting requiring intravenous fluids. Post surgery chemotherapy was received by (36%; 10/28). At a median follow-up of 12 months, 60% of the patients were still alive with an estimated median OS of 22 months for ITT population.

Conclusion: Compliance was largely affected by tumor progression preoperatively while toxicity was acceptable. We observed encouraging OS and pCR with NACTRT approach serving a good biological selection for these aggressive tumors.

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P-231 Clinical analysis of histopathologic mapping after endoscopic submucosal dissection of gastric neoplasm

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Background: The pathologic mapping process after endoscopic submucosal dissection (ESD) is the most important pathway, which is implicated with technical success, pathologic diagnosis, and prognosis. However, until now, the analysis of outcomes for post ESD mapping has been focused on microscopic features. So, we reviewed and designed the groups of surface distribution of tumors after post ESD mapping.

Methods: The aim of this study was to investigate post ESD outcomes relating to prognosis including post ESD mapping. From Jan. 2008 to Mar. 2012, ESD was performed in 141 patients, 158 lesions were diagnosed with adenoma and EGC confirmed by endoscopic biopsy in Eulji hospital. After ESD, all lesions assigned to one of two groups based on the final histological findings were as follows: same grade group (SG; LGD to LGD, HGD to HGD, EGC to EGC) or upgrade group (UG; LGD to HGD or EGC). Therefore, macroscopic type, size of the lesion, location of the lesion, and pathologic distribution of resected specimen were retrospectively investigated. Pathologic distribution of resected specimen was divided into four subtypes based on post-ESD mapping results.

Results: A total of 141 patients, 89 male and 52 female were included. Adenomas were 112 and cancers were 46. Surface nodularity of UG was 24 out of 35 vs SG was 75 out of 122. Some patients of UG showed upgrade pathology, which is beyond indications of endoscopic resection, with surface nodularity. Color of lesion, ulcer, and pathologic distribution of resected specimen were not correlated with pathologic outcomes. Pathologic distribution of resected specimen was divided into four subtypes as a result of post-ESD mapping (homogenous: 96, separated: 10, multiple skipped: 12, heterogenous: 14). 35/158(22.2%) patients had changes of pathologic grading, however incorrect lateral staging and incomplete resection rates tended to be high in multiple skipped groups with differentiated cell types.

Conclusion: There are several limitations in predicting the correct histopathologic diagnosis by conventional biopsy and endoscopic inspection. Because of heterogenous gastric histopathology, discrepancies and incomplete resection are influenced by topographic subtyping of post ESD mapping. Especially, some cases of differentiated cell type and multiple skipped subtype groups may have a negative impact on post ESD outcome.

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P-232 Clinical outcomes and characteristics according to localization of colorectal cancer in Fundacion Santa Fe De Bogota between May 2015-May 2019

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Background: In Colombia, colorectal cancer is the third neoplasm with the most incidence, with 9140 new cases in 2018. The objective of this study is to make a description using real-world data of the characteristics and clinical outcomes of patients according to location, in a cancer reference institution in Colombia.

Methods: This is an observational study of a cohort of patients with adenocarcinoma of colon and rectum. We did follow up for 51 months and analyzed molecular, epidemiological and clinical characteristics and overall survival (OSm). We use Kaplan-Meier as survival analysis.

Results: Forty patients were included, 42% had left colon cancer, 28% had rectum cancer and 30% right colon cancer. The distribution according to the sex was: left colon 70.5% female/29.5% male, in rectum 45.4% female/54.5% male, In right colon: 33.3% female/66.6% male. The 50% of the patients at the time of diagnosis had a level of CEA less than 5 ng and 25% had a CEA greater than 10ng. There were no differences in age according to location, the average was 60 years. At the time of diagnosis 32.5% were stage IV, 30% stage III, 22.5% stage II, and 10% stage I. The distribution of these stages according to location were: In left colon 38.8% stage IV, 27,7% stage III, 22.2% stage II and 5% stage I, in the rectum 36.3% stage IV, 27.2% stage III, 9% stage II and 27.2% stage I. For the right colon was: 16.6% stage IV, 50% stage III, 33.3% stage II and 0% stage I. In the cohort of patients with metastatic disease, concerning to molecular characteristics, the presence of RAS mutation was found in 50%, BRAF mutation in 7%, high MSI in 18%, and in relation to localization, the right colon had a 100% of RAS mutation, while left colon 28.6%, in rectum was 50% . In the context of advanced disease there was not differences in the average age between right and left colon. In the survival analysis the OSm in stage IV was 16m in right colon cancer vs 27,6m in left colon cancer and in rectum cancer was 21m. According with RAS status, in patients with mutation the OSm was 20m and in wild type 25m.

Conclusion: In our cohort of patients with colorectal cancer there were no age differences according to localization. Left side colorectal cancer was more frequent in women and the stage at diagnosis was IV in most of the cases. In patients with metastatic disease, the clinical outcomes as the OSm was better in left side and in Ras wild type tumors such as have been described in worldwide published literature.

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P-233 Metformin combined with irinotecan in patients with refractory colorectal cancer: A phase 2 trial

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Background: Patients with advanced colorectal cancer (CRC) have few and expensive treatment options. The combination of irinotecan and metformin had been tested in animal models with promising results. The primary end-point of this study was to determine if metformin combined with irinotecan increases the disease control rates in patients with CRC. The secondary endpoints were progression-free survival (PFS); overall survival (OS); and toxicity rates.

Methods: This was a single-arm optimal two-stage Simon phase 2 clinical trial enrolling CRC patients with RECIST 1.1 evaluable disease that had progressed on previous lines of chemotherapy including oxaliplatin, irinotecan, fluoropyrimidine, and anti-EGFR if RAS wild-type. The sample size calculation was designed for an alfa of 0,1, beta of 0,8, and at least 26.7% disease control at 12 weeks of treatment. Patients received metformin 2500 mg orally a day plus irinotecan 125 mg/m^2 intravenously weekly D1 and D8 every 21 days until disease progression, unacceptable toxicity, or withdrawal of consent.

Results: Forty-one patients were enrolled between December 2015 and January 2018, achieving the sample size calculation for the primary end-point. RAS mutation was identified in 27 patients (66%), 14 patients (34%) had 3 or more site of metastatic disease; and 11 patients (27%) presents body mass index equal or higher than 30. The median follow up was 8.2 months. Seventeen patients (41%) met the primary endpoint of disease control in 12 weeks; hence the study was deemed positive. The median progression-free survival was 3.2 months (CI 95%, 2.0 — 4.5) and the median overall survival 8,4 months (CI 95%, 5.9- 10.8). There was no objective response according to RECIST 1.1, only disease stabilization. Both KRAS mutation and disease control impacted in overall survival in the multivariate model, respectively (HR 2,28 (CI 95%, 1.12-4.7 — p=0.023; and HR 0,21 (CI 95% 0.08-0.5 — p=0.001). Patients who achieved and did not achieve disease control presented median OS of 11.2 months and 4.4 months, correspondingly. The treatment was well-tolerated, and the most common adverse event was diarrhea, which was grade 3 in 12 patients (29.2%).

Conclusion: This phase II trial demonstrated that the combination of metformin and irinotecan led to promising disease control in patients with refractory metastatic CRC, which correlated with OS. These results must be confirmed in prospective randomized studies.

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P-234 A SEER based analysis of clinical characteristics and survival in patients with functional endocrine tumors of gastrointestinal origin

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Background: Functional endocrine tumors (FETs) belong to the heterogeneous class of neuroendocrine tumors characterized by excess secretion of disease-specific hormones. These are uncommon tumors of low malignant potential, however, rarely these tumors can become metastatic. The main goals of treatment include amelioration of symptoms from the overproduction of hormones and to address tumor growth.

Methods: Using the SEER database, we identified 529 patients with malignant functional endocrine tumors identified as gastrinoma, insulinoma, glucagonoma, VIPoma and somatostatinoma (ICD-8150-8153, 8155, 8156). We conducted a retrospective, population-based analysis to evaluate the baseline patient and tumor characteristics. Overall survival (OS) and cancer-specific survival (CSS) were analyzed using Kaplan-Meier method and multivariate Cox proportional hazards model was used to determine the prognostic factors by SPSS 26.

Results: We identified 529 patients with FETs, excluding mixed pancreatic endocrine and exocrine tumors. FETs were more predominant in patients older than 50 (67.3%) and white patients (78.1%). The median age at diagnosis was 56 years. There were no gender differences seen in the incidence of FETs. The most common FETs were gastrinoma (56.3%) and insulinoma (23.8%), followed by glucagonoma (11.2%), VIPoma (5.3%) and somatostatinoma (3.4%). Most FETs were found in the pancreas (67.1%) with the second most common location in the small bowel (13.8%). Grade was only specified in 30% of the cases; however, grade I (well-differentiated), grade II (moderately differentiated) accounted for 26.1%. Surgery was the primary modality of treatment, employed in 55.8% of the cases. Median overall survival (OS) for the entire cohort was 9.8 months (95% CI 7.9-11.8), with 5-, 10- and 20- year OS of 63.7%, 49.3% and 26%, respectively. Median cancer-specific survival (CSS) was 8.5 years(95% CI 12.8-24.2) with 5-, 10-, 20- year CSS of 74.1%, 65.6% and 47.2%, respectively. As for histology, glucagonoma had the shortest median OS (5.8, 95%CI:6.3-17.6), followed by VIPoma (6.5; 95%CI 1.7-11.3), gastrinoma(10.6; 95%CI 8.5-12.7) and insulinoma (11.9; 95%CI 6.3-17.6). In multivariate analysis, age >50 (HR= 2.7; 95% CI 2.02-3.64), lack of surgical resection (HR=1.88; 95% CI 1.43-2.46), metastasis (HR=3.0; 95%CI 2.0-4.5) and poor differentiation were prognostic factors of poor survival. Site and histology did not have a significant impact on survival.

Conclusion: FETs have a favorable prognosis regardless of the histological type and site of occurrence, specifically when managed with successful surgical resection.

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P-235 Management of constipation associated with advanced cancers, chemotherapy and opioid-induced constipation by oral herbal supplement in heterogeneous group of gastrointestinal, hepatobiliary and pancreatic cancers

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Background: Constipation is third most common symptom in cancer. It is even worse in advanced stage cancers where 50-87% of patients experience constipation. This is also attributed to adverse effect of some chemotherapeutic agents [Chemotherapy-induced constipation (CIC)] or due to opioids taken for pain management [Opioid-induced constipation (OIC)]. Various classes of laxatives are indicated to manage constipation and its effects but that also does not relieve symptom completely which leads to treatment delay, dose limitation of chemotherapy, cessation of anti-cancer treatment greatly affecting cancer management and clinical outcomes. This also affects health-related quality of life (QoL) of cancer patients.

Methods: In this study total 90 patients of various malignancies complaining of unsatisfactory or difficult bowel evacuation were studied. Study drug *Aarewat Kalpa* (AK) is FDA (Local Regulatory Authority of India) sanctioned oral herbal supplement with main composition containing *Cassia senna* 125 mg and *Cassia fistula* 125 mg. One capsule of AK was administered in a capsule form with lukewarm water at bedtime daily. Effect was measured using Constipation Assessment Scale (CAS) at end of 15 days.

Significance of difference between mean scores of CAS after15 days of intervention was assessed using paired sample t-test whereas difference between post-interventional scores of patients receiving only study intervention and those receiving study medication along with conventional laxatives was assessed using independent sample t-test. CAS scores of patients receiving opioid derivatives was analysed separately.

Results: The mean age of study subjects was 60.9 years with 64.4% of male patients. Various cancers types of patients enrolled were colorectal (n=38), hepatobiliary (n=17), pancreas (n=17), oesophagus (n=14), stomach (n=7) with around 60% of patients being of stage IV.

The mean baseline CAS of patients taking chemotherapy (6±3.1) and patients not taking chemotherapy (4.8±2.7) was significantly different ($p < 0.05$). AK for 15 days significantly reduced constipation in chemotherapy patients (n=32) (6.0 vs 3.1 $p < 0.001$) as well as patients not taking chemotherapy (n=38) (4.8 vs 2 $p < 0.001$). However, there was no statistically significant ($p > 0.5$) difference in the reduction of CAS on day fifteen between patients taking only AK and patients taking AK along with conventional laxatives.

In patients with CIC, mean baseline CAS score of patients taking Chemotherapy was (6 ±3.1) which reduced to (3.1 ±2.8) ($p < 0.001$). However, post interventional (Day 15) scores of patients taking AK alone (n=14) was significantly lower than that of patients taking AK along with Conventional laxatives(n=18) (5.0 vs 2.1 $p < 0.001$).

In patients taking Opioid derivatives mean baseline CAS score was 6.7 ±2.9 which reduced to 3.6 ±3.9 post interventional ($p < 0.001$). Post-interventional score in a group of patients taking opioids along with AK was similar to those of patients taking opioids along with conventional laxatives and AK ($p > 0.5$). AK was well tolerated in all patients.

Conclusion: The findings of this study indicate the efficacy of Aarewat Kalpa can act as an effective and well-tolerated laxative for treating various types of constipation associated with advanced-stage cancers, chemotherapy-induced constipation, and opioid-induced constipation. However further randomized control trials are required to make any clinical recommendations.

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P-236 New polyclonal antibody therapeutic to treat esophageal adenocarcinoma and Barrett's esophagus by targeting EPHB4

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Background: We have previously shown that human ephrin receptor B 4 (EPHB4) is overexpressed in human mucosal biopsies from esophageal adenocarcinoma (AEC) and its precursor Barrett's esophagus (BE). With the current standard of care, overall survival at 5 years in patients with AEC is < 20%. Endoscopic ablation of BE in patients presenting with high-grade dysplasia has been shown to reduce the rate of progression to AEC, but ablation is costly and invasive. In non-dysplastic BE patients (the majority) treatment options are limited, mostly consist of reflux control with proton pump inhibitors to minimize further damage to the affected tissue, and their effectiveness and ability to prevent progression to AEC is debatable. To address this gap, new less invasive therapies are required. Accordingly, we have developed and characterised a new oral therapeutic agent consisting of bovine polyclonal antibodies against human EPHB4 with the potential to treat both BE and AEC.

Methods: Therapeutic bovine pAbs were raised in dairy cows and the immunoglobulin fraction was extracted. Binding of the pAbs to recEPHB4 was tested in vitro by ELISA and surface plasmon resonance. Binding to native human EPHB4 was tested by flow cytometry and immunofluorescence techniques using esophageal cell lines and engineered Chinese Hamster Ovary (CHO) cells expressing full-length human EPHB4. Additionally, we tested the ability of the EPHB4-specific pAbs to reduce the viability of cell lines expressing human EPHB4 originating from non-dysplastic BE, high-grade dysplastic BE, AEC, and healthy esophageal tissue.

Results: Bovine pAbs were able to bind their target EPHB4 sequence with high affinity (disassociation constant (KD)=66.34 ± 3.0 nM) with assay noise/signal ratios of < 4%. Specific binding to EPHB4 was confirmed in CHO cells expressing the full-length receptor and further proven in human esophageal cell lines. In both BE and AEC cells, viability was reduced 25-34% at 80 nM concentration of active EPHB4-specific pAbs. The viability of healthy esophageal cells was not affected.

Conclusion: This study provides preclinical evidence of a polyclonal antibody therapeutic that efficiently targets EPHB4 and kills BE and AEC cells. With limited options for the treatment of non-dysplastic BE and poor results in the treatment of AEC patients worldwide, novel EPHB4 polyclonal antibodies offer a potential novel treatment for AEC and a novel therapeutic ablation option for individuals with BE.

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P-237 Impact of adjuvant chemotherapy in poorly cohesive gastric carcinoma: Experience from the Peruvian National Cancer Institute

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Background: In Peru, the incidence of gastric cancer is around 16.1 per 100 000 inhabitants making it the 4th most common cause of cancer and the second most deadly (12.8 cases per 100 000 inhabitants). Fifty-percent of them are poorly cohesive gastric carcinoma (PCGC). PCGC is frequently highly infiltrative and resistant to chemotherapy. Although radical gastrectomy is a standard treatment for PCGC, recurrence is a critical issue for long-term survival of patients and so far, the role of adjuvant chemotherapy in these patients is controversial. In this study, we evaluated the effect on disease-free survival (DFS) and overall survival (OS) of adjuvant chemotherapy with capecitabine or 5-fluorouracil plus oxaliplatin after D2 gastrectomy compared with only D2 gastrectomy in PCGC.

Methods: We retrospectively reviewed patients diagnosed and treated for PCGC during 2014 – 2016 at the Peruvian National Cancer Institute (INEN). Patients with incomplete chemotherapy or those who died because of a postoperative complication were excluded. The Kaplan Meir method was used to estimate the OS and DFS and the Breslow test to compare the survival curves. The prognostic factors were identified with the Cox proportional hazard model.

Results: 116 patients were diagnosed and treated for PCGC. The median age was 54 (21-89) years and 62 (52.4%) patients were women. Fifty-six (48.3%) received only surgery while 60 (51.7%) received adjuvant chemotherapy and surgery. The median follow-up for DFS was 45.8 months (43.52-48.15) and 48.6 months for OS (44.85-52.34). Median DFS was 45.07 months in the chemotherapy and surgery group and not reached in the surgery group. The DFS rate was 50% in the chemotherapy and surgery group and 64.4% in the surgery only group (p=0.25). Median OS was 52.5 months in the chemotherapy and surgery group and not reached in the surgery group. The OS rate was 55% in the chemotherapy and surgery group and 64.3% in the surgery only group (p=0.56). On the other hand, univariate analysis identified lymphovascular infiltration, perineural infiltration, pT3, pT4, pN2, pN3, positive/resected nodes rate as prognostic factors for DFS and OS. In the multivariate analysis, pN3 was the only independent prognostic factor of DFS (HR=6.48; 95% CI: 1.09-43.05, p=0.001). The type of treatment was not a prognostic factor associated with DFS or OS (HR: 1.5, 95% CI: 0.85-2.64, p=0.164; HR: 1.32, 95% CI: 0.74-2.35, p=0.35).

Conclusion: These data suggest that adjuvant chemotherapy did not significantly reduce recurrence and mortality after curative resection and D2 lymph node dissection in poorly cohesive gastric carcinoma.

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P-238 Metformin reduces biliary tract cancer in patients with type 2 diabetes

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Background: This study evaluated whether metformin use in patients with type 2 diabetes mellitus might reduce the risk of biliary tract cancer (BTC).

Methods: New-onset type 2 diabetes patients aged 25-75 years from 1999-2005 were enrolled from Taiwan's National Health Insurance and followed up until December 31, 2011. A total of 287,995 ever users and 16,229 never users were identified (unmatched original cohort) and a 1:1 matched pairs of 16,229 ever users and 16,229 never users based on propensity score (PS) were created (matched cohort). Hazard ratios were estimated by three Cox regression models: 1) adjusted for PS; 2) incorporated with the inverse probability of treatment weighting using PS; and 3) all covariates treated as independent variables.

Results: In the unmatched cohort, 73 never users and 523 ever users developed BTC, with a respective incidence of 100.36 and 38.06 per 100,000 person-years. An overall risk reduction was observed in metformin users in all three regression models with a respective hazard ratio (95% confidence interval) of 0.442 (0.344-0.568), 0.377 (0.295-0.481) and 0.477 (0.370-0.615). The tertile analyses showed a dose-response pattern with a neutral effect in the first tertile when metformin use was $<$ 2 years and a significant risk reduction in the second and third tertiles. Findings in the matched cohort were consistent with those observed in the unmatched cohort.

Conclusion: Metformin significantly reduces the overall risk of BTC by 50%-60%. A dose-response effect is observed and users of more than 2 years show significantly reduced risk.

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P-239 Patient-reported outcomes in patients with metastatic gastric and esophageal cancers near end-of-life

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Background: Despite various advancements, the prognosis of patients with metastatic gastric and esophageal cancer remains poor. Further, such patients are likely to exhibit various symptoms, some of which may intensify near death.There are limited data on patient-reported outcomes near end-of-life (EOL) in patients with gastric and esophageal cancers. This study aimed to assess the pattern and burden of symptoms near EOL, using the Edmonton Symptom Assessment System (ESAS) in a real-world cohort.

Methods: We examined prospectively collected patient-reported outcomes (PROs) near the end of life (within six months of death) of patients diagnosed with metastatic esophageal and gastric cancer, using the revised Edmonton Symptom Assessment System (ESASr) questionnaire from a large Canadian province between 2016 and 2019. The ESASr was categorized into physical, psychosocial, and total symptom domains. Each domain was scored from 0-10 by the patient and the scores were classified as mild (0-3), moderate (4-6), and severe (7-10). While physical score included six individual domains- pain, tiredness, drowsiness, nausea, loss of appetite, and shortness of breath, psychological score consisted of anxiety and depression. The total score was derived from physical, psychological, and a domain of overall well being. The severity of symptoms was further analyzed for any associations with age, sex, time to death and primary tumor site (esophagus vs gastric) using multivariable logistic regression.

Results: We identified 288 patients (146 with esophageal, and 142 with gastric cancer) for the current analysis, of which 75% were males, and the median age at diagnosis of metastatic disease was 66 (interquartile range, 35-91) years. The ESASr questionnaire were self-administered at a median of 43 (interquartile range, 15-132) days before death. Overall, physical and psychological symptoms were severe in 17% and 12% of patients with gastroesophageal cancers, respectively. Around one-third of patients had moderate to severe symptoms in at least one domain of physical score. Within the psychological domain, anxiety and depression were reported at similar frequency and two-third of patients reported some severity of either symptom. Severe psychological symptoms were reported by 12% of patients. Further, severe nausea and loss of appetite were more common than other physical symptoms. There were no associations of symptom severity with age, sex, and primary tumor site (gastric vs esophagus). However, pain score was more likely to be rated as severe in patients with esophageal cancer, as compared to those with gastric cancer (P=0.02). In logistic regression, time to death was associated with the total (P=0.02) and physical (P=0.01) symptom scores, but not with the psychological score (P=0.32).

Conclusion: In the real-world setting, unique symptom trajectories may emerge for gastric and esophageal cancer patients near the end of life. Collection of PROs near death can help deliver targeted palliative intent treatments to improve not only the quality of life but also the quality of death in patients with gastric and esophageal cancer.

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P-240 Anal cancer treatment: Major reduction of acute toxicity with an approach using 4-fractions-per-week

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Background: The purpose of our study was to report the long-term excellent outcome in patients with squamous cell carcinoma of the anal canal (SCCA), who were treated with definitive chemo-radiotherapy (CRT) using an innovative approach of 4-fraction-per-week and conventional 3D radiotherapy technique.

Methods: Twenty-four patients who received definitive chemo-radiotherapy from January 2013 to December 2018 were included in this study. All patients received 5-fluorouracil with mitomycin C as this has been our institutional practice. No patients received cisplatin. All 24 patients were treated with conventional radiotherapy technique. The median dose was 5400 cGy (range = 5220-5580 cGy). Median follow-up was 36 months.

Results: All 24 patients were treated using a modified regimen of 5 fractions only for the first week, followed by 4 fractions per week thereafter (Fridays off starting the second week of treatment with no planned break). For a few patients receiving the highest dose of 5580 cGy in 31 fractions, this was equivalent to 7.5 weeks or 51 days. Acute skin toxicity was: grade I: 21 patients (88%), grade II: 3 patients (12%), with no grade III or IV skin toxicity. Acute hematologic toxicity: grade I: 16 patients (66%), grade II: 7 patients (29%), with no grade III or IV hematologic toxicity. Acute GI toxicity: grade I: 14 patients (58%), no grade II, III or IV GI toxicity. All patients completed treatment as prescribed. Treatment compliance was 100%. No patients required hospitalization from side effects of chemo-radiotherapy treatment.

Conclusion: This innovative approach of 4-fraction-per-week using conventional 3D radiotherapy technique was initially conceived to reduce skin toxicity. Interestingly, in addition to a significant reduction of acute skin toxicity, hematologic, and GI toxicity was also greatly reduced, with virtually no need for treatment breaks, and yielded excellent local-regional control and overall survival when compared with known randomized RTOG studies. This innovative approach of 4-fraction-per-week deserves further study by individual investigators and/or appropriate clinical trials.

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P-241 First- and second-line treatment with tyrosine kinase inhibitors after chemoembolization in intermediate-stage hepatocellular carcinoma patients

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Background: The benefits of sorafenib as first-line treatment and regorafenib as second-line treatment for HCC patients after recurrence to TACE is not yet adequately studied. Aim: To estimate the efficacy of sorafenib as first-line treatment and regorafenib as second-line treatment in patients with intermediate-stage HCC after recurrence to previous TACE treatment.

Methods: Retrospectively, we estimated the efficacy of sorafenib and regorafenib administration (overall survival [OS] and time to disease progression [TTDP]) in 12 patients (Group A) with intermediate-stage HCC after recurrence to treatment with TACE (1-3 TACEs; median, 2). The results were compared with those of a similar historical group of 15 HCC patients treated only with TACE (Group B).

Results: There were no significant differences in disease characteristics between the two studied groups. The index of disease control for group A was 67.2% and the mean TTDP was 4.2 months during sorafenib administration. Regorafenib was administered when progression of HCC was observed. The OS was 31.2 months. For Group B, the index of disease control was 30.6% (P = .001), the mean TTDP was 2.3 months (hazard ratio, 0.44; P $<$ .01), and the OS was 13.4 months (hazard ratio, 0.57; P $<$ .001). The

multivariate analysis revealed that the addition of sorafenib and regorafenib was the most important factor for OS and the prolongation of the TTDP.

Conclusion: The administration of sorafenib and regorafenib seems to be an attractive therapeutic approach for patients with intermediate-stage HCC after recurrence to previous TACE treatment.

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P-242 Germline mutations identified in Colombian patients with Lynch syndrome

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Background: Colorectal cancer (CRC) is the third cause of death from cancer in the world; in Colombia, it is the fourth neoplasm in men and the third in women. Approximately 70% can be classified as sporadic CRC cases and about 30% of CRC cases show a family history of the disease and about 6% have familial aggregation. In our previous studies, we identified 69 family cases among 1,278 patients, 14 were carriers of 48 mutations in high-risk genes such as APC, MLH1, MSH2, PMS2, PTEN, SMAD4, STK11, POLD1, and POLE, while for the remaining 55 family cases, the genetic basis was not established.

Methods: We performed whole-exome sequence analysis from 2 patients with Lynch Syndrome (LS01 and LS02) without high-risk gene mutations. The genomic DNA was extracted from blood samples, whole-exome sequencing was performed by Novaseq 6000 Sequencing System (Illumina) with 100X and 150 PE. Burrows-Wheeler Aligner (BWA-MEM) was used for read mapping to the human reference genome GRCh38; GATK HaplotypeCaller was used for variant calling and these were annotated by using Annovar. The variants were selected with a threshold of MAF $\leq$ 1% and CADD $>$10. The functional effect of variants was predicted with Polyphen, SIFT, MutationAssessor, and MutationTaster.

Results: A total of 101,230 SNPs and 15,363 InDels were identified in case LS01. Based in ClinVar classification, we identified seven pathogenic variants on SLC26A2, FGFR4, HFE, STOX, NOD2, DUOX2, and PRODH genes and 14 risk variants on IL6R, RNASEL, RET, ERCC6, ERBB2, among others; 12 variants of uncertain significance (VUS) in cancer-related genes. A total of 101,797 SNPs and 15,500 InDels were identified in case LS02. Among these variants, we found four pathogenic mutations on HADHA, HFE, BLM, and RAD51D. We identified a mutation on MHL1 gene classified as VUS, however, it is considered as class 4 (likely pathogenic) variant in InSiGHT databases.

Conclusion: We have reported new gene variant candidates to be associated with Lynch syndrome in Colombian cases. Currently, peripheral blood was obtained from two affected relatives with CRC and 20 asymptomatic relatives of case LS01 and one relative with CRC, two with gastric cancer and eight asymptomatic relatives of case LS02 to perform a segregation analysis to evaluate the concordance of the variant status and the presence of the disease.

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P-243 Incidence and survival of pancreatic neuroendocrine tumours in Girona, Spain

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Background: Pancreatic neuroendocrine tumours (pNETs) are rare cancers arising from neuroendocrine cells of the pancreas. We evaluated the incidence, demographic and survival outcomes of pNETS in the Girona region.

Methods: A retrospective review of patients treated between 2001-2018 in our center was undertaken. Clinical data were obtained from the hospital cancer registry and Girona cancer registry. We classified all the neuroendocrine tumors from this period and analyzed according to the 2010 World Health Organisation Classification: NET g1, NET g2 and neuroendocrine carcinoma (NEC).

Results: During this period 82 pNETs patients were treated. 34 were women (42%) and 48 were men (58%). The median age at diagnosis was 60 years. 77% of cases were classified into neuroendocrine tumors (NET) g1 and g2, and 23% into neuroendocrine carcinoma (NEC). 14% were functional tumours (5 gastrinomas, 2 insulinomas, 1 vipoma, 1 polypeptide secreting tumor, 2 carcinoid syndrome). Just 29 had metastatic disease at presentation (35%), mostly in the liver (90%). Chromogranin A (CgA) levels at diagnosis were determined in 62% of cases. It was elevated in 65% of the determinations. In terms of treatment, 34 patients were initially treated with radical surgery, chemotherapy was the front line in 18 patients (14 of them were NEC) and somatostatin analogues were used in 16 patients. 45 patients have died (5 patients died for nontumoral causes). Median Overall Survival (mOS) was 59 months. In the univariate analysis, only grade was significantly associated with OS (p=0.018). Sex, functional status, basal CgA and metastatic disease at presentation were not significant, probably because of the low number of cases. In the multivariate analysis, grade was the only factor having a significant impact on OS (HR 3.135, p=0.033).

Conclusion: Compared to previously published data, our report showed a smaller rate of metastatic disease at presentation. Survival was poorer, but we included NEC and 5 patients with other causes of death. Management of pNET has changed in the last 10 years and a deeper revision will be performed.

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P-244 Demographic data, risk factors, and clinical aspects of hepatocellular carcinoma (HCC) in Southeastern Europe during the last decade

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Background: Risk factors, clinical aspects, and demographic data of HCC patients in Southeastern Europe are not adequately investigated. Aim: Determination of demographic data, clinical aspects, and risk factors for HCC in Southeastern Europe during the decade 2007-2017.

Methods: Data from 328 HCC patients followed in our department from 2007 to 2017 were analyzed retrospectively.

Results: The median age of patients was 67 years (range, 42-89) and 242 (73.7%) were men. Overall, 179 (54.5%) were infected with HBV, 117 (35.6%) were infected with HCV, and 7 (2.1%) were co-infected with both viruses. A total of 12 (3.6%) patients reported chronic alcohol consumption, and for 13 (3.9%), the cause of HCC was NASH/NAFLD. Of the patients with viral hepatitis (B or/and C), 33 (11.1%) also reported chronic alcohol abuse. Cirrhosis stage A was diagnosed in 189 patients (57.6%), stage B in 79 (24.0%), and stage C in 34 (10.3%). The rest were noncirrhotics. A total of 219 patients (66.7%) were diagnosed with advanced disease, 78 (23.7%) with intermediate, and 31 (9.4%) with early HCC stage. In all, 144 (43.9%) patients presented with elevated AFP, and 57 of these (17.3% of total) had AFP levels $>$400 ng/mL. Of 328 patients, 99 (30.1%) presented with multinodular HCC and 20 (6.1%) had diffuse disease. At the time of diagnosis, 27 (8.2%) patients presented with local lymph node metastases and 13 (4.0%) had distant metastatic disease. Hepatectomy, RFA, chemoembolization, and sorafenib administration were the main therapeutic approaches.

Conclusion: In Southeastern Europe, HCC is 3-fold more common in men than in women. HBV and HCV infections and chronic alcohol consumption are the main etiological factors. Elevated AFP levels can be useful for early diagnosis in high-risk patients.

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P-245 GETNET-SILVELUL study: An original or modified immunohistochemical score (IPS or mIPS) in patients (pts) with pancreatic neuroendocrine tumors (PanNET) treated with everolimus or CAPTEM

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Background: Previously our group showed the potential use of a score (IPS) based on MGMT, NDRG-1 and PHLDA-3 immunohistochemistry (IHC) expression as strong prognosis factor in operated PanNET (Viúdez et al. Oncotarget 2016). The present retrospective multicenter project analyzes the predictive/prognosis role of MGMT, NDRG-1 and PHLDA-3 IHCs in patients with advanced PanNET treated CAPTEM or everolimus.

Methods: IHC nuclear staining for MGMT and PHLDA-3 is being scored as 0, 1-5%, 6-50% and $\geq$ 51%. For NDRG-1, we are using a cytoplasmic score from 0 to 2 based on distribution pattern (null, patched or diffuse). mIPS was calculated based on those IHC expressions 0% IHC expression for MGMT: 0 pt; $<$ 5% PHLDA3: 0 pt; null or weak intensity NDRG1 expression: 0 point (min: 0 pt, max: 4 pts).

Results: 78 of 105 pts have been fully analyzed, 39 of them women (50%) and median age of 61 (27-81). 35 pts were treated with CAPTEM and 43 pts with everolimus. Median previous lines were 2 (20.5% received chemotherapy previously), and 90.5% pts had ki67 $<$ 20%. 63%, 12% and 26.8% were null for MGMT, NDRG-1 and PHLDA-3 IHC analysis. In the entire cohort K-M analysis showed significant differences for PFS or OS based on best response and mIPS, p=0.0001 and p=0.002, respectively. Significant differenced were also observed for OS based on number previous lines received (p=0.011) or mIPS (p=0.016). In pts treated with everolimus, log rank analysis showed significant differences for PFS (p=0.007 HR: 0.136 CI95%: 0.032-0.575) based on our mSPI. Similar results were observed in CAPTEM cohort for PFS (p=0.033 HR: 3.56 CI95%: 1.11-11.45) according to original IPS.

Conclusion: From our knowledge it is the first time that a simple IHC score could be useful to predict outcome in PanNET pts treated with everolimus or CAPTEM. More mature results and analyses of our project are needed and will be presented during 2020 ESMO World Congress on GI Cancer.

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P-246 Taxane cross-resistance: An exploratory analysis of second-line chemotherapy for metastatic gastric cancer

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Background: Standard treatment for metastatic gastric cancer (GC) is chemotherapy (CT). Most commonly, first-line chemotherapy is based on a combination of fluoropyrimidines, platinum derivates, and, in case of a HER2 overexpression, trastuzumab. First choice for second-line chemotherapy is paclitaxel associated with ramucirumab. However, there is a dearth of data about the optimal second-line treatment in patients (pts) who progress on first-line treatment including taxanes. For these pts, second-line paclitaxel and ramucirumab could incur in lack of efficacy due to taxanes cross-resistance. This exploratory analysis aims to address effectiveness and safety of second-line treatment with paclitaxel and ramucirumab after a first-line treatment including docetaxel; moreover, it investigates clinicopathological features that could be associated with a better response and, thus, potentially drive clinical decision-making.

Methods: A retrospective analysis was conducted on a consecutive series of 22 GC pts previously treated with first-line docetaxel, oxaliplatin and capecitabine (1 pt with fluorouracil) at National Cancer Institute, IRCCS CRO Aviano (Italy). In the univariate survival analysis, overall survival (OS) and progression-free survival (PFS) were estimated using Kaplan-Meier method.

Results: In our analysis, 20/22 pts were males; median age was 58y (41-73). 7/22 pts had HER2-positive cancer. 7/22 pts had locally advanced tumors at diagnosis (T3 and N+/-); 15/22 pts had stage IV disease at diagnosis; 1/22 had more than 3 metastatic sites at diagnosis; 4/22 had more than 3 metastatic before paclitaxel. Median number of docetaxel cycles received before starting paclitaxel was 6 (1-12); median number of months since completion of docetaxel was 7 months (1-31). Paclitaxel and ramucirumab was usually given as second-line; 3/22 pts had it as third-line; median number of cycles administered was 3. 8/22 pts had a baseline performance status (PS) = 0; 12/22 a PS =1; 2/22 a PS =2. 15/22 pts underwent maintenance treatment after completion of first-line treatment. Only 2/22 pts had a partial response to paclitaxel and ramucirumab; 3/22 had stable disease; the disease control rate was 22.7%. 2/22 pts had G3/4 haematological toxicity; no patient had non-haematologic G3/4 adverse events; 5/22 patients had G2 neuropathy. 11/22 patients required a dose reduction while on paclitaxel, mostly due to neurotoxicity or PS deterioration. Median OS was 6 months, median PFS was 3 months. At the time of this analysis, 3 patients were still alive.

Conclusion: Our analysis showed that patients who undergo treatment with paclitaxel and ramucirumab after a first-line therapy including docetaxel have a median PFS of 3 months and an OS of 6 months, both shorter than the historical control of the randomised phase 3 RAINBOW trial. PS was the only feature significantly associated with OS. The main limits of our study are its retrospective design and the small number of patients included in the analysis. Interestingly, we noticed an imbalance in the number of male patients and of HER2-positive patients. As such, further studies are needed to determine whether paclitaxel is a viable option for GC patients who received docetaxel.

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P-247 Real-world clinical outcomes for third-line standard of care regimens in deficient mismatch repair or microsatellite instability-high metastatic colorectal cancer in France

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Background: Evidence suggests that deficient mismatch repair (dMMR)/micrsatellite-High (MSI-H) metastatic colorectal cancer (mCRC) patients are less responsive to conventional treatment (chemotherapy +/- targeted therapy) and have a worse prognosis than those with MMR-proficient or microsatellite stable mCRC. Immune checkpoints inhibitors (ICIs) have rapidly emerged as a key treatment modality for dMMR/MSI-H tumors including mCRC. However, these data were based on single-arm clinical trials and clinical outcomes data with standard of care (SOC) regimens are lacking since dMMR/MSI-H advanced CRC represents only ~5% of all CRC. The study objective was to evaluate real-world clinical outcomes in dMMR/MSI-H mCRC patients receiving third-line (3L) SOC regimens.

Methods: Two tertiary French University hospitals participated in a retrospective chart review study in which adult patients previously diagnosed with mCRC (stage IV), with a dMMR and MSI-H status and treated with 2 or more prior lines of SOC therapy for advanced disease were enrolled. Key exclusion criterion was prior or current treatment for 3L with ICIs. A minimum of 6 months of follow-up was required, including patients who died during this time period. Overall survival (OS) from the start of 3L treatment (index date) was reported using Kaplan-Meier analysis. The best overall response rate (BORR) was reported along with complete response (CR) and partial response (PR).

Results: 36 dMMR/MSI-H mCRC patients were included. Majority were male (56%) with a mean age of 61.8 years and with synchronous metastatic disease (78%). RAS and BRAF mutations were observed in 31% and 42% of patients, respectively; 22% were RAS/BRAF wild type and 6% had unknown mutational status. 17% (N=5/29 reported) of patients were identified with Lynch syndrome (germline mutation). Of the surgeries performed in the pre-index period, 76% were for primary tumor resections and 24% for metastatic disease. Most common metastatic sites were hepatic (57%) and peritoneum (50%). Prior to 3L treatment, all patients received combination therapy in 1L with fluoropyrimidine + oxaliplatin (53%) and fluoropyrimidine + oxaliplatin + bevacizumab (11%) being the most common regimens. In 2L, 97% of patients received combination therapy with fluoropyrimidine + irinotecan + bevacizumab (23%), fluoropyrimidine + irinotecan (17%) and fluoropyrimidine + irinotecan + cetuximab (11%) being the most common regimens. For 3L and later, combination therapy was preferred over monotherapy but decreased in usage (75% for 3L vs. 57% for 4L). Fluoropyrimidine + irinotecan with or without an EGFR/VEGF inhibitor was the most common combination regimen (N=12) and 5 patients received regorafenib in 3L. The median OS for dMMR/MSI-H mCRC patients

receiving 3L therapy was 9.0 months (95% Confidence Interval (CI): 4.0-14.1). Median OS decreased to 4.1 months (95% CI: 4.0-9.0) when survival data of patients receiving ICIs at 4th or later lines were censored at progression date of prior treatment line. BORR was 5.7% (2 patients with PRs), and 31.4% (11 patients) showed stable disease (SD) for 3L treatment.

Conclusion: Real-world clinical outcomes observed for dMMR/MSI-H mCRC patients treated in 3L are suboptimal. Study results suggest a high unmet need that could be addressed with ICIs.

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P-248 Quality of life among Tunisian gastrointestinal cancer patients undergoing chemotherapy

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Background: The impact of disease and treatment on gastrointestinal (GI) cancer patients' well-being is a topic of growing interest. The aim of our study was to assess the quality of life (QoL) among GI cancer patients undergoing chemotherapy and to evaluate the association between the QoL and demographic and clinical characteristics.

Methods: We conducted an exploratory survey using the QLQ-C30 between February and April 2019. We included all cancer patients, all stages and under treatment. Global health, functional scales, and symptoms of GI cancer patients were then compared through the Student's t-test or the Mann-Whitney after testing the normality of the distribution.

Results: We included 40 GI cancer patients among 131 patients who responded to the questionnaire. Twenty-three patients had colon cancer, eight patients had rectal cancer, five patients had stomach cancer, two patients had pancreatic cancer and two patients had cholangiocarcinoma. The mean age of GI cancer patients was 54.5 years (SD=11.9). GI cancer patients were male in 52.5% and had recurrent or metastatic disease in 45%. Among all cancer patients, GI cancer patients had worse physical functioning (p=0.04) and less appetite (p=0.029). Female GI cancer patients were more likely to have altered physical functioning (p=0.005), nausea and vomiting (p=0.044), pain (p=0.006) and insomnia (0.036). GI cancer patients over 55 years old had worse role functioning (p=0.02) and those who were married had better cognitive functioning (p=0.024). Fatigue was significantly important among patients receiving one to three cycles of chemotherapy compared with 4 to 6 cycles (p=0.005). The metastatic disease did not affect scales in our study.

Conclusion: We found a correlation between QoL and age, gender and social status. Fatigue reduced significantly in patients after 3 cycles of chemotherapy.

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P-249 Resecting the unresectable: Superior survival of tri-modality pancreatic adenocarcinoma patients

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Background: The majority of patients with pancreatic adenocarcinoma are deemed unresectable on initial diagnosis due to locally advanced or metastatic disease. Their overall median survival is approximately 10 – 12 months. This is largely due to the dissemination of pancreatic tumour cells early prior to its formation via epithelial-to-mesenchymal transition. Recent publications showed the use of chemotherapy converting unresectable to resectable tumours, resulting in better survival outcomes. The aim of this study was to: 1. Identify our Oncology Unit's experience in downstaging unresectable locally advanced pancreatic adenocarcinoma using long course chemotherapy and radiotherapy with infusional 5-fluorouracil (5-FU/RT) 2. Examine the overall survival rate of our Oncology Unit's locally advanced pancreatic adenocarcinomas receiving tri-modality of long course chemotherapy, 5-FU/RT, then surgery.

Methods: We conducted a retrospective analysis of patients diagnosed with unresectable locally advanced pancreatic adenocarcinoma between January 2014 and December 2019. Follow-up patient data with subsequent multidisciplinary meetings were obtained for those who were deemed resectable with tri-modality of treatment: chemotherapy, chemo-radiotherapy and surgery. Overall survival (OS) was estimated via Kaplan-Meier method.

Results: Of the total 68 patients identified, there were 20 patients (29%) who became resectable and underwent surgery after chemotherapy (7 patients) or 5-FU/RT (13 patients). Median chemotherapy treatment time was 6 months (4 – 8 months), whereas 5-FU/RT treatment time was 6 weeks (55 Gy). The regimens were as follows:- a) 6 months gemcitabine/nab-paclitaxel (Gem/NabP), then RT-5U (11 patients) b) 6 months Gem/NabP, FOLFIRINOX, then RT-5FU (2 patients) c) 6 months Gem/NabP, then FOLFIRINOX (3 patients) d) 6 months Gem/NabP (4 patients). The overall survival for patients that received triple modality after deemed resectable was 51.0 months (95% CI, 32.0 – 89.0).

Conclusion: Approximately one-third of patients who have unresectable locally advanced or metastatic pancreatic adenocarcinoma could be rendered potentially resectable through the use of neoadjuvant therapy. Our Oncology Unit's treatment regimen of 6 months chemotherapy followed by 5-FU/RT for the selected patient cohort resulted in significantly prolonged OS. There is an improved OS for patients who had conversion from unresectable to resectable pancreatic adenocarcinoma after receiving tri-modality treatment.

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P-250 Significance of microsatellite instability PCR evaluation for metastatic colorectal cancer patients: Dynamic changes during disease course (preliminary results)

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Background: Microsatellite instability (MSI) is an important biomarker in colorectal cancer (CRC) used for multiple purposes. In this study, we evaluated the significance of MSI measurement as a prognostic factor in patients with metastatic CRC (mCRC).

Methods: The study included 42 consecutive patients who underwent chemotherapy for mCRC between January 2019 and January 2020. The clinicopathological data of the patients were obtained from their medical records through a retrospective review. MSI status was determined by PCR/fragment analysis on ABI3130 Genetic analyzer. DNA was extracted from paraffin-embedded tumor tissues and compared to the patient's DNA isolated from peripheral blood. A set consisting of 8 microsatellite markers was used – two mononucleotide (BAT25 and BAT26), three dinucleotide markers (D2S123, D5S346, and D17S250) and three tetranucleotide markers (L17686, MYCLI and D9S242). Patients were divided into two groups: MSI (with instability in two or more markers) and MSS (with zero or one unstable markers). Statistical analyses were performed using SPSS version 21.0.

Results: 31 % of the patient population was female and 69 % was male with a median age of 61,5 years. 78,6 % of patients had comorbidity. 76,2% of the tumors were left-sided and 23,8 % were right-sided. 92,9 % of patients had their primary tumor removed. 31% of patients had resection of one metastatic site. 28,6 % of patients presented with lung metastases at diagnosis, 83,3 % with liver metastases, 11,9 % with peritoneal metastases. 61,9 % of patients had metastases at more than one organ site. The ORR to first line of treatment was 52 %. 71,4 % of patients received second line therapy, 50 % received third line. 27,5 % of all tumors were MSI, whereas 72,5 % were MSS. All MSI tumors showed instability at BAT25. Mean PFS in the MSS group was 11,7 months, whereas the mean PFS in the MSI group was 18,6 months. Mean OS in the MSS group was 24,1 months, whereas the mean OS in the MSI group was 33,5 months. There was no statistically significant relationship between MSI status and age (p=.428), CEA level (p=.16), PFS (p=.09), or OS (p=.151). 39 patients were BRAF wild-type and 3 were BRAF mutated. 45,2 % were RAS mutated and 54,6 % were RAS wild-type. Six of patients who underwent surgery for metastases were tested twice – at the time of removal of primary tumor and then at operation for metastatic spread. Two patients whose tumors were originally MSS changed to MSI, two remained MSS with instability at zero markers. The last two remained MSS but exhibited instability at one marker in comparison to zero at the time of diagnosis.

Conclusion: Our study is in agreement with some prior studies of mCRC which had not found a significant difference in OS and PFS in MSI and MSS tumors. Despite the small number of patients tested twice in the course of their disease and the little available information, the change instability in one or more nucleotide markers might be explained by tumor heterogeneity and will require additional studies.

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P-251 Diversity of Helicobacter pylori genotypes in tumoral, antral and normal tissue of Colombian patients with gastric cancer

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Background: Infection with Helicobacter pylori (H. pylori) is the major risk factor for gastric cancer (GC), the first cause of death in men and the fourth in women for Colombia. Studies suggest that there exists a positive selection of pathogenic strains according to advance the severity of gastric lesions.

Methods: We evaluated the virulence profile of H. pylori strains present in antral, normal and tumoral tissue of 78 patients with GC from Ibagué-Colombia. The DNA from the gastric tissues was extracted using the DNeasy Blood & Tissue Kit of QIAGEN. The bacterium was identified by PCR amplification of a fragment of the 16s rDNA gene and the genotypes were identified by amplification of fragments of the cagA, cagE genes and the signal (alleles s1 and s2) and medium (alleles m1 and m^2) regions of vacA gene. The PCRs were performed separately in a Biorad Dual-Touch 1000 thermocycler. The amplification products was visualized by electrophoresis in agarose gels.

Results: The prevalence of H. pylori infection was of 58% in antral, 20% in normal and 30% in tumoral tissue. A total of 14 genotypes of strains were identified; in the antral, we observed the highest number of genotypes. In the antral and the adjacent normal tissue, just one strain had the vacA $s2m^2$ genotype, the remaining strains had the cagA or cagE genes and the alleles of vacA gen in different combinations. 63% (27/45) in antral tissue and 50% (8/16) strains in normal tissue had a cagA/cagE/vacAs1m1 genotype. In tumoral tissue we did not find the vacA $s2m^2$ genotype and 63% of strains in tumoral tissue were cagA/cagE/vacAs1m1 and all strains had the oncogene cagA and different combinations of the presence or absence of cagE and the alleles of vacA gene. In 13 patients, we observed the cagA/cagE/vacAs1m1 genotype in the antral, normal and tumoral tissue.

Conclusion: The low percent of vacA $s2m^2$ genotypes and the high frequency of the cagA/cagE/vacAs1m1 genotype and the persistence of this genotype in the different tissues suggest a positive selection and persistence of the cagA/cagE/vacAs1m1 pathogenic genotypes in patients with GC.

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P-252 Serial cytokines as potential predictive/prognosis biomarkers in potentially resectable pancreatic adenocarcinoma

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Background: Mortality rate in pancreatic adenocarcinoma (PDAC) is similar to its incidence rate due to that almost 50% of the patients are diagnosed having metastasis and 1yOS for all stages barely over 20%. For this reason, new biomarkers (BKs) are urgently needed in order to improve patient outcomes in PDAC. In this sense, the main aim of this multicenter and prospective project is to find predictive and/or prognostic BKs based on many cytokines that are produced in cancer microenvironment and can nowadays be accurately analyzed.

Methods: Patients diagnosed with potentially resectable PDAC with poor prognostic factors (CA 19.9 > 150 U/ml; suspected micrometastasis or low PS) and treated with neoadjuvant treatment are being prospectively included. Serial analyses (basal, with TC, with surgery and time of relapse/or after 1y of follow-up) of serum levels of 80 cytokines are being done.

Results: Since February 2018, with a median follow-up of 11,25 months (m) (4,67-38,28) 22 patients (pts) with median of age of 62,5 y-0, most of them men (63.6%) have been included, with radical surgery performed in 14 of them (2 pts with bypass). Seven operated pts received adjuvant treatment and 12 operated pts developed progression of disease. 18 pts have received nab-paclitaxel and gemcitabine as perioperative treatment and 4 received Folfirinox. Perineural and vascular invasion were confirmed after surgery in 45,5% and 27,3% of cases, respectively. Positive nodes were found in 40,9% of them, being the median of positive and resected nodes of 1 (0-14) and 26 respectively. Surgical margins were negative (R0) in 64,3% of cases (35,7% R1). Pathological response was described as partial in 13,6%, with no changes in 31,8% and progression in 13,6%. Globally, PFS and OS were 13,50 m (CI95%: 6,44-20,55) and 17.31 m (CI 95% 8,86-25,76), respectively. In K-M analysis, significant differences (p=0,002) were observed in cases in which radical surgery had been performed with a mean disease-free survival of 13,5 m (9,34-17,66) and 3.97 m (0-8,23) for unresectable patients. Regarding the cytokine array, we observed different PFS outcomes based on MCP3 levels (low: 16,32 m CI 95%: 5,02-27,63; high: 7,52 m CI95%: 6,23-8.81, p=0,023), oncostatin (high: 7,12 m CI95%: 3,09-11,15, low: not reached; p=0,007), eotaxin (low: 7,12 m CI 95%: 5,75-8,50; high: not reached, p=0,029). A cytokine score was created based on these results, which maintained significant differences in K-M for PFS (16,32 m CI95%: 5,07-27,57 vs 6,53 m CI95%: 2,75-10,32, p=0.003). Our cytokine score showed a significant role as an independent prognosis factor in multivariate analysis (HR: 0,196 CI95%: 0,042-0,918; p=0.039).

Conclusion: In potentially resectable/borderline pancreatic adenocarcinoma, our basal cytokine score seems to be able to discriminate as an independent prognosis factor between those patients who will get significant benefit from neoadjuvant treatment from those who will not.

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P-253 Monitoring circulating epithelial tumor cells (CETCs) in patients with locally advanced colorectal cancer during therapy as a tool to predict therapy response

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Background: Since the first results of the CAO/ARO/AIO-94 trial were published, a combination of neoadjuvant therapy with subsequent total mesorectal excision (TME) has been established as a standard treatment for patients suffering from locally advanced (stage II and III) rectal cancer. Replacing the postoperative by a preoperative (chemo-) radiotherapy (C/RT) led to an impressive improvement in the rates of local tumor recurrence (6% vs 13%) and of toxicity (27% vs 40%). Significant decreases in metastatic relapses, the main reason for therapy failure, have not been achieved, resulting in a poorer outcome in patients with rectal vs colon cancer. Circulating epithelial tumor cells (CETCs) are an important link between primary tumors and metastases and provide a readily accessible source of tumor material from patients with solid cancer.

Methods: Our study was designed to use the immunofluorescence-based maintrac® method to identify and quantify CETCs in the blood of patients with colorectal carcinoma (C18/20) before and during neoadjuvant and/or adjuvant C/RT. Moreover, the ratio of CETCs expressing the proliferation marker Ki-67 was determined during the course of therapy. Sample size of the study is 18 patients and still recruiting.

Results: Stage II and III colon cancer patients were predominantly treated with surgery followed by adjuvant chemotherapy, whereas patients with locally advanced rectum cancer (stage II and III) received neoadjuvant C/RT. The CETC numbers, as well as the ratio of Ki-67 positive CETCs decreased in blood samples of patients with colon cancer during adjuvant therapy. In rectal cancer patients, the number of CETCs before initiation of neoadjuvant chemotherapy correlated with lymph node involvement. Overall, 71% of patients with locally advanced rectal cancer (stage II and III) did not or only partially responded to neoadjuvant C/RT; 60% of the latter had increasing CETC numbers during therapy.

Conclusion: The presence of cells from the tumors circulating in the blood is assumed to be a prerequisite for metastasis formation. Changes in the number of CETCs during neoadjuvant C/RT could directly reflect response to therapy. This rationale is supported by an improvement of therapy results by additional adjuvant chemotherapy following surgery in patients with rectal cancer. The clinical relevance of our findings needs to be analyzed.

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P-254 An experience of two Croatian centers in the treatment of gastroenteropancreatic neuroendocrine neoplasms with long-acting octreotide treatment

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Background: Neuroendocrine neoplasms (NENs) are a heterogeneous group of tumors whose incidence has increased steadily over the past decades. Octreotide is a somatostatin analogue which has traditionally been used for the relief of symptoms that result from the release of peptides and amines (carcinoid syndrome), although a substantial amount of evidence suggests that it has anti-proliferative effects and lengthens the time to progression of the disease. We've aimed to evaluate the relationship between octreotide use and progression-free survival (PFS) and overall survival (OS).

Methods: Medical records of 76 patients with gastroenteropancreatic NENs treated with long-acting octreotide in the University Hospital Centre Zagreb and University Hospital Center Sisters of Charity were collected in the period from March 2011 to March 2019. A retrospective analysis was completed with the Kaplan-Meier method using the PFS and OS as a primary endpoint. Previous to octreotide treatment patients had confirmed high expression of somatostatin receptors (sst-rs) by tetroktyde scintigraphy.

Results: All patients were followed for a median of 38 months, all of them where grade 1 (27%) or grade 2 (73%). Median PFS for all patients was estimated at 12 ± 2,5 months (95% CI 9,62-14,38). Median PFS for patients with pancreatic NETs was estimated at 10 ± 0,5 months (95% CI 7,03-12,97; median Ki-67 10%), patients with NET of large intestine at 10 ± 3,67 months (95% CI 2,87-17,13; median Ki-67 14%), patients with NETs of unknown primary at 12 ± 2,6 months (95% CI 4,93-19,07; median Ki-67 6%) and for patients with NETs of small intestine at 30 ± 14,5 months (95% CI 1,57-58,48; median Ki-67 5%). Median OS was not reached in any subgroup of patients.

Conclusion: Although overall median PFS is lower than in the PROMID study, the fact that the median OS was not reached renders long-acting octreotide as an effective treatment option with acceptable tolerability. This patient population was more heterogenous than in clinical trials and reflects the real-life setting of clinical practice.

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P-255 Effects of tumor treating fields (150 kHz) in combination with FOLFOX on gastric cancer cells in vitro

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Background: Gastric cancer is the third most common cause of cancer mortality worldwide. Long-term survival in gastric cancer remains poor despite advances in systemic therapies. FOLFOX (oxaliplatin, fluorouracil [5-FU], and leucovorin) is an approved chemotherapy regimen for the treatment of gastric cancer. Tumor Treating Fields (TTFields) are an antimitotic, loco-regional anticancer treatment delivered via non-invasive application of low intensity (1-3V/cm), intermediate frequency (100-500 kHz) alternating electrical fields. TTFields target rapidly dividing cancer cells by disrupting microtubules leading to mitotic catastrophe, abnormal chromosome segregation, and apoptosis induction. We investigated the effect of TTFields alone and in combination with FOLFOX in gastric carcinoma cells.

Methods: Gastric cells (AGS and KATO III) were treated for 72 hours with TTFields (1.1 and 1.7 V/cm, respectively) at frequencies of 100-400 kHz using the Inovitro system. Effectiveness of TTFields alone and in combination with FOLFOX as well as TTFields combined with the individual FOLFOX components (oxaliplatin, 5-FU, or leucovorin) was tested by applying TTFields at the optimal frequency in combination with various drug concentrations. Cell counts, apoptosis induction, clonogenic potential, and overall effect were evaluated.

Results: The optimal TTFields frequency that resulted in the greatest cell count reduction (AGS, 55%; KATO III, 52%) was 150 kHz. The clonogenic potential was reduced by >70% in both of the cell lines. TTFields combined with each FOLFOX component (oxaliplatin, 5-FU, or leucovorin) led to a significant reduction in AGS and KATO III cell survival (2-way ANOVA, $P < 0.001$ for each cell line) versus each treatment alone. In AGS cells, TTFields plus FOLFOX combination treatment led to a further reduction in the overall effect (cytotoxic and clonogenic; 79%) versus TTFields alone (65%) and FOLFOX alone (34%). Similar results were observed in KATO III cells.

Conclusion: These results suggest that TTFields at 150 kHz (optimal frequency for gastric cancer cells) show potential as an effective gastric cancer treatment. Combining TTFields with standard-of-care chemotherapy may further enhance clinical efficacy in gastric cancer. TTFields (150 kHz) concomitant with XELOX (oxaliplatin/capecitabine) as the first-line treatment is currently under investigation in a phase 2 trial.

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P-256 Survival rates of locally advanced and metastatic pancreatic cancer in Western Australia

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Background: Pancreatic adenocarcinoma has one of the poorest survival rates, with median overall survival (OS) commonly ranging between 10 to 12 months. Lancet Oncology details that Australia, in particular Western Australia, has one of the best survival rates for pancreatic cancer globally given a 5-year net survival rate of 18.1%. This retrospective analysis:- 1. Examines overall survival rates of patients with locally advanced or metastatic pancreatic adenocarcinoma receiving treatment in Western Australia 2. Identifies factors that may contribute to pancreatic cancer patient survival time in Western Australia.

Methods: A retrospective cohort study identified patients with locally advanced and metastatic pancreatic adenocarcinoma diagnosed between January 2014 and December 2019. All patients had an ECOG performance status of 2 or less. Patients' treatment lines and modalities were collected and analysed. Overall survival (OS) was estimated via Kaplan-Meier method.

Results: A total of 157 patients were identified in our cohort. Out of these, 74 patients (47%) had metastatic disease. Patients were further identified as having the following treatment: chemotherapy only (70 patients), chemotherapy then chemo-radiotherapy (43 patients), chemotherapy and surgery (23 patients) and tri-modality (21 patients). Treatment lines for patients are as following:- a) Chemotherapy only — First line Gemcitabine/nab-Paclitaxel (Gem/NabP) (64 patients) was used, followed by second-line mFOLFIRINOX (48 patients), and third line re-treatment of Gem/NabP (6 patients). b) Chemotherapy then chemo-radiotherapy — Routine incorporation of infusional 5-Fluorouracil were performed for all patients undergoing radiotherapy, where first line Gem/NabP (39 patients) was used, followed by second line mFOLFIRINOX (18 patients), and third line re-treatment Gem/NabP (6 patients). c) Chemotherapy and surgery — First line Gem/NabP (11 patients) was used, followed by second-line mFOLFIRINOX (8 patients), and third line re-treatment of Gem/NabP (4 patients). d) Tri-modality — First line Gem/NabP (19 patients) was used, followed by second-line mFOLFIRINOX (13 patients), and third line re-treatment of Gem/NabP (5 patients). Overall survival (OS) of both locally advanced and metastatic pancreatic adenocarcinoma was 22.0 months (95% CI 20.0 — 28.0). Locally advanced disease patients had OS of 34.0 months (95% CI, 24.0 — 26.0) whereas metastatic disease patients had OS of 19.0 months (95% CI, 12.0 — 21.0).

Conclusion: This retrospective study showed a significant prolonged overall survival for both locally advanced and metastatic pancreatic cancer, with the combined and individual median survival being vastly superior in comparison to global standards. The use of second-line mFOLFIRINOX, as well as third-line re-treatment with Gem/NabP in those of good performance status, could be influencing the overall survival rate.

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P-257 Deep polychromatic flow cytometry characterization of circulating endothelial cells in metastatic colorectal cancer patients

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Background: Circulating endothelial cells (CEC) and their progenitors (EPC) are restricted subpopulations of peripheral blood (PB), cord blood (CB), and bone marrow (BM) cells, involved in the endothelial remodeling and turnover. Both CEC and EPC have been studied as potential biomarkers in colon cancer, but a lack of specificity has limited their clinical application. In this work, a highly sensitive polychromatic flow

cytometry method has been applied for CEC characterization, exploring the role of different circulating endothelial cell subpopulations as potential and predictive biomarkers in colorectal cancer patients.

Methods: A novel polychromatic flow cytometry approach based on optimization of gating strategies and dual-platform counting technique was employed for characterization and enumeration of different CEC phenotypes based on the combination of expression of surface markers as CD45, CD34, CD146, VEGFR2, and annexin-5. Blood samples of 38 metastatic colon-rectal patients were collected at baseline and at the moment of first radiological assessment. A total of 50 healthy subjects were enrolled as controls.

Results: The CD34bright CEC subpopulation resulted differently expressed in the bloodstream of colorectal cancer patients and healthy subjects. In detail, we observed that the concentration of CD34bright CEC in patients raised to a double median value when compared with healthy subject numbers (median, 10.9 CEC/mL).

Conclusion: Our findings suggest a meaningful difference of the CEC subpopulation framework between colorectal cancer and healthy blood samples, identifying the CD34bright phenotype as an appealing marker for further investigation.

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P-258 Evaluation of volumetric modulated arc therapy with simultaneous integrated boost in carcinoma of the anal canal

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Background: This study aimed to retrospectively analyze the benefit of simultaneous integrated boost volumetric modulated arc radiotherapy (VMAT-SIB) in patients experiencing acute gastrointestinal, genitourinary and cutaneous adverse events for anal canal cancer patients.

Methods: Since 2016, T1-4N0-1M0 anal canal cancer patients (pts) received VMAT-SIB, prescribed per stage: T1-2N0, 42 Gy elective nodal and 50.4 Gy anal tumor planning target volumes (PTVs) in 28 fractions; T3-4N0-1, 45 Gy elective nodal, 54 Gy metastatic nodal and anal tumor PTVs in 30 fractions. These pts were compared with those previously treated with sequential boost VMAT (VMAT-SB) to a total dose of 59.4 Gy. The primary endpoint was assessment of acute side effects (gastrointestinal, genitourinary, and cutaneous) according to RTOG/CTCAE scale. Dosimetric parameters were analyzed by dose-volume histogram. Planned secondary endpoints assessed local control and overall survival.

Results: Twenty out of 55 pts were treated with VMAT-SIB. Tumor stage included 13% I, 42% II, 20 % IIIA, 3% IIIB, and 22% IIIC according to AJCC 8th edition. In primary endpoint analysis, among the VMAT-SIB group, 60% of pts experienced G2 skin toxicity, 5% G2 genitourinary, and 15% G2 gastrointestinal toxicity. None pts experienced G3 toxicity. Among VMAT-SB, 51% of pts experienced G2 and 6% G3 skin toxicity, 3% G2 genitourinary and 20% G2 gastrointestinal acute toxicity. Two coplanar arcs were employed for VMAT delivery. Dosimetric results were consistent in terms of both target coverage and normal tissue sparing. In regard to dosimetric findings, mean V40Gy of bladder were 11% (range 5-21.3%) and 16.5% (range 2.2-63.9%) in the VMAT-SIB and VMAT-SB group, respectively; mean V45Gy of bowel were 27.8cc (range 0.5-97 cc)and 43.2 cc (range 1.9-252.9 cc) in the VMAT-SIB and VMAT-SB group, respectively. At 3 months, a complete response was observed in 16/20 pts (80%) in the VMAT-SIB group, and in 32/35 pts (91%) in VMAT-SB. Finally, in the VMAT-SIB group, OS rate was 95% with a mean follow-up of 14 months (3-36 months), while it was 77% in VMAT-SB with a longer mean follow-up of 44 months (3-120 months).

Conclusion: VMAT-SIB was feasible, safe, and effective. There was a dosimetric advantage in the VMAT-SIB group for bladder and bowel dose-volume histogram; however, there were no clinical differences in terms of acute toxicity. Larger accrual and longer follow-up are warranted in order to understand local control and survival benefit.

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P-259 Pembrolizumab as second-line therapy of hepatocellular carcinoma: A cost-effectiveness analysis

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Background: Recently, checkpoint inhibitors have been approved for the second-line therapy of hepatocellular carcinoma (HCC) in patients who previously received sorafenib. Pembrolizumab has demonstrated substantial anti-tumor activity and favorable toxicity profile as second-line treatment of HCC. However, considering the high cost of pembrolizumab, there is a need to assess its value by considering both efficacy and cost. We aimed to evaluate the cost-effectiveness of pembrolizumab vs. placebo as second-line therapy in hepatocellular carcinoma (HCC) patients from the US payer perspective.

Methods: We developed a Markov model to compare the lifetime cost and effectiveness of pembrolizumab with those of placebo as second-line treatment of HCC using outcome data from the KEYNOTE-240 randomized control trial. Life-years, quality-adjusted life-years (QALYs), lifetime costs, and incremental cost-effectiveness ratio (ICER) were estimated, at a willingness-to-pay threshold of $100,000 to $150,000 per QALY. Univariable, 2-way, and probabilistic sensitivity analyses were performed to evaluate the model uncertainty. Cost threshold analysis was also performed.

Results: In the base-case analysis using data from KEYNOTE 240 trial, pembrolizumab provided a gain of 0.15 life-year and 0.14 QALY with additional cost of $ 47,057. The ICER was $340,409 for pembrolizumab compared with placebo and BSC. Overall survival hazard ratio (0.78; 95% CI: 0.61-1.00) cost of pembrolizumab ($6914.5 per cycle, range: 5532.6 – 8297.4), and utility of placebo (0.76, range: 0.59-0.93) had the strongest influence on ICER. The ICER for pembrolizumab was > $200,000 per QALY in all of our univariable and probabilistic sensitivity analyses. In cost-threshold analysis, pembrolizumab would have to be priced 57.7% lower to be cost-effective considering a willingness to pay of $ 150,000 per QALY.

Conclusion: At current cost, pembrolizumab is not a cost-effective second-line therapy of HCC at a willingness-to-pay threshold from $100 000 to $150 000 per QALY.

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P-260 Naïve indirect treatment comparison of PanCO, a pilot study of OncoSil P-32 microparticles combined with gemcitabine + nab-paclitaxel or FOLFIRINOX chemotherapy versus standard-of-care treatment in unresectable locally advanced pancreatic cancer

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Background: Pancreatic cancer is a malignancy with a very poor prognosis and remains an area of high unmet medical need. Current standard treatment for patients with unresectable locally advanced pancreatic cancer (LAPC) is limited to chemotherapy (CT-only) or chemoradiotherapy following induction CT (ICT+CCRT). International guidelines (e.g. ESMO, ASCO and NCCN) recommend gemcitabine monotherapy as well as other regimens containing gemcitabine or fluoropyrimidines (capecitabine, 5FU) plus other agents, or ICT+CCRT, for the treatment of LAPC. Brachytherapy using beta-emitting phosphorus-32 (P-32) microparticles enables a predetermined radiation dose to be implanted into pancreatic tumours via endoscopic ultrasound (EUS) guidance. The results of a prospective, interventional, open-label, single-arm pilot study of P-32 microparticles (OncoSil TM ; OncoSil Medical) combined with gemcitabine + nab-paclitaxel or FOLFIRINOX chemotherapy demonstrated encouraging safety and efficacy in patients with unresectable LAPC (the PanCO study: NCT03003078). In the absence of a head-to-head randomised controlled trial, a naïve indirect treatment comparison was used to assess the results of the PanCO study against state-of-the-art (SOTA) therapy obtained from a systematic literature review (SLR) of published scientific literature from prospective clinical studies.

Methods: A SLR was conducted to identify published clinical data on SOTA/'standard-of-care' treatments from prospective phase II and III clinical studies in patients with unresectable LAPC treated with CT-only or ICT+CCRT. The SLR outcomes were then compared with the results of the PanCO study in a naïve indirect treatment comparison and analysed using a binomial test.

Results: The SLR identified clinical outcomes including overall survival (OS), progression-free survival (PFS), one-year survival, resection rate, disease control rate (DCR) and overall response rate (ORR). In total, there were 46 included studies, comprising 57 arms and 4,327 patients, 2,350 of whom had LAPC. The PanCO study enrolled 50 patients (Intention-to-Treat [ITT] population) of which 42 were implanted with P-32 microparticles (Per Protocol [PP] population), with a median follow-up of

16.1 months. Median OS was significantly longer ($p<0.001$) in the PanCO study than CT-only and/or ICT+CRT regimens (PanCO PP: 16.0 months; ITT: 15.5 months; *vs*. SLR combined: 12.7 months; CT-only: 12.7 months; ICT+CCRT: 12.6 months), representing a ~20% reduction in the risk of death compared to CT-only and ICT+CCRT studies (Hazard Ratio PP: 0.79; ITT: 0.82). One-year survival rates in PanCO were significantly higher than SOTA ($p<0.001$; PanCO PP: 64.0%; ITT: 63.4%; *vs*. SLR combined: 52.5%; CT-only: 50.4%; ICT+CCRT: 55.2%). The rate of surgical resection in PanCO was significantly greater than SOTA ($p<0.001$; PanCO PP: 23.8%; ITT: 20.0%; *vs*. SLR combined: 9.9%; CT-only: 7.7%; ICT+CCRT: 11.5%). Median PFS was significantly longer ($p<0.001$) than the SLR combined or CT-only regimens (PanCO PP and ITT: 9.3 months; *vs*. SLR combined: 7.6 months; CT-only: 6.6 months; ICT+CCRT: 9.1 months). DCR and ORR were also significantly higher than the combined SLR or CT-only regimens (ORR/DCR: PanCO PP 31.0%/100%; ITT: 29.8%/95.7%; *vs*. SLR combined: 18.2%/80.1%; CT-only: 14.7%/71.3%; ICT+CCRT: 24.2%/88.5%, respectively).

Conclusion: The naïve indirect treatment comparison to state-of-the-art therapy indicated that P-32 microparticles combined with standard-of-care chemotherapy may provide significant and clinically relevant benefits for patients with unresectable LAPC and a valuable treatment option in an area of high unmet medical need.

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P-261 Safety and effectiveness of tumor treating fields combined with sorafenib in preclinical models of hepatocellular carcinoma

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Background: Hepatocellular carcinoma (HCC) is a leading cause of cancer-related mortality worldwide. Sorafenib, an oral multikinase inhibitor, is approved for patients with advanced HCC; however, survival benefit is limited. Tumor Treating Fields (TTFields) is an anti-mitotic treatment FDA-approved for glioblastoma and malignant pleural mesothelioma. TTFields are low intensity, intermediate frequency, alternating electric fields delivered non-invasively to the tumor site. We investigated the effectiveness and safety of TTFields alone and in combination with sorafenib in HCC preclinical models.

Methods: HepG2 and Huh-7D12 HCC cells were treated with TTFields (100-400 kHz) for 72 hours using the inovitroTM system. Effectiveness of TTFields plus sorafenib was with TTFields at the optimal frequency plus various sorafenib concentrations. Cell counts, induction of apoptosis, and clonogenic potential were determined. Additionally, N1S1 HCC cells were injected into the left lobe of the liver of Sprague Dawley rats and after 1 week, TTFields (1.2 V/cm) and sorafenib (10 mg/kg) were applied for 6 days and then evaluated for tumor growth using MRI. Healthy rats were used to study the safety of TTFields (150 kHz) applied to the abdomen.

Results: The optimal frequency of TTFields was 150 kHz in both HCC cell lines. TTFields (1.0 - 1.7 V/cm, 72 hours) at 150 kHz led to a 53-55% reduction in cell counts and an additional reduction (65-69%) in clonogenic potential. The combination of TTFields and sorafenib led to a significant reduction in cell count (2-way ANOVA, $P < 0.05$) compared to either treatment alone. HCC tumor growth was significantly reduced in the combined group compared to the control group (student t-test, $P < 0.01$). On average, the HCC tumor volume (fold-increase) in the combination group (1.6-times) was significantly lower than in the control group (5.9-times, $P < 0.0001$), TTFields alone group (3.3-times, $P < 0.01$), and sorafenib alone group (2.3-times, $P < 0.05$). Histological analysis of the KI67 proliferation marker in HCC tumors showed reduced proliferation in all treated groups. Based on preliminary analysis of autophagy marker (LC3) in tumors, we hypothesize the involvement of autophagy as one of the mechanisms underlying increased treatment efficacy. Safety studies did not reveal any adverse events associated with TTFields application to the rat abdomen.

Conclusion: These results demonstrate that TTFields can be safe and effective in the treatment of HCC and that the combination with sorafenib leads to further enhancement in treatment effectiveness. Based on these results, a phase 2 clinical trial evaluating the effects of TTFields and sorafenib treatment in patients with HCC is ongoing (HEPANOVA; NCT03606590).

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P-262 Effect of neoadjuvant chemotherapy in patients with gastric cancer: A retrospective study

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Background: The use of neoadjuvant chemotherapy has significantly improved the prognosis of locally advanced (LA) gastric cancer. The aims of this study were to determine the safety and efficacy of the neoadjuvant chemotherapy in patients with LA gastric and gastroesophageal junction (GOJ) cancer in daily clinical practice.

Methods: We retrospectively analysed patients with LA gastric cancer who were offered neoadjuvant chemotherapy from January 2015 to December 2017. Clinical outcomes included response, disease-free survival (DFS), overall survival (OS), and toxicity.

Results: Among 98 patients with gastric cancer, 23 received NAC. Median age was 55 years (22-69); 73.9% of patients were male. At diagnosis, 34.8% of patients were classified as stage II and 65.2 % stage III. Neoadjuvant treatment regimens CF, FOLFOX/XELOX, and FLOT were applied in 87%, 4% and 9% of cases, respectively. 22 patients (95.6%) completed neoadjuvant chemotherapy, 15 (65.2%) underwent R0 resection, 4 (17.4%) had exploratory procedure and 9 patients (39.1%) completed adjuvant chemotherapy. Post-operative complications were observed in one patient (anastomotic leakage). Disease control rate was achieved in 82.6 % of cases, downstaging in 34.7% and 17.4% had a pathologic complete response. We reported grade 3/4 adverse events including gastrointestinal (GI) side effects in 8.7% of patients, leukopenia and anaemia in 13% and 8.7%, respectively. 3-year OS was 56% for the whole population and 78.6% for patients treated with surgical resection. No relapse was observed in patients with pathological complete responses. The median survival has not been reached after 51 months of median follow-up.

Conclusion: Our study is limited by the retrospective design and small sample size. However, we have provided evidence that the neoadjuvant treatment approach is important both to facilitate operation procedure and to evaluate efficacy of systemic treatment.

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P-263 The role of biologic targets in metastatic colorectal cancer in non-elderly patients: A single institutional analysis

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Background: The paradigm for the treatment of metastatic colorectal cancer (mCRC) has shown great advances in recent years. With the increasing use of targeted therapies, including epidermal growth factor receptor (EGFR) and anti-vascular endothelial growth factor (VEGF) antibody, the median overall survival (OS) of mCRC has been raised to approximately 30 months over the last 10 years [1]. Hence, for patients whose tumors are RAS wild-type, anti-EGFR monoclonal antibodies (cetuximab, panitumumab) have shown clinical efficacy. Study aims were to I) describe pts with mCRC; II) assess overall survival (OS) at 1 and 2 years of pts that underwent target therapy or chemotherapy alone.

Methods: We performed retrospective and descriptive analysis of patients under 65 years old with mCRC from January 2013 to December 2017. Data were processed using SPSS®. Survival rate was evaluated using the Kaplan-Meier estimator with log-rank test.

Results: There were 54 pts with mCRC under 65 years old. Median age at diagnosis was 57 [24-65] years old; 55,6% (30/54) were male. Twenty-seven (50%) of pts were KRAS/NRAS wild-type and 81,5% of those received anti-EGFR, cetuximab, as first-line therapy, associated to FOLFIRI or FOLFOX. Eleven (32,3%) patients were prescribed bevacizumab in first-line and one (2,9%) patient was prescribed panitumumab associated to FOLFOX. In the second line, 6 patients that had cetuximab as first-line treatment switched to bevacizumab associated with FOLFOX or FOLFIRI and 5 patients continued with cetuximab associated with FOLFIRI or FOLFOX. In the third line, 5 patients that received second-line chemotherapy plus bevacizumab had a rechallenge with cetuximab plus irinotecan with a median time of treatment of 1,4 months. Twenty pts (37%) had 5-FU + Irinotecan/oxaliplatin based chemotherapy alone. According to BRAF mutation status, only one patient with RAS wild-type had the mutation V600E in BRAF gene. All the others were BRAF and RAS wild-type. High level of microsatellite instability (MSI-high) was observed in 2 patients and another 2 had a low level of microsatellite instability (MSI-low). All other patients tested were MSI stable (MSS). Median follow-up was 27 months. In the group of patients that made target therapy, survival rate at 1 year was 82,4% and 61,5% at 2 years. In the other group of patients, survival rate at 1 year was 63,5% and 42,4% at 2 years (HR 0,833, IC: 0,407-1,703, p=0,613).

Conclusion: Although there is no significant difference between the two groups, survival rate at 1 and 2 years was superior in the group of patients that made target therapy.

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P-264 Clinical validation of next-generation sequencing as a liquid biopsy for the monitoring of patients with metastatic colorectal cancer

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Background: Colorectal cancer is the third most frequently diagnosed neoplasm worldwide, with more than a third of cases being associated with the presence of metastases. Diagnosis of metastatic disease requires the acquisition of a tissue specimen which undergoes further analysis for molecular biomarkers that eventually guide treatment selection. Resistance usually appears as a result of tumour alterations occurring at a molecular level, which dictates a shift in therapeutic strategy. This phenomenon has long been known as tumour evolution, it was however not routinely tested at disease progression due to the risks and impracticality of re-biopsy. This has now changed with the advent of liquid biopsy, which allows for the molecular characterisation of the tumour in real-time, through the analysis of circulating tumour elements, such as circulating tumour DNA (ctDNA) in the blood and other bodily fluids.

Methods: 10mL of peripheral venous blood was collected from 33 patients with available tissue at diagnosis of metastatic colorectal cancer, as baseline liquid biopsy. Both tissue and plasma ctDNA were tested with Next-Generation Sequencing (NGS) with Unique Molecular Identifiers (UMIs) for the status of 23 and 50 genes, respectively, to describe the molecular landscape of the tumours. Baseline plasma NGS results were compared with all patients' tissue NGS results and were validated with plasma digital PCR (dPCR) in a subgroup of 15 patients. Repeat liquid biopsies were performed at disease progression to assess tumour clonal evolution over time.

Results: In around 20% of tumours, mutations in genes other than RAS and BRAF, such as TP53, PIK3CA, FBXW7 and APC, were present. Comparison of plasma with tissue results revealed plasma NGS sensitivity of 85% and 100% for the detection of RAS and BRAF mutations, respectively. Overall agreement for the clinically actionable KRAS, NRAS and BRAF was 84%. Baseline plasma RAS mutation detection rate was 51.52% with NGS versus 53.33% with dPCR, in the subgroup of patients whose plasma was additionally tested with this method. With regard to RAS mutation status, plasma NGS results were in agreement with plasma dPCR in 93% of cases, while agreement of all three testing approaches (tissue NGS, plasma NGS and plasma dPCR) was 80%. At disease progression, repeat liquid NGS revealed a change in the tumour mutational landscape with appearance/disappearance of mutations in the plasma of 75% of patients with disease progression.

Conclusion: In the present study, plasma NGS reliably generated tissue results regarding the clinically actionable mutations KRAS, NRAS and BRAF . This is one of a few studies using the same high-sensitivity method for tissue testing, allowing for a method-independent and more objective interpretation of the liquid biopsy results, pointing to heterogeneity-derived discordance, rather than analytical discrepancies of different methods applied on different materials. Additionally, the application of dPCR as a validation method confirms that NGS with UMIs is accurate for ctDNA testing in this disease setting. The appearance/disappearance of mutations at disease progression underlines the role of liquid biopsies to guide further treatment and multigene NGS panels represent useful tools that are worth further development and validation in randomised controlled trials.

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P-265 The study of mutations of the KRAS, NRAS, and BRAF genes in patients with colorectal cancer depending on gender, age, race in the population of the Republic of Kazakhstan

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Background: Of 3218 patients with colorectal cancer (CRC) who were registered in the Republic of Kazakhstan in 2018, 1476 have died. In the structure of mortality, colorectal cancer is ranked 4th. Recently, studies of the frequency of the KRAS gene mutation and analysis of its correlation with the clinical course of CRC have been conducted in different countries. The relationship of sex, age, race, and localization of the primary tumor to the status of the KRAS, NRAS, and BRAF genes in CRC remains the subject of discussion.

Methods: The research material was paraffin blocks of the primary tumor of patients with CRC ($n = 332$). Using genomic DNA, real-time PCR revealed the most common mutations: the KRAS gene (exon 2, 3, 4), the NRAS gene (in codons 12,13, 61,146), V600E of the BRAF gene.

Results: For the first time, the occurrence of mutations in the KRAS and NRAS genes (42.5% and 2.4%), which is equivalent to the international ($\sim$ 40%), was determined, and 183 (55.1%) patients were of the wild type. Mutation of the BRAF gene occurred in 9.3% of cases, and all of them had unmutated RAS status. The frequency of mutations among women and men was the same and was more often observed in the G12D codon. An analysis of the dependence of the type of mutation on gender did not show significant differences, however, there was a tendency to an increase in the frequency of mutations in women. For a pair of "female KRAS mutations," the value of the correlation coefficient was $rp = 0.04$, $p = 0.06$. An analysis of the relationship between mutations and race revealed the predominance of the wild type in the Asian group - 94 (51.4%), in Europeans the KRAS gene mutation was more often detected - 81 (54.4%) patients. When studying the occurrence of mutations in two age groups (group 1 - from 25 to 59, 2 - from 60 to 89 years), it was found that patients of group 2 were more likely to have a mutated type of RAS genes, and group 1 was significantly more likely to have a wild type. In the study, gene mutations were more common with primary tumor localization in the right compared to the left ($p = 0.001$). There was a tendency towards increase in the number of gene mutations with an increase in the frequency of damage to the distal colon and especially the rectum.

Conclusion: The obtained results point to the need to continue research on the comprehensive study and identification of molecular genetic characteristics of CRC. With a more in-depth analysis of the relationship of mutations, it is possible to achieve improved therapy results and increase prospects for long-term survival.

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P-266 LDH levels as predictors of efficacy in second-line treatment for metastatic gastric cancer: The LINE study

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Background: Serum lactate dehydrogenase (LDH) levels are recognized as an indirect biomarker of tumor hypoxia and angiogenesis for several solid tumors. Ramucirumab represents the first molecularly targeted agent proven to be effective in second-line therapy for advanced gastric or gastro-oesophageal junction adenocarcinoma, alone or in combination with chemotherapy. However, little is known so far about potential predictive factors of benefit from antiangiogenic treatment. Thus, we conducted an observational retrospective study aimed at evaluating the possible differential prognostic impact of baseline serum LDH levels in advanced gastric cancer (GC) patients treated or not with ramucirumab in the second-line setting.

Methods: We retrospectively analyzed a cohort of consecutive advanced GC patients treated with second-line therapy at our Institution (Centro di Riferimento Oncologico CRO in Aviano, Italy) from January 2010 to December 2019. Baseline LDH levels prior to the start of second-line treatment were classified according to laboratory ranges as low, normal and high. The association of LDH with survival outcomes (PFS and OS calculated from the start of second-line treatment) was explored through the Kaplan-Meier method and compared using the Log-Rank test. Subsequently, subgroup analyses according to LDH levels were carried out to assess its differential prognostic impact on antiangiogenic-based schemes. Statistical analyses were performed using the STATA Software 14.2.

Results: Overall, 94 patients were identified. After progression to first-line treatment, 65 patients (69%) were treated with ramucirumab in association with paclitaxel or as a single-agent, while 29 (31%) received taxanes (10%) or fluoropyrimidine-based chemotherapy regimens combined with irinotecan (21%). At the start of the second-line therapy, median age was 67.5 years, 87 (93%) patients had an ECOG PS of 0 or 1, 18 (20%) had HER2 positive disease, MMR status was known only for 9 (10%) cases.

Median follow up was 17 months (25th-75th percentiles: 14-30 months). In the whole population, median second-line PFS was 3.7 months (25th-75th percentiles: 2.6-7.2 months) and median second-line OS was 7.9 months (25th-75th percentiles: 4-15.7 months). Baseline serum LDH levels were reported for 66 out of 94 patients. High LDH levels prior to second-line start confirmed to be associated with worse PFS (HR 2.15, 95% CI 1.04-4.45, p=0.034) and OS (HR 2.56, 95% CI 1.18-5.55, p=0.0016) when compared to low or normal LDH levels. At subgroup analyses, patients treated with ramucirumab-based regimens who had elevated baseline LDH levels had a trend towards worse PFS (HR 2.76, 95% CI 1.09-6.94, p=0.031) (p of interaction 0.31) and OS (HR 4.29, 95% CI 1.59-11.51, p=0.004) (p of interaction=0.096).

Conclusion: High baseline LDH levels prior to the start of the second-line treatment are confirmed as predictors of a worse outcome in patients with advanced gastric cancer. Moreover, subgroup analyses suggest their role in predicting the activity of antiangiogenic agents. Case expansion and prospective validation are needed in order to confirm these findings.

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P-267 Signet-ring cell carcinoma of the colon: 10-case experience of the Medical Oncology Department at Hassan II University Hospital

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Background: Signet-ring cell carcinoma of the colon was first described by Laufman and Saphir in 1951. It is a very rare tumor representing 0.7% to 2.4% of all colorectal carcinomas. These tumors are diagnosed in an advanced stage and their prognosis seems poorer than colorectal adenocarcinomas (ADK).

Methods: This is a retrospective study conducted in the Department of Medical Oncology of the Hassan II University Hospital in Fez, including all patients followed for signet-ring cell carcinoma of the colon from January 2015 to September 2019.

Results: Overall, 10 cases were noted, including 7 men and 3 women, and representing 2% of all colorectal cancers collected during the study period. The average age of the patients is 33 years (range, 28-69 years). The average age at diagnosis was 32 years. 50% of patients had stage IV disease at diagnosis; 4 cases had synchronous peritoneal dissemination. The sites of metastasis, in order of frequency, were pulmonary, hepatic, and ovarian. In all, 3 patients were operated on occlusion and one in peritonitis. A total of 4 patients with stage III disease underwent curative surgery followed by adjuvant chemotherapy. The metastatic patients received palliative chemotherapy based on 5FU +/- oxaliplatin or irinotecan. Overall, 2 patients had stable disease and 2 have progressed; 2 patients relapsed after a free interval of 12 months, and 1 patient died of a pulmonary embolism. The median survival was 7 months.

Conclusion: These tumors affect young subjects and are characterized by an advanced stage at the time of diagnosis with low rates of curative resection and a poor prognosis. Early diagnosis and a multidisciplinary strategy are essential for better management.

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P-268 Diabetes and risk of pancreatic cancer

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Background: Pancreatic cancer is the fourth leading cause of cancer mortality in the world. Half of all patients with pancreatic cancer are diabetic at the time of diagnostic. We aimed to analyze the association between pancreatic cancer and diabetes in patients treated at our institute.

Methods: A retrospective observational study of patients with pancreatic cancer treated between January 2010 and December 2019 was conducted. The concept of diabetes was researched by interrogation.

Results: Our cohort comprised 115 people with pancreatic cancer, with a male to female ratio of 1.5/1. Diabetes was described in 42% of cases of which 10% were diagnosed in the 2 years preceding the diagnosis of cancer, 30 had diabetes type II, 18 patients had diabetes types I. 82%of patients with diabetes had stage IV disease with predominantly liver metastases. The mean age was 61 years (range: 52-85 yrs) with a male predominance. All patients had pancreatic adenocarcinoma. The tumor was located in 55% in the head of the pancreas, 32% in the body and 19% in the tail.

Conclusion: People with diabetes, especially type 2, have high risk for pancreatic cancer.

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P-269 Lenvatinib in hepatocellular carcinoma: QoL surveys and radiological imaging markers predicting clinical outcome in patients with hepatocellular carcinoma treated with lenvatinib as first-line treatment (SULENVA-HCC)

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Background: Hepatocarcinoma (HCC) is the most frequent primary liver neoplasm. In most cases, the diagnosis of HCC occurs in a context of non-operability or metastatic disease for which systemic treatment is indicated. In Italy, two drugs are indicated and reimbursed as first-line setting for HCC: sorafenib and lenvatinib. Lenvatinib is a small multitarget molecule that selectively inhibits kinase activities of pathway-related proangiogenic and oncogenic receptors. The efficacy of lenvatinib has been demonstrated in the randomized phase III REFLECT clinical trial. The study demonstrated the non-inferiority of lenvatinib compared to sorafenib, in patients with preserved liver function, in terms of overall survival (OS), the primary endpoint of the study. Moreover, lenvatinib showed an advantage in terms of progression-free survival (PFS) and the objective response rate (ORR). The toxicity profiles and data for quality of life (QoL) were similar for both drugs. Furthermore, there is an unmet need for predictive biomarkers of toxicity and efficacy/resistance for multitarget kinases drugs. However, some studies suggest the possibility of using the cavitation of lung metastases as a radiological marker of response to cancer therapy especially when the treatment has antiangiogenic properties.

Trial design: The proposed study is a monocentric observational trial that involves data collection about possible associated factors for the effectiveness of the treatment and side effects associated with lenvatinib. Moreover, the study plans the administration of QoL questionnaires and the acquisition of images relating to CT scan re-evaluations. We will use the EORTC QLQ-C30 V.3 questionnaire and the NCI-PROCTCAE ITEMS-ITALIAN V1.0 questionnaire, which will be administered at baseline, after 8-12 weeks after the start of treatment in concomitant with the CT-scan re-evaluation and at the end of the first-line treatment. The images of the instrumental re-evaluations performed with CT scan will be acquired at baseline, at the first reassessment and at the end of the treatment. The cavitation of the pulmonary metastases will be analyzed by an expert radiologist at the center who will not be made aware of individual patients' PFS and OS responses. Cavitation will be evaluated according to criteria drawn up in the RadioCORRECT study: - at baseline, the cavitation of lung metastases as defined as the presence of a cavity full of air occupying $\geq$10% of the maximum diameter of one or more lung metastases with a maximum diameter $\geq$10 mm; - on re-evaluation after an interval of 8-12 weeks, cavitation of lung metastases is defined as the appearance of full cavities of air in lung metastases or as an increase in cavitations existing. The study will last for 12 months.

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P-270 Early tumor shrinkage as a predictor of favorable outcomes in patients with unresectable metastatic colorectal cancer treated with first-line chemotherapy plus bevacizumab

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Background: Obtaining early tumor shrinkage, defined as ≥ 20% shrinkage in tumor size per RECIST criteria at the first radiological assessment (8 weeks of treatment), has been shown to be prognostic for improved survival of patients with mCRC treated with cetuximab with or without chemotherapy. The aim of our study was to evaluate the impact of this parameter in patients treated with first-line of chemotherapy combining fluoropyrimidine, irinotecan, and bevacizumab.

Methods: All pts who received first-line chemotherapy combining fluoropyrimidine, irinotecan, and bevacizumab for unresectable mCRC, between March 2012 and May 2015, were included in an exploratory analysis of survival based on the presence or not of ETS. The univariate analysis of the PFS and OS was based on the Kaplan-Meier method and the Log-Rank test. Multivariate analysis was performed using a Cox model including ETS, sex and Köhne prognostic score.

Results: Fifty-two patients were enrolled; median age was 59 years (range 32-75), performance status 0-1 was 84.6%. 69.2% had multi-organ involvement. The median follow-up was 40 months. Fifty-one patients were evaluable for response: ORR 39.2%, SD 43.1 for a clinical benefit of 82.3%. 33% qualified for early response. Median PFS and OS for the whole group was 11 months (95% CI: 7.8-14.2) and 20.8 months (95% CI: 16.5-25.1), respectively. ETS was associated with prolonged PFS and OS (22.5 vs 10.3 months, p = 0.001; 52 vs 20 months, p< 0.0001).

Conclusion: Early response to chemotherapy may predict favorable outcomes in patients with metastatic CRC treated with first-line bevacizumab plus chemotherapy, but large prospective analysis and validation are mandatory.

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P-271 Meta-analyses on mutation status concordance between tumor tissue and circulating tumor DNA and prognostic value of ctDNA in pancreatic cancer

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Background: Liquid biopsy is a promising method of diagnostics in pancreatic cancer (PC). Concordance of mutational status between tumor tissue and circulating tumor DNA (ctDNA) and the prognostic significance of the latter have been actively studied in recent years but results are heterogeneous. We carried out a systematic review and meta-analyses to address these issues.

Methods: PubMed, ASCO and ESMO databases were searched to identify studies that have been published until February 2020. Inclusion criteria for publications were the following: more than 10 participants enrolled in the study, presence of the data concerning concordance of mutations identified in paired tumor and blood samples; for articles on prognostic significance — presence of HR and 95% CI for PFS and OS. Random effects were used for analyses due to potential heterogeneity of the studies. Meta-analyses were performed using Review Manager (RevMan), version 5.3.

Results: 16 studies including 549 patients were enrolled to assess mutational status concordance. The data of these studies were significantly homogeneous (p=0.31, I2=12%). Our results showed that the mutational status of ctDNA and tumor tissue was significantly different (16%, HR 0.84, 95% CI 0.78-0.90, p< 0.00001). Analysis of ctDNA prognostic significance included 17 studies, 5 of which were dedicated to resectable PC. Meta-analysis of the studies evaluating the importance of ctDNA at any stage of disease showed that detection of ctDNA before treatment adversely affected OS (HR 2.21, 95% CI 1.35-3.33, p=0.001) (I2=84%, p< 0.00001). Presence of ctDNA both before and after surgery was a negative predictor of PFS (HR 2.32, 95% CI 1.54-3.5, p< 0.0001; I2=0%, p=0.47) and OS (HR 2.01, 95% CI 1.12-3.63, p=0.02; I2=51%, p=0.08). Patients with undetectable ctDNA after surgery also had better PFS (HR 3.06, 95% CI 1.63-5.76, p=0.0005; I2=45%, p=0.18) and OS (OP 3.39, 95% CI 2.12-5.44, p< 0.00001; I2=0%, p=0.78) compared with patients with detectable ctDNA.

Conclusion: The possible discordance of the mutational status between ctDNA and the primary tumor has been shown. The detection of ctDNA in the blood of patients was a negative prognostic factor in resectable and advanced PC.

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P-272 Sarcopenia in metastatic colorectal cancer patients during first-line chemotherapy

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Background: Sarcopenia is a condition characterized by skeletal muscle mass decrease due to physiological aging or concomitant disease such as neoplasia. In cancer patients, a low lean body mass represents a negative prognostic factor for survival and development of dose-limiting chemotherapy toxicities, independent of the stage of disease. The aim of our study was to analyze the association between sarcopenia and overall survival (OS), response to therapy and toxicity in patients with metastatic colorectal cancer (mCRC) in first-line chemotherapy treatment.

Methods: Our retrospective analysis included 56 mCRC patients who received first-line chemotherapy from 2014 to 2017 at the Medical Oncology Unit of our hospital. Sarcopenia was assessed using the Skeletal Mass Index [SMI = muscle area in cm^2 / (height in m)2], evaluated on a cross-sectional area at the third lumbar vertebra by CT scans. We used lumbar SMI cutoffs specific to sex and body mass index (BMI). CTs were performed before starting chemotherapy (baseline) and at first disease re-evaluation. Toxicities were analyzed during the first four cycles of therapy and graded according to the Common Terminology Criteria for Adverse Events v4.0.

Results: Median age was 67 years (37-85), and 20/56 patients (35.7%) were ≥ 70 years old. 14 patients (25%) were sarcopenic at baseline CT scan (7/33 M; 7/23 F); 5/14 sarcopenic patients were 70 years or older. BMI distribution was 23.2% obese, 39.3% overweight, 37.5% normal weight, 0% underweight. SMI varied within each BMI category: 6/21 normal-weight patients, 6/22 overweight patients, and 2/13 obese patients were sarcopenic at baseline CT scan. 18 patients (32.1%) had a neutrophil/lymphocyte ratio ≥ 3 (inflammation index). At the time of the first diagnosis, 23 patients (41.1%) presented with pTNM stage II or III disease and they subsequently developed metastases; 33 patients (58.9%) received the diagnosis at the metastatic stage. No statistically significant correlation was found between baseline sarcopenia and age (p=1), BMI (p=0,728), stage at diagnosis (p=0,355), neutrophil/lymphocyte ratio (p=0,751). The median follow-up was 26.8 months (3.8-66.8) and the median overall survival (OS) was 27.2 months (95% CI 23.3-37.3). Sarcopenia was correlated neither to OS (p=0.362) nor to higher toxicity reported during the first 4 cycles of chemotherapy (p=1). During the first four cycles of therapy, 4/14 (28.6%) sarcopenic patients and 13/42 (31%) non-sarcopenic patients had at least a reduction in drug dosage for toxicity (p=1). 27 patients (48.2%) obtained a partial or complete response, 24 patients (42.8%) had disease stability and 5 patients (8.9%) reported disease progression as best response to first-line treatment. Response rate was not correlated with baseline sarcopenia (p=0.221). At first disease re-evaluation, a skeletal muscle loss ≥ 5% was found in 17 patients (30.3%); 3 of these patients were already sarcopenic at baseline CT scan, while 7 patients became sarcopenic. Muscle mass loss was not correlated with OS.

Conclusion: In our study, neither baseline sarcopenia nor muscle mass loss during first-line chemotherapy influenced survival. In addition, baseline sarcopenia did not worsen treatment toxicities. However, these results must be interpreted with caution in consideration of the limited sample size.

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P-273 Real-world experience of definitive chemoradiation in esophageal cancer: Correlation of tumour length, toxicity and disease control

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Background: Definitive chemoradiation (dCRT) is an accepted modality for treating esophageal cancer if the tumour is deemed unresectable or the patient is unfit for or unwilling to consider surgery. Local control and overall survival with dCRT have been comparable to surgery in recent trials. However, most trials limit the length of tumour to 6-8 cm for concerns of normal organ toxicity. With advances in RT techniques, it is feasible to deliver radiotherapy to longer tumours without violating the organs at risk.

Methods: The study analysed patients with advanced or inoperable oesophageal cancer managed in Queen's Centre of Oncology and Haematology, Hull University Teaching Hospital NHS Trust. The cohort comprised of 84 patients treated with definitive chemoradiotherapy or radiotherapy alone between March 2014 to January 2017. Data were collected retrospectively for patient and tumour characteristics including age, gender, stage and histology and treatment planning including type, dose, toxicity and response (including radiological and pathological) from the medical record system (Lorenzo and ARIA report system). Survival (both overall survival and progression-free survival) was calculated from the date of diagnosis and comparisons

were performed for different tumour lengths. All analyses were performed with SPSS v25, IBM Corp ™. Survival analyses were performed with the Kaplan Meier. KM curve comparisons were performed with the log-rank test; a probability level of 5% was used as the cut-off for statistical significance in all analyses.

Results: Among the 84 patients included in the study, 31(36.9%) patients were alive at the time of database closure. Median age at diagnosis was 78.4 ± 9 years. The majority of the patients were male (65.5 %) with a performance status of 1 (73.8%). The majority had stage III (40.5%) and stage IVa (25%) disease. Adenocarcinoma was the predominant histology (65.2%). 61.9% had a GTV of < 0.002) and Heart DVHs-V30 (Correlation Coefficient 0.394, p < 0.001). Overall survival (OS) and progression-free survival (PFS) for the whole cohort was 22.5 months (95% CI 13.9, 31.2) and 10.7 months (95% CI 6.8, 14.5). Comparison of both OS and PFS for different tumour length category did not demonstrate a statistically significant outcome (p=0.247 for OS and p=0.233 for PFS).

Conclusion: The data demonstrates that it is feasible to treat longer tumours without increasing clinically significant toxicities and it is also feasible to achieve good local control for patients with longer tumours who would otherwise not have any radical treatment options. In future trials, it will be feasible to include patients with longer tumours, especially if modern RT techniques like VMAT are adopted and mandated.

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P-274 RELEVANT study: Patient and physician perspectives on clinically-meaningful outcomes in advanced pancreatic ductal adenocarcinoma

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Background: No previous studies have investigated patient and physician views on treatment decision-making, goals and clinically-meaningful outcomes in advanced pancreatic ductal adenocarcinoma (PDAC).

Methods: This prospective observational study recruited consecutive patients with newly-diagnosed advanced PDAC who were due to start palliative chemotherapy and their physicians. Patients completed 2 Quality-of-Life questionnaires (EORTC QLQ-C30 and PAN26) and a study survey at 3 time points: (T1) before starting chemotherapy, (T2) before, and (T3) after 1st on-treatment CT scan. Paired surveys were completed by physicians at each time point.

Results: Seventy-one patients consented, median age 65years, 52%male, 93% stage III-IV, 76% ECOG 0-1; 32% started triplet chemotherapy, 38% doublet and 23% monotherapy. Baseline EORTC QLQ-C30 scores (out of 100) were: QoL 57 points (mean, SD ±21), physical functioning 73 points (±22), fatigue 46 points (±26) and pain 45 points (±33) (lower scores indicated worse symptoms). Both physical functioning (p=0.003) and pain (p=0.02) worsened over time. 61% of patients died during the study timeframe. Survey compliance at timepoints: T1: 65/71, T2: 39/61, T3: 36/45; reasons for non-compliance were patient deterioration or death. Chemotherapy adverse event acceptability was similar between patients and physicians, but rash and alopecia were more acceptable (both p=0.004) and diarrhoea was less acceptable to patients (p< 0.001) than physicians thought. Tiredness became less acceptable for patients between timepoints (p=0.05). For 45% of patients, the most important aspect when selecting between chemotherapy options was overall-survival (OS); most physicians (58%) favoured OS/side-effect balance (p< 0.001). Over 80% of patients indicated that they had a personal goal that they wanted to reach with the help of treatment, whilst only 12% of clinicians were aware of this. The importance of some priorities also varied: being able to travel (mean 3.7 compared to 5.1, for clinicians and patients, respectively, p< 0.001), spending time with family (1.4 to 2.4, p< 0.001) and special events (3.2 to 4.7, p< 0.001) were all rated as more important by patients than clinicians. Significant differences regarding the length of time chemotherapy was expected to extend patients' lives were identified (p< 0.001); 81% of physicians and 12% of patients and 0% of physicians and 58% of patients thought that this would be between 1-6 months or 1-5 years, respectively. Differences were also identified regarding the minimal survival gain considered to be important: 76% of physicians and 17% of patients and 0% of physicians and 43% of patients thought that it would be 1-6 months and 1-5 years of minimal survival gain, respectively (p< 0.001). 47% of patients would accept chemotherapy with large amounts of side-effects as a trade-off for minimal important time gain; 9% of physicians predicted this (p< 0.001). Physicians underestimated the willingness of patients to accept chemotherapy if it controlled symptoms of cancer, but did not extend survival (physicians 46% vs patients 67%, p=0.05).

Conclusion: This study revealed that there is a clear mismatch between patient and physician views about the goals, priorities and expected benefits from treatment. Patients largely overestimated the expected length of time extension that chemotherapy would offer, and when making decisions about treatment options, patients prioritised survival, while physicians thought that patients would prioritise the best balance between side-effects and survival.

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P-275 Quality of life and symptoms in patients undergoing CRS-HIPEC with or without perioperative systemic treatment for colorectal peritoneal metastases: Results from the randomised CAIRO6 trial

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Background: To investigate the effect of perioperative systemic therapy in addition to cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) on quality of life (QoL) and symptoms during and after treatment for colorectal peritoneal metastases.

Methods: During this phase II, randomized, controlled trial, all consecutive patients were randomized 1:1 for a) CRS-HIPEC (control group) and b) CRS-HIPEC with perioperative systemic treatment (experimental group). Analyses were performed on the per-protocol study population. QoL and symptoms were measured at baseline, after neoadjuvant treatment (experimental group only), and at 3 and 6 months after surgery. The EORTC QLQ-C30, QLQ-CR29, and EQ5D-5L questionnaires were used.

Results: Eighty patients were included: 43 in the control group and 37 in the experimental group. Response rates were 100%, 94.9%, 83.5%, and 74.9% at baseline, after neoadjuvant treatment, at 3 and 6 months after surgery, respectively. The C30 summary score, EQ-VAS score, and index score were similar between the groups at baseline, at 3 and at 6 months after CRS-HIPEC. Also, all EORTC QLQ-C30 and CR29 functional and symptom scores were not significantly different between the groups at any point. In the experimental group, higher index scores were observed in patients who received adjuvant systemic treatment compared with patients who did not at 6 months after surgery.

Conclusion: Perioperative systemic therapy in patients undergoing CRS-HIPEC for colorectal peritoneal metastases did not significantly deteriorate QoL or worsen symptoms. Furthermore, in both groups, all QoL and symptom scores returned to baseline values at 3 or 6 months after surgery.

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P-276 Neutrophil/lymphocyte ratio (NLR) predicts survival after curative treatments for rectal cancer patients

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Background: Inflammation presents a connection with tumorigenesis. Simultaneously, ionizing radiation causes tumour cell death and an immune response takes place. Patients' baseline immune response can be a predictor of tumour response to rectal cancer treatments. Our aim was to evaluate the role of neutrophil-lymphocyte ratio (NLR) patient survival in rectal cancer.

Methods: Patients, treatment, and survival data were retrospectively collected, concerning radiotherapy treatments administered with curative intent, from 2013 to 2017. Survival data were evaluated through Cox-analysis, log-rank and survival tables. For the 5-y overall (OS) and disease specific-survival (DSS), the discriminative cut-off NLR was estimated applying Area Under Curve (AUC), receiver operating characteristic (ROC), DeLong method. All analyses were performed using an IBM-SPSS v.25 and, for all, a level of significance α=0.05 was noted.

Results: 268 patients were included, with male prevalence (165, 61.6%), mean age at diagnosis of 64 y/o (SD=11.96), and 127 patients were aged 65 or above. The category was ECOG-PS 0 for 215 (80.2%), ECOG-PS1 for 48 (17.9%), and ECOG-PS2 for 5 (1.9%) patients. Anaemia at diagnosis was found in 111 (41.4%) patients. Diabetes was described for 51 (19%), heart disease 39 (14.6%), vascular disease 115 (42.9%), alcohol consumption 66 (24.6%), and smokers 88 (32.8%). Age-adjusted comorbidity index was 6 or higher for 92 (34.3%) patients. The tumour was located at the low rectum in 113 (42.1%), medium 71 (26.5%), and proximal 84 (31.3%) patients. The mean follow-up time was 34 months (SD=19.27). Regarding treatment approach, the most frequent was long-course neoadjuvant CRT (210, 78.4%), and the remaining were short course neadjuvant RT (27, 10.1%), adjuvant RT plus CHT (28, 10.4%), and adjuvant RT (3, 1.1%). Only 2 patients did not receive CHT. AUROC analysis showed the discriminative values of NLR>3.36 and NLR>3.36, for 5y-OS and 5y-DSS, respectively. Cox analysis revealed that patients with NLR above 3.36, were at higher risk for death related to rectal cancer [HR=2.07; 95%CI 1.04-4.14, p=0.039] and for all cause-death [HR=1.93; 95%CI 1.05-3.54, p=0.033]. The NLR cut-off estimated for our cohort (>3.36) was compared with other ones described in the literature (NLR>3.0). Eighty-two (30.6%) patients had NLR>3.36 and for 102 (38.1%) NLR was higher than 3. For those patients with NLR ≤3.36 and >3.36, the 5y-DSS was 79,2% and 46.3% [p(log-rank) 3.0, respectively. For the patients with NLR ≤3.36 and >3.36, the 5y-OS was 73.3% and 56.0% [p(log-rank) 3.0, respectively.

Conclusion: Our data are in accordance with recent studies, affirming the predictive role of NLR for rectal cancer patients treated with curative intent. The AUROC discriminative value of NLR we found overwrites the existing reports in the literature. Regarding survival patterns, there were no significant differences between NLR>3.0 and NLR>3.6.

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P-277 Epidemiology of pancreatic cancer: Experience of the medical oncology department of CHU Hassan II Fez

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Background: Pancreatic cancer is a malignant tumor developed at the expense of pancreatic tissue, represents 2% of all cancers, and is the 4th leading cause of death from cancer worldwide. Its life expectancy at 5 years is 5%. The prognosis for this cancer is dire. Its incidence and mortality rate are similar.

Methods: This is a descriptive study, retrospective over 4 years from January 2016 to September 2019, conducted in the medical oncology department of CHU Hassan II of Fez. The aim was to determine the epidemiological, clinical and therapeutic aspects of this cancer.

Results: During this period, we collected 80 cases of pancreatic adenocarcinoma. The median age of the patients was 59.25 years with extremes of 20 and 81 years, with a clear male predominance and a sex ratio of 1.7. The main risk factors found were smoking in 33.3% of our population and 5.12% of chronic alcoholism. Of the cases, 20% were diabetic patients on insulin therapy. Two of our patients had a first-degree relative followed for a gastric tumor and the other for pancreatic cancer. The clinical symptomatology was dominated by mucocutaneous jaundice, weight loss and abdominal pain, with an average onset time of 4.5 months. Imaging revealed that the cephalic localization was the most frequent (47.5%). The diagnosis was confirmed by a CT scan biopsy in the majority of patients (88.75%). CA19-9 and ACE were increased in 23% and 13% of cases, respectively. The extension report revealed 78 metastatic cases. In our series, 2 patients had localized disease having undergone a duodeno-pancreatectomy followed by concomitant radiotherapy after R1 resection. Metastatic patients received palliative chemotherapy based on gemcitabine in 80% of cases and Folfirinox in 20%.

Conclusion: Pancreatic cancer appears to be increasing, probably related to the development of diagnostic imaging techniques. It is discovered at an advanced stage thus preventing any curative gesture. In the absence of an early diagnosis, management is dominated by palliative treatment. Hence there is a need for early diagnosis, by the popularization and the practice of ultrasound and abdominal scanner at the slightest sign of an appeal, especially in the setting of risk factors (first-degree family history and chronic pancreatitis).

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P-278 Neutrophil-to-lymphocyte, lymphocyte-to-monocyte and platelet-to-lymphocyte ratios as predictive markers of pathological response to FLOT neoadjuvant strategy in locally advanced gastric/gastroesophageal junction cancer

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Background: Locally advanced gastric and gastroesophageal junction (LAG/GEJ) cancers are responsible for the third leading cause of cancer-related mortality worldwide. FLOT perioperative chemotherapy showed improved prognosis in patients with LAG/GEF cancers, but predictive biomarkers have not been established. Neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR) and platelet-to-lymphocyte ratio (PLR) are inflammation biomarkers already reported as independent prognostic factors in several solid tumours. This study investigated the importance of NLR, PLR, and LMR in patients with resectable LAG/GEF and assesses the clinical potential of risk stratification for tumour behaviour prediction.

Methods: We conducted a multi-institutional retrospective study in Portugal, including patients from 9 different oncological centres, diagnosed with LAG/GEJ cancer, that underwent surgery after at least one FLOT cycle, since its initial use in the institutions until December 31st, 2019. Analysis of receiver operating characteristics curve defined a cut-off value for group stratification. Univariate regression analysis was used to estimate the risk of disease progression/absence of response.

Results: A total of 107 patients (67,3% males) were included, with mean age of 65,2 years (40-84 years). All were adenocarcinomas (92,5% gastric; 6,5% GEJ; 0,9% oesophageal) and 41,1% poorly differentiated. Median number of preoperative FLOT cycles was 4 (2-8 cycles). Subtotal gastrectomy was performed in 53,2% of patients, while 38,3% had total gastrectomy, 7,4% Ivory-Lewis esophagectomy and 0,9% distal gastrectomy. Complete standard lymphadenectomies were 73.7% (56% D2, 17,7% D1+), with R0 resection achieved in 89,7% patients. Tumour downstaging (TD) was observed in 64,5% patients. Of the 86 surgical specimens evaluated for tumour regression grade (TRG), 45,3% showed partial response, 36% no response, and 18,6% pathological complete response. Optimal cutoff values for NLR, MLR and PLR were determined regarding TRG and TD, respectively. High NLR (>2.95 vs. >2.13) and PLR (>135.6 vs. >128.5), as well as low LMR (< 0.05, 95%CI): NLR OR 3.66, 1.59−8.41, P=.002 / MLR OR 2.88, 1.27−6.51, P=.011 / PLR OR 2.25, 1.0−5.0, P=.05). To better stratify risk, we combined ratios by ascending risk order, classifying two groups: 1) "Lower Risk" - [high LMR, low NLR & PLR] < [high LMR & PLR, low NLR] < [low LMR, NLR & PLR] < [high LMR & NLR, low PLR]; and 2) "Higher Risk" - [high PLR, low LMR & NLR] < [high NLR, LMR & PLR] < [high NLR, low LMR & PLR] < [high NLR & PLR, low LMR]); the second group had higher risk of progression or not responding (OR 4.1, 95%CI: 1.75−9.45, P=.001).

Conclusion: NLR, LMR & PLR have the potential to be used as biomarkers to predict pathological response to preoperative FLOT. Through risk assessment, we suggest stratification of 2 groups to better evaluate patients and predict outcomes. Higher risk patients should be considered for more active surveillance during chemotherapy, to detect progression early and possibly reconsider therapeutic strategies.

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P-279 Clinical utility of circulating tumor DNA in resectable and advanced pancreatic cancer

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Background: Circulating tumor DNA (CtDNA) has shown its negative prognostic value in a number of studies, however, data on the role of ctDNA in resectable pancreatic cancer (PC) are lacking. The aim of our study was to determine the prognostic value of ctDNA at various stages of the disease using our simple and cheap test.

Methods: This prospective study included patients with diagnosis of PC who received treatment at the Russian cancer research center n.a. N.N. Blokhin from 2017 to 2019. In cases of resectable PC (N=37), blood samples were taken before and after surgery. The median time between surgery and blood sampling was 7 days (5−9 days, σ = 0.6). In cases of advanced disease (N=29), two blood samples were taken − before

and during chemotherapy. Primary tumors were sequenced to identify somatic mutations in 50 genes. Personalized tumor-specific digital polymerase chain reaction assays were used to identify these mutations in plasma samples. Absence or decrease of the mutant allele fractions by $\leq$ 2% were considered a negative result.

Results: At the time of the first blood sampling median ctDNA concentration was significantly higher in advanced setting than in localized cancer (2.31 versus 0 copies/µl, Mann-Whitney U-test p=0.005). In cases of advanced PC change of ctDNA concentration in two consecutive blood samples did not show its prognostic significance (HR=1.14, p=0,53 for PFS and HR=1.08, p=0.77 for OS). In 15 (40,5%) cases ctDNA was detected before operation. Detection of ctDNA before surgery did not affect PFS (HR 1.0, p=0.9) and OS (HR=0.02, p=0.4). There was no correlation between the stage of disease and the presence of ctDNA before surgery (k -0.003, p=0.9; HR 0.9, 95% CI 0.2-3.9, p=0.9), T parameter (k -0.02, p=0.9; HR 0.9, 95% CI 0.2-3.5, p=0.9) and N parameter (k -0.14, p=0.4; HR 0.6, 95% CI 0.2-2.1, p=0.4). In 10 (27%) cases ctDNA was determined after surgery. In these cases there was significant association between ctDNA+ with the stage of disease (k 0.34, p=0.04; HR 5.4, 95% CI 1.01-28.5, p=0.05) and T parameter (k 0.4, p=0.014, HR 8.2, 95% CI 1.3-51.1, p=0.02). 7 out of 14 (50%) patients with ctDNA+ and 3 out of 23 (13%) with ctDNA- after surgery had disease progression (p=0.02), which affected PFS (HR 2.9, 95% CI 1.01-8.5, p=0.04) but not OS (HR 1.2, 95% CI 0.2-6.6, p=0.8). The presence of ctDNA after surgery was associated with a higher rate of progression regardless of adjuvant chemotherapy (p>0.05).

Conclusion: The median concentration of ctDNA in the plasma of patients with metastatic PC is significantly higher than in the plasma of patients with localized PC, which may reflect tumor burden. The presence of ctDNA after surgery increases the risk of disease progression regardless of adjuvant chemotherapy.

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P-280 The comparison of mFOLFOX-6, mDCF, mFOLFIRINOX in the first-line treatment of advanced gastric cancer

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Background: The prognosis of patients (pts) with advanced gastric cancer is poor. There is no single, global standard regimen for the first-line treatment of metastatic disease. We performed a randomized trial to evaluate the safety and efficacy of first-line mFOLFOX-6, mDCF, mFOLFIRINOX in metastatic gastric cancer pts.

Methods: Pts were randomly assigned to mFOLFOX-6 (oxaliplatin 85 mg/m^2 IV on day 1, folinic acid 400 mg/m^2 IV on day 1, fluorouracil (5-FU) 400 mg/m^2 IV bolus, 5-FU 2400 mg/m^2 IV continuous infusion over 46 hours), mDCF (docetaxel 40 mg/m^2 IV on day 1, cisplatin 40 mg/m^2 IV on day 1, 5-FU 2000 mg/m^2 IV continuous infusion over 48 hours) and mFOLFIRINOX (Irinotecan 180 mg/m^2 IV on day 1, oxaliplatin 85 mg/m^2 IV on day 1, Folinic acid 200 mg/m^2 IV on day 1, 5-FU 250 mg/m^2 IV bolus, 5-FU 2200 mg/m^2 IV continuous infusion over 46 hours). The primary endpoint was overall survival. Sample size: 178 pts in each arm to decrease rate of progression in mFOLFOXIRI/mDCF arms comparative to mFOLFOX-6 arm (HR 0.75, $\alpha = 0.05$; $\beta = 0.80$; 10% of estimated data loss).

Results: We included 50 pts in the preliminary analysis: 20 pts in mFOLFOX-6 arm, 17 pts in mDCF arm, 13 pts in mFOLFIRINOX arm. Median age was 61 years (27-74). No complete responses were achieved. Disease control rate was 85% (17/20) in mFOLFOX-6 arm, 58,8% (10/17) in mDCF arm, 84% (11/13) in mFOLFIRINOX. Partial response rate was 30% (6/20) in mFOLFOX-6 arm, 17.6% (3/17) in mDCF arm, 23% (3/13) in mFOLFIRINOX arm. Pts in the mFOLFIRINOX arm had more frequent reduction in chemotherapy doses 61,5% (8/13) vs 15% (3/20) in mFOLFOX-6 arm and 17,7% (3/17) in mDCF arm. Grade 3—4 neutropenia was observed in 30% (6/20) of cases in mFOLFOX-6 arm, 23,5% (4/17) - in mDCF arm, 38,5% (5/13) - in mDCF arm. Pts in mFOLFIRINOX arm and mDCF arm received G-CSF. Rates of grade 3/4 non-hematologic adverse events (asthenia, cardiotoxicity, hepatotoxicity) were 46,2% (6/13) in mFOLFIRINOX arm, 5% (1/20) in mFOLFOX-6 arm.

Conclusion: mFOLFOX was comparable in efficacy to three-drug chemotherapy regimens (mFOLFOXIRI/mDCF) in the first-line setting of advanced gastric cancer. mDCF arm was closed and changed to FLOT arm.

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P-281 Colon cancer in elderly patients: Experience of the Medical Oncology Department of CHU Hassan II Fez

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Background: This is a retrospective study of patients over the age of 70 with colonic cancer who were followed up and treated in the Department of Medical Oncology at Hassan II University Hospital in Fez from January 2015 to June 2019.

Results: Overall, 15.38% of patients aged over 70 years were listed among the 247 cases of histologically confirmed colon cancer collected over a period of 4 years. The median age was 79.44 years (range, 70-103 years), with a slight male predominance of 57%. In all, 28% of patients had hypertension-type comorbidities and diabetes, and only 1 patient had well-controlled prostate cancer under medical castration. Colonic adenocarcinoma was the histological type in all cases. Overall, 65% of patients were metastatic with a predilection for the liver and the lungs as sites of metastasis. RAS status was sought only in 7.69% of cases and was mutated. A total of 23.07% of patients had received mono-chemotherapy based on intravenous or oral fluoropyrimidines; 53.84% received bi-chemotherapy based on 5FU in combination with irinotecan or oxaliplatin; and 61.53% received bevacizumab in combination with chemotherapy. In all, 8.69% of patients were put on maintenance after a partial response to the first line of treatment with good tolerance. Only 19.23% were able to receive a second therapeutic line. Overall, 11.53% were lost to follow-up after diagnosis and 11.53% who had a PS of 4 were placed in supportive care. Of the patients, 31.57% were operated without any postoperative complications. One-quarter were classified as stage II with the achievement of microsatellite status, which was stable in 66.6% and unstable in 33.3%. Overall, 45.45% had received 5FU bi-chemotherapy whereas 36.36% had received only a mono-chemotherapy. Of the patients who received adjuvant chemotherapy, 22.2% are currently under good control. The safety profile was generally good without any grade 3 or 4 toxicity.

Conclusion: The treatment of elderly patients with colon cancer remains similar to that of young people. However, their treatment must be adapted according to their physiological conditions and their comorbidities within the framework of a multidisciplinary collaboration for a better quality of life.

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P-282 Long-term outcomes after neoadjuvant chemoradiotherapy and R0 resection in ESCC using: A propensity-matched analysis of PF versus CROSS regimen

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Background: Carboplatin-paclitaxel-based (CROSS) neoadjuvant chemoradiotherapy (NACRT) has been widely adopted despite that no randomized study has ever confirmed its superiority over the conventional cisplatin-5FU-based (PFRT) regimen. In fact, only 41 patients with squamous cell carcinoma received CROSS regimen in the landmark study. Emerging evidence has suggested its excellent efficacy in the squamous cell histology (ESCC) could not be reproduced in the real-world setting and PFRT may achieve better outcomes. Here, we report the propensity-matched analysis of one of the largest prospectively-maintained database of Asian ESCC treated with standard NACRT regimens.

Methods: This is a single-center retrospective propensity score-matched analysis. Records of all ESCC patients who have received neoadjuvant PF with 40Gy radiotherapy (PFRT Group) or CROSS with 41.4Gy radiotherapy (CROSS Group) during the period 2002-2019 were retrieved from a prospectively maintained database. Patients with radiation dose beyond 40-46Gy, double primary tumor, double level tumor and treatment received from other centers were excluded from the analysis. Propensity score was calculated using a multivariable logistic regression model in which R0 resection, age, gender, ECOG performance status, tumor length, tumor level and tumor stage according to American Joint Committee on Cancer (AJCC) 6th edition were the independent variables. Patients from the CROSS and PFRT groups were matched (1:1) according to the closest propensity score on the logit scale and caliper (0.25) matching. The primary and secondary endpoints were survival and pattern of recurrence, respectively, in those who had R0 resection.

Results: Fifty-nine patients in the CROSS group with R0 resection and 59 (out of 211) propensity score-matched patients in the PFRT group were included. The median FU time was 22.5 months in the CROSS group and 47.8 months in the PFRT group. The median overall survival (mOS) and median disease-free survival (mDFS) of the whole population were 45.5 months and 39.3 months, respectively. Both mOS and mDFS were comparable in the two groups (mOS, 39.9 months in CROSS vs 48.6 months in

PFRT, p=0.395; mDFS, 37.8 months vs 41.9 months, p=0.609). The overall recurrence rate was 33.9% in the CROSS group and 44.1% in the CROSS group. The patterns of recurrence were similar in both groups and distant failure predominated in this R0 cohort (23.7% in CROSS and 30.5% in PFRT).

Conclusion: While the jury is still out for the best NACRT regimens for ESCC, our results suggest similar efficacy of both CROSS and PFRT regimens in those who achieved R0 resection. The pattern of recurrence was similar to those reported in the landmark CROSS study but the survival outcomes could not be reproduced in the Asian community-setting with ESCC. Further studies to optimize patient selection and treatment intensification are unmet needs for this aggressive disease.

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P-283 Analysis of KRAS mutation allele in circulating cell-free DNA derived from urine in colorectal cancer patients

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Background: Liquid biopsy is widely introduced in various malignant diseases and it provides crucial clinical information on genetic profiles. Cell-free DNA (cfDNA) derived from peripheral blood has been studied mainly. However, other body fluids also have potential to provide molecular information. Urine could be a novel and completely noninvasive source to provide genetic information. The aim of this study was to evaluate the quantity of cfDNA derived from urine in colorectal cancer patients. The accuracy of KRAS mutation allele detection was also analyzed using droplet digital PCR (ddPCR).

Methods: Urine, peripheral blood and tissue samples were collected from consecutively resected colorectal cancer patients. DNA was extracted from each sample and the quantity was measured. From each DNA sample, ddPCR was performed to detect common point mutations in KRAS oncogene.

Results: A total of 143 patients were enrolled. In all patients, plasma and urine cfDNA were successfully extracted and the quality and quantity were appropriate for genetic analysis. The concentration of urine cfDNA was significantly higher than that of plasma (2448 ng/ml vs. 267 ng/ml, $p< 0.05$). Neither plasma nor urine cfDNA concentration correlated with cancer staging. In tumor tissue DNA, KRAS mutation allele was detected in 95 patients (66.4%), KRAS mutation was detected in 21 patients from plasma and 13 patients from urine. The concordant rate of KRAS mutation allele detection between tumor tissue DNA and plasma cfDNA was 22.1%, and between tumor tissue DNA and urine cfDNA was 13%. In the early stage patients (stage I and II), the detection rate of KRAS mutation allele was similar in plasma and urine cfDNA (15.6% vs. 15.6%), however, in advanced-stage patients (stage III and IV), the detection rate in urine cfDNA was lower than that in plasma DNA (15.9% vs. 25.4%). Furthermore, urine cfDNA had a lower detection rate of KRASmutation than plasma cfDNA in stage I and IV patients (stage I; plasma cfDNA 14%, urine cfDNA 0%, stage IV; plasma cfDNA 52%, urine cfDNA 12%), however, the detection rates were equivalent in stage II and III patients (stage II; plasma cfDNA 16%, urine cfDNA 20%, stage III; plasma cfDNA 16%, urine cfDNA 16%).

Conclusion: Our data indicated that urine cfDNA is a useful source in complementing genetic analysis in colorectal cancer patients. The sensitivity seems to be inferior especially in advanced stage, however, it will be considered useful for evaluation of minimal residual disease in stage II and III colorectal cancer patients.

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P-284 Clinico-epidemiological and therapeutic profile of metastatic and locally advanced pancreatic adenocarcinoma: Experience of medical oncology department of CAC ORAN

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Background: Pancreatic cancer is a devastating illness with extremely poor survival. Pancreatic adenocarcinoma is still the fourth most frequent tumor-related cause of death in the world. Surgical resection represents the only hope for cure but only occurs in 10-20%. The aim of this study was to investigate the clinicopathological characteristics and prognosis in patients with pancreatic cancer.

Methods: We retrospectively analysed 65 patients with locally advanced and metastatic pancreatic adenocarcinoma, from January 2015 to December 2019.

Results: In all, 65 patients were recruited; mean age was 61,8 years, range (40-89 years). 60% were male, 40% were female. The performance status were OMS 0: 1,53%, OMS1: 50,76%, OMS2: 24,61%, OMS3: 23,7%. Body mass index (BMI) was $>$ 25 in 21,54%, BMI between 18 and 25 in 64,62 %, $<$ 18 in 13,84%. Personal history: pancreatic adenocarcinoma was the second primary neoplasm after breast and bladder cancer, diabetes was observed in 28 pts, (43,07) hypertension in 20 pts (30,76%), cholecystectomy in 3pts (4,61%). Family history: Neoplasms were observed in 22 pts (33,84%) with PAC in 2 pts. The main symptoms at diagnosis were abdominal or epigastric pain in 65 (100%), vomiting in 22 (33,84%), thromboembolic disease in 14 (21,53%), jaundice in 10 (15,58%), anaemia in 10 (15,38%). High quality imaging plays a crucial role in the diagnosis of pancreatic tumors: CT Scan of the abdomen was positive in 65 (100%), MRI of the abdomen in 7 (10,76%). Tumor location was in the pancreatic body in 28 (43,07%), pancreatic head in 27 (41,53%), pancreatic tail in 23 (35,38%). Extensive vascularization occured in 41 (61, 53%). The final histological diagnosis of adenocarcinoma was confirmed in 60 (92,30%). At diagnosis, locally advanced disease was in 19 (29,23%), metastatic disease in 46 (70,76%). Metastatic sites: liver metastasis in 40 (61,53%), peritoneal carcinomatosis in 8 (12,30%), lung metastasis in 6 (9,23%), lymph nodes metastasis in 5 (7,69%). CA 19-9 concentration was normal in 15 (23,07%), elevated in 18 (27,69%). 52pts (80%) received first-line chemotherapy, GMZ Mono in 25 (38,46%), GMZ- CDDP in 8 (12,30%), GEMOX in 7(10,76%), FOLFIRINOX in 5 (7,69%), GMZ—CAP in 4 (6,15%), FOLFOX and 5FU—CDDP n= 2. 14pts (21,53%) received second-line chemotherapy, and derivation was performed in 2pts. Median survival was 6 months.

Conclusion: Prognosis of locally advanced or metastatic pancreatic adenocarcinoma is poor with extremely reduced survival despite patients undergoing potentially curative resection. International collaboration is required to further improve the management, survival, and quality of life of patients.

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P-285 Therapeutic management of exocrine pancreatic cancer in elderly patients

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Background: The cancer of the exocrine pancreas is a pathology of the elderly and its incidence does not cease increasing. It is the digestive cancer whose prognosis is the most unfavourable.

Methods: A retrospective study was carried out at the Medical Oncology Department of the Tlemcen University Hospital on the files of patients aged 65 years and over treated for pancreatic cancer.

Results: We collected 115 cases of pancreatic cancer of which 47 patients were 65 years of age and older, 42% were women. The mean age of the patients was 74 years [65-93] .65% had at least one medical history of diabetes (60%), hypertension (55%), heart disease (8%); 19% had at least one family history of cancer. The reason for consultation was abdominal pain in 70% of cases, the average duration of evolution was 4.5 months [1-12]. The tumor site was at the level of the head (50%), body (38%), tail (12%). The histological type was adenocarcinoma in 100% of cases. The tumor was metastatic in 82% of which the most frequent sites were liver (70%), lung (12%) and carcinosis (18%). After oncogeriatric evaluation, 54% of the patients had received palliative first-line chemotherapy. The most used chemotherapy protocol was gemcitabine with an average of 3 courses [1-9] per patient, and 12% received second-line chemotherapy. The safety profile was good, with an average overall survival of 6 months [1-9].

Conclusion: Pancreatic cancer is a serious pathology linked essentially to the fact that the diagnosis is made late and that radical surgery in the majority of cases is not possible.

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P-286 Exploring chemotherapy holiday in pancreatic cancer patients responding to upfront nab-paclitaxel-gemcitabine containing regimens

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Background: To date, no information about the optimal duration of upfront chemotherapy in patients affected by pancreatic adenocarcinoma (PDAC) is available. We explored the role of chemotherapy holiday in patients who responded to nab-paclitaxel-gemcitabine (AG) based regimens.

Methods: We retrospectively analyzed the outcome of 40 PDAC patients who had disease control (DC = partial response [PR] or stable disease [SD]) after 4-8 cycles of 1st-line AG-based chemotherapy (i.e. AG or PAXG = cisplatin, nab-paclitaxel, gemcitabine, capecitabine), allowing a chemotherapy holiday until progression, then retreated with AG/PAXG.

Results: Between 2015 and 2019, 40 chemo-naïve patients had DC with AG-based chemotherapy for stage IV (N=21; 17 AG, 4 PAXG) or stage II-III PDAC (N=19; 14 AG, 5 PAXG) at our Institution. Median age was 61 (28-75), 19 patients were males (47.5%) and 21 females (52.5%), ECOG performance status was 0-1 for all patients. Seventeen metastatic patients had PR (81%) and 4 had SD (19%). CA19-9 response was recorded in 18/20 assessable patients (90%). Median (m) PFS1 and OS1 were 10.3 and 23.2+ months (mo), respectively. Stage II-III patients had PR in 12 cases (63%) and SD in 7 (37%). CA19-9 response was recorded in 16/17 evaluable patients (94%). mPFS1 and mOS1 were 11.7 and 21.4+ mo respectively. Grade 3-4 side effects were neutropenia (57%), fatigue (15%), infections (12.5%), thrombocytopenia (10%) and anemia, nausea, peripheral neuropathy (2.5%). At time of PD, 34 patients were retreated for stage IV (A; 31 AG, 3 PAXG) and 6 for stage II-III (B, all AG). In group A, the median duration of chemotherapy holiday was 6.1 mo (3-25.7), 14 patients (41%) had PR and 12 (35%) had SD (DCR 76%). CA19-9 response was recorded in 22/32 evaluable patients (69%). mPFS2 and mOS2 was 5.3 and 12.1+ mo respectively. Patients with chemo holiday between 3 and 6 mo had a mPFS2 of 4.2 as opposed to 6.2 mo for patients with holiday lasting >6mo. Similarly, mOS2 was 10.3 versus 12.1 mo, respectively. At PD, 8 patients (36%) were still re-treated with AG yielding 2 PR, 4 SD (DC 75%) and mPFS3 of 5+ mo, with a chemo holiday period of 5.1 (2.6-8.9). After AG failure, further chemotherapy was administered to 19 patients (56%). In group B, the median duration of chemotherapy holiday was 7.4 mo (5.8-13.5), 1 patient (17%) had PR and 4 (67%) had SD (DC 84%). CA19-9 response was recorded in 4/5 evaluable patients. mPFS2 and mOS2 was 5.6 and 24 mo, respectively. Grade 3-4 neutropenia (50%), peripheral neuropathy (10%), anemia and thrombocytopenia (7.5%), fatigue, nausea and infection (5%) were reported.

Conclusion: Re-treatment with the same schedule after a durable chemotherapy holiday seems to be a valuable option, reaching a clinically relevant DC rate and mPFS2, preserving a manageable safety profile, and allowing 2nd-line chemotherapy in a large number of patients. This strategy may provide a potential remarkable benefit for patient quality of life.

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P-287 Does endemic gallbladder cancer behave differently? Data of clinical spectrum, management and outcome of gallbladder cancer patients from a north Indian tertiary cancer centre

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Background: Gallbladder cancer (GBC) is the most common malignancy of the biliary tract. The global rates for GBC exhibit striking variability, reaching epidemic levels for some regions of Asia. An increased frequency of gallbladder cancer occurs in northern Indian females, Pakistani females, and Korean males. It is the commonest malignancy of the gastrointestinal tract and the commonest cause of malignant jaundice in northern India. But the data regarding the clinical scenario of GBC from the north Indian population is still not clear.

Methods: An analysis of a prospectively maintained computerized GBC database of the Department of Surgical Oncology, AIIMS, New Delhi was performed. The medical records of patients with histo-pathologically proven GBC were analyzed to assess the epidemiology, clinical profile, staging, treatment patterns, and outcomes. A total of 250 GBC patients operated between the period of January 2012 to January 2018, with multimodality treatment (especially radical surgical approach) were analysed.

Results: A total of 250 patients were analysed, including 69 (27.6%) males, and 181 (72.4%) females. A clear female predominance was found with the male-female ratio being 1:2.6. The mean age was 50 years in both males and females. Abdominal pain was the most common clinical presentation, invariably present in the majority of the patients 201 (80.5%) followed by jaundice 35 (14%). The majority of patients (136, 54.4%) were of an incidental group (GBC found during cholecystectomy done outside for other causes) and the primary upfront cases were 114 (45.6%). Out of the total patients operated, 161 (64.4%) patients underwent curative treatment with either radical cholecystectomy or completion radical cholecystectomy and 89 (35.6%) patients underwent explorative laparotomy and closure due to metastasis or local unresectability. The reason for exploration and closure was metastasis 43 (48%), local unresectability 39 (43%) and dense fibrosis at porta 7 (8%) in the patients. The final Staging after the histopathological assessment, was stage 1 (17.05%), stage 2 (15.8%), stage 3 (21.17%), stage 4 (42.35%) and unknown (3.70%) among the patients. The average number of nodes harvested was 9.5 with a nodal positivity rate of 8.2%. Out of the patients who underwent curative surgery, adjuvant CTRT was given in 30.68%, CT alone in 31.81% and observation in 37.5% of the patients.

Conclusion: Gallbladder cancer patients from the endemic zone present in early age groups, the mean age at presentation being 50 years as compared to 65 to 72 years reported in most of the published literature. The majority of them were from an incidentally detected group with higher curative resection (64.4%) in comparison to other studies. Multimodality management with surgery/revision surgery and chemoradiation will yield a better outcome.

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P-288 Nerve fibers in the tumour microenvironment are co-localized with tertiary lymphoid structures and is associated with better survival in pancreatic cancer patients

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Background: Pancreatic ductal adenocarcinoma (PDAC) is one of the most lethal cancer types and it has not shown any benefit since the revolution of immunotherapy. The role of other immune components, such as B cells and tertiary lymphoid structures (TLS) are reported to be important in the improvement of survival and response to immunotherapy. Besides immune cells, there is some limited data about the influence of nerve fibers on cancer progression. However, the precise roles of these tertiary lymphoid structures and nerve fibers remain unknown.

Methods: Histological slides from 155 patients with PDAC were selected from the Pathology of RWTH University Hospital Aachen and used for the immunostaining Protein Gene Product 9.5 (PGP9.5). The study was approved by the Ethics under protocol number EK 106/18. Nerve fiber density: an experienced pathologist read all the slides and nerve fiber density (NFD) was evaluated by counting the number of nerve fascicles with diameters of 10 nerve fibers. Type of immune cells and their spatial arrangements: the dominant type of immune cells was determined by the pathologist on the corresponding H&E slide and scored into three categories: 1) lymphocyte-predominant, 2) neutrophil-predominant or 3) no immune cells. Their spatial arrangement was determined by QuPath by using a classifier for the distance from each immune cell to the nearest annotated tumor gland. Spatial distribution of nerve fibers: the small nerve fibers are colocalized within the tertiary lymphoid structures mostly located at the edge of the tumour. We used Multipleximaging to confirm the existence of TLS by immunohistochemical staining for T cells, B cells and dendritic cells.

Results: We found a highly significant correlation in the group with a high NFD (group 3; having more than 10 positive nerve fibers) and overall survival (HR 0.58 (95% CI 0.41-0.87) p< 0.01). Univariate analysis showed that lymphocytes are present in the tumors containing more stroma. By machine learning, we determined the mean distance from the nearest tumor gland from each immune cell. The patients with a high NFD have lymphocytes more distant from the nearest tumor gland (OR 1.01 (95% CI 1.00-1.01) p=0.01 in the binary logistic regression analysis).

Conclusion: Here we showed that small nerve fibers are located at the tertiary lymphoid structures and correlate significantly with better survival in patients with pancreatic cancer. Secondly, by using machine learning we showed that the lymphocytes are located at a greater distance from the tumour glands in patients with a

high NFD. Our findings confirm the importance of the TLS on survival for patients with PDAC and the relationship between nerve fibers and TLS is undiscovered. This association will unravel future pathways for a better response to immunotherapy.

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P-289 Role of the neoadjuvant chemoradiotherapy in esophageal cancer: Our center's experience

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Background: Initial results of Chemo-Radiotherapy for esophageal cancer followed by Surgery Study (CROSS) in locally advanced resectable esophageal and esophagogastric junction (EGJ) cancer showed better outcomes in favor of the neoadjuvant chemoradiotherapy plus surgery group. Our goal is to describe the overall survival (OS) and its correlation with the response by PET-CT (rPET) in esophageal cancer (EC).

Methods: We performed a retrospective study of locally advanced esophageal and EGJ cancer patients treated in our center using the CROSS trial scheme of weekly administration of carboplatin and paclitaxel for five weeks and concurrent radiotherapy (41.4 Gy in 23 fractions, five days per week) followed by surgery. We calculated the metabolic response with the SUVmax difference between the diagnostic PET-CT and the assessment after the chemoradiotherapy (CRT). We used Kaplan-Meier curves plotted for OS and log-rank test for association between rPET and OS.

Results: A total of 92 patients were diagnosed between 2013 to 2018 with resectable EC. All patients were diagnosed with upper gastrointestinal endoscopy and histologic biopsy. 87% underwent endoscopic ultrasonography (EUS). Extension staging was made with PET-CT in 88 patients. 45 (48.9%) had adenocarcinoma and 47 (51.1%) had squamous-cell carcinoma. Most tumors were located in the distal esophagus (28.3%) or EGJ (37%), the rest were middle and proximal esophagus. 78.6% of patients had positives lymph nodes by EUS. All patients completed concurrent CRT. The main toxicity related to CRT was hematologic (23%) and esophagitis (27%), with no grade 3 or higher toxic effect reported. The evaluation after CRT was assessed with PET-CT through morpho-metabolic response in 84 (91.3%) patients, with partial response in 62 (67.4%) and complete response in 8 (8.7%) patients. The median difference between PET-CT at diagnosis and post-CRT evaluation, assessed by SUVmax, was 10.8. Sixty-three (68.5%) patients underwent surgery, the remaining patients progressed during CRT or during the interval to surgery, or refused the intervention. One patient died after surgery, with no other major postoperative complications. Complete resection was achieved in 85.7%. Pathological complete response was seen in 14 (15.2%) patients. With a median follow-up of 30 months, we observed a median OS of 28 months, being significantly higher in operated patients (70 vs 15 months; $p < 0.0001$). There was no survival benefit in relation to the rPET, observing an OS of 28 months vs 29 months, in patients with differences greater than 10.8 vs. lower than 10.8, respectively ($p = 0.79$).

Conclusion: The results of this study are in accordance with published reports, confirming that trimodality therapy for potentially resectable EC brings benefit in OS with a safe toxicity profile. Results indicate that there is no correlation between rPET and OS. Further data is necessary to validate the metabolic response as an outcome predictor.

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P-290 Neutrophil-to-lymphocyte ratio and platelet–lymphocyte ratio as predictive and prognostic markers in patients with pancreatic cancer in Tlemcenian patients

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Background: Pancreatic cancer (PC) is one of the most lethal malignant neoplasms in the world. The long-term prognosis of patients with PC is poor, The neutrophil-to-lymphocyte ratio (NLR) and platelet–to-lymphocyte ratio (PLR) are representative blood markers of systemic inflammatory responses. However, the clinical significance of the combination of these markers is unclear. This study aimed to evaluate the impact of NLR and PLR before the start of multimodal treatment on patients with pancreatic cancer and to assess the clinical utility of a new blood score combining the NLR and PLR (NLR-PLR score) as a predictor of tumor response and prognosis.

Methods: A retrospective study was conducted at the Department of Medical Oncology (CHU Tlemcen), including 114 patients treated for pancreatic cancer before receiving treatment. Complete blood count, NLR, and PLR before initiation of treatment was evaluated and correlated with survival. Value cutoffs were adopted to discriminate patients as follows: low NLR < 3 and high NLR ≥ 3; PLR < 8000 and PLR ≥ 24000.

Results: A total of 114 patients with pancreatic cancer were enrolled in this period of study. NLR and PLR at baseline were available for 82 patients (72%). 32 patients (39 %) with a low NLR < 3 and PLR < 8000 had an average age of 63.6 years [46-89]. 21 of them were men (65 %), and 50% had performance status (PS) 0–1 with 16 cases. Low NLR and PLR were associated with a median survival of 9 months [1-72]. 50 patients (61 %) with a high NLR ≥ 3 and PLR ≥ 24000 had an average age of 61 years [41-76], with 27 males (54 %), ECOG 0 - I in 22 patients (44 %) and ECOG II-III in 28 cases (56 %). High NLR and PLR were associated with a poor median survival of 2 months [1-7].

Conclusion: Initial NLR > 3 and PLR ≥ 24000 were associated with shorter survival in patients with pancreatic cancer. The NLR and PLR score can be a useful blood marker to predict therapeutic responses in treatments. In the future, the NLR- PLR scoring system is expected to be useful in decision-making of therapeutic strategies as a key marker in the clinical management of patients with pancreatic cancer. The ratio is a simply accessed and inexpensive but useful biomarker in pancreatic cancer before receiving chemotherapy.

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P-291 Retrospective comparison efficacy and toxicity FOLFIRI plus aflibercept or bevacizumab in patients with metastatic colorectal cancer: Results of the multicenter observational study

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Background: The aim of this study was to compare FOLFIRI with aflibercept or bevacizumab efficacy and toxicity in the 2nd line chemotherapy (CT) in patients (pts) with metastatic colorectal cancer (mCRC).

Methods: We analyzed a prospective database of pts with mCRC in 18 cancer clinics in Russia who received FOLFIRI with aflibercept or bevacizumab in 2nd line CT. The primary endpoints were progression-free survival (PFS) and objective response rate (ORR). A multivariate regression analysis was performed with the SPSS v.20 software package.

Results: The study included 271 pts (81 in the bevacizumab group and 190 in the aflibercept group). There were no differences between groups by age, sex, number of organs with metastases, localization of metastases, mRAS (43% vs 42%), synchronous metastases (72% vs 67%), adjuvant CT (17% vs 8%), comorbidities and concomitant therapy. ORR was achieved in 15 (18.5%) pts with bevacizumab and in 39 (20.5%) pts with aflibercept (p=0.4). Median PFS was 5 months (95%CI 3.8-6.1) in the aflibercept group and 7 months (95% CI 5.7-8.3) in the bevacizumab group (HR 1.5, 95%CI 1.09-2.1, p=0.01). Cox regression analysis did not show any statistical difference between treatment groups in terms of PFS after adjusted by age and mRAS (HR 1.3, 95%CI 0.9-1.8, p=0.12). Adverse events (AEs) were reported in 216 (79.7%) pts. There were no significant differences between treatment groups in terms of overall toxicities (58% vs 72%, p=0.1), Gr1-2 (54% vs 61%, p=0.6), Gd3-4 (20% vs 22%, p=0.4). Among Gd3-4 nonhematologic AEs arterial hypertension (2 vs 9.5%), and diarrhea (0 vs 5.4%) were often seen in pts with aflibercept. Thrombosis was associated with bevacizumab only (10% vs 1.8%, p=0.015).

Conclusion: There were no statistical differences in terms of ORR and PFS between bevacizumab or aflibercept plus FOLFIRI in 2nd line treatment of pts with mCRC. AEs were more often seen in the aflibercept group except for thrombosis.

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P-292 Locally advanced esophageal cancer: Pattern of care, treatment outcomes and prognostic factors over a 20-year experience at the Modena Cancer Centre

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Background: Esophageal cancer produces a considerable burden worldwide, being responsible for 1 in every 20 cancer deaths every year (>500.000 deaths/year). A multimodality treatment strategy including a combination of chemotherapy, radiotherapy, and surgery is the standard of care for patients with locally advanced esophageal cancer (LAEC). However, patient (pt) outcomes have improved only a little and > 50% of pts succumb to their disease. In this study, we aimed at describing the pattern of care, treatment outcomes, as well as prognostic factors in a real-world cohort of LAEC, treated over a 20-year period.

Methods: Electronic medical records of patients with T2-T4 and/or N-positive AC or SCC of the esophagus followed at the Modena Cancer Center (MCC) between 2001 and 2018 were retrospectively reviewed. Clinicopathologic variables deemed of potential interest were collected. Continuous variables were reported as the median and 25−95 percentile, while categorical variables were reported as absolute and percentage frequencies. OS was calculated using Kaplan-Meier estimators and comparisons between curves were performed with the log-rank test. Cox proportional hazards in univariate and multivariate regression were used to assess the effects of the prognostic factors on OS.

Results: 95 pts (51%) were included in the analysis. Median age was 67 years, 68 (72%) pts were males. 67 (71%) and 18 (19%) pts presented with stage III and II, respectively and 70 pts (74%) were node-positive. The most frequent histology was SCC (69%), followed by ADC (30%). While SCCs were mainly localized at the mid-thoracic (65%) and cervical (23%) esophagus, the vast majority of ADCs developed in the distal esophagus (90%). Among SCC (n=65), 15 pts (23%) underwent curative-intent surgery within a multimodality strategy (Group A), consisting of neoadjuvant chemoradiation in 11 pts (17%). 20 pts (31%) with SCC were treated with definitive chemoradiation (Group B), whilst the other 25 (38.5%) received palliative chemotherapy ± radiotherapy (Group C). Median OS was significantly better in Group A (45 months) compared to Group B (10 months) and Group C (7 months) (p< 0.001). At both univariate and multivariate analysis, ECOG PS (p< 0.001) and surgical resection (p=0.02) retained independent prognostic value. Among ACs, 18 pts (64%) were treated with a multimodality strategy (Group A1): 9 pts (32.1%) received perioperative treatment and other 9 neoadjuvant or adjuvant chemotherapy alone. 7 (25%) pts were treated with palliative chemotherapy ± radiotherapy (Group B1). Median OS was significantly higher in Group A1 vs Group B1 (40 months vs 6 months; p=0.048). Surgery (p=0.02) and receipt of adjuvant (after neoadjuvant) chemotherapy (p=0.07) were associated with better OS in AC. Pts treated during 2011-2018 experienced improved OS than those treated during 2001-2010 (43 vs 21 months; p< 0.001). Notably, a significantly higher proportion of them received perioperative treatment (8 pts vs 1 pt) in the most recent subgroup.

Conclusion: In this large tertiary cancer center experience, a multimodality strategy encompassing radical surgery and good PS confirmed to yield the best treatment outcomes regardless of histology. The increasing number of candidates to perioperative chemotherapy and the completion of the adjuvant phase seems to result in better OS in the AC subgroup.

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P-293 Overall survival according to mutation frequency of BRAF, NRAS genes, and MSI status in patients with wild-type KRAS metastatic colorectal cancer treated with cetuximab

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Background: The treatment of colorectal cancer (CRC) has been progressively based on its molecular profile. This study was justified by the prognostic relevance of BRAF and NRAS genes and microsatellite instability (MSI) status in CRC, and the small number of studies evaluating the mutation frequency of these genes as well as the status of MSI in colorectal tumors in Brazil. In addition, it is one of the first studies in the Brazilian population that aimed to confirm previous findings regarding the efficacy of cetuximab in the treatment of advanced CRC in an enriched population of refractory poly-treated patients. The primary endpoint of this study was to evaluate the survival and frequency of BRAF, NRAS gene mutation, and MSI status in patients with advanced colorectal cancer treated with cetuximab in a Brazilian Cancer Center.

Methods: A retrospective cohort study was conducted through the medical records of patients diagnosed with metastatic or locally advanced colorectal cancer, wild-type KRAS, treated with cetuximab at the Barretos Cancer Hospital. Demographic, clinical and pathological data were evaluated descriptively. Univariate analyzes were performed for overall survival by variables and Cox regression was used for multivariate analysis.

Results: Two hundred eleven patients from January 2011 to December 2016 were included in the final analyses. The median survival for patients treated with cetuximab was 10.4 months; for right colon tumors it was 6.6 months and for left colon tumors 11.5 months (p=0.02). BRAF mutation frequency was 3.8% and had a median survival of 4.9 months, while NRAS mutation was found in 3.3% of patients with a median survival of 6.9 months. A frequency of MSI-H of 3.3% was found, with a median survival of 4.6 months. In multivariate analysis for survival only, the laterality variable was statistically significant (HR = 2.6, [95% CI 1.41−4.72]), with the risk of death being higher in patients with right colon tumors.

Conclusion: Overall survival of cetuximab-treated patients, as well as NRAS mutation and MSI frequency, were approximate to that found in other studies evaluating cetuximab in poly-treated patients refractory to other treatment lines. BRAF mutation frequency was not as high as in other studies previously done. BRAF, NRAS mutation and MSI were associated with a smaller survival in univariate analyses, but only laterality, the right side of the colon, maintained statistical significance after the multivariate analysis.

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P-294 Incorporating genetic counseling service into the gastrointestinal tumor board: Experience, obstacles, and opportunities in a Mexican center

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Background: Germline mutations explain about 5 to 10% of cancers; it is important to recognize patients (pts) with hereditary cancer in order to refer them to Genetic Counseling (GC) and Genetic Testing (GT). Guidelines have been published to help identify those individuals according to the type of tumor, age and family history. Those individuals could have benefits such as adjusted surveillance, risk reduction strategies, cascade testing and directed therapy. Nonetheless, many barriers to offering GC have been described, including criteria that are difficult to manage, lack of coverage of GC, and high cost of GT. Herein, we describe our pilot project incorporating a genetic counselor into the Gastrointestinal (GI) Tumor Board.

Methods: This was a retrospective and descriptive study. We reviewed the electronic medical records of pts in which cases were discussed in the GI tumor board from January 2018 to December 2019. Additionally, we added 20 pts previously referred to the genetics department. We explored the percent of pts referred to GC according to criteria. Clinical, familial and demographic data were gathered. GT was discussed with patients, but GT should be covered by them. GT was performed by NGS and CGH. We used descriptive statistics.

Results: 943 cases were discussed, among them, 114 (12%) met criteria to GC. Nonetheless, only 46 (40.4%) pts received GC. Among the 66 pts who had GC, the mean age was 43.71 y (SD 14.26). 32 (49%) had family history. 48 (72.7%) had colorectal cancer (CRC), 6 (9.1%) pancreatic adenocarcinoma (PAAD), and 6 (9.1%) diffuse gastric cancer (DGC). 10 pts (15%) had a second primary tumor. Only 1 pt with Neurofibromatosis type 1 had a GIST. We found no clinical suspicion of other

syndromic GIST. 61 (92.4%) met criteria for GT. 8 pts underwent GT: 2 tested positive for MSH2, 1 CRC pt for BRCA1, and 1 for APC. Two pts had negative testing, and 1 pt had a VUS in MSH2. 2 families had cascade testing. Then, we analyzed the 68 pts who were not referred to GC, mean age was 43 (SD 12.3), 32 (47%) had CRC; 11 (16%) had PAAD, 8 (11%) DGC. 9 (13%) pts had no cancer or medical record available. 9 pts were deceased: 4 of DGC, 2 of PAAD, 2 of CRC, and 1 of GIST.

Conclusion: We observed that nearly 12% or pts met criteria for GC, but only 40% of them were actually referred. Comprehensive GT is not offered by most public health care centers in Mexico; also, immunochemistry is not routinely performed at our center due to the cost of reagents. Only 6% of identified pts underwent genetic testing. Half of pts with positive findings performed cascade testing. We still lack referral of PADD. Recent guidelines suggest GT in all pts in order to identify pts who would benefit from PARP inhibitors. Unfortunately, we could not explore the barriers affecting referral to GC in this study. Finally, we should also focus on pts in palliative care to discuss the possible advantages of GT.

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P-295 Patterns of failure following neoadjuvant and definitive radiation strategies in carcinoma thoracic esophagus: Do we need to rethink targets?

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Background: This study aimed to document the patterns of failure in patients with carcinoma esophagus treated with neoadjuvant and definitive intent radiation strategies.

Methods: Between January 2011 to December 2014, a total of 157 consecutively treated patients with radical intent chemoradiation strategies were identified. Group 1 included patients undergoing radical RT while Group 2 included patients undergoing NACRT followed by Sx. Data regarding demographics, disease, treatment, and failure patterns were extracted from patient case files and hospital medical records. Demographic data and failure patterns were summarized using crude percentages while differences between the groups were evaluated using Pearson's chi-square test. Locoregional failure (LRF) was defined as persistence of residual disease or recurrence locally or in the regional nodal areas including the mediastinal, celiac and supraclavicular regions irrespective of the location of disease. LRF was mapped on the treatment planning system as infield if located within 50% isodose or out of field if recurrence was located outside the 50% isodose line. Distant metastasis included all nonregional nodal and visceral sites.

Results: Median age of the entire population was 57 yrs, median length of 7 cm (Range 2-15) with 95% of patients with SCC and the majority were located in middle±lower thoracic in 57.3%. Group 1 had 99 patients and Group 2 had 58 patients. Overall locoregional failure (LRF) was documented in 36.3 % (n=57) and distant metastasis in 17.2% (n=27) patients. LRF was documented in 38.3% (n=51) of patients in Grp 1 and 25% (n=6) patients in Grp 2 (p=0.25). Dissecting patterns of failure further revealed local recurrence was higher in Grp, 1 33%(n=44), as compared with Grp 2, 8.3%(n=2), whereas isolated regional failures were significantly higher in patients undergoing surgery, (Grp 1 vs 2: 5.3% vs 16.7%, p=0.033). These regional failures were infield for Grp 2, 100 % (n=4) while out of field for Grp1, 85.7%(n=6) with statistically significant difference (p=0.021). For Grp 1 patients, the most common site of nodal failure was supraclavicular 31.2% followed by celiac axis 18.8% while for Grp 2 patients, the most common site of nodal failure was upper paratracheal (50%) followed by mediastinal nodes (25%). Most of the LRF was infield in 78.9 % (n=45) followed by out of field failure in 15.8% (n=9) and both components of failure in 5.3 % (n=3). All out of field failures were seen in Grp 1, 17.6% patients as opposed to none in Grp 2 and mostly located in supraclavicular and celiac nodal regions. Distant metastasis was seen in 18% Grp 1 (n=24) patients as opposed to 12.5% (n=3) in Grp 2 patients, (p=0.37) which was predominantly lung and nonregional nodes for Grp1 and Grp 2, respectively.

Conclusion: Regional nodal infield failures were commonly seen in patients undergoing Sx whilst local recurrence was uncommon. For patients undergoing radical radiotherapy, local infield recurrence was common and regional nodal failures although uncommon were mostly out of field. Hypothesis-generating studies are needed to help refine our targets, particularly in radical RT setting.

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P-296 Chemosensitivity and outcome in advanced and metastatic gastric signet-ring cell carcinoma (GSRC)

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Background: GSRC accounts for 4-17% of all cases of gastric cancer (GC), is associated with a worse prognosis compared with non-SRC, and its chemosensitivity is uncertain.

Methods: A retrospective analysis of all patients (pts) with locally advanced and metastatic GSRC treated in our oncology department from Jan 2012 to Dec 2017 was done to characterize clinical, demographic, and treatment data, and to evaluate the response to chemotherapy (CT) and overall survival (OS).

Results: From the 560 pts with GC treated in our Institution, a total of 71 with GSRC were included with a median age of 65 years (range, 21-83). Localized disease was present in 70% (50 pts) and metastatic in 30%. The anatomic site was esophagus/cardia in 15 pts and others in 56 pts. Total/subtotal gastrectomy was performed in 47pts. Perioperative CT was given to 31 pts, mostly with epirubicin (E), cisplatin (C), and capecitabine (X), with minimal histological tumor regression in 85% and moderate in 15%. N2/N3 was found in 16 operated pts. Twelve pts underwent primary surgery, followed by adjuvant CT with doublet or triplet oxaliplatin-X (in association with E). Twenty-four pts recurred (50%); 20 with metastasis. The median time to relapse was 11 months. A first-line palliative CT for metastatic or recurrent disease was administered in 33 pts. Response was complete in 1 pt, partial in 3, stable disease in 2; 28 progressed. The regimen most used in first-line CT was ECX. The 1-year OS for metastatic pts was 33%. The 5-year OS for localized GSRC was 34.4% and 25% for the global cohort.

Conclusion: Neoadjuvant CT use did not result in tumor downstaging/downsizing. The observation of a group of CT responses in the neoadjuvant and metastatic settings presents the possibility of subtypes with better prognosis despite high lymph node involvement. Further studies are required to clarify the differences between subgroups and to explore the effectiveness of the new docetaxel-based triplet FLOT regimen.

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P-297 Outcomes of combined modality treatment neoadjuvant chemo-radiotherapy and surgery in resectable esophageal carcinoma patients treated at a tertiary cancer care centre

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Background: We present the results of trimodality treatment in squamous cell carcinoma (SCC) of the thoracic esophagus in terms of compliance and outcomes treated at a tertiary care institution.

Methods: Between 2006-2015, 95 consecutive patients of SCC of thoracic esophagus presenting to the Department of Radiotherapy and deemed operable after discussion in multidisciplinary tumor board were identified. Patients received NACRT that comprised of external beam radiotherapy (EBRT) 45Gy/25# along with weekly concurrent cisplatin (dose @ 35mg/m^2). Those deemed fit were taken for surgery while those deemed as unfit or those who refused surgery continued a radical dose between 60Gy-66Gy based on normal tissue tolerance. Patient demographics, clinicopathological features, and response to treatment were retrieved through case files and electronic records. Statistical methods comprised of descriptive analyses for demographic variables and compliance to treatment while Kaplan Maier analysis was performed for overall survival (OS) and progression-free survival (PFS). Univariate and multivariate logistic regression analysis was done to identify various predictors of OS and PFS. The cut-off date for all time-to-event analyses was September 1st, 2019.

Results: The median age (range) was 56 years (20-75) with male predominance 66%. Median duration of dysphagia was 4 months (range 1 -18), and 42% (n=40) had grade 3 dysphagia. About 27% (n=26) had >10% weight loss of the usual body weight in the preceding 6 months. Disease was located in the mid or lower third location with a median length of 6cm (2-15). Amongst those planned for Sx, 60% (n= 57) underwent Sx with pathological complete response (pCR) documented in 35% (n=20/57) while in 12% (n=7/57) disease was inoperable or metastatic disease. Additionally, 40% (n=38) could not be taken for planned surgery due to financial constraints/refusal (n=17), tumor progression/treatment toxicity (n=13) at time of reassessment and were lost to follow-up (n=8)[S1]. At a median follow-up of 69 months (Range: 52 - 175) for surviving patients, 21% (n=20) were alive, 65% were dead (n=62) and 14% (n=13) lost to follow up (LFU) with or without disease. The median OS for entire cohort was 18 months (Range:11-25). On multi-variate analysis, patients with age ≤56 yrs and pCR had better OS [Age; [H.R. 0.28; 95%C.I. (0.12 − 0.66); p= 0.004], pCR [H.R. 0.45; (0.22 − 1.01); p= 0.05] and PFS [Age; [H.R. 0.28; 95%C.I. (0.12 − 0.67); p= 0.004], pCR [H.R. 0.40; (0.18 − 0.92); p= 0.03]. Patients who achieved pCR had significantly better median OS (38 months versus 18 months; p= 0.05), and PFS (47 months versus 12 months; p= 0.009).

Conclusion: Patients achieving pCR and younger age had better OS and DFS. Compliance with treatment was 60%, largely affected by financial constraints in a resource-limited setting which emphasizes the importance of multidisciplinary clinics and cautious patient selection.

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P-298 Surgical resection of primary tumor as a prognostic factor in stage IV colon adenocarcinoma

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Background: Stage IV colon adenocarcinomas represent 22% of all colon cancer cases at diagnosis. There are some known prognostic factors such as left vs right sidedness, microsatellite instability, and KRAS and BRAF mutations. We seek to identify if surgical resection of the primary tumor is a prognostic factor for overall survival (OS).

Methods: We identified histologically confirmed cases of colon adenocarcinomas with metastatic disease and information about surgery status and OS diagnosed between 2004 and 2016 from the National Cancer Database (NCDB). Kaplan-Meier method and log-rank test were used to estimate and compare OS. Recursive partitioning analysis (RPA) analysis was performed on the entire cohort.

Results: 169,001 patients met our inclusion criteria: 102,369 patients underwent surgical resection of the primary tumor and 66,632 patients did not. Surgical status, age, and sidedness were significant prognostic factors for OS by RPA, in that order. Patients who underwent surgery, younger than 75 years, with left-sided tumors had median OS of 30.7 months, compared with patients who did not undergo surgery, were younger than 75 years, with left-sided tumors had a median OS of 14.5 months ($p< 0.0001$). A similar improvement in OS was seen with patients with right-sided tumors. In the older than 75 years group, patients who underwent surgery had improved median OS of 10.2 months, compared with non-surgery patients who had median OS of 4.1 months ($p< 0.0001$).

Conclusion: Surgical status, age, and sidedness were significant prognostic factors for OS, in that order. Patients who underwent surgery, were younger than 75 years, with left-sided tumors had the best OS.

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P-299 Cytoreductive surgery with gastrectomy and HIPEC for gastric cancer with limited peritoneal metastases treated with neoadjuvant systemic therapy is feasible and safe

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Background: Peritoneal metastases (PM) from gastric cancer are associated with very poor survival inferior to one year in the majority of patients. Systemic chemotherapy with palliative intent is the standard treatment but a select group of patients may benefit from a more aggressive approach that includes radical surgical resection coupled with intraperitoneal chemotherapy (HIPEC). Preoperative systemic therapy has been shown to be safe prior to gastrectomy but the feasibility of gastrectomy associated with more extensive peritoneal resections and HIPEC following systemic chemotherapy is not definitively established. The aim of this study was to evaluate the results of patients undergoing gastrectomy, peritonectomy, and HIPEC following neoadjuvant systemic chemotherapy for limited gastric PM.

Methods: This is a retrospective cohort study of adult patients gastric PM metastases (PM) treated within the peritoneal malignancies program of Catalonia. Patients with limited peritoneal metastases defined as peritoneal cancer index (PCI) of <12 were considered potential candidates. The standard clinical pathways included diagnostic laparoscopy, systemic chemotherapy for 4 cycles, repeat diagnostic laparoscopy prior to gastrectomy, cytoreductive surgery and cisplatin-based HIPEC. All data regarding the activities of the center have been maintained in a dedicated prospective database.

Results: There were 53 patients with a mean age of 52.2 years. In 7 patients (13.2%), PM presented as recurrent disease after a prior gastrectomy. All patients received preoperative systemic chemotherapy. Positive cytology was the indication in 9 patients (18.4%), molecular positive peritoneal lavage in 5 (10.2%). Mean affected regions were 3.6/13 and the mean PCI was 5.5/39. The majority (42/53) had a total gastrectomy with D1+ plus lymphadenectomy. Significant postoperative morbidity included: ICU readmission 1 (2.2%), hospital readmissions 8 (16%), urgent reoperation 1 (2.2%). After a median follow up of 12.1 months, 28 patients died (64.2%), 5 were alive with disease (9.4%) and 14 were disease-free (26.4%). Median survival was 20.6 months (IC 95%: 13.9 — 27.2 months) but reached 32 months in patients with a PCI of 0, complete macroscopical resection and no signet ring histology.

Conclusion: Gastrectomy coupled with cytoreductive surgery and HIPEC is feasible and safe after neoadjuvant systemic chemotherapy in an expert center. A select group of patients with very limited peritoneal metastases and the absence of signet ring histology can be identified for whom this approach offers promising survival rates.

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P-300 Overall survival with single vs multi-agent chemotherapy in stage IIIA colon adenocarcinoma

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Background: Stage IIIA (T1-2, N1) colon cancers are considered low-risk cancers and treated with either single or multi-agent chemotherapy. However, it is not known if survival is improved with the addition of a second chemotherapeutic agent.

Methods: We identified histologically confirmed cases of colon adenocarcinomas stage T1-2 and N1 with information about chemotherapy use, surgery, and overall survival (OS) diagnosed between 2004 and 2016 from the National Cancer Database (NCDB). Kaplan-Meier method and log-rank test were used to estimate and compare OS. Recursive partitioning analysis (RPA) analysis was performed on the entire cohort.

Results: 21,837 patients met our inclusion criteria: 3,394 patients received no chemotherapy (NC), 5,227 received single-agent chemotherapy (SAC), and 13,216 patients received multi-agent chemotherapy (MAC). Age, insurance, chemotherapy status, and comorbidity were significant prognostic factors for OS by RPA, in that order. Patients older than 75 years of age who did not receive chemotherapy had the worst OS at 41.7 months, and patients younger than 75 years of age with private insurance, and Charleson Deyo score less than 2 had the best OS at 166.1 months. Median OS was 57.5 months for NC, 130.1 months for SAC, and 166.1 months for MAC ($p< 0.0001$).

Conclusion: Age, insurance, chemotherapy status, and comorbidity were significant prognostic factors for OS by RPA, in that order, for stage IIIA colon cancer. Patients younger than 75 years, with private insurance, and Charleson Deyo score less than 2 had the best OS. Multiple-agent chemotherapy improved OS significantly by 3 years compared to single-agent chemotherapy ($p< 0.0001$).

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P-301 Gastrointestinal stromal tumors: 10 years of experience in the medical oncology department at Mohammed VI university hospital in Marrakech, Morocco

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Background: The development of molecular biology has revolutionized the diagnostic and therapeutic management of gastrointestinal stromal tumors (GIST). The objective of our study was to identify the epidemiological, diagnostic, therapeutic and evolutionary characteristics of our patients followed for GIST.

Methods: This is a retrospective descriptive study conducted within the medical oncology department of the Mohammed VI University Hospital Centre in Marrakech. The study is spread over a 10-year period from January 1, 2010, to December 31, 2019.

Results: We have identified 70 patients followed for GIST. The average age of our patients was 53.3 years (range 21-81). The sex ratio was 1.25 (39 men / 31 women). The most frequent reason for consultation was abdominal pain (58.5%). gastric localization was most frequent in 3 cases in 40 cases (57.5%). The histological diagnosis was made on analysis of the surgical specimen in 37 cases (52.8%). Fusiform cell type was the most observed type in 57 cases (81.4%). The expression of CD117 was observed in 68 cases (97.1%). Research for mutations of the c-KIT and PDGFR genes by molecular biology was not carried out. After staging the disease, the tumor was

localized in 38 cases (54.3%), locally advanced in 9 cases (12.8%) and metastatic in 23 cases (32.9%). The liver metastases were the most marked in 14 cases (20%). 40 patients (57.1%) received surgical treatment, with R0 resection in 36 cases (51.4%). Palliative surgery was performed in 4 metastatic patients, with an occlusion for 2 patients and gastrointestinal bleeding for the other 2 patients. Regarding medical treatment, imatinib was indicated in the neoadjuvant setting in 3 cases. Among the 36 patients (51.4%) who underwent R0 resection, 34 patients (48.5%) were classified as intermediate or high risk for recurrence and received imatinib 400 mg/d as an adjuvant for 3 years. For metastatic patients, all were treated first with imatinib at 400 mg/day, then at 800 mg/day in 8 cases (11.4%) after progression. Only one patient received second-line treatment with sunitinib according to the 50 mg/d regimen 4 weeks out of 6. Regorafenib was not used in any of our patients. The average follow-up was 30 months and was marked by complete remission in 26 cases (37.1%), tumor recurrence in 5 cases (7.1%), control of the metastatic disease under medical treatment in 13 cases (18, 5%) and death in 5 cases (7.1%). The estimated progression-free survival at 5 years was 88.6% and overall survival at 5 years was 92.8%.

Conclusion: GISTs are rare tumors, the diagnosis of which is essentially histological and immunohistochemical. The treatment is mainly surgical for localized forms. The development of therapies targeting the causative molecular anomalies, in particular the anti-c-Kit and anti-PDGFR tyrosine kinase inhibitors, have enabled a real therapeutic revolution.

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P-302 Prognostic factors in stage IV appendiceal adenocarcinoma

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Background: Appendiceal carcinomas (AC) account for 1-2% of colorectal cancers (CRC), but there is limited data to guide treatment. We sought to identify prognostic factors for overall survival (OS).

Methods: We identified histologically confirmed cases of appendiceal adenocarcinomas with metastatic disease and information about OS diagnosed between 2004 and 2016 from the National Cancer Database (NCDB). Kaplan-Meier method and log-rank test were used to estimate and compare OS. Recursive partitioning analysis (RPA) analysis was performed on the entire cohort.

Results: 6,792 patients met our inclusion criteria: 5,742 patients underwent surgical resection of the primary tumor and 1,050 patients did not. Surgical status, age, comorbidity status, cancer center type, chemotherapy use, and income were significant prognostic factors for OS by RPA, in that order. Patients who underwent surgery, were younger than 75 years, were treated at an academic institution, and were from communities with median income >=$63,000 (N=1,309) had the best median OS of 60.8 months, followed by similar patients from communities with median income < 0.0001). For patients who did not undergo surgery, OS decreased by 6 months if they had comorbidities (11 vs. 17 months, p< 0.0001).

Conclusion: Surgical status, age, comorbidity status, cancer center type, chemotherapy use, and income were significant prognostic factors for OS by RPA, in that order. The best OS was seen in patients who underwent surgery, were younger than 75 years, were treated at an academic institution, and from communities with median income >=$63,000.

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P-303 Definitive radiation for esophageal cancer: Experience of a Portuguese cancer center

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Background: Definitive radiation (DR), preferably with concurrent chemotherapy (CCT), is the recommended treatment for either cervical, unresectable or non-surgical esophageal carcinoma with no distant metastasis. To evaluate toxicities, patterns of failure and survival rates associated with DR in a Portuguese cancer center, a retrospective study was carried out.

Methods: Medical records from consecutive patients with esophageal squamous cell carcinoma treated with DR between January 2013 and December 2018 were reviewed. Clinical-pathological data, treatment variables, and oncological outcomes were collected and analyzed. Kaplan Meier survival curves with a Log-rank test for significance were used for survival analysis.

Results: A total of 122 patients were included. The median age at diagnosis was 61 (interquartile range [IR] 54 - 69) years and 89% were male; 91% had a PS $\leq$1, the median Charlson Index was 4 (IR 3 - 5) and the majority were active (46%) or past (34%) smokers. Tumors were located in the cervical (29%), upper thoracic (32%), middle thoracic (28%), and lower thoracic (11%) esophagus. Nineteen percent of tumors were staged cT1 - T2, 55% cT3 and 23% cT4 (3% cTx); 82% were node-positive. A gastrostomy was placed in 64% of patients before the start of the treatment and it was partially (49%) and completely (37%) used as a feeding support in the majority of patients. Radiation dose was prescribed according to the treatment volume (PTV of the tumor $\pm$ nodal disease) and planned CCT: 115 (94%) patients received 50 - 54Gy and 7 (6%) patients had > 54.0Gy (1.8 - 2Gy/fx). IMRT/VMAT techniques were used in the majority (70%) of patients. Twenty-seven (22%) patients did not receive CCT due to comorbidities, 80 (66%) patients received cisplatin/5-FU and 15 (12%) had carboplatin (AUC 2)/paclitaxel. Thirteen patients (11%) had neoadjuvant chemotherapy (2 - 5 cycles). Four (3%) patients did not complete DR due to unrelated acute events; 118 patients were included in survival analysis. After a median follow-up of 22 months, 60 (51%) patients had relapsed - 29% locoregional, 16% distant and 6% as both sites; of these, 20 (17%) patients had locoregional progression within 6 months after treatment; 17 (14%) patients were lost to follow up. Median overall survival was 27 months (CI 95% 22.4 - 30.7). There was a significant increase in overall survival for patients who have received CCT compared to radiation alone (26 vs 13 months, p=0.001). Acute toxicity grade $\geq$3 was present in 22 patients (19%). Of the 41 patients who remained disease-free, 15 (36%) developed stenosis grade $\geq$2, 2 (5%) developed fistulae grade 4-5 and 1 (2%) patient developed hypothyroidism grade 2, as late toxicity.

Conclusion: Our data are in concordance with the existing literature in terms of toxicity, failure rates, and survival curves. Although the omission of CCT carries a significant worst overall survival, DR alone remains a feasible radical option in patients who are not candidates for CCT or surgery.

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P-304 Effectiveness and safety of thermal ablation of pulmonary metastases in patients with colorectal cancer

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Background: Pulmonary oligometastatic disease in colorectal cancer can be managed with either resection or ablation. Radiologically guided thermal ablation procedures have the benefit of disease control, preservation of adjacent normal tissue and improved quality of life, based on a short hospital admission and recovery time. We sought to report the effectiveness and safety of radiofrequency and microwave ablation for pulmonary metastases in patients with colorectal cancer.

Methods: We undertook a retrospective observational cohort study of 38 patients with colorectal cancer who were treated with thermal ablation to pulmonary metastases between 2009 and 2019 at our Regional Centre. Data were collected from hospital electronic records. Ablations were undertaken by specialist radiologists using CT guidance and under general anaesthesia.

Results: The median age at diagnosis of colorectal cancer was 67.5 [IQR 60.3-73] years and 55% (21/38) patients were male. Performance status was 0-1 in all patients. At diagnosis 66% (25/38) had moderately, 5% (2/38) poorly differentiated adenocarcinomas and 29% (11/38) had incomplete data: 50% [19/38], 39% [15/38] and 11% [4/38] patients had a rectal, left colon, or right colon cancer, respectively. 21% [8/38] patients presented with pulmonary metastatic disease at diagnosis. The median time to diagnosis of pulmonary metastases in the remainder was 2.2 [IQR 1.1-4.7] years. 92% (35/38) had either neoadjuvant, adjuvant or palliative chemotherapy. The median number and size of pulmonary metastases at the time of first thermal ablation were 2 [IQR 1-3], and 1 [IQR 0.7-1.3] cm, respectively without predilection for any lobe of the lung. The median number of lesions treated per patient was 3 [IQR 1-5]: 39% [15/38] patients received radiofrequency ablation and 61% [23/38] patients microwave ablation. Cox proportional hazard ratios did not show any difference in overall survival according to the type of thermal ablation (HR 0.72 (0.21-2.4) p = 0.58). Recurrence occurred at 35% (41/116) of previously ablated sites. Most patients, 80% (12/15) underwent re-ablation at the site of local recurrence: the estimated time to re-ablation was 2 [IQR1.2-3.0] years and no differences were seen between types of thermal ablation. Pneumothoraces complicated 28% [33/116] sites ablated and required aspiration and/or chest drain insertion in 45% [15/33] leading to a median length of stay of 2 [IQR 1-3.5] days. Further complications were uncommon: 2% [2/116] patients had minor bleeding, 2% [2/116] patients suffered a phrenic nerve injury. Complication rates were similar in patients treated with MWA and RFA.

Conclusion: Thermal ablation is an effective treatment for colorectal cancer pulmonary metastases. We found no difference in outcome according to the type of thermal ablation used. Small pneumothoraces were common with both types of thermal ablation, but otherwise, both techniques were well-tolerated.

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P-305 Efficacy and safety of IMATINIB in gastrointestinal stromal tumors: Experience of the medical oncology department of the CHU Hassan II of Fez

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Background: Gastrointestinal Stromal Tumors (GIST) are a very rare form of cancers of the digestive tract belonging to the sarcoma family. They are characterized by an overexpression of C-kit in immunohistochemistry and by activating mutations of tyrosine kinase receptors. Targeted therapies against these receptors such as IMATINIB and then SUNITINIB have transformed the management and prognosis of advanced and metastatic forms. The aim of this work was to study the efficacy and tolerance of IMATINIB in gastrointestinal stromal tumors.

Methods: A retrospective study was carried out in the medical oncology department of the Hassan II University Hospital in Fez, collecting 67 patients with a gastrointestinal stromal tumor during the period from April 2013 to April 2019. The statistical analysis of the results was done by SPSS version 23 software, the survival was calculated by the Kaplan-Meier method.

Results: The average age of the patients was 59 years with a clear male predominance (sex ratio of 1.5). The most frequent localization was gastric in 33 cases, followed by the small intestine in 21 cases, then other localizations in 13 cases. The most common symptom was pain, reported in 85% of cases. Surgery was the means of diagnostic confirmation in 76% of the cases. At the end of the radiological and histological assessment, the diagnosis of localized GIST was retained in 38 cases, locally advanced in 11 cases and metastatic in 18 cases. Surgery was performed in 46 patients. All patients received treatment with IMATINIB. The most common side effects were: * Asthenia: observed in 30% of patients. * Hematotoxicity: 15% thrombocytopenia, 20% anemia and 10% leukopenia. * Cutaneous-mucous: 47% of hand-foot syndrome, 25% of mucositis, 15% of skin rash and depigmentation of the hair was observed in 5% of patients. * Digestive: vomiting and nausea occurred in 20% of patients. 35% of patients developed edema of the lower limbs and 25% of periorbital edema. 20% of patients developed dysthyroidism and hypertension was observed in 10% of patients. After a median follow-up of 23 months, all the patients were alive and the median progression-free survival was 7 months.

Conclusion: The safety profile of IMATINIB used in our study was comparable to the global tolerance reported in the literature. More studies are needed to investigate the relationship between their toxicity and their efficacy in the Moroccan population.

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P-306 Survival and recurrence of patients operated on for stomach cancer and its determinants

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Background: Despite the decrease in incidence, gastric cancer remains a major public health problem worldwide. The prognosis of this cancer has shown little progress in 25 years, despite the standardization of surgical techniques and the introduction of multimodal therapy.

Methods: This is a descriptive and analytical retrospective study over a period of 15 years from January 1st, 2000 to December 31st, 2015. The study included 192 patients who underwent surgery for gastric adenocarcinoma in the General Surgery Department of Sahloul Teaching Hospital. Survival rates and recurrence were analyzed by the Kaplan—Meier and Mantel—Cox method, and multivariate analysis was done using the Cox proportional hazards model.

Results: The median overall survival was 13 months. The overall survival at 1 year was 57.5%, at 3 years, it decreased to 27%, at 5 years, it was 22% and at 10 years it was 14%. The presence of a tumor residue, larger tumor size, and the advanced tumor stage were independent prognostic factors of poor prognosis for survival in operated patients. The locoregional recurrence rate was 21.7%. The multivariate analysis showed that subtotal gastrectomy increased the risk of locoregional recurrence by 2.81 times. The distance recurrence rate was 41.37%. Serosal invasion and the presence of an infiltrative component were independent prognostic factors of distant recurrence with HR = 2.88 (p = 0.023) and HR = 3.49 (p = 0.002), respectively.

Conclusion: Overall survival in patients operated on for gastric adenocarcinoma depends mainly on the disease, namely the tumor size and the stage of the disease, but also on the efficiency of the surgical procedure through the presence of a tumor residue which is retained as an independent prognostic factor of poor prognosis. The choice of gastrectomy type is involved in loco-regional recurrence: a subtotal gastrectomy is a risk factor for loco-regional recurrence. Hence there is a need for a broader indication of total gastrectomies. Distant recurrence is conditioned by factors related to the tumor, namely serosal invasion and the presence of an infiltrative component.

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P-307 Colorectal cancer in young people under 45: Experience of the medical oncology service of the Hospital Hassan II of Fez

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Background: Colorectal cancer in young people is a rare condition with a poor prognosis. Several studies have objectified the increase in its incidence as well as its aggressiveness. Family screening, genetic analysis, and early diagnosis are necessary to improve one's prognosis when risk factors exist. The aim of this work was to study the epidemiological, anatomical-clinical, therapeutic and progressive characteristics in order to assess the factors of poor prognosis in this young population.

Methods: We performed a retrospective study including 40 cases aged less than 45 years with colorectal cancers diagnosed and managed within the medical oncology department of the Hassan II teaching hospital in Fez, between January 2013 and June 2017.

Results: 40 cases were included which represented 22% of all colorectal cancers during the study period. Average age was 33 years (range 19 and 45). The sex ratio was 1.7 with a clear male predominance. Colorectal cancer-predisposing history was present in 11% of patients. The tumor was located in the right colon in 37.5% of cases and in the rectum in 32.5% of cases. Over 18% of cases were discovered during a complication (13.6% during an occlusion and 5.5% continued perforation). 13% of patients had mucous (mucinous) colloid carcinoma. The cancers were poorly differentiated in 35% of the cases. Existence of vascular emboli and nerve sheaths were found in only 22 files; the presence of emboli was noted in 37.5% of cases. 41% of patients were stage III or stage II with MSS status and poor prognosis factors and received a adjuvant chemotherapy following surgical treatment. 4% of patients were stage II with MSI status, without risk factors and received no adjuvant therapy. 55% of patients were metastatic from the start and received basic chemotherapy (fluoropyrimidine). Radiation therapy was performed in 26% of patients with cancer of the middle or lower rectum. The median survival time, all stages included, was 16 months (1-60 months).

Conclusion: According to these results, colorectal cancer in young people has a poor prognosis, mainly due to the advanced disease stage at the time of diagnosis, as well as the frequent occurrence of recurrences in the case of undifferentiated tumors. Multidisciplinary care and genetic analysis seem essential to improve the prognosis of these patients.

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P-308 Prognostic nomogram for gastric cancer after surgical resection

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Background: A small number of nomograms have been previously developed to predict the individual survival of patients who undergo curative resection for gastric cancer. TNM staging does not always accurately predict prognosis. Some studies have shown infiltration of M2 macrophages in many tumors indicated a poor prognosis,

which might have the potential to predict prognosis more accurately together with TNM staging. The aim of this study was to develop and validate a survival predict nomogram for gastric cancer patients incorporating the recognized TNM stage and the degree of M2 macrophage infiltration.

Methods: We investigated the clinicopathological and survival data of 112 patients who underwent curative resection for gastric cancer between 2008 and 2013 at our hospital, and all the cancer tissues were received immunostaining evaluation for macrophage infiltration. Patients from 2008 to 2011 were assigned to the training set, and the others from 2011 to 2013 were assigned to the validation set. Multivariate analysis using the Cox proportional hazard regression model was performed to establish the nomogram prognostic model, and discrimination and calibration were evaluated by training, validation and whole sets.

Results: Multivariate analyses revealed that TNM stages, age, gender and CD163 expression in macrophage were independent risk factors and had significant prognostic value for overall survival. These variables were subsequently recruited into the prognostic model to construct a monogram. In the training, validation and whole sets, the concordance index was more than 0.6 (from 12 to 120 months). The five-year survival calibration curves of this model were of very good fit with a standard curve in all three sets, and the calibration was higher only in the training and the whole set. The prognostic ability was available with threshold probabilities of 10—38% for 1-year survival, 10—75% for 3-year survival, 35—80% for 5-year survival.

Conclusion: We combined the CD163 expression level in macrophage, TNM stages, age, and gender to develop and validate a nomogram as a useful tool in predicting 5-year overall survival after curative resection for gastric cancer. This model may provide further diagnostic and prognostic value for patients with gastric cancer.

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P-309 Correlation between baseline CEA levels and TNM stage at presentation in colorectal cancers in an Indian population

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Background: CEA is an oncofetal antigen that is increasingly expressed in colorectal cancers. We aimed to examine the relationship between carcinoembryonic antigen (CEA) levels in the preoperative period and TNM staging in patients with colorectal cancer in the north Indian region.

Methods: In the present study, 166 cases diagnosed with colorectal cancer between January 2015 and December 2019. We analyzed CEA values and stage retrospectively.

Results: 166 patients diagnosed with colorectal cancer between 2010 and 2019 were evaluated; 62% were males and 38% were females with the mean age of 42.8 years. CEA levels of 120 cases were measured; 54.1% of the samples were within normal limits. Cases with CEA $\leq$5 ng/mL were mostly in Stage II and stage III, whereas those with CEA $>$5 ng/mL were predominantly in Stage IV. The correlation value between TNM Stage and CEA was 0.187 and the p-value by Anova analysis was 0.086. Therefore, the correlation between the TNM stage and CEA levels was not statistically significant for any tumor stage.

Conclusion: The CEA levels of 52.2% of participating cases were within normal limits. There was no statistically significant relationship between the CEA levels and the TNM stage in colorectal cancers. After analysis of data, it was seen that CEA levels may be within normal limits in the majority of patients with colorectal cancer. Hence, normal levels of CEA will not rule out colorectal cancer diagnosis, nor is CEA value predictive of tumor extent.

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P-310 Fatigue and digestive cancers: A monocentric prospective study

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Background: Cancer-related fatigue is often an underdiagnosed symptom. The aim of this study was to screen and to assess fatigue in patients with digestive cancers during chemotherapy.

Methods: This was a prospective study of 44 patients followed for digestive cancer in the university department of medical oncology in Sfax during a 3-month period. We evaluated fatigue according to the fatigue assessment scale (FAS). The fatigue was defined with a FAS greater than 21. Extreme fatigue was defined with a FAS greater than 34.

Results: The mean age was 56 years with 25 men (57%) and 19 women (43%). The disease was metastatic in 52.3%. The site of the tumor was colic in 65%, rectal in 11.4%, gastric in 11.4% and pancreatic in 6.8 %. 59.1% had fatigue. In the non-metastatic subgroup, 47.6% of patients had fatigue. No patient had extreme fatigue. 71.4% of the patients were operated. 52.4% of patients received adjuvant chemotherapy based on FOLFOX. 42.9% of the patients had a sleep disorder. 28.6% of patients had anorexia and 19% had depression. In the metastatic subgroup, 69.9% of patients had fatigue, with 12.5% having extreme fatigue. Palliative chemotherapy was FOLFOX and FOLFIRI in 60.9% and 17.4% of cases, respectively. 39.1% of patients had a sleep disorder. 60.9% of patients had anxiety and 17.4% of patients had depression. Anxiety was correlated with fatigue ($p=0.015$). Extreme fatigue was correlated with metastatic disease ($p=0.01$), pancreatic site ($p=0.017$) and the type of chemotherapy (FOLFIRINOX) ($p=0.018$).

Conclusion: Fatigue is an extremely common complaint among cancer patients (75%-80%). Our study showed that fatigue was associated with digestive cancers in 59.1% using the FAS. Extreme fatigue was correlated with metastatic disease, pancreatic site, and chemotherapy regimen.

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P-311 Low risk of advanced neoplasms for up to 20 years after negative colonoscopy: Potential for personalized follow-up screening intervals

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Background: Within ten years after a negative colonoscopy, advanced colorectal neoplasms (ADN) were shown to be rare. However, evidence on longer intervals is very sparse, and little is known on the potential of personalized screening intervals based on individual risk profiles. The objective of our study was to investigate the prevalence of ADN after longer colonoscopy intervals and the possible role of easy-to-collect factors for risk stratification.

Methods: We determined the prevalence of neoplasms among 2456 participants of the German screening colonoscopy program who had a previous colonoscopy without polyp findings and compared the findings to 12,033 first-time screening colonoscopy participants, adjusting for potential confounding factors by log-linear regression models. Prevalences were assessed according to time interval since last negative colonoscopy, overall and in subgroups defined by sex, age, smoking history, family history, body mass index and a scoring system to assess colorectal cancer (CRC) risk.

Results: Within 20 years of a negative colonoscopy, the prevalence of ADN was 5.5% compared to 12.6% among people without previous colonoscopy (adjusted prevalence ratio, aPR, 0.45, 95% CI 0.37 — 0.53). The prevalence showed little variation across 5-year time windows after negative colonoscopy up to 20 years, and was still 41% lower even $\geq$20 years after a negative colonoscopy (7.4%) as compared to first-time screening participants (aPR, 0.59, 95% CI 0.39 - 0.91). Analyses combining risk factors of CRC into a scoring-system yielded a consistent pattern of markedly elevated ADN prevalences in those scored at very high risk.

Conclusion: Currently recommended colonoscopy screening intervals could potentially be extended beyond ten years for the majority of people with low or intermediate CRC risk.

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P-312 Perioperative chemotherapy versus surgery alone on resectable advanced gastric cancer in a Moroccan population

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Background: Gastric cancer represents the fifth most common tumor and the third-leading cause of cancer-related death worldwide. The results of surgical treatment of locally advanced gastric cancer remain generally poor due to the high rate of relapse after surgery. In the last decade, neoadjuvant chemotherapy has become the standard of care for patients with stage ≥IB resectable advanced gastric cancer. The benefit in progression-free and overall survival was confirmed by several randomised trials and meta-analyses compared to immediate surgery. However, data in the "real-life" setting are rare. We conducted a retrospective study to clarify the question of whether this benefit is achievable under real-life conditions.

Methods: Our retrospective study concerned patients with histologically-confirmed advanced gastric cancer clinical stage II-IIIc according to UICC (8th edition) treated at the University Hospital of Marrakech between January 2017 and December 2018. They received 2-4 cycles/3 weeks of neoadjuvant chemotherapy based on FLOT, FOLFOX, XELOX, EOX or 5FU-Cisplatin protocols.

Results: 48 patients with a median age of 56 years were diagnosed with advanced gastric cancer. 67% of them are male were. Only 16 patients (33,3%) had received neoadjuvant chemotherapy and 19 were operated immediately (39,5%). Protocols used in perioperative were FLOT in 8 patients (50%) and FOLFOX in 4 patients (25%). The rest have received either EOX (1 patient), XELOX (2 patients) or 5FU-cisplatin (1 patient). 7 patients (43,75%) received 4 cycles of neoadjuvant chemotherapy. Side effects were represented by mycosis grade 2 in 2 patients, neutropenia grade 2 in 4 patients and only one patient had grade 3 toxicity. After neoadjuvant chemotherapy, we observed 3 cases of partial response and 4 of stable disease. 5 patients (31,25%) underwent surgery (R0 in all cases) by total gastrectomy and D2 lymphadenectomy. 68,42% of the group who did not receive neoadjuvant chemotherapy, were treated by concomitant chemoradiotherapy. The median overall survival in the neoadjuvant group was 21 months compared to only 12 in the second group.

Conclusion: Despite the small number of patients treated, our analysis showed that selected patients with locally advanced adenocarcinoma can be safely managed with perioperative chemotherapy in daily clinical practice and our results confirm the survival benefit of perioperative treatment.

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P-313 Management of frail patients with metastatic pancreatic ductal adenocarcinoma: A single-institution experience

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Background: Metastatic pancreatic ductal adenocarcinoma (mPDAC) is an aggressive disease with dismal survival rates. Frail patients (pt) represent a high percentage of the mPDAC population, but they are understated in clinical trials. Management of these pt is challenging due to increased comorbidity and risk of deterioration. We aimed to describe the outcome of mPDAC frail pt at our Institution.

Methods: We conducted a retrospective study of 179 newly diagnosed mPDAC pt between 2009 and 2018. All pt had clinic-laboratory and treatment characteristics available. Frail pt were defined as pt with Performance Status (PS) ≥ 2 and/or age ≥ 75 years. We assessed survival differences between frail versus (vs) non-frail pt.

Results: 78 pt (44%) were frail, with a median age of 75 (range 65-78). Frail pt received less chemotherapy (CHT) compared with non-frail (37% vs 92%), and if treated were more likely to receive gemcitabine monotherapy than combinations (48% vs 21%). Combination regimes used in frail pt were gemcitabine-nab-paclitaxel, 5FU-leucovorin-oxaliplatin (FOLFOX) and gemcitabine-oxaliplatin (GEMOX). Median overall survival (mOS) in the treated population was 4.6 months (m) in frail vs 8.9 m in non-frail pt (HR 1.853; IC 95% 1.200 − 2.863; p 35 g/L and IMC > 20 Kg/m^2) and less than 3 metastatic sites. PS ≥ 2 was identified as the worst prognostic factor for decreased mOS (HR 3.816; IC 95% 2.587 − 5.628), and mPFS (HR 2.251; IC 95% 1.157 − 4.379).

Conclusion: Frail mPDAC pt encompass a heterogeneous group in which systemic CHT improves mOS. Our study suggests that PS ≥ 2, age ≥ 75 years, poor nutritional status and higher tumoral burden are strongly associated with worse prognosis. Hence, geriatric tools could identify predictive biomarkers and help in delineating optimized strategies for these pt.

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P-314 Supine VMAT versus prone 3D-EBRT in preoperative rectal cancer: Dosimetric comparison and pathological response with each radiotherapy technique

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Background: The use of belly-board as an immobilization system with a full bladder protocol to receive radiotherapy for rectal cancer has been a standard of care for many years. Doing this, we reduce doses to organs at risk, but the position is difficult to maintain and hardly reproducible. With advanced techniques of radiotherapy, we can achieve this protection regardless of the position of treatment. Therefore, making a dosimetric comparison between 3D-EBRT (external beam radiotherapy) in prone versus VMAT (volumetric arc radiotherapy) in supine position and pathological response achieved with these two radiotherapy techniques were the aims of this study.

Methods: We chose 10 patients for each treatment group. 3D-EBRT was carried out in a Siemens Primus LINAC using three 15MV static fields of treatment and VMAT in a Varian TrueBeam with two 6MV arcs of treatment. Planning target volume (PTV) was delimited in both CT by the same facultative as the organ at risk (bladder, small bowel, and femoral heads). The total dose to PTV was 25Gy, short-course preoperative radiotherapy in 5 fractions. PTV coverage data were evaluated according to ICRU recommendations and limiting doses to risk organs. All patients underwent surgery at least 8 weeks after radiotherapy, and data from pathological findings were recorded.

Results: In terms of coverage, VMAT offered better dose homogeneity minimizing hot spots inside and outside of the PTV and better protection of organs at risk (OAR) with an average dose reduction of 26,8 to 8,39% in the volume of the bladder which receives 20Gy (V20), 63,6 to 21,6% in V11 and without significant differences for the maximum dose of the femoral heads. With VMAT technique, we have achieved a greater number of pathological responses, but in both cases, all patients benefited from downstaging.

Conclusion: In addition to the best reproducibility and comfort for the supine position, we choose VMAT for preoperative treatment in rectal cancer due to better PTV coverage and OAR protection. Although we have had a higher rate of pathological responses associated with VMAT treatment, it is not a significant sample to establish its superiority.

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P-315 Impact of tumor location (right vs left) as a prognostic and predictive factor in colon cancer in a Moroccan population: A single-center study

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Background: The impact of laterality is likely to recur in colon cancer literature. Controversial studies have examined the relationship between tumor location and the clinicopathological features, prognosis, and response to treatment. However, data in the "real-world" setting are rare and the correlation remains unclear. In our retrospective study, we sought to investigate whether this effect is clinically relevant.

Methods: From January 2012 to September 2019, all consecutive patients with a diagnosis of primary, stage I—IV colon adenocarcinoma, treated at the Department of Medical Oncology at Mohamed VI University Hospital of Marrakech, were enrolled and divided by location and stage. Incidence data, clinical and pathological features, chemotherapy regimens and outcomes were systematically collected. Survival data were modeled by statistical analysis. Primary endpoints of this study were disease-free survival, progression-free survival, and overall survival. Secondary endpoints

were correlations between laterality and clinicopathological features including molecular markers (RAS, BRAF) and microsatellite instability.

Results: We queried the data of 320 patients. Due to the lack of follow up data (n = 21), stage (n=17), and location (n=11), 49 patients were excluded from the analysis (Final number=271). Right colic cancer (RCC) and Left colic cancer (LCC) proportions in our population were 29% (38 males, 45 females, median age 57, range 22-84) and 67%, (93 males, 100 females, median age 56, range 23-88), respectively. For stages III-IV, 81% of patients (n=220) were identified. Of those, 40,5 % had left-sided tumors and 42% had right-sided tumors. Patients presenting with surgical emergencies such as obstructive or perforated tumor were most likely to have a left-sided location (35% vs 21%). For stage II tumors, patients with right-sided tumors had significantly greater rates of poor prognosis histopathologic features (RCC vs LCC: vascular emboli: 75% vs 65%, perineural invasion: 54% vs 46%, positive Lymph nodes: 64% vs 61%). For stage III tumors, left-sided tumors showed better clinical outcomes than proximal colon cancers after adjuvant chemotherapy. For stage VI, although a more marked number of metastatic sites was observed on right-sided tumors, there was no significant association with clinical outcome and survival with regard to the number of metastatic sites between the two locations. Available data of the MSI, KRAS, NRAS, and BRAF mutation status were too scarce for statistical analysis to report the correlation between molecular markers and laterality. We concluded that patients with left-sided tumors were observed to reach longer benefit for first-line chemotherapy progression-free survival (13 vs 8 months). Stage IV right colon tumors were less responsive to systemic therapy and had a poorer overall survival (OS: 13 vs 16 months). Thus, our patients exhibited lower median overall survival compared to literature data. This can mainly be attributed to limited early screening programs, as most patients were diagnosed with late-stage disease, and lack of treatment facilities, in the era of target therapies and immunotherapy.

Conclusion: Colon cancer laterality seems to maintain clinical relevance, most likely in the advanced and metastatic stages. These findings are convincing arguments to support the standardization of this indicator for better prognosis grading.

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P-316 Profile of microbiota is associated with early onset of colorectal cancer in Egyptian and Kenyan patients

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Background: Colorectal cancer (CRC) is a global burden, with an expected 2.2 million annual cases and 1.1 million deaths by 2030. Nearly 90% of CRC cases occur in people over the age of 50. However, early-onset (< 50 years) CRC is increasing in Egypt and Kenya. Prior studies suggest that alteration in microbiome composition (dysbiosis) disturbs the symbiotic relationship between the colorectum and resident micro-organisms and promotes CRC. We hypothesized that, for Egyptians and Kenyans, microbiome dysbiosis is responsible for early-onset CRC. We further hypothesized that there is cross-talk between the microbiome, tumor molecular features, and the immune microenvironment.

Methods: We assessed the colonic microbiota and the expression of specific host response genes in normal colonic mucosal samples from 8 healthy individuals and samples from 20 Egyptian CRC patients and 20 Kenyan. A retrospective convenience sample design was employed. Colonoscopy was performed on these patients at the Alexandria University Hospital, in Alexandria, Egypt. Microbiota composition was determined by 16S rRNA amplicon sequencing. A panel of 784 genes involved in tumor, microenvironment, and immune response were used to characterize differential expression across patient groups by the Nanostring method. This panel facilitates the estimation of immune cell abundance for 15 tumor-infiltrating immune cell types. Differential abundance and cross-talk between the relative abundance of microbiota and tumor RNA expression were evaluated using negative binomial model fitting and Wald statistics.

Results: One third of our CRC patient population was under 50 years old at the time of diagnosis in Egyptian patients and 80% in Kenyan, and most were female. Healthy controls were even younger than CRC cases, and most were females. There were differences in relative abundances of bacteria between healthy controls and those with CRCs. Analysis showed a low abundance of Mitsuokella multacida, a short-chain fatty acid (SCFA)-producing bacterium, in CRC patients when compared with healthy individuals. In particular, this trend was evident for older CRC patients (≥ 50 years); of note, this bacterium was absent in younger patients (< 50 years) (adj. p-value = 0.01). Further, there was a high abundance of Fusobacterium nucleatum in all CRC patients compared with healthy individuals (adj. p-value = 0.04). In cross-talk analysis for healthy controls, elevated abundance of M. multacida was inversely associated with macrophage abundance (global p-value =0.055). For Egyptian patients, the absence of SCFA-producing multacida in younger patients may be a reason for early-onset CRC. In Kenyan patients, similar results will be presented at the conference.

Conclusion: These findings suggest that the oncoprotective effect of Mitsuokella multacida should be further investigated.

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P-317 Survival outcomes among patients with locally advanced esophageal cancer treated within a multidisciplinary gastro-esophageal cancer functional unit

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Background: Management of locally advanced esophageal cancer (LAEC) is challenging given its aggressive behaviour and that it is often diagnosed in patients (pt) with significant comorbidities. A multimodal approach could enhance treatment results and quality of life. We aimed to assess outcome differences in a non-clinical trial scenario in our LAEC cohort, according to multidisciplinary management in a highly specialized gastro-esophageal cancer functional unit (UFEG) integrated with different specialists.

Methods: From 2012 to 2018, 150 newly diagnosed esophageal cancers were referred to our UFEG, of whom 90 were LAEC. Several UFEG specialists at this first consultation evaluated every case, in order to establish a multimodal therapeutic plan. UFEG is comprised of digestive surgeons, medical oncologists, radiation oncologists, nutritionists, nurses, radiologists, digestive endoscopists, pathologists, social workers and supportive care physicians. All demographic, treatment and survival data were extracted retrospectively from available electronic medical records.

Results: Median age was 65 years (range 30 – 90), with 83% men, 68% were squamous carcinomas and 32% adenocarcinomas. 81% pt were eligible for radical treatment, whilst 7% received palliative chemotherapy (CHT) and 12% were deemed candidates only for best supportive care, mostly due to poor performance status ≥ 2. Focusing on pt that underwent curative treatments, 58% received definitive chemo-radiotherapy (dCRT) and 42% pt received neoadjuvant chemo-radiotherapy (nCRT), followed by surgery in 94% of the cases. CRT was based on cisplatin-5FU and carboplatin-paclitaxel, depending on histology and comorbidities. 59% achieved a pathological downstaging, including 24% (n=7) pt with a complete pathological response (pCR). 30% pt presented surgical complications and in-hospital mortality was 6%. The 3-year median overall survival (mOS) was 29% in the nCRT group and 27% in the dCRT group. The recurrence rate was higher in the dCRT (52%) compared to nCRT (32%). Distant relapses were more frequent than local-regional ones (79% vs. 21%).

Conclusion: In our LAEC cohort, 3-year mOS was similar in dCRT and nCRT groups. However, pt that underwent nCRT followed by surgery had lower recurrences, achieving similar pCR to those reported in the literature. Of note, 24% pt were ≥ 75 years, which prompted us to implement a geriatric assessment among all elderly pt. Multidisciplinary management at a UFEG ensures that LAEC pt receive optimized world-class care, and seems warranted to further improve the outcomes of these pt.

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P-318 Survival outcomes among patients with locally advanced gastric cancer treated within a multidisciplinary gastro-esophageal cancer functional unit

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Background: Gastric cancer is a complex disease and the third leading cause of cancer deaths worldwide. To date, surgery remains the only curative strategy in locally advanced gastric cancer (LAGC) patients (pt), although the results of the MAGIC trial supported the implementation of a perioperative treatment (ttx) with epirubicin-cisplatin-5FU (ECF). Since 2019, the FLOT4-AIO trial showed that perioperative 5FU-leucovorin-oxaliplatin-docetaxel (FLOT) improved median overall survival (mOS) compared to ECF. We aimed to assess outcome differences in a non-clinical trial scenario in our LAGC cohort, according to multidisciplinary management in a highly specialized gastro-esophageal cancer functional unit (UFEG) integrating different specialists.

Methods: From 2012 to 2018, 114 newly diagnosed LAGC pt were referred to our UFEG. Several UFEG specialists at this first consultation evaluated every case, in order to establish a multimodal therapeutic plan. UFEG is comprised of digestive surgeons, medical oncologists, radiation oncologists, nutritionists, advanced practice nurses, radiologists, digestive endoscopists, pathologists, supportive care physicians, and social workers. All demographic, treatment and survival data were extracted retrospectively from available electronic medical records.

Results: Median age was 72 years (range 37-92), with 64% men. Almost 29% underwent upfront surgery, due to symptomatic tumour (active bleeding or gastrointestinal obstruction) or being considered frail to complete properly preoperative chemotherapy (pCHT). 34% of these resected pt received postoperative ttx afterwards. Despite being assessed as LAGC, 5% received palliative chemotherapy and 13% were candidates only for best supportive care, mostly due to poor performance status $\geq$ 2. The other 53% pt received pCHT with ECF. Among pCHT pt, 93% underwent surgery with 25% achieving a tumour or nodal downstaging. Of note, 1 pt presented complete pathologic response, who had received pCHT. Regarding surgical morbi-mortality, 21% had postoperative complications and 8% died in the postoperative period (30 days after surgery). Differential mOS in the pCHT group was 38.4 months (95% CI, 29.3 to 47.4) versus 35.1 months in the upfront surgery group (95% CI, 25.0 to 45.2).

Conclusion: In our LAGC cohort, mOS was similar in pCHT and upfront surgery groups. These results could have been due to the accurate selection of individualized ttx for each pt and early identification of those with a higher risk of tumour complications. Of note, 45% were $\geq$ 75 years, which prompted us to implement a geriatric assessment among all elderly pt. Multidisciplinary management at a UFEG ensures that LAGC pt receive optimized world-class care and seems warranted for further improving the outcomes of these pt.

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P-319 How coordinated and integrated multidisciplinary work improved the return to intended oncologic treatment in colon cancer

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Background: International research reveals that the time between the decision to treat to treatment and time to Return to Intended Oncologic Treatment (RIOT) are important outcomes of the quality of care, impacting both overall survival and disease-free survival. To fulfill the RIOT, a coordinated and efficient multidisciplinary approach for the optimal postoperative recovery is mandatory. 77% of patients diagnosed with colon cancer treated at A.C. Camargo Cancer Center in 2018, initiated adjuvant therapy until the ideal time of 56 days. Factors that impacted in the RIOT were scheduling delays for appointments with specialties and postoperative complications. The postoperative complications directly interfered with the RIOT. In those patients who did complicate, 50% had the time between surgery and the first infusion of adjuvant chemotherapy within 56 days. Of those who did not, 80% underwent chemotherapy within 56 days. So, the aim of the research was to increase the percentage of patients who start adjuvant therapy within 56 days.

Methods: An action plan was established with the hospital's multidisciplinary team, operations and quality departments to optimize appointment scheduling and reduce the incidence of postoperative complications (paralytic ileus and fistula), through the Improvement Science methodology of the Institute for Healthcare Improvement (IHI). The actions implemented for colon cancer patients were nutritional and physical therapy assessment in the pre and postoperative period, strict glycemic control below 180mg/dl during the perioperative period and a new anesthesia management protocol aiming to reduce opioid use.

Results: 40 patients were followed up from July 2019 to January 2020. 100% of the patients were attended by nutrition and physiotherapy in the pre and/or postoperative period and 100% of diabetic patients were included in the institutional glycemic control protocol. 15% of patients had paralytic ileus and 2,5% fistula. The median time from surgery to the beginning of adjuvant treatment (RIOT) dropped from 46 days (2018) to 42 days. Since August 2019, 100% of patients started adjuvant chemotherapy within 56 days.

Conclusion: The results reinforce the importance of coordinated and integrated multidisciplinary work, focusing on optimizing the patient's journey and reducing complications. It also reinforces the need for institutional support and the activation of areas indirectly related to assistance such as operations and quality departments to achieve the goal.

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P-320 Genetic testing for microsatellite instability and KRAS mutation in stage IV colorectal cancer: Trends and outcomes from the National Cancer Database

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Background: Microsatellite and KRAS status affect the development of colorectal carcinoma (CRC) and can warrant specific clinical management. This study assesses current trends and outcomes of testing for microsatellite and KRAS status in stage IV CRC patients in the US.

Methods: The 2010-2016 United States National Cancer Database was queried for adult patients diagnosed with stage IV colorectal adenocarcinoma. Patients were excluded if the CRC localization was unspecified. Genetic testing was stratified as microsatellite (MS), KRAS, and MS+KRAS testing. Demographic, cancer-related and treatment variables were compared across genetic testing strata. The impact of genetic testing on overall survival (OS) was analyzed using multivariable Cox proportional hazards models adjusting for demographic, cancer-related and treatment variables.

Results: A total of 88,389 patients met inclusion, of which the majority did not receive genetic testing (n= 50,139, 56.7%). KRAS testing was conducted in n= 22,893 patients (25.9%), MS testing in n=7,079 (8%), and combined MS+KRAS testing in n=8,278 (9.4%). Genetic testing rates continuously increased from 31.2% of all patients in 2010 to 50.7% in 2016. Genetic testing was generally more common in younger patients (any genetic testing mean age 61 yo vs. no genetic testing 66 yo; $p< 0.001$) and those with private insurance (44% vs. 32%; $p< 0.001$). Genetic testing was also more likely in academic centers (33% vs. non-academic centers 31%; $p< 0.001$) and according to specific US geography, i.e. in New England States (6.5% vs. 4.5%; $p< 0.001$). On multivariable analyses, MS and MS+KRAS testing was associated with longer overall survival compared to no genetic testing (MS testing vs. no genetic testing HR=0.94, 05% CI: 0.9-0.97, $p< 0.001$; MS+KRAS testing vs. no genetic testing

HR=0.94, 95% CI: 0.91-0.98, p=0.001). Corresponding OS rates at 1, 2, 3, and 5-years were: MS testing 68.1%, 48.1%, 33.8%, 18.7%; MS+KRAS testing 77.6%, 54.1%, 35.8%, 17.1%; no genetic testing 53.2%, 34.5%, 22.3%, 11.4%. KRAS testing alone did not significantly affect overall survival (KRAS testing vs. no genetic testing HR=0.98, 95% CI: 0.96-1.0, p=0.11).

Conclusion: Genetic testing for microsatellite and KRAS status is increasingly used for stage IV CRC patients in the United States. Testing for microsatellite status and combined MS+KRAS testing demonstrate longer overall survival, which may correlate with individualized treatment regimens in these patients. In this context, demographic and geographic discrepancies in testing rates were highlighted, which may indicate an underutilization in specific populations, i.e. those without private healthcare insurance or access to academic healthcare centers.

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P-321 The voice beyond the clinic: Delineation of young-onset cancer patient profiles using a digital social network

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Background: In recent years, colorectal cancer rates have escalated disproportionately in young adults as compared to older individuals, and increasing efforts to target their unique needs and improve their experiences is needed. Adept usage of social media has defined this new generation, creating a parallel reality beyond the traditional patient-doctor office encounter. Herein, we present user-profiles from StopCancer, a digital social network designed for patients aged 18-44. Our primary purpose was to delineate patient and disease characteristics; moreover, to correlate these parameters with usage patterns and satisfaction measures.

Methods: A questionnaire was distributed within the online platform. Patients were stratified by marital status, religion, education, and employment, as well as by type and stage of malignancy and treatment received. They were asked to rate the utility of the network in gaining health and legal information, relieving feelings of loneliness or fear, and their general satisfaction. Reported outcomes were considered statistically significant using the Fisher Exact test (p=0.05).

Results: During the five days it was made available, the survey was completed by 523 participants. Colorectal cancer was the third most common malignancy following breast and hematological cancer. Most patients (73%) had non-metastatic disease at diagnosis, 25% experienced disease recurrence and 79% had no evidence of disease at the time of survey completion. Participants accessed the network primarily for emotional coping (77%), medical and legal information (47% and 48%, respectively), and finally, family issues. Forty percent reported relief of loneliness to a large degree. In 11%, online discourse increased fears and anxiety. No significant differences in platform usage patterns were observed between survivors and those with active cancer, nor between patients with metastatic and localised disease; however, survivors related greater relief of loneliness to the platform. Half of the participants were married, and they demonstrated superior satisfaction levels. Most (62%) attended university, a group that sought out information on health and social rights, and reported higher satisfaction, whereas those with lower educational background reported more stressful or fearful emotions. Only 12% of participants considered themselves religious, and they tended to express lower satisfaction with coping and were less likely to recommend the platform than the nonreligious. At the time of survey completion, 36% of subjects maintained a full-time job. Most participants (75%) highly recommended the platform.

Conclusion: This snapshot of young-onset cancer patient characteristics demonstrates the high-yielding, easily accessible source of information available via online resources. Moreover, the large fraction of survivors with comparable utilisation patterns as active patients, alongside a low employment rate, suggest challenges in the transition to survivorship and reintegration into society that can be addressed through specialised social media outlets or otherwise. Additionally, the relatively homogenous nature of the patient user-profiles suggests greater efforts should be directed toward metastatic, religious or less-educated patients who are underrepresented, show higher anxiety levels and lower satisfaction rates. Limitations include recall and selection bias as well as a lack of follow-up. By identifying those who use digital networks and for what causes, management can be tailored to young patients' needs and ultimately improve their outcomes.

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P-322 Nutritional intervention impact on body mass index and toxicities related to 1st-line metastatic colorectal cancer treatment with targeted therapy

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Background: Colorectal cancer (CRC) is the 2nd most common cancer in Europe and 1st in Portugal. 1st-line metastatic CRC (mCRC) treatment is based on chemotherapy (QT) in combination with an inhibitor of epidermal growth factor receptor (i-EGFR) such as panitumumab or an inhibitor of vascular endothelial growth factor (i-VEGF) such as bevacizumab. The choice is based on molecular analysis. Low body mass index (BMI) at diagnosis is usually associated with worse prognosis and increased toxicities.

Methods: Retrospective analysis of patients with mCRC who received 1st-line treatment with QT plus i-EGFR or i-VEGF, in two Portuguese hospital units between January 2015 and December 2018 was performed. IBM SPSS v25 software was used for statistical analysis. The main goal was to analyse the impact of nutritional intervention (NI) on BMI, toxicities, and outcomes.

Results: 178 patients with median age of 65 years old were included; 63% were male and the majority had ECOG PS of 0. Metastasis were present in only one organ in 2/3 of patients, more common in the liver. 65 patients underwent QT plus i-EGFR, all RAS wild-type, with overall response rate (ORR) 64%, progression-free survival (PFS) 13 months and overall survival (OS) of 21 months. 113 patients underwent QT plus i-VEGF with ORR 58%, PFS 9 months and OS of 20 months. Toxicities due to i-EGFR were mainly cutaneous with grade 3 and 4 cutaneous toxicity present in 21,6% of patients. Discontinuation of treatment occurred in 18,5%. The discontinuation of treatment with i-VEGF was 7,4%. The mean BMI was 24,8 Kg/m 2 . An association between BMI at the beginning of treatment and OS and severe toxicities was observed. A negative mean BMI difference (BMIdif) was observed after treatment progression with both therapies. No correlation was evident between BMIdif and OS, but an association between BMIdif and severe cutaneous toxicity (p=0,033; OR 1,99; IC 95%[1,05-1,49]), and i-EGFR discontinuation (p=0,044; OR 2,33; IC 95%[1,02-5,31]) was perceptible. 17,6% of patients were referred to NI, with a positive association with BMIdif as these patients gained weight.

Conclusion: NI seems to be useful for preventing weight loss in an early phase of the mCRC. More awareness should be given to early referral for NI as it may improve the patient's quality of life and reduce unwanted severe toxicities.

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P-323 RAS mutations in metastatic colorectal cancer in central Tunisia

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Background: Colorectal cancer (CRC) is the most common cancer worldwide. RAS oncogene is one of the most important targets for drug development in metastatic colorectal cancers. Its mutation predicts cetuximab resistance and a worse prognosis. To our knowledge, the prevalence of RAS mutations in central Tunisia has not been previously reported.

Methods: This was a retrospective study including metastatic colorectal cancer patients treated in the department of Medical Oncology in Farhat Hached Hospital in Tunisia from 2015 to 2019 who had RAS testing. RAS mutation was detected by PCR-based tests. RAS mutation status was performed using Lightmix kit. The aim of this study was to assess the histopathological, epidemiological and RAS mutation data in locally advanced and metastatic CRC. Correlation studies were based on Chi-squared test.

Results: Fourty three patients were included, 21 males (48.8%) and 22 females (51.2%). Median age was 54 years old [16 to 83 years old]. 18% of patients had a familial history of colorectal cancers. Three patients had a personal medical history of familial adenomatous polyposis (7%). Patients were smokers in 27.9% of the cases. Colon cancers represented 55.8% of cases (left colon cancer 46.5% and right colon cancer 9.3%) whereas rectal cancers represented 44.2% of cases. Performance status was between 0 to 1 in 90.7% of cases. The liver was the most common metastatic site (54.8%). Other metastatic sites were observed such as lungs (19.1%), peritoneum (14.3%) and ovaries (4.8%). RAS mutation was found in 37.2% of patients. Patients received an average of 2 lines of chemotherapy. Only 36.1% of the patients received targeted therapy. Bevacizumab was used in 47.1% of the cases and cetuximab in 35.3% of the cases. Overall survival was 16 months and progression-free survival was 9 months. RAS mutation was correlated with an advanced TNM stage (p=0.032) and shorter progression-free disease (p=0.022). There was no correlation between RAS

mutation and the degree of differentiation or node invasion (p=0.46 and p=0.24 respectively).

Conclusion: The prognostic impact of RAS mutation was demonstrated in our patients. Treatment for metastatic cancers remains challenging in Tunisia despite recent advances. Thanks to the identification of RAS status, unjustified expenses of anti-EGFR targeted therapy could be avoided.

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P-324 Advanced hepatocellular cancer: Current systemic treatment sequencing and outcomes in the United States

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Background: There are several systemic treatment strategies for advanced hepatocellular carcinoma (HCC), including tyrosine kinase inhibitors (TKIs) and immunotherapy. This study assessed the current utilization of systemic HCC treatment strategies in the United States and associated outcomes.

Methods: We queried the Flatiron Health EHR-derived de-identified database in October 2019 for adult patients with advanced HCC and data on treatment timing. Patients were excluded if they were treated with local therapies (i.e. resection, TACE, TARE, SBRT). Treatment was stratified as PD-1 targeted immunotherapy (PD-1 IMT; including nivolumab and pembrolizumab), tyrosine kinase inhibitors (TKI), chemotherapy, and VEGF inhibitors. The course of systemic HCC treatments was descriptively analyzed. Overall survival (OS) was assessed using Cox proportional hazards models.

Results: A total of 1,167 patients with advanced HCC met inclusion criteria, of which the majority were male (n=930, 79.7%; female n=236, 20.2%) and of Caucasian race (n=651, 55.8%). Viral hepatitis was present in n=561 patients (48.1%), and alcohol abuse in n=434 patients (37.2%). The median age at advanced HCC diagnosis was 66 years (interquartile range IQR: 60-74 years). The majority of patients received TKIs (n=1,073, 91.9%) or PD-1 IMT (n=227, 19.5%), followed by chemotherapy (n=63, 5.4%) and VEGF inhibitors (n=11, 0.9%). PD-1 IMT was administered as first-line treatment in n=79 patients (6.8%). The median duration of TKI treatment was 4 months (IQR: 2-8 months), comparable to that of PD-1 IMT (median 4 months, IQR: 2-7 months). At a median follow-up time of 27.3 months (IQR: 10.9-46.2 months), a total of 873 patients had died (74.8%). Overall survival correlated with treatment, with those patients receiving PD-1 IMT showing longer survival versus those receiving no PD-1 IMT (HR=0.53, 95% CI: 0.43-0.63, p< 0.001). On multivariable analyses, these differences proved independent from potential confounders including demographics (age, gender, race, diabetes, obesity), etiology and extent of liver disease (hepatitis, alcohol abuse, ascites, encephalopathy), and year of diagnosis: PD-1 IMT vs. no PD-1 IMT HR=0.45, 95% CI: 0.37-0.56, p< 0.001. Associated survival rates at 1/2/3/5 years were 54.0%, 36.1%, 19.5%, 12.4% for PD-1 IMT, and 30.0%, 15.0%, 7.4%, 1.7% for no PD-1 IMT.

Conclusion: In the United States, TKIs are most commonly used for systemic treatment of advanced HCC, followed by PD-1 targeted immunotherapy. Currently, PD-1 IMT is primarily used as a 2nd-line treatment option. Patients receiving PD-1 IMT demonstrated longer overall survival compared to those without PD-1 IMT, highlighting the clinical relevance of immune therapy for the treatment of HCC.

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P-325 Oral delivery of a single microbial strain, EDP1503, induces anti-tumor responses via gut-mediated activation of both innate and adaptive immunity

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Background: Systemic immunity is regulated by interactions of commensal bacteria with immune cells in the gut, the outcomes of which are the amelioration or promotion of inflammation influenced by microbial strain. We demonstrate that a single non-colonizing, pro-inflammatory strain of Bifidobacterium animals ssp. lactis, designated EDP1503, is a novel modality for the immunotherapy of cancer.

Methods: The clinical efficacy of EDP1503 was investigated in subcutaneously implanted isograft tumor models and in an intravenous lung metastasis model. Mechanism of action was dissected by ex vivo analysis of the tumor microenvironment (TME) and gut-draining lymph nodes, and was further interrogated by in vitro functional studies with murine and human cells. Results from an ongoing phase 1b clinical study (NCT03775850) will be reported.

Results: Preclinically, EDP1503 attenuates tumor growth similar to inhibition of the PD-1 pathway, with enhanced activation of both NK cells and CD8+ T cells within the tumor. EDP1503 promotes immunogenic remodeling of the tumor microenvironment (TME) by decreasing the activation of immunosuppressive cells, such as myeloid-derived suppressor cells and regulatory T cells, and increasing the number of activated immunostimulatory dendritic cells, IFN-g-producing tumor-infiltrating lymphocytes, and CD8+ cytotoxic T cells. The orchestrated activation of the innate and adaptive immune compartments originates with the stimulation of antigen-presenting cells within the small intestine that engage and activate recirculating lymphocytes in an IL-12p70-dependent manner. This signaling cascade promotes the differentiation and mobilization of tumor antigen-specific central memory CD8+ T cells into potent CX3CR1+ cytotoxic effectors that traffic to the tumor bed. These data demonstrate that an orally delivered non-colonizing monoclonal microbe enhances innate and adaptive anti-tumor immunity in preclinical mouse models.

In a phase I/II clinical trial, the safety, tolerability, and pharmacological effects of orally administered EDP1503 in combination with pembrolizumab are being evaluated in multiple tumor types: microsatellite stable (MSS) metastatic colorectal cancer, triple-negative breast cancer, and a basket of PD-1 relapsed solid tumors. In a 32-patient metastatic MSS colorectal cancer cohort, EDP1503/pembrolizumab combination therapy was safe and well tolerated without significant treatment-related serious adverse events. Histological assessments and gene expression analysis of paired tumor biopsies revealed enhanced CD8+ T cell-to-Treg and CD8+ T cell-to-exhausted CD8+ T cell ratios within the tumor following a run-in period with EDP1503 monotherapy.

Conclusion: We provide clinical evidence to support further therapeutic investigation of oral delivery of single microbial strains for additional cancer cohorts. EDP1503 is being evaluated in two ongoing clinical studies (NCT03775850, NCT03595683).

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P-326 Chemoradiotherapy treatment in gastroesophageal junction tumors

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Background: The esophagogastric junction (EGJ) and gastric cardia, represent anatomical sites with a remarkably high and rapidly rising incidence of adenocarcinoma. Although surgery is the primary curative modality for EGJ tumors, long-term outcomes are not satisfactory with resection alone, even if microscopically complete. This poor long-term outcome has prompted an evaluation of neoadjuvant (preoperative) and adjuvant (postoperative) combined modality therapy. The best form of multimodality therapy is not established.

Methods: The clinical histories of patients with locally advanced gastroesophageal junction cancer from the Oncology Section of the Italian Hospital in Buenos Aires from 2014 to 2019 were analyzed retrospectively. The clinical characteristics of the patients and their treatments were evaluated. For the analysis of global survival and progression-free survival, the Kaplan-Meier method was used.

Results: 105 patients were diagnosed with EGJ, 63 patients underwent concomitant neoadjuvant chemotherapy and radiotherapy, with a median of 62 years ranging from

20 to 84 years, 85% (51) men, 91% (55) ps 0-1, 65% (39) smoking, 17% (10) had Barret's esophagus. The diagnosis was made with high videoendoscopy with biopsy in 100%, staging with PET/CT in 77% (46), 73% (44) had positive nodes and 48% (29) had siewert II location. 92% (55) of the tumors corresponded to adenocarcinomas and 35% (21) were tested for her2 of which 24% (5) were positive. The radiotherapy dose was 180 Gy with 41 Gy per session. 98% (59) completed radiotherapy, of which 96% did 3D radiotherapy and 4% (2) IMRT. 92% (55) received carboplatin 2 AUC and paclitaxel weekly. 58% (35) had toxicity, and of these, 51% (18) had hematological toxicity grade 1-2. The objective response rate was 78% (47), evaluated by pneumotomography, and 10% (6) patients progressed intra-treatment. Surgical compliance was 72% (43), 67% (29) underwent esophagectomy. 14% (6) had a complete pathological response in the post operative part, it was a subrogant of OS with HR 0.4 (CI 0.16 to 0.96) p = 0.041. 22% (13) patients performed adjuvant, the majority of these with capecitabine, there were no significant differences in DFS or OS with the addition of adjuvant treatment. With a mean follow-up of 25 months, 19% (8) of the operated patients relapsed, with 50% systemic relapses. All relapsed patients received FOLFOX. 32% (16) died during follow-up with an OS of 18 months and a DFS of 16 months. Neutrophil/lymphocyte ratio greater than 3 at diagnosis was 45% (27) and a statistically significant association with mortality was observed (p=0,034).

Conclusion: Good surgical compliance was observed, with acceptable toxicity, and the objective response rate was high. Adjuvant treatment offered no benefit in OS or DFS. The complete pathological response was a surrogate for survival. Neutrophil/lymphocyte ratio at diagnosis was associated with mortality. The results in our center were similar to those of the CROSS study.

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P-327 Gastric cancer in elderly patients

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Background: Gastric cancer is considered to be a cancer of the elderly. In 80% of cases, gastric cancers are detected after the age of 65 years. The mean age of diagnosis is 71 years for men and 74 years for women.

Methods: We conducted a retrospective study including patients over 70 years old treated for gastric neoplasia in the Medical Oncology Department of Tlemcen Hospital. The object of our work was to describe the epidemiological characteristics of gastric cancer in elderly patients and their therapeutic management.

Results: Thirty-five patients were included. The mean age was 77 years [70-84]. A male predominance was noted (sex ratio: 1.7). The average consultation time was 6 months [1-12]. 35 % of patients were smokers. The tumor was revealed by epigastralgia, deterioration of performance status, vomiting, and digestive hemorrhages. Endoscopy was performed in 27 patients. The tumor had an antral site in 10 patients and cardio-tuberosity in 9 cases. 24 patients had a moderately differentiated gastric adenocarcinoma; the signet ring cell was found in 5 patients. Curative surgery was indicated in 14 patients with localized disease. The anatomopathological study revealed adenocarcinoma in all patients, with lymphatic ganglions invasion in 12 patients. 3 patients received adjuvant chemotherapy according to the XELOX protocol. The treatment was well tolerated. For the 21 patients with metastatic disease, a geriatric evaluation was done before any chemotherapy treatment, and palliative chemotherapy was recommended for 10 patients according to the XELOX and XELODA protocol. The mean number of cures was 3. The toxicities were hematological and digestive. Symptomatic treatment only was proposed for 10 patients.

Conclusion: Elderly people with gastric cancer are candidates for the same treatment as younger patients. Only a collaboration of oncologists and geriatricians will facilitate the treatment.

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P-328 Biliary tract cancers: Epidemiology and trends in Tunisian patients

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Background: Biliary tract cancers (BTCs) are rare tumours and are known for their poor outcome. This group of cancers comprises intrahepatic cholangiocarcinomas (ICCs), gallbladder cancers (GBCs), extrahepatic cholangiocarcinoma (ECCs), Klatskin tumours and ampulla of Vater carcinomas (ACs). The aim of our study was to determine the epidemiological characteristics and trends of these rare tumours in Tunisian patients.

Methods: We retrospectively reviewed all data of patients with BTCs from 2012 to 2019 in our center. Data analysis was performed with SPSS 21st version.

Results: From 2012 to 2019, fifty patients with CTCs consulted our department, thus representing 2.2% of all cancer cases during that period. Mean age at diagnosis was 63± 10 years old. Male to female ratio was 1.14. Twenty-seven percent of the patients had ICCs, 27% had ICCs, 20% had GBCs,13 % had Klatskin tumours and 13% had ACs. Almost half of the patients (47%) had a history of cholecystectomy, 30% had diabetes and 30% had a history of hypertension. Ten percent were alcohol consumers, and 40% were active smokers. About half of the patients (52%) had a body mass index over 25kg/m^2. A history of chronic viral hepatitis was noted in 8%. Revealing symptoms were hepatic colic (76%), jaundice (60%), vomiting (10%), generalized pruritus (10%) and weight loss (43%). Cholecystitis revealed the disease in 6% of cases. Biological findings showed cholestasis in 25% of patients with ICCs, in 75% of patients with ECCs, in all patients with Klatskin tumours, in 83% of patients with GBCs and in 25% of patients with ACs. High serum levels of CA19-9 were noted in 60% of cases. In ECCs and Klatskin tumours, high levels of CA19-9 were noted in 75% of cases while only 33% of patients with GBC tumors had elevated CA19-9 levels. CEA serum levels were high in 40% of patients, half of them had ECCs. As for stage at diagnosis, seventy percent of our patients had metastatic disease, 20% had stage III and 10% had stage II tumours. All patients with localized disease had upfront surgery, but only 43% of them had complete resection (R0). The main first-line chemotherapy regimens in metastatic patients were gemcitabine+oxaliplatin in 70% and gemcitabine+cisplatin in 14% of cases. Survival analysis showed that patients (all stages taken together) had an overall survival of 27 months. At one year 70% of them were alive. At twenty months, survival rate was 55%. Prognostic factors with statistically significant value in bivariate and multivariate analysis were high levels of Alkaline phosphatase (p=0.024), extrahepatic invasion (p=0.043), vascular invasion (p=0.013) and TNM stage III and IV (p=0.001).

Conclusion: Our findings highlight the epidemiological characteristics of Tunisian patients with BTCs. We note that viral hepatitis is not a common risk factor when compared to Western countries. Diagnosis is revealed at advanced stages, mainly stage IV disease (70%). The most important prognostic factors were high levels of alkaline phosphatase, vascular and extrahepatic invasion, and TNM stage III and IV.

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P-329 Clinico-epidemiological profile of pancreatic cancer

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Background: With a dramatically increased incidence and a very poor prognosis, the treatment of pancreatic cancer remains a challenge. Unfortunately, the majority of cases are diagnosed at an advanced stage, where palliative chemotherapy can be administered to alleviate the symptoms and prolong life. Although pancreatic carcinogenesis has not yet been explained, familial agregation, tobacco smoking, and hypercaloric intake are associated with pancreatic carcinogenesis. To date, either prevention or screening programs have yet to be proposed.

Methods: This is a retrospective study for patients followed in the Medical Oncology Department of Anti-cancer Center Blida between January 2010 and December 2016. The aim of this study is to report the epidemiologic profile for patients with pancreatic cancer.

Results: Overall, 140 patients were followed in the department; the median age was 59.8 years (range, 21-80), and the sex ratio was 2. A family history of cancer was present in 16.7%, 29.7% had diabetes in their antecedents, tobacco smoking was present in 42.8% of cases, and 29% had obesity. The most common reasons for consultation were pain in 45.2% of cases and jaundice in 16.4%, with an average consultation time of 3 months. The histological type was adenocarcinoma in 95.3% of patients, with stage IV and stage III disease in 77.5% and 14.3%, respectively, at diagnosis.

Conclusion: As cancer of the pancreas becomes symptomatic, the diagnosis is made at a late stage, which testifies to the gravity of this cancer. To improve this situation, prevention by acting on risk factors, such as smoking and obesity, is important.

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P-330 Is CA 19.9 a prognostic predictor in advanced or metastatic pancreatic cancer (AMPC)

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Background: CA 19.9 is considered the most specific and sensitive serological marker of pancreatic adenocarcinoma. CA 19.9 elevated levels are associated with a poor prognosis. Serum carbohydrate antigen basal levels are widely used to predict prognosis and response to treatment in patients with advanced or metastatic pancreatic cancer.

Methods: Our study was conducted in patients who had histologically proven advanced or metastatic pancreatic cancer. These patients were treated with systemic chemotherapy (gemcitabine/cisplatin), and CA 19.9 was assessed before and after treatment in order to determine effectiveness. The assay was also assessed in consultation control to detect a recurrence of the disease. The primary objective is to demonstrate the expression of CA 19.9 among patients with pancreatic cancer.

Results: Between 2010 and 2017, 147 patients were admitted in the Department of Medical Oncology. The median age was 57.8 years (range, 25-80 years), stage III representing 43.9% of cases, and stage IV representing 28.7% of cases. The marker was elevated at disease diagnosis in 57.4% of cases, at normal levels in 16% of cases, and decreased in 29.8% of cases with good clinical and radiological response. CA 19.9 increased in 11.5% of cases with radiological progression.

Conclusion: Serum carbohydrate antigen (CA 19.9) in advanced or metastatic pancreatic cancer may be used to evaluate treatment effectiveness. When levels are high at disease diagnosis, it can be used to help in the diagnosis but cannot be used to confirm a diagnosis without histological evidence.

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P-331 Adjuvant chemotherapy for stage II colon cancer following complete resection: Experience of the Mohammed VI University Hospital Centre oncology center in Marrakech

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Background: The goal of this study was to report the experience of our center regarding stage II colon cancer and the use of adjuvant systemic chemotherapy following curative-intent surgery.

Methods: This is a retrospective, descriptive study conducted within the Medical Oncology Department of the Mohammed VI University Hospital Centre in Marrakech. The study was spread over a period of 8 years from January 1, 2012, to December 31, 2019.

Results: We identified 60 patients followed for stage II colon cancer. The average age of our patients was 58.6 years with extremes of age between 36 and 80 years. The sex ratio was 1.22 (33 women/27 men). The disease was revealed by occlusion in thirty-five percent of cases. The most common tumor site was left colon in 43 cases (71.6%) and right colon in 17 cases (28.3%). All patients underwent surgical treatment; the surgery was complete. The histological factors of poor prognosis were: tumor poorly differentiated in 2 cases (3.4%), stageT4 in 16 cases (26.6%), presence of vascular emboli in 32 cases (53.4%), insufficient lymph node dissection 15 cases (25%). MSI was observed in 20.8% of patients. Adjuvant chemotherapy was indicated in 40 cases (66.6%). Only 35 patients received adjuvant chemotherapy with 8 cycles of XELOX or 12 cycles of FOLFOX. The average follow-up was 3 years, and was marked by relapses in patients who already benefited from chemotherapy in 3 cases (8.5%) and in patients who did not receive adjuvant treatment in 2 cases (8 %).

Conclusion: The adjuvant chemotherapy of patients with stage II colon cancer is an area of controversy in medical oncology.

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P-332 Real-world data study of BRAF mutant metastatic colorectal cancer patients across the Greater Manchester region prior to BEACON trial results

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Background: BRAF mutations are known to impact both prognosis and anti-EGFR response in metastatic colorectal cancer (mCRC).

Methods: All consecutive pts (n=80) with BRAF mutation from 2016 to 2018 were included in this real-world data (RWD) study. Data were obtained from electronic patient records. Survival univariate analysis (UVA) was performed with Kaplan-Meier curves and log-rank test. Multivariable survival analysis (MVA) was performed by Cox regression.

Results: Median age for the 80 pts was 68y (range 32 to 82). Median follow up was 10.2 months (ms). Females 36 pts (45%) and males 44 (55%). Anatomically, 42.5% were ascending colon, 13.7% transverse, 21.9% sigmoid and 17.8% rectum; in summary, right colon tumours accounted for 51.5%. Seventy (87.2%) pts had BRAF V600E mutation. KRAS mutation was present in 7 cases (8.8%), 4 (5%) were co-expressed with BRAF V600E mutations. Sixteen (20%) had a PIK3CA mutation. The most common first-line chemotherapy backbone was FOLFOX (41.5%), followed by FOLFIRI (40%). Only 12 pts (15%) received anti-EGFR antibodies, 9 of them with BRAF V600E mutations. The median variant allele frequency for BRAF variants was 22%, ranging from 2 to 56%. Responses by RECIST criteria to first line were, complete response (CR) in 4 (6.5%) out of 61 evaluable patients, partial response (PR) in 12 (19.7%), stable disease (SD) in 16 (26.2%) and progressive disease (PD) in 29 (47.6%). Overall survival (OS) for the full cohort was 11.4 ms 95%CI (9.2-13.7). First-line progression-free survival (PFS) for the full cohort was 5.3 ms 95%CI (3.7-6.9). In the UVA for OS, sidedness was statistically significant (p=0.048) with right-sided tumours having a median OS of 9.7 ms 95%CI (5.6-13.7) vs left-sided 13.6 ms 95%CI (5.4-21.8). However, when the analysis was stratified by BRAF mutation, the difference was not statistically significant (p=0.204); a trend was observed for the non-V600E (p=0.058). No differences in OS were found regarding the chemotherapy backbone or anti-EGFR antibodies. In the first line, responders had a better OS of 14.8 ms (95% CI 0.0-30.2) vs the OS of non-responders which was 9.2 ms (95%CI 6.9-11.4, p=0.005). There were no differences regarding baseline ECOG. In the UVA for PFS, responders had a better PFS 9.7 ms (95%CI 5.0-14.3) vs non-responders PFS 3.2 (95%CI 2.5-3.9, p=0.001) and it was the only significant variable. In the MVA analyses for OS, response by RECIST remained as an independent prognostic factor when adjusted for BRAF variant, gender, EGOG and sidedness (HR: 0.6 95%CI 0.4-0.8 with p=0.003). In the MVA analyses for PFS, response by RECIST remained significant when corrected for BRAF variant, gender ECOG and sidedness (HR: 0.6 95%CI 0.4-0.7, p< 0.001).

Conclusion: In our RWD study, response to treatment was the main independent factor associated with PFS and OS for the first line of treatment. This is in keeping with the utility of chemotherapy triplets in this subgroup.

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P-333 Clinical and epidemiological characteristics of gastric cancer in young Algerian patients (aged 45 and under): Experience of the Department of Medical Oncology in Blida, Algeria

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Background: Gastric cancer is the second leading cause of cancer-related mortality and the fourth most common cancer globally; the average age at diagnosis is generally ≥50. In our Department of Medical Oncology in Blida (north of Africa), we have observed an increased number of young patients with gastric cancer.

The aim of this study is to determine the epidemiologic and clinical characteristics of this cancer in young patients aged ≤45 years.

Methods: This is a retrospective study of patients diagnosed with gastric cancer aged 45 years and under, treated in the Department of Medical Oncology in Blida between January 2014 and December 2017. We were interested in the clinico-epidemiological characteristics of this population.

Results: During this period, 56 patients with gastric cancer aged 45 years and under were seen, which is about 25.3% of all patients with gastric cancer (total, 221 patients); 38 were male (67.8 %) and 18 were female (32.1%), the median age at diagnosis was 36 years (range, 21 to 45 years). Body mass index (BMI) was higher than 25 in 15 patients (26.7%); smoking was found in 18 patients (32.1%); consumption of salted and preserved products was observed in 23 patients (41%); a diet high in meat and fat was observed in 25 patients (44.6%); oil of cade intake was noted in some patients; family history of gastric cancer was seen in 3 patient; and a family history of other cancer was seen in 10 patients. The most common symptom was epigastralgia; diagnosis delay was >3 months in 64% of cases; the gastric antrum was the most frequent seat; the histological type was adenocarcinoma in 91%; helicobacter pylori infection was determined in 29 biopsies; locally advanced (III) and metastatic stages (IV) were identified in 35.7% and 48% of cases, respectively.

Conclusion: There was a high incidence of gastric cancer in young people in our series. The main risk factors in young people are smoking, HP+, low socioeconomic status, intake of salty and smoked food, oil of cade, a diet rich in meat and fat and low in vegetables and fruits, physical inactivity, excess weight, and unknown behavioral factors. Eating habits and lifestyle factors of our young population must be analyzed carefully. Gastric cancer remains a serious health problem in Algeria; therefore, other prospective studies designed to identify other risk factors are highly recommended.

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P-334 Perioperative chemotherapy in the treatment of resectable and locally advanced gastric and junctional esophagogastric adenocarcinoma: Experience of a Portuguese central hospital

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Background: Gastric cancer is the 5th most prevalent cancer in Portugal and the 3rd most deadly worldwide. Currently, perioperative chemotherapy is the standard of care for resectable and locally advanced gastric and junctional esophagogastric (JEG) adenocarcinoma. During several years, the MAGIC study catapulted ECF/ECX/CF regimens into the spotlight. Since publishing the FLOT4-AIO trial results in 2017 - associated with higher R0 resection and pathological response ≤T1 rates, as well as extended overall survival in 15months - the FLOT regimen has become the preferred perioperative option in most national and international clinical centers. The aim of this study was to compare in the real-life setting the FLOT vs ECF/ECX/CF perioperative regimens used in the treatment of resectable and locally advance gastric adenocarcinoma, in terms of safety and efficacy.

Methods: We conducted a retrospective and observational study, which included patients diagnosed with resectable and locally advanced gastric and JEG adenocarcinoma treated with perioperative chemotherapy regimens between 01/01/2016 and 31/06/2019, namely FLOT (Group A) and ECF/ECX/CF (Group B). Toxicity assessment was made according to CTCAE V.5.0.

Results: The study included 64 patients [A:58%(n=37); B:42%(n=27)]. Most patients were male [A:57%(n=21); B:82%(n=22)], median age was 64 years old [A:63 years [39-78]; B:70 years[53-79]] and had cT3/T4 [A:70%(n=26); B:85%(n=23);p=0,164] and cN+ [A:67%(n=25); B:93%(n=25);p=0,017] disease at diagnosis. The median follow-up time was 10 months [2-22] and 21 months [0-37] for groups A and B, respectively. The preoperative regimen was completed by 81% of patients in both groups. Most patients underwent curative surgery [A:84%(n=31); B:81%(n=22);p=0,533]. Most patients initiated postoperative cycles [A:54%(n=20); B:63%(n=17)] but only 43% (n=16) of the patients in group A and 63%(n=17) of group B completed the perioperative treatment. Treatment readjustments was performed in 70% of patients in the group A and 96% of the group B, including delays [A: 40%(n=15); B: 44%(n=12);p=0,755], suspension [A: 27%(n=10); B: 96%(n=26);p< 0,01] and dose reduction [A: 27%(n=10); B: 41%(n=11);p=0,249]. Except for one patient in group A who had R1, all the other patients in the two groups had R0 resection. Compete pathological response (ypT0N0) was reported in 13% of the patients in group A and 9% of group B (p=0,511). Overall survival (OS) was 19 (IC95% 17-21) and 26 months (IC95% 21-32) (p=0,368) and Disease-Free Survival (DFS) was 20 (IC95%:18-22) and 31 months (IC95%:27-36) (p=0,098) in groups A and B, respectively. During the perioperative treatment, the majority of patients experienced grade 3-4 toxicity at some point in treatment [A:57%(n=21); B:70%(n=19);p=0,267], most common being neutropenia [A:35%(n=13); B:63%(n=17);p=0,028]. Two patients died of infectious complications in group A.

Conclusion: According to our study, there was no significant difference between the two groups regarding complete pathological response (ypT0N0). The higher incidence of grade 3-4 toxicity especially neutropenia and treatment suspension seemed to occur in the ECX/ECF/CF group. The short follow-up time and small sample size can justify the OS and DFS results.

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P-335 Self-reported prescribing practices in the setting of adjuvant treatment for colorectal cancer

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Background: The Short Course Oncology Treatment (SCOT) trial demonstrated non-inferiority of 3 versus 6 months of adjuvant treatment for colorectal cancer (CRC). It was the largest contributor to the Duration of Adjuvant Chemotherapy for Stage III Colon Cancer (IDEA) Collaboration. The aim of this study was to explore the impact of these results on clinician prescribing one-year post-publication.

Methods: An online survey was developed and piloted using OnlineSurveys®, and was disseminated using email, an ESMO GI mailing list, and Twitter® in April 2019. Descriptive statistics were used for the main analysis and Chi2 tests for comparison of proportions.

Results: In total, 265 clinicians from 21 countries responded. Most were oncologists (97%) and worked in non-academic roles (63%). Response rate was 51% for UK consultant oncologists. Most (91%) were aware of the SCOT trial or IDEA collaboration results, and 94% of these clinicians reported a corresponding practice change. Listening to conference presentations of trial results was the most common (30%) mechanism of dissemination which influenced practice change. There was a clear division in the approach to treatment based on stage III CRC risk group. In total, 78% of clinicians used 3 months of CAPOX for patients with low-risk stage III CRC (T1-3N1) versus 15% for high-risk disease (T4 or N2 disease) (p< 0.001). Most clinicians (69%) preferred to use 6 months of either CAPOX or FOLFOX for high-risk stage III CRC, whereas only 4% used this strategy for low-risk disease (p< 0.001). UK clinicians were more likely to choose CAPOX when giving 6 months of doublet chemotherapy for high-risk stage III CRC (68% CAPOX, 32% FOLFOX p< 0.001), however, this preference was not apparent for non-UK clinicians (48% CAPOX, 52% FOLFOX p=0.302). Overall, there was more heterogeneity in practice for patients aged over 70 compared to younger patients, and for patients with stage II versus stage III CRC. In total, 91% of respondents agreed that 3 months of CAPOX could be considered standard care for patients with low-risk stage III disease versus 44% for high-risk stage III disease. Using 3 months of FOLFOX was a less favourable option for both stage III risk groups. There was most uncertainty regarding stage II disease, with 23% of clinicians indicating they were unsure about using 3 months of doublet chemotherapy in this situation.

Conclusion: Approximately half of patients with CRC present with stage II or stage III disease at diagnosis. It is therefore paramount to know how these patients are treated in real life. This survey shows that the SCOT trial and IDEA collaboration can be considered practice-changing. Despite SCOT meeting its non-inferiority end-point in the overall trial population, clinicians are using sub-group analyses to guide treatment. Clinicians are more reluctant to use a shorter duration of doublet treatment for high-risk compared to low-risk stage III CRC, and rarely use 3 months of FOLFOX for any disease stage. This survey will be repeated in April 2020 to explore if and how practice has altered over time.

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P-336 Clinical outcomes of 49 consecutive patients admitted with malignant obstructive jaundice

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Background: Biliary obstruction as a consequence of primary biliary malignancy or secondary metastatic disease from extrabiliary sites is often accompanied by significant symptoms, resulting in poor quality of life. Clinical symptoms vary depending upon the location of cancer but commonly include jaundice in up to 90%, pruritus in 66%, pain and malabsorption leading to weight loss in 30-50% patients. The relief of obstructive jaundice is a key aim in the palliation of biliary tract cancers and has been shown to prolong life, and equally importantly, quality of life.

Methods: We carried out a retrospective review of electronic health records to look at aetiology, post-decompression treatment, and survival in 49 patients who presented with obstructive jaundice and had percutaneous trans-hepatic cholangiogram

(PTC) and biliary stenting over a period of 4 years (5/08/15 to 21/09/19) in a tertiary care centre.

Results: 49 patients with obstructive jaundice had 76 PTC procedures during the review period. Median patient age was 66 years (range 42 − 90 years). 18 patients (36%) were male and 31 patients (63 %) were female. 20 patients (40 %) had gallbladder and cholangiocarcinoma, 11 patients (22 %) had pancreatic cancer, 8 patients (16 %) had colorectal cancer, 2 had melanoma, 2 had ovarian cancer, 1 had hepatocellular carcinoma, 1 had small bowel cancer, 1 had duodenal cancer, 1 had RCC and 1 had a neuroendocrine tumour. Median time from admission with obstructive jaundice to PTC was 7 days (range 1-42 days). The median duration of hospital stay was 20 days (range 1-65 days). Post PTC 26.5 % patient had further systemic treatment with a median survival of 99 days while 73.5 % of patients had no further treatment, median survival in this sub-group was 44 days. Reasons for no further treatment included frailty in 61 % patients, a decline in performance status post-PTC in 11 %, unsuccessful PTC in 8%, no further treatment available in 5 %, further treatment declined in 3%, stable disease and surveillance in 3% and deaths during the admission in 11% patients. Post PTC, 24% of patients died within 30 days, 32% died between 31- 90 days while 44 % of patients survived beyond 90 days. We noticed a 10% complication risk post-PTC with sepsis being the commonest. Re-procedure bilirubin levels did not have any impact on overall survival. Median overall survival post-PTC was 52 days.

Conclusion: Obstructive jaundice is a debilitating oncological complication leading to increased patient morbidity and mortality. Fit patients with potential for further treatment should be considered for urgent intervention to improve jaundice, but terminally ill patients with poor performance status and no therapeutic option could be considered for best supportive care.

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P-337 Perioperative FLOT experience: Pathological regression and toxicity

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Background: The prognosis of gastric cancer patients is poor. Surgical resection is curative in about 90% of early-stage (T1) tumours, but survival drops dramatically for more advanced tumours (T2-4) or those with regional lymph node involvement. To improve survival, multidisciplinary strategies including perioperative chemotherapy with FLOT protocol (fluorouracil plus leucovorin, oxaliplatin, and docetaxel) is the current standard.

Methods: We report our experience in perioperative chemotherapy with the triplet docetaxel, oxaliplatin and 5FU (FLOT) in resectable gastric adenocarcinoma patients stage cT2 or cN +, to evaluate the toxicity, tolerability, and clinical and pathological response. In this descriptive and prospective study, 34 patients were treated in the medical oncology department of the Oran Cancer Center of Algeria between January 2018 and December 2019.

Results: The median age at diagnosis was 59 years (42-75), and most patients were women 61.7% (n =21), 9 patients had a risk factor (26.4%) including atrophic gastritis, gastric metaplasia, and Helicobacter pylori in 5 patients). The most common symptom was epigastralgia in 21 patients (61.7%) associated or not with other symptoms like vomiting, melena, anorexia. Performance status (PS) prior to treatment were 0 (n=8, 23.5%), 1 (n = 25, 73.5%), 2 (n = 1, 2.9%). Clinical tumor stage: cT2 in 7 patients (20.5%), cT3 in 13 patients (38%), cT4a in 14 patients (41%), clinical node-positive in 31 patients (91%), the tumor was antro-pyloric in 47% of cases. 32 patients (94%) completed 4 preoperative cycles and two patients (5.8%) discontinued treatment after 1 and 3 cycles because of toxic deaths. 32 patients (94%) were able to undergo surgery and R0 was achieved in 24 patients (75%) compared with 85% in the AIO-FLOT4 trial, total gastrectomy was performed in 12 patients (50%), lymphadenectomy D2, D1.5 and D1 in 11 (45.8%), 12 (50%), 3 (12.5%) patients, respectively, metastatic disease was discovered during surgery in 3 patients. Pathological regression with FLOT patients was detected with a proportion of postoperative stage ypT1, ypT2, or ypT3 tumours in 17 patients (70.8%) contrasted with 58% in the AIO-FLOT4. Pathological nodal stage ypN0 was reached in 16 patients (66.6%) with clinical node-positive disease compared with 49% in the AIO-FLOT4. According to tumour regression grade (TRG), there was no complete histological response (TRG 1a). Pathological subtotal regression (TRG 1b) was reached in seven patients (29%), partial tumor regression (TRG2) in 13 patients (54%) and no regression (TRG 3) in 8 patients (33.3%). 4 patients (16.6%) did not start postoperative FLOT (PS 2/3). Nine patients (37.5%) completed 4 postoperative cycles and 8 patients (33.3%) discontinued postoperative FLOT because of toxic effects. The most common grade 3/4 toxicities were neutropenia (n=15, 44%), diarrhoea (n=1, 3%), neurological toxicity (n=1, 3%), fatigue (n=2, 5.8%), and anorexia (n=1, 3%). 19 patients (55.8%) had at least 1 treatment delay and eight patients (23.5%) required dose reduction.

Conclusion: FLOT is the new standard of perioperative chemotherapy for gastric cancer and has been integrated into European standards. It showed improve pathologic response rate and the toxicity was controlled.

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P-338 Advanced pancreatic adenocarcinoma in daily clinical practice: A single-center experience

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Background: Pancreatic adenocarcinoma (AC) is a systemic disease with early metastatic spread and poor survival rate. Palliative chemotherapy (CT) is the treatment of choice for advanced stages. Also, palliative surgical and endoscopic techniques are meant to improve quality of life and make the patient more comfortable. Moreover, the majority of pancreatic cancer patients present with pain at the time of diagnosis. Pain management can be challenging in light of the aggressive nature of this cancer. The aim of this study was to evaluate the oncological approach to advanced pancreatic ductal AC in daily clinical practice.

Methods: We conducted a retrospective analysis of all patients diagnosed with pancreatic AC treated at our Medical Oncology Department between 2008 and 2016, then we analyzed the cohort of patients with metastatic disease. We evaluated gender, clinical history, performance status (ECOG), tumour location, tumour stage, biliary stent, albumin rate, white blood cell rate, liver function, and treatment approach. Univariate analysis for OS was estimated using the Kaplan-Meier method with statistical significance ($p < 0.05$) of differences evaluated by log-rank test. Cox regression model was carried out for multivariate analysis. All statistical analysis was performed using SPSS version 25.0.

Results: 114 patients were identified; 43% female and 57% male; median age at diagnosis was 63.3 years (range 41-111). All patients had AC histopathological type. We evaluated 78 patients (68,4%) with metastatic disease. They had a baseline ECOG performance status at cycle 1 of first-line CT of 1, 2, 3, 4 in 40%, 40%, 16%, 4% patients. The primary tumor was located in the head of the pancreas in 59,6% patients. T3 and T4 stages were found in 64,9% of patients. Liver/peritoneum/lymph node/lung/multiorgan metastases were present in 17/10/09/19/23 patients. Time to diagnosis was less than three months in 50.9% of patients. 21 patients had been treated for pain at baseline, and 22 had undergone biliary drainage prior to the initial CT. 60,3% of patients received CT. 58% of patients received first-line CT. The most used first-line CT regimen was gemcitabine (46,2%). Second-line CT was performed in 13 patients (16,7%), and 4 patients received third-line CT. The most used CT regimen in the 2nd and 3rd lines was capecitabine. The median overall survival (mOS) was 3,9 months (95% CI, 0.2-7.1) from diagnosis. mOS from diagnosis was 2.4 months (95% CI, 0.2-11.6) for patients who received 1 line only, 8.3 months (95% CI, 0.5-16.5) for patients who received 2 lines and 16.3 months (95% CI, 4.1-35.2) for those who received 3 lines. Univariate and multivariate analysis showed that ECOG PS ($p = 0.002$) was associated with poor prognosis.

Conclusion: This retrospective analysis highlighted the prescribing profile of systemic CT at Algerian Tlemcen Hospital. We demonstrated poor overall survival of metastatic pancreatic cancer. Survival was poorest in those receiving a single line of CT. Patients should receive multiple sequences of chemotherapy whenever possible. We are aware of the limitations of a retrospective study. Further studies like these are needed to evaluate the management of advanced pancreatic cancer in real-world clinical practice.

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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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P-342 Margetuximab combined with anti-PD-1 (MGA012) or anti-PD-1/LAG-3 (MGD013) +/- chemotherapy in first-line therapy of advanced/metastatic HER2+ gastroesophageal junction or gastric cancer

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Background: Trastuzumab (T), a monoclonal antibody (mAb) targeting HER2, is the standard of care 1st-line therapy for advanced HER2+ GEJ/GC patients (pts). Margetuximab (M), an investigational Fc-engineered anti-HER2 mAb, targets the same HER2 epitope but with higher affinity for both 158V (high binding) and 158F (low binding) alleles of activating Fc receptor CD16A. Data suggests M coordinately enhances both innate and adaptive immunity, including antigen-specific T-cell responses to HER2. PD-1 and LAG-3 are T-cell checkpoint molecules that suppress T-cell function. MGA012 (INCMGA00012) is a humanized, hinge-stabilized, IgG4 K anti-PD-1 mAb blocking binding of PD-L1 or PD-L2 to PD-1. MGD013 is a humanized Fc-bearing bispecific tetravalent protein that binds to both PD-1 and LAG-3, inhibiting their respective ligand binding. We previously reported that a chemotherapy (CTX)-free regimen of M+PD-1 blockade was well tolerated in gastroesophageal junction or gastric cancer (GEJ/GC) pts, and induced a 30% objective response rate (ORR) in a double-positive biomarker population. This was 2- to 3-fold greater than in historical controls with checkpoint inhibitors alone. This registration-directed trial assesses efficacy, safety, and tolerability of M+checkpoint inhibition ± CTX in metastatic/locally advanced, treatment-naïve, HER2+ GEJ/GC pts.

Trial design: This is a 2-cohort, adaptive open-label phase 2/3 study. The first single-arm, CTX-free cohort A evaluates M+MGA012 in HER2+ (immunohistochemistry [IHC] 3+) and PD-L1+ (excluding microsatellite instability-high) pts. After 40 pts are evaluated for response/safety, additional pts will be enrolled if the threshold for continuation is met. In randomized cohort B, HER2+ (IHC 3+ or 2+/fluorescent in situ hybridization+) pts are enrolled irrespective of PD-L1 status. Part 1 randomizes pts to 1 of 4 arms (50 pts each): control arm (T+CTX) or 1 of 3 experimental arms (M+CTX; M+CTX+MGA012; M+CTX+MGD013). CTX is investigator's choice XELOX or mFOLFOX-6. Part 2 consists of control (T+CTX) vs 1 experimental arm (M+CTX) + either MGA012 or MGD013, depending on results from part 1; with 250 pts each. The primary efficacy endpoint for cohort A (both parts) is ORR per RECIST 1.1; for cohort B part 2 it is overall survival.

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P-343 Gastroenteropancreatic neuroendocrine tumors: A single-centre experience

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Background: Pancreatic adenocarcinoma (AC) is a systemic disease with early metastatic spread and poor survival rate. Palliative chemotherapy (CT) is the treatment of choice for advanced stages. Also, palliative surgical and endoscopic techniques are meant to improve quality of life and make the patient more comfortable. Moreover, a majority of pancreatic cancer patients present with pain at the time of diagnosis, pain management can be challenging in light of the aggressive nature of this cancer. The aim of this study was to evaluate the oncological approach in advanced pancreatic ductal AC in daily clinical practice.

Methods: We conducted a retrospective analysis of all patients diagnosed with pancreatic AC treated at Our Medical Oncology Department between 2008 and 2016, and then we analyzed the cohort of patients with metastatic disease. We evaluated gender, clinical history, performance status (ECOG), tumour location, tumour stage, biliary stent, albumin rate, white blood cell rate, liver function, and treatment approach. Univariate analysis for OS was estimated using the Kaplan-Meier method with statistical significance ($p < 0.05$) of differences evaluated by log-rank test. Cox regression model was carried out for multivariate analysis. All statistical analysis was performed using SPSS version 25.0.

Results: 114 patients were identified; 43% female and 57% male; median age at diagnosis was 63.3 years (range 41-111). All patients had AC histopathological type. We evaluated 78 patients (68,4%) with metastatic disease. They had a baseline ECOG performance status at cycle 1 of first-line CT of 1, 2, 3, 4 in 40%, 40%, 16%, 4% patients. The primary tumor was located in the head of the pancreas in 59,6% of patients. T3 and T4 stages were found in 64,9% of patients. Liver/peritoneum/lymph node/lung/multiorgan metastases were present in 17/10/09/19/23 patients. Time to diagnosis was less than three months in 50.9% of patients. 21 patients had been treated for pain at baseline, and 22 had undergone biliary drainage prior to the initial CT. 60,3% of patients received CT. 58% of patients received first-line CT. The most used first-line CT regimen was gemcitabine (46,2%). Second-line CT was performed in 13 patients (16,7%), and 4 patients received third-line CT. The most used CT regimen in the 2nd and 3rd lines was capecitabine. The median overall survival (mOS) was 3,9 months (95% CI, 0.2-7.1) from diagnosis. mOS from diagnosis was 2.4 months (95% CI, 0.2-11.6) for patients who received 1 line only, 8.3 months (95% CI, 0.5-16.5) for patients who received 2 lines and 16.3 months (95% CI, 4.1-35.2) for those who received 3 lines. Univariate and multivariate analysis showed that ECOG PS ($p = 0.002$) was associated with poor prognosis.

Conclusion: This retrospective analysis highlighted the prescribing profile of systemic CT at Algerian Tlemcen Hospital. We demonstrated poor overall survival of metastatic pancreatic cancer. Survival was poorest in those receiving a single line of CT. Patients should receive multiple sequences of chemotherapy whenever possible. We are aware of the limitations of a retrospective study. Further studies like these are needed to evaluate the management of advanced pancreatic cancer in real-world clinical practice.

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P-344 The role of postoperative prognostic nutritional index as a prognostic factor and its association to systemic inflammatory response markers in stage III colon cancer

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Background: Increasing evidence has shown that systemic inflammatory response (SIR) in cancer has a great influence on survival. As chronic inflammatory state contributes to nutritional depletion and to the development of cachexia, some tools based on inflammation may be considered useful in the evaluation of nutritional status. The aim of this study was to evaluate the role of the Prognostic Nutritional Index (PNI) as a prognostic factor and determine its association with SIR markers in stage III colon cancer (CC) patients.

Methods: This was a retrospective study of 235 stage III CC patients submitted to curative surgery followed by adjuvant chemotherapy between January 2013 and September 2018. PNI was calculated according to this formula: serum albumin level (g/L) + 5 x total lymphocyte count (/L). Lymphocyte-to-monocyte ratio (LMR), neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were calculated. Analytical values were obtained upon the date of first oncology doctor's appointment, excluding clinical evidence of infection or inflammation. PNI cut-off was estimated through analyses of the ROC curve. Survival analyses were estimated through Kaplan-Meier method and multivariate analyses through Cox regression.

Results: The median age of diagnosis was 63 (21-82) and 57% were men. The cut-off value of PNI was 51.70 with sensitivity of 48.1% and specificity of 71.4% [area under the ROC curve (AUC), 0.55; 95% CI 0.45-0.65; $P = 0.05$]. PNI was > 51.70 in 112 (47.7%) patients and ≤ 51.70 in 122 (51.9%) patients. Overall survival (OS) and disease free survival (DFS) were significantly lower in PNI ≤ 51.70 group vs. PNI > 51.70 (OS: 90.9% vs. 95.4%, $P = 0.014$; DFS: 72.7% vs. 87.3%, $P = 0.007$). In the multivariate analyses, PNI ≤ 51.70 maintained negative impact only in DFS (HR 1.457; CI 95% 1.215-1.749; $P < 0.001$). PNI correlated positively with lymphocytes ($r = 0.707$, $P < 0.001$) and with LMR ($r = 0.480$, $P < 0.001$), and negatively with NLR ($r = -0.394$, $P < 0.001$) and with PLR ($r = -0.410$, $P < 0.001$).

Conclusion: It has been found that a low PNI value is significantly associated with SIR markers, with the worst results in stage III CC patients that were submitted to curative surgery and adjuvant chemotherapy. Several studies have identified the PNI as a useful marker for oncologic prognosis, mainly when used before surgery. This study demonstrated it may also have a prognostic role in the post-surgery period, before beginning adjuvant chemotherapy. Timely identification of patients with malnutrition risk allows the implementation of nutritional support strategies at an earlier stage.

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P-345 Evaluation of a fully automated Idylla test system for microsatellite instability in a cohort of Spanish patients with colorectal carcinoma in a single institution

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Background: Approximately 12-15% of all CRCs are associated with defects in the DNA MMR pathway. CRC patients whose tumors exhibit high-level microsatellite instability (MSI-H) have an increased probability of LS and these tumors are sensitive to immune checkpoint blockade with anti-ICK inhibitors. dMMR is defined as the loss of any protein by IHC. There is an excellent (but not perfect) correlation between IHC and PCR. Decisions about which screening test to use depend primarily on the availability of resources and expertise. Guideline-recommended; complementary to PCR.

Methods: We evaluated 20 formalin-fixed paraffin-embedded tumor tissues, which were cataloged as dMMR using the method of immunohistochemistry, and were tested for MSI status using the polymerase chain reaction with the Idylla MSI detection system, a new fully automated MSI detection system released by Biocartis without the need for prior DNA extraction or concurrent testing of a normal control. MSI status by IHC testing of expression of the MMR proteins was performed. A four-antibody panel of MMR proteins, including MLH1, MSH2, MSH6, and PMS2, was conducted. Positive external controls from CRC positive for MLH-1, MSH-2, MSH-6, and PMS2 were used. According to the CAP protocol for immunohistochemistry interpretation, any nuclear staining, even patchy, was assessed as "no loss of expression". Only absolute absence of nuclear staining was considered "loss of expression" provided that internal controls were positive. MSI status was assessed by the Idylla MSI Test using an integrated, real-time PCR-based system (Idylla - Biocartis). The test analyzes a set of 7 novel proprietary biomarkers located in the ACVR2A, BTBD7, DIDO1, MRE11, RYR3, SEC31A andSULF2 genes. Based on these markers, instability of $>2/7$ markers = MSI-H, $<1/7=$ MSS (microsatellite stable). Results of these methods are highly concordant with other MSI testing approaches (MSK-IMPACT, MSI-PCR (Promega) and/or MMR IHC).

Results: The initial results showed a degree of agreement of 65% (by Idylla 13 were IMS and 7 MSS), which was much lower than those reported in the literature. The IHQ data of these 7 MSS patients were reviewed by a second pathologist. 4 of them with loss of PMS2 and another patient with loss of MLH-1 were reclassified as pMMR (by default of fixation of Ac in the previous test, mainly of PMS-2). 1 patient with PMS2 deficit and 1 patient with MSH2/MSH6 deficit remained classified as dMMR. After this second revision of the IHQ, the degree of concordance amounted to 86.6%, which was more consistent with what was reported in the literature (Maertens et al. Annals of Oncology 2017; 28 (suppl_5): v22-v42).

Conclusion: The Ac for PMS2 and MSH6 are the ones that give less robust positivities which makes it difficult to interpret. This reinforces the need for a second interpretation by another pathologist in cases of doubt and the recommendation of clinical practice guidelines to supplement with PCR prior to deciding whether to treat with immunotherapy. The Idylla MSI detection system showed a high concordance rate with previously used methods. Moreover, this fully automated system proves to be a powerful tool to accurately detect MSI status in tumor cells in a rapid and almost labor-free manner.

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P-346 Endoscopic profiling of various GI malignancies in CMOSH Medical College Hospital, Chattogram, Bangladesh

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Background: The prevalence of GI malignancies in Chattogram, Bangladesh, is mostly unknown. We, gastroenterologists, often find various GI malignancies during gastro-duodenoscopy, colonoscopy and ERCP. However, we have no DATA regarding the epidemiology of these malignancies which are diagnosed endoscopically. We did this study to profile various GI malignancies diagnosed endoscopically at our centre. Moreover, we audited the endoscopy reports with diagnosis of GI cancer to improve the quality of our performance and reporting.

Methods: Endoscopy reports of 93 consecutive patients presenting to the endoscopy suits of CMOSH from May 2017 until April 2019 and diagnosed as GI malignancies were retrospectively analyzed. The DATA regarding various procedures performed, age, and gender were recorded from the endoscopy reports. DATA on carcinoma of oral cavity, oesophagus, stomach, duodenum, ampullary, peri-ampullary region, bile duct, colon and rectum were analyzed using STATA software; version 13 (StataCorp, College Station, TX).

Results: Total number of subjects: 93; male 56 and female 37.

Site of cancer:

We found cancers in the oral cavity 3 (3.23%), oesophagus 22 (23.66%), stomach 31 (33.33%), Duodenum 3(3.23%), ampullary and periampullary 20 (21.51%), biliary 1 (1.08%), and rectum and colon 13 (13.98%). Among 22 oesophageal cancers the majority 18 (81.82%) involved lower oesophagus, 2 (9.09%) involved middle oesophagus. 2 (9.09%) involved upper oesophagus. Among 31 carcinoma stomach cases majority 17 (54.84%) involved antrum, 7(22.58%) involved body, 3 (9.68%) cardia, 2 (6.45%) fundus and 2(6.45%) pylorus. Among 13 colorectal cancers, 6 (46.15%) involved rectum, 4 (30.77%) sigmoid colon, 1 (7.69%) each in ascending, descending and transverse colon.

Age group distribution of GI cancers:

Age group distribution of our subjects was: 20 and below: 1 (1%), 21-30: 6 (6.45%), 31-40: 10 (10.75%), 41-50: 17 (18.28%), 51-60: 22 (23.66%), 61-70: 25 (26.88%), 71-80: 6 (6.45%), 81-90: 4 (4.30%) and 91 and above: 2 (2.15%).

The subjects belonging to the 61-70 years age group had the most GI cancers in our study. Prevalence of cancer in this age group was: oral cavity 2, oesophagus 8, stomach 9, Duodenum 5 and rectum 1. Second age group was 51-60 years. Cancers found in this age group was: oesophagus 5, stomach 5, duodenum 9, rectum 1 and colon 2. Third age group was 41 to 50 years. Cancers which were prevalent in this age group were: oesophagus 2, stomach 5, duodenum 6, biliary 1, rectum 1 and colon 2.

Gender distribution of GI cancers:

Commonest cancer in female subjects was oesophagus 12, which was followed by stomach 8, colorectal 8, ampullary/preiampullary 4, duodenum 3 and biliary 1. Most common cancer in male subjects was gastric cancer 23, which was followed by ampullary/periampullary 16, oesophagus 10 and colorectal 5.

Conclusion: Our subjects were predominantly male belonging to age group 61-70 and predominant cancer in our study was gastric cancer. The most common cancer in female subjects was carcinoma oesophagus and the most common cancer in our male subjects was carcinoma stomach. Although there were some minor differences in the reporting and occasional omission of details, we found the reporting quality as optimum.

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P-347 A phase 3, randomized, double-blind, placebo-controlled study of transarterial chemoembolization combined with durvalumab or durvalumab plus bevacizumab therapy in patients with locoregional hepatocellular carcinoma: EMERALD-1

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Background: Patients with intermediate-stage hepatocellular carcinoma (HCC) are treated with locoregional therapy such as transarterial chemoembolization (TACE) because curative therapy is not always an option and there is no standard systemic therapy. TACE therapy achieves tumor responses, but progression and recurrence are common and often occur within 1 year. Early evidence shows encouraging activity and durable clinical response for checkpoint inhibitors (CIs), such as durvalumab, as treatment for advanced HCC (Kelley, et al. ASCO 2017) and combined with TACE (Duffy, et al. J Hepatology, 2017). CIs combined with VEGF inhibitors (Cheng, et al. ESMO Asia 2019) also show promise in advanced HCC. Taken together, combining D, VEGF inhibitors, and TACE therapies warrants evaluation in patients with locoregional HCC. EMERALD-1 (NCT03778957) is a randomized, double-blind, placebo-controlled, multicenter phase 3 study assessing efficacy and safety for durvalumab monotherapy when given with either drug-eluting bead (DEB)-TACE or conventional TACE (cTACE) followed by durvalumab with or without bevacizumab therapy in patients with HCC not amenable to curative therapy.

Trial design: 600 patients will be randomized 1:1:1 to Arm A (DEB-TACE or cTACE + durvalumab and following last TACE procedure, durvalumab + placebo), Arm B (DEB-TACE or cTACE + durvalumab followed by durvalumab + bevacizumab), or Arm C (DEB-TACE or cTACE). Durvalumab therapy will begin after at least 7 days following the initial TACE procedure. Durvalumab ± bevacizumab will begin after at least 14 days following the last TACE procedure. Eligible patients must have confirmed HCC not amenable to curative therapy, have Child-Pugh score class A to B7, and an Eastern Cooperative Oncology Group performance status of 0 or 1. Patients with a history of nephrotic or nephritic syndrome, clinically significant cardiovascular disease, extra-hepatic disease, or main portal vein thrombosis (Vp3/Vp4) are excluded. Patients with active (controlled) or past hepatitis virus B or C infection may be enrolled. The primary endpoint is progression-free survival (PFS) for Arm A versus Arm C by blinded

independent radiology review using RECIST v1.1. Secondary endpoints include PFS for Arm B versus Arm C, overall survival, health-related quality of life measures, and safety.

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P-348 A multi-institutional retrospective study of stage I-IV transverse colon cancer: Diagnosis, treatment and outcome analyses

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Background: Transverse colon cancer (TCC) accounts for 10% of all colon cancers. Unlike right (RCC) and left colon cancer (LCC), TCC shows neither reliable prognostic factors nor specific outcome data yet.

Methods: We retrospectively studied patients affected by TCC, defined as originating distally to the hepatic flexure and proximally to the splenic flexure, diagnosed between 2007 and 2018 in 5 Italian centres. Patients' clinicopathological characteristics, treatments, objective response rate (ORR), progression-free survival (PFS) and overall survival (OS) were analysed, with the aim of describing the outcome of multi-institutional stage I-IV TCC.

Results: We identified 89 Patients, with a median age of 67 (range 41-90) years, 54 (61%) male, most of them with good performance status. TCC presented as IV, III, II and I stage in 52%, 21%, 24%, and 3% of cases, respectively. Intestinal occlusion was the first symptom in 29% of cases, anaemia in 41%, and pain in 10%. Molecularly, 7(8%) tumours were microsatellite instability-high, 40 (45%) were RAS wild type, and 13 (15%) were BRAF-mutant. Most of them underwent chemotherapy in the adjuvant setting. Thirty-three percent of patients developed metachronous metastases, especially in the liver (54%), peritoneum (30%) and the lung (11%). Treatment options for stage IV patients in first-line setting included 5 fluorouracil-based chemotherapy alone (29%), eventually added to a targeted anti-VEGF (45%) or anti-EGFR (26%) drugs according to the tumor molecular profile. The ORR was 33%, 59%, and 54%, respectively. With a median follow up of 50 months, the median PFS was 7 v 11 v 21 months (HR = 0.76, 95%CI 0.58-1.01) and OS was 16 v 34 v 32 months (HR = 0.85, 95%CI 0.64-1.13) with chemo alone, plus anti-VEGF and anti-EGFR targets, respectively.

Conclusion: Diagnosis of TCC is often delayed, thus TCC occurs more frequently in an advanced stage, similar to RCC. On the contrary, the TCC molecular profile seems closer to LCC. This study suggests that the therapeutic choice in TCC patients should be more like that considered in LCC and first-line chemotherapy with an anti-EGFR target should not be underestimated in order to improve their outcome and properly build a TCC therapeutic algorithm.

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P-349 Clinical significance of lymph node radio to predict prognosis in colon cancer

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Background: Metastases to regional lymph nodes (LN) has been considered to be a strong outcome predictor following surgical resection and a key determinant factor for adjuvant chemotherapy in colon cancer. According to the tumor-node-metastasis system reflected by the American Joint Committee on Cancer (AJCC), which has been the most popular cancer staging system, patients with positive LN involvement without distant metastasis are classified as stage III and they are subclassified into pN1 and pN2 based on the number of involved LN. However, in the current staging system, low LN harvest may lead to inadequate nodal staging which might result in overestimation of patient prognosis. In this perspective, recent studies recommended the lymph node ratio (LNR; the number of positive LN divided ty the number of harvested LN) as a prognostic indicator, rather than current nodal staging by AJCC. In the present study, we investigated the clinical significance of LNR to predict survival outcomes in colon cancer.

Methods: Patients who underwent radical resection for colon cancer and presented with positive LN involvement from January 2014 to December 2016 were included in the present study. Among the included patients, who were candidates for adjuvant chemotherapy, patients who had not undergone chemotherapy were excluded. Patient medical records were reviewed retrospectively and the number of harvested LN, positive LN and other pathological factors for prognosis including pT stage by AJCC, lymphovascular invasion, perineural invasion and histologic grade were recorded. As survival outcomes, disease-free survival (DFS) and overall survival (OS) were investigated.

Results: A total of 84 patients with positive LN involvement who underwent adjuvant chemotherapy were enrolled in the present study. Their median duration of follow-up was 43.5 months (interquartile range, 29.8-56.8 month). The median number of harvested LN was 22 (interquartile range, 16-27) and positive LN was 2 (interquartile range, 1-5). Median LNR was 14.3% (interquartile range, 5.3-25.0%). Hazard ratio (HR) for DFS of LNR by multivariate Cox regression analysis including putative confounding factors for prognosis was 1.009 (95% confidence interval [CI], 0.991-1.027), which was not statistically significant. (p=0.338). For OS, the HR of LNR was 1.005 (CI, 0.667-1.005) and it was not significant either.

Conclusion: In the present study, LNR was not a significant predictor for prognosis in colon cancer. Further evaluation with a larger cohort with detailed co-variate investigation would be required to verify the clinical significance of LNR.

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P-350 Maintenance trastuzumab in the setting of second-line treatment in HER2 overexpressing metastatic gastric and gastroesophageal junction adenocarcinoma: Experience of our centre

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Background: Standard of care (SOC) in patients with advanced gastric or gastroesophageal junction (G/GEJ) adenocarcinoma after progression to 1st line platinum/fluoropyrimidine-based treatment is the combination of paclitaxel and ramucirumab (P/R), based on the results of the RAINBOW trial. Trastuzumab (T) has shown clinical benefit in HER2 overexpressing cases. Nevertheless, literature published so far is scant regarding trastuzumab combination with second-line P/R. We report here our experience in the use of maintenance trastuzumab in combination with P/R in HER2 overexpressing G/GEJ adenocarcinoma patients.

Methods: Correlative HER2 positive G/GEJ patients with progression of disease as per RECIST criteria after first-line treatment based on platinum, fluoropyrimidines, and trastuzumab were included in this study and treated between January 2017 and December 2019. Statistical analysis was performed according to non-parametrical tests based on the Mann-Whitney U test to compare progression-free survival (PFS) between both groups. Overall Response Rates were evaluated according to Fisher's exact test.

Results: A total of 12 patients were included in this analysis. 8 of them (66,6%), underwent maintenance T together with P/R after confirmed progression to first-line. The remaining cases (n=4; 33,3%) were treated according to with to SOC based on P/R without T. ORR in the T+P/R group was 62.5% (n=5) reaching a disease control rate up to (DCR) of 87% (n=7) in contrast to SOC in which no response was observed showing a DCR of 50% (n=2). Statistical comparison using Fisher's exact test did not reveal statistical significance (p=0.07) likely due to insufficient sample size. Moreover, median PFS was 5.5 months among patients receiving T+P/R and 4.5 months in the P/R group. No significant differences were found between groups (Mann Whitney U test p=0.55). In terms of toxicity, maintenance trastuzumab did not demonstrate treatment-related increased cardiotoxicity. The overall incidence of grade 3 or 4 adverse events according to the CTCAE 5.0 was 25%, 2 cases in the P/R group (1 bleeding, 1 nonfebrile neutropenia) and 1 in the combination with trastuzumab (thrombosis).

Conclusion: Combination of trastuzumab and SOC P/R could offer benefits in terms of response and progression-free survival, although no statistical differences were seen probably as a result of our limited sample size. Nevertheless, combination therapy does neither seem to add more toxicity than that expected with the SOC based on P/R alone, nor does it appear to have remarkable cumulative cardiovascular toxicity in our series. Despite our limitations, in patients with HER2 overexpressing GEJ adenocarcinoma, maintenance trastuzumab with second-line P/R until further progression could be a feasible option in patients with good performance status who are fit for combined therapy.

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P-351 RNA sequencing for personalized therapy prescription in colon cancer

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Background: Analysis of mutation profiles in cancer patients has no clinical benefit in 80-90% of cases [1]. Gene expression analysis could potentially complement standard detection of clinically relevant mutations. We previously used gene expression and pathway analysis based method Oncobox for prescribing off-label sorafenib and pazopanib in an unresectable metastatic cholangiocarcinoma case, which resulted in successful management of the disease [2]. In addition, it allowed prediction of tumor response and time to progression in gastric cancer patients treated with ramucirumab [3]. In this study, we focused on the retrospective analysis of patients with colorectal cancer.

Methods: RNA was extracted from FFPE tumor biopsies and gene expression was profiled using RNA sequencing. Gene expression profiles were analyzed using Oncobox platform, which provided personalized rating of target drugs for each case. The Oncobox method is based on calculating "balanced efficiency score" (BES) for each drug and ranking of target drugs according to this parameter [4]. Performance of the Oncobox predictions was statistically assessed by calculating area under receiver operating characteristic curve (AUC).

Results: We profiled gene expression in colorectal cancer samples (n=14) with known target drug response status and calculated BES for each sample. We enrolled 14 colorectal cancer patients: 11 females and 3 males, age range: 37-72 years. 9 patients had distant metastases at time of the diagnosis. In total, 30 therapy outcomes were collected for 14 patients. Control over disease was reported for 8 therapies (5 stable disease and 3 partial responses), 22 therapies resulted in progressive disease. Then we assessed the performance of BES as a predictor of tumor response. We found that the rank of the drug in the Oncobox report, based on BES, could effectively predict tumor response (AUC = 0.76). First-line target therapy outcome was available for 12 patients. The outcomes were control over disease for 5 patients (3 stable disease, 2 partial responses), and progressive disease for 7 patients. Performance of BES scores in this case (AUC = 0.94) was higher than in the analysis of all available outcomes. This suggests that using fresh biopsy is essential for the quality of treatment response predictions using Oncobox system.

Conclusion: Analysis of RNA sequencing data for tumor biopsies may potentially be helpful for personalized prescription of targeted therapeutics in advanced gastrointestinal tumors. References: 1. Marquart J, et al. Estimation of the Percentage of US Patients With Cancer Who Benefit From Genome-Driven Oncology. JAMA Oncol. 2018. 2. Poddubskaya EV, et al. Personalized prescription of tyrosine kinase inhibitors in unresectable metastatic cholangiocarcinoma. Exp Hematol Oncol. 2018. 3. Sorokin M, et al. RNA sequencing profiles and diagnostic signatures linked with response to ramucirumab in gastric cancer. Cold Spring Harb Mol Case Stud. 2020. 4. Tkachev V, et al. Oncobox Method for Scoring Efficiencies of Anticancer Drugs Based on Gene Expression Data. Methods Mol Biol. 2020.

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P-352 Docetaxel, oxaliplatin, and 5-fluorouracil in metastatic gastric/gastroesophageal junction adenocarcinoma: A single-center experience

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Background: The combination of docetaxel, cisplatin, and 5-fluorouracil (5-FU) demonstrated high response rates in advanced gastric cancer, albeit with increased toxicity. Given the efficacy of platinum-taxane-fluoropyrimidine regimens, in this retrospective study we evaluated the efficacy and toxicity of docetaxel, oxaliplatin, and 5-FU (DOF) for the treatment of metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma.

Methods: In this study, 34 patients with metastatic gastric or GEJ adenocarcinoma who were treated with DOF regimen between January 2017 and June 2019 were retrospectively evaluated. Chemotherapy was administered every 14 days, with combined docetaxel (50 mg/m^2) and oxaliplatin (85 mg/m^2) followed by 5FU (2400 mg/m^2).

Results: Overall Response Rate (ORR) and Disease Control Rate (DCR) were 58.8% and 70.6%, respectively. Median Progression Free Survival (PFS) and Overall Survival (OS) were 9.4 months (95% CI [6.4-11.3]) and 14.6 months (95% CI [11.8-21.6]), respectively. Grade 3-4 toxicities occurred in 21 patients (61.7%), including neutropenia (20.3%), neurologic (18.9%), and diarrhea (16.0%).

Conclusion: DOF demonstrated a high response rate, expected safety profile, and prolonged survival and remains an option for select patients with metastatic gastric or GEJ adenocarcinoma.

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P-353 Colorectal cancer liver metastases challenges and potential opportunities: Systematic review and meta-analysis

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Background: Colorectal cancer liver metastases (CLMs) occur in 25%-30% of CRC patients which represent a heterogeneous cohort of patients based on the extent of the disease and the eligibility for resection. Resectable liver-confined metastasis is the best scenario as surgery can offer cure with a 5-year survival of about 40%. The caveat is that only 25% of CLMs are initially resectable so preoperative treatment could confer conversion of unresectable and borderline CLMs into respectability. Practical speaking, there are no guidelines that help clinical decision-making in the management of CLMs with regards to resectability criteria and best systemic treatment to be used.

Methods: A literature search of the Scopus and Ovid databases was conducted to identify studies of perioperative systemic treatment in liver-confined resectable and unresectable CLMs. The analysis was stratified according to study design either RCTs or single-arm cohort studies and systematic review was performed of all identified studies. SPSS version 20 was used to calculate the overall response rate (RR), resection rate R0 and correlation between RR and R0.

Results: From 1440 articles initially retrieved, 28 studies were included in the analysis, of them 8 were RTCs and 20 were cohort studies so the were analyzed in two seperate analyses. Regarding the 8 RTCs, there was no impact of different treatment protocols on the R0 resection rate (p=0.734), with no added benefit of targeted agents on the R0 rate of resection (p=0.634). The correlation between the overall response rate and the resection rate was not significant so achieving a high response rate was not a predictor factor for R0 resection (P=0.305). For the other 20 cohort studies, chemotherapy alone was used in 9 studies while in 11 studies chemotherapy was used in combination with either bevacizumab or cetuximab in wild KRAS. The mean response rate for cetuximab in combination with chemotherapy was (68.8%) which was significantly higher than chemotherapy with bevacizumab or chemotherapy alone (P=0.048). There was a correlation between RR and R0 rates (R=+0.496) but not significant (P=0.06). According to the resectability status, EORTC 40983 study showed that the RR was (43%) for FOLFOX4 preoperatively with same R0 rate when compared to upfront surgery. FOLFOX4 was also used in 3 cohort studies and achieved higher RR and R0 rate as primary endpoints when compared with other regimens. Anti-EGFR monoclonal antibodies combined with chemotherapy, resulted in detrimental effects when used preoperatively in resectable CLMs in one RCT and one cohort study. For unresectable CLMs, chemotherapy alone was used in 6 studies and the irinotecan-based regimen achieved the highest R0 rate (33%). Bevacizumab was used in two trials with a conversion rate of 42% when combined with CAPOX. Cetuximab was used in 7 studies with RR (79.7%) and R0 (80%) in one study.

Conclusion: For initially resectable CLMs, surgery is the cornerstone for treatment albeit the question about the value of preoperative chemotherapy in absence of clear survival benefit remains. In unresectable CLMs achieving higher RR, using targeted agents correlates with a higher R0 rate but further RTCs are needed to investigate the significant effect of the combination on conversion rate and survival.

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P-354 Association between tumor regression with tumor location and inflammatory biomarkers in patients with resectable gastric cancer and gastroesophageal junction cancer who underwent perioperative chemotherapy: Multicentric data from Peru

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Background: FLOT perioperative chemotherapy is the standard treatment in patients with resectable gastric and gastroesophageal junction (GEJ) cancer. There is a lack of information if tumor location or inflammatory biomarkers are associated with tumor regression after chemotherapy treatment. The aim of this study is to determine associated factors with tumor regression after FLOT therapy.

Methods: This is a retrospective observational study of a single patient cohort. Clinical records of patients with clinical stage II and III gastric and GEJ cancer were recollected, since January 2018 to December 2019, in ALIADA cancer center and Rebagliati Hospital, in Peru. Clinical stage was determinate using AJCC 8th edition and was evaluated before therapy and after surgery to determine tumor regression. Tumor location was evaluated in endoscopy reports; meanwhile NLR and PLR were calculated from blood counts before the beginning of chemotherapy. Clinical records with incomplete data were excluded. The bivariate statistical analysis was performed with Chi-squared test, Odds ratio and logistical regression was performed with a confident level of 95% ($p< 0.05$).

Results: 52 clinical records were evaluated and finally 41 were included. 63% were male and the mean age was 58 years. All patients had adenocarcinoma type histology, 65% of them had diffuse subtype and the rest intestinal subtype. The 63% of patients had gastric cancer distributed as follows: 50% in corpus, 35% in antrum, 10% in cardia and 5% fundus. 37% of patients had GEJ cancer; the 53% of them were siewert II and 47% siewert III. The 90% of patients had clinical stage III and 10% clinical stage II. All patients received four cycles of FLOT and the 82% were operated. 78% of patients had tumor regression after chemotherapy; 12% of them achieved pathological complete response. The 17% of patients had stable disease and 24% had progression of disease, 71% of them progressed to peritoneum. Diarrhea (27%) and emesis (20%) were the most frequent adverse events presented in our population meanwhile neutropenia (8%) and anemia (5%) were the most frequent grade III-IV adverse events. There was no statistic difference between patients who had tumor regression compared to patients who did not have response to chemotherapy with respect to mean NLR (2.61 ± 0.27 vs 2.84 ± 0.31, $p>0.05$) and mean PLR (2.61 ± 0.27 vs 2.84 ± 0.31, $p>0.05$). Tumor regression was more frequent in patients with gastric cancer (69% vs 63%, $p=0.02$). There was no statistic difference in the multivariate analysis (OR = 148, IC95% = 0.34-6.40).

Conclusion: Tumor regression was associated with tumor location in bivariate analysis, being more frequent in patients with gastric cancer; however there was no statistic difference in multivariate analysis. Studies with bigger amount of patients are needed to validate this association.

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P-355 Trastuzumab-based treatment of HER2-positive metastatic gastric cancer

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Background: The study aimed to evaluate trastuzumab-based chemotherapy in HER2 positive gastric cancer.

Methods: The data of 63 patients were retrospectively reviewed. The demographic, histopathological, treatment, and clinical features of the patients were recorded. Chemotherapy regimens that were DCF+T (docetaxel, cisplatin, fluoropyrimidine, and trastuzumab), PF + T (platinum, fluoropyrimidine, and trastuzumab), and C+T (capecitabine and trastuzumab) were compared to by log-rank test.

Results: The median follow-up period was 12.9 months (range: 1.2-80,2 months). The median age at diagnosis was 60,5 years (range: 27-91 years). The percentages of female and male patients were 27% and 73%, respectively. The number of de novo metastatic patients was 44 (69.8%). The median OS was 13.6±2.8 months (8-19.3 months). With trastuzumab-based chemotherapy, the complete response rate was 6.3%, partial response 39.7%, and stable response 9.5%. Chemotherapy regimens were not different in terms of overall survival (OS) ($p=0,452$) and progression-free survival (PFS) ($p=0,893$). The ratio of grade 1-2 toxicity was 79.6% and grade 3-4 toxicity 20.6%. In multivariate analysis, ECOG performance status ($p< 0,001$) and having three or more sites of metastasis ($p=0,001$) were negative prognostic factors for OS.

Conclusion: In this study, we determined that adding taxane chemotherapy in fluoropyrimidine and platinum regimens did not affect OS and PFS.

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P-356 phase Ib study of irinotecan, bevacizumab and biweekly trifluridine/tipiracil in patients with metastatic colorectal cancer refractory to fluoropyrimidine and oxaliplatin: Preliminary report of MODURATE study

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Background: Trifluridine/tipiracil (FTD/TPI) showed survival benefit as monotherapy and in combination with bevacizumab (BEV) in the late-line treatment for metastatic colorectal cancer (mCRC). Preclinical studies showed FTD/TPI additively enhanced the anticancer effect of irinotecan (IRI), and a phase Ib study of a standard schedule of FTD/TPI with biweekly IRI demonstrated the expected antitumor activity although further investigation is warranted due to high incidence of febrile neutropenia. This phase Ib study of biweekly FTD/TPI with IRI and BEV for previously treated mCRC was conducted.

Methods: This study consisted of 2 parts: a dose-escalation part (part 1) to determine the recommended phase II dose (RPTD) and an expansion part (part 2) to further evaluate the safety and efficacy. Key eligibility criteria included histologically confirmed colorectal adenocarcinoma, failure or intolerance to fluoropyrimidine and oxaliplatin, no prior therapy with FTD/TPI and IRI, age of 20-75 years, ECOG PS of 0—1. Pts received two-week cycles of treatment with FTD/TPI (twice daily, days 1 to 5), IRI (day1) and BEV (5mg/kg, day1). Five dose levels of FTD/TPI and IRI are planned as follows; Level 1: 25 mg/m 2 and 180 mg/m 2, Level 2a: 30 mg/m 2 and 180 mg/m 2, Level 3a: 35 mg/m 2 and 180 mg/m 2, Level 2b: 30 mg/m 2 and 150 mg/m 2, Level 3b: 35 mg/m 2 and 150 mg/m 2 . In part 1, patients underwent a 3+3 design schema to evaluate the dose limiting toxicity (DLT). The RPTD was defined as the highest dose level where no more than 2 of 6 pts experienced a DLT during 2 cycles.

Results: Between Oct 2016 and May 2019, 18 pts were enrolled to part 1 (3 pts in Level 1/2a/3a/2b and 6 pts in Level 3b). Pts characteristics were as follows; median age, 68 (33-74) years; male/female, 10/8; PS 0/1, 13/5; right-/left-sided tumor, 5/13; number of metastatic site 1/>1, 6/12; RAS mutant/wild, 12/6; prior history of BEV/anti-EGFR, 7/6. DLT was observed in 5 pts; grade 3 febrile neutropenia in 2 pts, grade 3 gastrointestinal perforation, grade 2 anorexia resulting >2 week delay in subsequent cycle initiation, and grade 3 ALT elevation in each 1 pt. Among 6 pts enrolled to Level 3b, 2 pts experienced DLT and the RPTD was determined Level 3b. At the data cut-off date as of Mar 14, 2019, 16 pts terminated protocol treatment, due to disease progression in 12 pts and adverse events in 4 pts, and the median cycle of treatment administrated was 7 (range, 1-42+). As preliminary efficacy analysis in part 1, partial response and stable disease was observed in 4 (22%) and 11 pts (61%), respectively. The most common grade 3/4 adverse event was neutropenia (61%), and the incidence of febrile neutropenia was 11%. No treatment-related death was observed.

Conclusion: The RPTD of biweekly FTD/TPI with IRI and BEV was determined to be 35 mg/m 2 of FTD/TPI, 150 mg/m 2 of IRI, and 5mg/kg of BEV. An additional 10 pts were already enrolled in the expansion part of the study at this dose and follow-up is underway.

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P-357 The frequencies and prognostic significance of ABO blood and rhesus (D) groups in HER2-positive gastric cancer

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Background: The ABO antigens are highly expressed on the surface of epithelial cells of the gastrointestinal tract. Alterations in surface glycoconjugates on the cell may trigger the development of gastric cancer. The relationship between gastric cancer

and blood group A was firstly discovered by Aird et al. The study aims to evaluate the cancer distributions and prognostic significance for the HER2 positive gastric cancer.

Methods: The data of 112 patients were retrospectively reviewed. The ABO blood groups, clinical, and histopathological data of the patients were recorded. The ABO blood group distributions of the patients were compared to healthy donors (n:130,909) by chi-square test.

Results: The median follow-up period was 15.5 months (range: 1.07-81.1 months). The percentages of female and male patients were 29% and 71%, retrospectively. The median age at diagnosis was 61 years (range: 24-91 years). The median OS was 17.9±2.3 months (13.2-22.5 months). Overall distributions of ABO blood groups were different between patients (57.1% A, 10.7% B, 6.3% AB, 25.9% O) and controls (41.87% A, 15.29% B, 7.91% AB, 34.93% O) (p=0.013). The distribution of Rh factor was comparable between patients and the control group (p=0.074). In univariate analysis, ABO blood groups were not a prognostic factor on OS.

Conclusion: In this study, we determined to the A blood frequency in HER2 positive gastric cancer is more common than other blood groups. 0 blood groups may be protective for HER2 positive gastric cancer.

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P-358 Mutational status in Ras/Raf/MAPK signaling pathway in Moroccan colorectal cancer patients

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Background: Activation of multiple signaling pathways of the Epidermal Growth Factor Receptor (EGFR), the RAS-RAF or the PI3K-PTEN-AKT pathways, is considered the most common carcinogenic mechanisms in colorectal cancer (CRC). Mutated RAS genes and BRAF gene encode constitutive activation of the Ras/Raf/MAPK Signaling Pathway, even in the absence of growth factor signaling. The result is a sustained proliferation signal within the cell. In our study, we aimed to report the frequency of RAS/RAF mutations in Moroccan colorectal cancer (CRC) patients.

Methods: A retrospective analysis conducted in the Department of Medical Oncology at Cheikh Khalifa Hospital in Casablanca, Morocco, between January 2018 and December 2019. All patients diagnosed with CRC and studied for KRAS/NRAS/BRAF status were included in this study. The samples were tested and analyzed using the MassARRAY System and software.

Results: Fifty-one patients were included in our investigation: 27 males (52,9%) and 24 women (48,1%). Median age of patients was 59,8 years. Forty-three patients (84,3%) had metastatic colorectal cancer, and eight patients (15,7%) were non-metastatic. Twenty-two patients (43,1%) had a KRAS mutation confirmed by PCR. In this population, exon 2 was mutated in twenty-six patients (92,8%) and exon 4 in two cases (7,2%). One patient had an NRAS mutation (2%), while twenty-eight other patients (54,9%) had RAS wild-type. Two patients (3,9%) had a BRAF mutation in the V600E protein.

Conclusion: Almost half of our patients (49%) presented with a mutation in the Ras/Raf/MAPK signaling pathway. Further studies, in larger numbers of patients, are needed to confirm these findings.

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P-359 Biliary tract carcinoma: Management patterns and outcome

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Background: Biliary tract cancer (BTC) is relatively rare. It can be intrahepatic, extrahepatic or in the gallbladder. The disease is difficult to diagnose and usually fatal due to its delayed clinical presentation and lack of effective non-surgical treatment modalities. We aimed to report epidemiological features and outcomes of BTC in a Tunisian population and to identify its potential prognostic factors.

Methods: We retrospectively reviewed 67 cases of BTC treated between 2012 and 2016. Clinical, radiological, pathological and therapeutic results were investigated. We used Kaplan-Meier method to evaluate survival.

Results: Median age was 60 years old (range 40-89), with a male predominance (sex-ratio = 1.48). Smoking was the most common known risk factor (43.3%). Tumours were intra-hepatic in 23.9% and extra-hepatic in 76.1% of cases (40.3% in the gallbladder, 20.9% in the hepatic hilum and 14.9% in the distal bile duct). Non-metastatic cases (43%, n=29) were localized in 11% and locally advanced in 32%. Metastatic sites were mostly liver in 22 cases and peritoneum in 7. Biliary drainage was indicated in 22.4% (n=15) using a percutaneous procedure in 7 cases, endoscopy in 3 cases and surgery in 5 cases. Surgical resection performed in 19 patients was R0 in 61.9%, R1 in 23.8% and R2 in 14.3%. Adjuvant chemotherapy was given to 22.7% (n=15) of patients using GEMOX protocol in 62.5%. The most commonly used first-line chemotherapy was gemcitabine in 56.7% of cases. All grade toxicity was seen in 74.5% of cases, which was mainly haematological with thrombocytopenia in 23.7% and neutropenia in 18.4%. Seventy percent (n=28) of patients received 2nd-line chemotherapy and only 18% of patients received 3rd-line chemotherapy. Overall survival for all sites was 12.75 months. Good PS (0-1) (16 months vs 8 months, p = 0.005), surgical treatment (22 months vs 10.9 months, p=0.003) and stage were significantly associated with OS. Surgical resection showed a non-significant tendency toward better survival in R0 resection compared to R1 and R2 (21 months, vs 14 months vs 11 months, p=0.4).

Conclusion: Biliary tract cancer has a poor prognosis. Surgery remains the most effective therapy, in patients with good performance status.

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P-360 EGFR-inhibitors in metastatic wild-type RAS colorectal cancer: Experience of the oncology department of Mohammed VI University Hospital in Marrakech

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Background: Cetuximab and panitumumab obtained approval from the FDA in the treatment of metastatic colorectal cancer wild-type RAS in 2004 and 2006, respectively. Since June 2016, these anti-EGFRs became available in our training, which gave hope to our patients.

Methods: We conducted a retrospective study of patients with metastatic colorectal cancer wild-type RAS under EGFR inhibitors, admitted to our department between June 2016 and September 2018. The endpoints were to describe the epidemiological, clinical, anatomopathological features of the Moroccan population and report their therapeutic characteristics to compare them to the literature data. SPSS software was used for statistical analysis. Data collection was carried out while respecting the anonymity and confidentiality of our patients.

Results: 24 patients received treatment with EGFR-inhibitors (panitumumab or cetuximab), sex ratio F/M = 1.6. Mean age was 52 years (range 25 to 71years). Rectal syndrome was the most frequent revelation mode (37.5%). The right colon, left colon and lower rectal localizations were met respectively in 37.5%, 25% and 37.5% of the cases. 50% of the patients in our series were immediately metastatic and 50% recurred after adjuvant treatment with a median of disease-free survival of 18 months (range: 6- 32 months). The most frequent metastatic sites were the peritoneum (75%) and the liver (62.5%). Adenocarcinoma represented the main histological type. All patients had wild type RAS and BRAF. EGFR-inhibitors were received in third-line treatment in combination with chemotherapy in 62.5% of cases, on the first-line treatment with chemotherapy in 25% of cases and both in first- and third-line in 12.5% of cases as part of a rechallenge strategy of EGFR-inhibitors. The evolution after 6 months of treatment was marked by a partial response, stability, and progression in 50%, 25%, 25% of the cases, respectively. After 18 months of median follow-up, median progression-free survival in the first-line was 10.3 months and 6.9 months in the third-line.

Conclusion: EGFR-inhibitors improved outcomes of metastatic wild-type RAS colorectal cancer in first-line treatment. However, the majority of our patients received EGFR-inhibitors in third-line treatment with modest results in progression-free survival compared to those who received it in the first line. Hence favoring EGFR-inhibitors in the first-line treatment in order to improve survival outcomes of our patients.

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P-361 High expression levels of circulating miRNA-618 and miRNA-203a-3p are associated with prolonged survival in patients with metastatic colon cancer

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Background: Circulating microRNAs (miRNAs) are promising non-invasive biomarkers for colorectal cancer (CRC). The aim of the present study was to evaluate the role of five circulating miRNAs — miRNA-618, miRNA-26a-1, miRNA-15b-5p, miRNA-200c, miRNA-203a-3p which are involved in key cell signal processes in tumors such as proliferation, migration, and apoptosis. These miRNAs are thoroughly investigated in tumor tissue, but little is known regarding their levels of expression in the blood of patients with CRC.

Methods: 97 patients with colorectal metastatic disease before starting the chemotherapy and 80 healthy controls were investigated. miRNAs were isolated from serum samples by commercial kit. cDNA was generated from each sample. All miRNA data were analyzed by normalization using U6 as a constitutively expressed endogenous control. qRT-PCR was performed and the relative expression of each miRNAs was calculated by using 2 -ΔΔCt method.

Results: Serum miRNA-618, miRNA-26a-1, miRNA-15b-5p, miRNA-200c, and miRNA-203a-3p were significantly overexpressed in CRC patients. Among all investigated miRNAs only two of them were associated with CRC patient survival. Patients with low expression levels of circulating miRNA-618 had significantly shorter median overall survival (OS) of 14 months (95% CI, 8.63-19.37) as compared with those with high expression - 21 months (95% CI, 14.36-27.64) (p=0.003). Also, patients with low levels of miRNA-203a-3p had a significantly shorter median OS of 14 months (95% CI, 8.81-19,19) compared with 20 months in patients with higher expression in the blood (95% CI, 17.05-22.95) (p=0.012). In addition, Cox proportional hazards regression model showed that low levels of miRNA-618 and miRNA-203a-3p expressions were associated with a shorter OS, HR=2.02 (95% CI, 1.24-3.29; p=0.005) and HR=1.77 (95% CI, 1.08-2.91; p=0.025), respectively.

Conclusion: Our data suggest that only expression levels of anti-oncogenic miRNA-618 and miRNA-203a-3p in sera could be useful as non-invasive prognostic biomarkers in CRC patients.

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P-362 SIBO and lactose intolerance in patients receiving chemotherapy treatment for colorectal or gastric cancer

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Background: Worldwide, colorectal cancer (CRC) and gastric cancer (GC) are respectively the third and the fifth most prevalent cancers. Diarrhea (characterized by ≥3 episodes a day) is a common symptom in chemotherapy or radiotherapy treatment of GC or CRC cancer. Treatment-related diarrhea is the most common toxicity, which may reduce treatment tolerance. However, in addition to surgical resections and chemotherapy, changes in intestinal microbiota can lead to lactose intolerance and small intestinal bacterial overgrowth (SIBO), which cause diarrhea. The aim of the study was to evaluate SIBO and lactose intolerance incidence and the relationship with nutritional status and presence of diarrhea.

Methods: This is a descriptive and observational study with patients of both sexes, over 18 years old, in treatment in the Gastro-Oncology outpatient clinic of the Universidade Federal de Sao Paulo. The study was submitted to the Local Ethics Committee and was approved under CAAE no 81597517.0.0000.5505. Patients with a confirmed diagnosis of CRC or GC during chemotherapy treatment were included. To detect bacterial overgrowth and lactose intolerance, the expired hydrogen test was used. The number and aspects of the evacuations and toxicity degree were collected. For the nutritional assessment, weight and height were performed to calculate the BMI and the Patient-Generated Subjective Global Assessment (PG-SGA).

Results: Thirty tree patients were included, 29 with CRC and 3 with GC. The majority were male (57.57%), mean age of 60.03 (±10.1) years old and 60.6% were more than 60 years old. Most of the tumors were adenocarcinoma (84.9%). Most of the patients underwent chemotherapy with a fluoropyrimidine (5FU or capecitabine) and oxaliplatin (54.5%). Diarrhea was present in 57.5% cases and 13 (39.4%) had grade II/III toxicity. According to BMI, 78.9% were eutrophics, obese or overweight, but according to PG-SGA, 84.9% had moderate or severe nutritional risk grade. Between the patients, 45% had lactose intolerance and 9% SIBO. Although the number of patients was very small, we did not find any relationship between SIBO or lactose intolerance and undernutrition or diarrhea.

Conclusion: Diarrhea was a frequent symptom in patients receiving chemotherapy treatment for CRC or gastric cancer independent of the presence of SIBO or lactose intolerance. Surgery and chemotherapy treatment impacted in the intestinal habit of patients. Diagnosis of other causes of diarrhea may contribute to better tolerance of treatment and improved quality of life.

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P-363 Clinical-pathological correlation of the presence of microsatellite instability in patients diagnosed with locally advanced gastric adenocarcinoma from Costa Rica

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Background: In Costa Rica gastric adenocarcinoma is the second leading cause of cancer-related death. The development of this malignancy is a complex multistep process involving numerous genetic alterations. Gastric cancer development proceeds through three different molecular pathways: the chromosomal instability (CIN) pathway, the mutator phenotype (or microsatellite instability pathway, MSI) pathway and the CpG island methylator phenotype (CIMP) pathway. The mutator phenotype pathway is characterized by frequent mutations in regions of the DNA containing microsatellite sequences. Microsatellite stable tumours have low levels of microsatellite instability (MSS/MSI-L), and they are developped through the CIN pathway, whereas tumours with high microsatellite instability (MSI-H) are considered to develop through the mutator phenotype carcinogenic pathway. The objective of the study is to analyze the clinical, demographic and disease-free survival characteristics of patients with stage II and III clinical cancer who have microsatellite instability.

Methods: An observational retrospective cohort study was formalized; it was developed in patients with confirmed diagnosis of stage II & III gastric adenocarcinoma at the San Juan de Dios Hospital in the period from 2010 to 2015. Data were retrieved from clinical records and MSI was determined by immunohistochemistry.

Results: A total of 255 cases diagnosed with stage II and III gastric adenocarcinoma were analyzed. 60.4% of which were male and 39.6% female, with a mean age of 67.5 years. Moderately differentiated adenocarcinoma was the most frequent reported histology for 37.2%, located in the antrum 45.9%, intestinal type 49%. Clinical stage II was the most frequent stage (91,3%%). A total of 9.2% patients presented MSI, with MLH1 absent in 100%. For patients with MSI, the clinical-pathological characteristics were female sex in 60,8%, with a median age of 67.2 years, predominance of intestinal histology 87%, predominantly antrum location 43,5% and less nodal invasion in 52,2%. The determination of median progression-free survival for the group without MSI was 36.7 (range: 0.07-137.6) months and a median of 17.9 months for the group with MSI present was 73.2 (range: 21.4-120.1) months with a median 65.8 months.

Conclusion: MSI status could be a useful biomarker in local or locally advanced gastric cancer to predict its prognosis. The presence of MSI in gastric cancer was associated with higher progression-free survival than the MSS tumours, as reflected in a more favorable clinical and pathological characteristics.

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P-364 Higher amount of KRAS mutations in pre-operative plasma cell-free DNA predicts shorter survival after liver metastasectomy in colorectal cancer patients

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Background: The liver is the most common site of colorectal cancer metastasis. Liver metastasectomy provides potentially curative treatment for a certain portion of patients with liver metastases. Novel biomarkers predicting patient survival in this specific clinical scenario are urgently needed. Determination of circulating cell-free tumor DNA (ctDNA) can be used as a liquid biopsy method for minimally invasive assessment of the disease course. In this study, we assessed the possibility of liquid biopsy based on KRAS-oncogene mutated ctDNA from peripheral blood to predict survival of colorectal cancer patients undergoing liver metastasectomy.

Methods: The quantitative estimation of 7 KRAS G12/G13 mutations was performed by ddPCR in 71 liver metastasis tissue samples (FFPE) and in 47 preoperative and postoperative plasma samples. Tissue DNA was isolated by AllPrep DNA/RNA FFPE kit (Qiagen, Hilden, Germany). Total circulating DNA was isolated from 1 ml plasma by the QIAamp Circulating Nucleic Acid Kit kit (Qiagen, Hilden, Germany). Quantitative estimation of 7 KRAS G12/G13 mutations was done by ddPCR™ KRAS G12/G13 Screening Kit (Bio-Rad Laboratories, Hercules, USA) on QX200 Droplet Digital PCR System (Bio-Rad Laboratories, Hercules, USA).

Results: Tissue KRAS positivity in colorectal cancer liver metastases (CLM+) was detected in 33 of 69 pts. (47.8%). Pre-operative plasma samples (PL) were available in 30 patients, 11 (36.7%) of them were KRAS positive (PL+). Both tissue and plasma samples were available for 29 pts. Of them, PL+ was detected in 10 of 16 CLM+ pts. (62.5%), whereas 12 of 13 CLM- patients were PL- (92.3%). Pre-operative PL+ compared to PL- pts. showed a trend to shorter DFS after liver surgery (357 vs. 470 days, P=0.074), but not OS (P=0.234). Percentage increment in pre-operative plasma KRAS fractional abundance (FA; proportion of the mutant allele in total DNA) predicted shorter OS (HR 1.04, P=0.049) and a trend to shorter DFS (HR 1.037, P=0.073). Pts. positive for KRAS mutations in both tissue and pre-operative plasma samples CLM+/PL+ (n=10) compared to CLM+/PL- pts. (n=6) showed shorter DFS (329 vs. 470 days, P=0.051), but not OS (P=0.328). Both pre- and post-operative plasma samples were available in 17 pts. Of them, 12 pre-operative PL- remained negative after surgery, whereas 5 pre-operative PL+ became negative after liver surgery as well. There was no one plasma KRAS positive pt. after surgery.

Conclusion: KRAS mutations can be detected and quantified in pre-operative plasma cell-free DNA before resection of colorectal cancer liver metastases with an incomplete overlap with quantification from tissue biopsy. Higher fractional abundance of pre-operative plasma KRAS mutations predicts shorter post-operative OS. Patients with dual positivity of KRAS mutations in both pre-operative plasma and tumor tissue experienced the worst DFS after liver metastasectomy. Liquid biopsy, based on the detection of ctDNA can serve as a prognostic factor for colorectal cancer patients undergoing liver metastasectomy.

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P-365 Association between baseline serum levels of miRNA-143 and hepatocyte growth factor in patients with RAS wild type metastatic colorectal cancer treated with first-line anti-EGFR therapy

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Background: Recently the prognostic role of microRNA-143 has been proven by ours and several studies and one meta-analysis. Additionally, high serum levels of hepatocyte growth factor (HGF) were found to be associated with resistance to anti-EGFR antibodies in KRAS wild-type metastatic colorectal cancer (mCRC). The possible interplay between miRNA-143 and HGF as predictive factors in RAS wild mCRC is unknown.

Methods: Sera samples from 38 patients with mCRC before first-line therapy with anti-EGFR antibodies and chemotherapy and from 35 healthy controls were collected. The expression levels of miRNA-143 in sera samples were determined. U6 was used as endogenous constitutively expressed control. Relative gene expression was calculated using the 2-ΔΔCt method. HGF concentrations in sera were measured by using a commercially available ELISA. Statistical analyses were done by SPCC 23 version.

Results: Reduced levels of miR-143 expression in sera were detected in mCRC patients compared to healthy controls. There was a difference between HGF serum levels in mCRC patients and healthy controls. The estimated disease control rate was 47.3% with mean PFS=9.94 (±10.9, SD) months. ANOVA results showed higher levels of expression of miRNA-143 and HGF (767.5 pg/ml) in patients with progressive disease in comparison to patients with remission and stable disease, in patients with progressive disease, and in comparison to patients with remission and stable disease (for miRNA-143 — 1,06 and for HGF 452,4 pg/ml), but without statistical significance (p=0.1). A trend to statistical significance was found between expression levels of miRNA-143 and HGF and response rate (Pearson, r=0.30 and r=0.25, p=0.06). In addition, a statistically significant correlation was established between expression levels of miRNA-143 and HGF (Pearson, r=0.35, p=0.04).

Conclusion: Small patient numbers preclude definitive conclusions, but positive correlation between miRNA-143 and HGF baseline levels confirm their mutual role in the EGFR signaling pathway. In addition, high miRNA-143 and HGF baseline levels are potentially predictive markers of resistance to anti-EGFR therapy in mCRC patients.

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P-366 Long-term quality of life in patients treated for anal cancer: Self-reported bother of symptoms

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Background: Survivorship after treatment for anal cancer includes living with side-effects. Few studies have explored the long-term effects of poor function in relation to Quality of Life (QoL). The aim of this study was to explore QoL in patients treated for anal cancer up to 6 years after treatment and to evaluate the effect of patient-reported bother related to dysfunction.

Methods: We conducted a cross-sectional national study inviting all surviving patients treated for anal cancer between 2011 and 2013 in Sweden. Patients identified using the Swedish Cancer Registry were contacted three and six years after treatment and were asked to answer a comprehensive questionnaire. Clinical data were extracted from patient charts. Risk for poor quality of life was calculated adjusting for known factors (depression, Sense of Coherence, age, and sex) that can have influence QoL. Results were compared to a Swedish reference population.

Results: 195 patients (3 years) and 152 patients (6 years) participated in the study. 150/195 (77%) were women. Median age 65 years. 99% were treated with a curative intention and 51% received chemoradiotherapy. 60% of the patients reported impaired QoL both at 3 and 6 years. Patients reported more than three times higher bother of urinary and bowel function compared to the reference population but only twice as much bother of sexual function. Bother of anal pain and bowel function were significantly related to poor QoL at three years in multivariate analysis (RR 1.36 (1.06-1.73) and RR 1.54 (1.06-2.23)). At six years this was true for bother of bowel function and urinary function. At no time point did bother of poor sexual function affect QoL. Patients with bother of several functions had more reduced QoL both at 3 and 6 years which was similar to the reference population.

Conclusion: Many survivors of anal cancer have impaired QoL up to six years after diagnosis. It is important to address the patients self-reported bother of symptoms to improve QoL. A combination of reducing side-effects to treatment by careful treatment planning and patient-centered care may improve QoL. It is also possible that increased communication before treatment regarding expectations of treatment-related side-effects together with active follow-up and interventional measures to address bother of symptoms could be beneficial.

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P-367 A novel patient-derived orthotopic xenograft model of esophageal adenocarcinoma provides a platform for translational discoveries

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Background: Mouse models of gastroesophageal junction (GEJ) cancer strive to recapitulate the intratumoral heterogeneity and cellular crosstalk within patient tumors to improve clinical translation. Current GEJ models have limited applications in the tumor microenvironment, immune-oncology, and metastatic studies. GEJ cancers remain to be a therapeutic challenge due to a lack of reliable mouse models for preclinical drug testing.

Methods: A novel patient-derived tumor orthotopic xenograft (PDOX) was established from GEJ cancer via transabdominal surgical implantation. Patient tumor was compared to subcutaneously implanted patient-derived tumor xenograft (PDX) and PDOX by H&E, IHC, and next-generation sequencing (T200.1 panel). Drug efficacy studies of 5-fluorouracil with and without radiotherapy are being performed.

Results: Mechanical abrasion of mouse GEJ prior to surgical implantation of patient-derived tumor in situ promotes tumor engraftment (100%, n=6). Complete PDOX engraftment was observed with rapid intra and extraluminal tumor growth as evidenced by Magnetic Resonance Imaging. Patient-derived stroma co-engrafts with tumor cells in GEJ-PDOX. PDOXs contain fibroblasts, immune and inflammatory cells, vascular and lymphatic vessels. Stromal hallmarks of aggressive GEJs are recapitulated in GEJ-PDOX mouse model. PDOXs demonstrates tumor invasion into vasculature. GEJ-PDOXs is a clinically relevant model for metastases and immunological studies. Next-generation sequencing with the T200.1 revealed that the loss of heterozygosity of NOTCH3, TGFβ1, EZH2, and MLL3 are maintained with similar allelic frequency between the patient tumor and the two xenografts. Additional somatic SNVs such as ARID1A, NSD1 (CDS157-158), NSD1 (CDS158-159), KDM6A, XPO1, MAPK1 and EGFR were found to be acquired in xenograft tumor tissues that were not observed in patient tumor. Targeted radiation resulted in (60%) partial response as assessed by RECIST and tumor volume measurements. Drug and radiation efficacy studies are currently ongoing. It will be important to note if the PDOX model reproduces the results observed in clinical trials for these patients.

Conclusion: A GEJ-PDOX model exhibits remarkable fidelity to human disease and captures the precise tissue microenvironment present within the local GEJ architecture facilitating it as a novel tool in translating to clinics. This model can be applied to address the importance of tumor microenvironment in metastatic and immunological studies and to develop novel therapeutic approaches for the treatment of GEJ cancer.

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P-368 Primary tumor location in synchronous and metachronous liver metastases: Impact on patterns of recurrence and survival after hepatic resection

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Background: It has become widely accepted that colorectal cancer (CRC) is no longer viewed as a unique pathological entity because of the considerable differences in terms of prognosis between the right-sided colon cancer (RCC) and the left-sided colon cancer (LCC) location. In this study, we evaluated the prognostic implications of primary tumor location (PTL) among patients who underwent curative-intent hepatectomy for synchronous and metachronous colorectal liver metastases (CRLM).

Methods: The study population included all consecutive patients affected by CRLM scheduled for first liver resection between 2008 and 2017 at three Italian oncological centers (Parma, Modena, and Bologna). Patients who underwent palliative surgery (R2 resection) were excluded. Clinicopathologic and long-term survival data were collected and reviewed to explore the prognostic implication of PTL in patients with synchronous (SM) and metachronous (MM) CRLM. RFS (relapse-free survival) and OS (overall survival) curves were constructed using Kaplan-Meier method, and differences were analyzed using log-rank (Mantel-Cox) test. A Cox proportional hazards model analysis was performed to determine the joint association of several clinical factors investigated (sex, age at the diagnosis, primary tumor location and the presence of SM/MM). The p-value was bilaterally tested, and values less than 0.05 were regarded as statistically significant.

Results: A total of 204 patients who underwent CRLM resection were included, 51% with RCC and 49% with LCC. Synchronous lesions were prevalent (n=133, 65%). Median OS was respectively 40 months for SM-RCC, 53,5 months for SM-LCC, 64,5 months for MM-RCC and 81,6 months for MM-LCC. Patients with MM-LCC showed an OS significantly better than patients with SM-RCC (p=0.008) and SM-LCC (p=0.002). Strikingly, Cox proportional hazards model analysis showed that age and the presence of SM vs MM were associated with a significantly higher hazard ratio (HR) for death (HR=1.024; 95%CI=1.005-1.043; p=0.011 and HR=2.010; 95%CI=1.328-3.043; p=0.001, respectively).

Conclusion: Our study confirms the worse survival of patients with synchronous liver metastases and right-sided primary tumors. These patients should be considered for different treatment approaches.

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P-369 Quality of life of caregivers of patients with gastrointestinal cancer

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Background: Caregivers of cancer patients may experience changes in their routine and environment that affect their quality of life. These alterations of quality of life can be measured through validated instruments using specific domains in health. The aim of the study was to identify the domains that compromise the quality of life of the caregiver of patients with gastrointestinal cancer through the questionnaires SF-36 (Short Form Health Survey 36) and CBS (Caregiver Burden Scale).

Methods: A descriptive, observational study with caregivers who spend most of the time with patients diagnosed with gastrointestinal cancer during chemotherapy with or without radiation therapy was done. The study was approved by a local ethics committee no 04338518.2.0000.5505 and was carried with outpatients of the gastro-oncology department of the Universidade Federal de São Paulo. Caregivers over 18 years old answered 2 questionnaires, the SF-36 and the CBS. The SF-36 has eight health domains based on mental and physical components that range (0-100) where 0 is the worst and 100 is the best. The domains evaluated were functional capacity, limitation due to physical aspects, ache, and health status. The CBS contains 22 items where each item has a score ranging from 1 (score meaning never) to 4 (score meaning frequently). The scale includes five subdimensions that are general tension, isolation, disappointment, emotional involvement and environment. Higher scores indicate higher caregiver burden levels, while lower scores indicate lower caregiver burden levels.

Results: We investigated 124 caregivers who spend most of the time with 100 patients undergoing treatment for cancer of the gastrointestinal tract. Most of the patients were elderly (with an average age of 69.58), married (74%) and males (52%). Patients with colorectal cancer (59%) and with III/IV tumor stage (66%) were more frequent. Among the caregivers, 102 (82.3%) were less than 60 years old and 96 (77.4%) were female. The quality of life, according to SF-36, presented low levels in the domains of emotional aspects (32), physical aspects (39.8), vitality (47.7), ache (54.8) and mental health (61.3). The best mean value was verified on functional capacity (82.7). Regarding the caregiver burden, assessed by the CBS instrument, it was observed that general tension (21) and the disappointment (14.6) domains had the highest score, indicating a more severe caregiver burden level. The least affected domains were emotional involvement (5.0), isolation (7.2) and environment (7.9).

Conclusion: Most of the caregivers were women and younger compared to the patients. The caregivers of the patients studied showed changes in quality of life in both physical and mental aspects.

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P-370 Comprehensive targeted genomic profiling and comparative genomic analysis to identify molecular mechanisms driving cancer progression in young-onset sporadic colorectal cancer

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Background: Despite screening guidelines and recent advances in cancer treatment, colorectal cancer (CRC) remains the second most commonly diagnosed cancer and the second and third leading cause of cancer-related mortality in Canadian men and women. By 2030, the incidence rate will increase by 90% in this patient population. Generally, young-onset CRC is the "hallmark" of hereditary CRCs with highly penetrant germline mutations. However, the majority of young-onset CRCs appear to be sporadic and the molecular mechanisms driving cancer initiation and progression are unclear. Recent large-scale genome-wide studies including the comprehensive genomic analysis of somatic alterations in metastatic CRCs continue to identify mutations in several genes including members of WNT, RAS, and PI3K signaling pathways and ERBB2 and MET amplification. However, there is a limited understanding of differences in genomic mutational landscape between young-onset sporadic CRC

(<50 years of age) and late-onset sporadic CRC (>50 years of age) with the former group showing poorer prognosis. Whereas late-onset CRCs are prevalent in the proximal colon and are usually driven by MSI, CIN and CIMP, young-onset CRCs tend to be localized in the distal colon and rectum, diagnosed at later stages with histological features showing mucinous/singlet ring and with poorly differentiated features and these cancers are typically microsatellite and chromosome stable. Moreover, these younger groups of patients are often diagnosed with aggressive forms and advanced stages of the disease.

Methods: In this project, we set out to perform "comprehensive" targeted genomic profiling to identify every relevant DNA and RNA variants in over 500 genes implicated in cancer using biopsies obtained from 30 patients with young-onset sporadic CRC. Further, we are applying integrated bioinformatics and machine learning techniques on the largescale high throughput genomic profiling data from sporadic late-onset CRC patients to identify molecular signature driving cancer in this group of patients. We then perform a comparative analysis to determine distinct molecular features between these two groups.

Results: The young-onset CRCs tend to be localized in the distal colon and rectum and were diagnosed at advanced stages in our set of patients. Genomic profiling data from the first set of samples from this group of patients indicated that these cancers appear to be microsatellite stable (MSS) with low tumor mutation burden (TMB). There appears to be a distinct mutational landscape in this group of patients with a significant mutation frequency in PIK3R1, PDGFRA, FLT3, KDR gene mutations.

Conclusion: Early detection of cancer is critical for effective management in patients with sporadic colorectal cancer (CRC) in young adults. However, the lack of relevant biomarkers to identify this vital group of patients has been a major challenge. Understanding the genomic mutational landscape in young-onset CRCs will also guide treatment optimization, surveillance as well as screening protocols. References: 1. Canadian Cancer Statistics 2017. Canadian Cancer Society; 2017 Canadian Cancer Society. 2. Siegel, R.L., et al., 2017. 109(8). 3. Bailey, C.E., et al., 1975-2010. JAMA Surg, 2015. 150(1): p. 17-22. 4. Dozois, E.J., et al., 2008. 87(5): p. 259-63. 5. Deen, K.I., et al., 2016. 8(6): p. 481-8.

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P-371 The use of gastric acid suppression in surgical oncology patients

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Background: The use of gastric acid suppression medications during oncologic surgery has become a mainstay within the perioperative period. Recent literature suggests that the use of these medications may be associated with significant adverse effects, including an increase in post-operative infections. However, surgical oncology patients have never been particularly studied and the impact of acid suppression in this cohort is generally unknown. We intended to compare the rates of postoperative morbidity including various types of infections and organ dysfunction in cancer patients who take acid-suppressing medications versus those who are not taking said medications during their surgical course.

Methods: We studied all patients in a 10-year period at our community hospital who underwent surgical oncologic intervention for a gastric, liver, small bowel, biliary, and pancreatic cancers and assessed their outcomes. We stratified patients based on those who did and did not receive acid-suppressing medication during their hospital course. Our outcome measures included postoperative fever, infection, AKI, pancreatitis, liver failure and pneumonia.

Results: Our study included 96 patients who underwent a pancreatic oncologic surgical intervention between 2008 and 2018. Of these 96 patients, 72 received acid-suppressing medication (PPI or H2 blocker) while 24 patients did not receive any acid-suppressing medication during the perioperative period. When examining outcomes, both groups had patients that experienced post-operative infections, acute kidney infections and postoperative fever with the acid-suppressing group having these at higher rates. These differences were deemed clinically significant between the two groups. While there were more patients who received acid suppression that were found to have pancreatitis, liver failure, and pneumonia post-operatively, these results were not significant.

Conclusion: While previous studies on acid-suppressing agents' effects on patients have been done, these studies have largely excluded a critical and vulnerable patient group: surgical oncology patients. We found that those patients receiving acid-suppressing medications during the perioperative period had higher rates of all postoperative complications. This begs to wonder if these agents alter the patient's ability to heal in this critical postoperative time period. While other patient factors may play a role in these outcomes, the effects of acid suppression cannot be overlooked as a mitigating factor in these events. Thus, it questions the necessity for acid-suppressing agents in all surgical oncology patients. Having specific and strict criteria for which patient may benefit from these medications may help to eliminate some of the deleterious outcomes that are likely associated with these medications.

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P-372 Safe moderate dose regimens retain full survival benefits for aged patients with and without resistant gastrointestinal cancers

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Background: Elderly patients (pts) are often considered ineligible for effective cancer (Ca) treatments (TXS) because of reported inferior survival (S) compared to (vs) ideal trial pts and concerns due to high risk of severe adverse events (AEs). Pts with gastrointestinal (G)I cancer are often un- or undertreated even when the goals are a potential cure. Development series 2000 -2019 found that palliative regimens GFLIO which exploit 3 simultaneous 1/2-1/3 dosage drug interactions, in preference to standard dosages, are effective and safe (Anticancer Research 2016, 2018 ACR).

Methods: The study involved intent to treat Kaplan-Meier (KM) combined analyses of new series including resistant (R), all ages, performance (PS) 0-2, high-risk patients (R 50 colorectal CRC; R, -53/+53, advanced pancreatic cancer (APC) and R, -18/+18, intrahepatic advanced cholangiocarcinoma (CCA) in the context of A.L.A.N. score (AS) and standard blood tests. (Salati: Eur J Ca 2019). Treatment consisted of the GFLIO algorithm. TX given every 2 wks in mg/M2 was gemcitabine 500, fluorouracil 1200-1500 over 24 hrs; leucovorin 180; irinotecan 80 and day 2: oxaliplatin 40, upon progression, the sequence added a taxane (except for CRC pts.) -/+ mitomycin C, and upon further progression, targeted therapy as indicated.

Results: M s of 122 pts with resistant GI Cas: 13.5 months (mos) median S; 24+mos, 25th percentile: 60%, at 12; 45% at 15 and 38% at 24 mos. Number in subsets were: (122)71, 65- 70- 75. Pts of all ages did equally well. For 69 pts with non-resistant GI Cas S: 14 mos S median ; 24+mos, 25th percentile; 60%, at 12 mos; 50% at 15 mos and 32% at 24 mos. Number in subsets were: (69) 26, 65- 70- 75. Pts of all ages did equally well. During early TX, safety, severe toxicity, was $<$ 5%, not limiting. The frequency of favorable prognostic tests was the same, some present in $\sim$ 75% of patients, at all ages. AS 0; AS1-2 identify subsets pts with R CRC and R APC median survival 15+ mos and when absent S of 3-6 mos.

Conclusion: For GFLIO algorithm series, age is not an adverse prognostic factor for survival or safety. At the median, 25th percentile, 12 and 24 mos. all age groups feasibly outperform results of the ideal standard registry series. A.L.A.N. score identified pts with best chances to safely benefit from GFLIO. PTs expanded eligibility for effective 1/2 dosage treatment. Pts who may not benefit from the GFLIO treatment may be identified at the outset for an alternative therapy or palliative care.

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P-373 Moderate dose chemotherapy retains efficacy and improves safety in conjunction with high dose ascorbic acid (HDAA)

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Background: HDAA has been reported to improve quality of life (QOL). It has reduced risks of chemotherapy toxicity and severe intensive care infections. In vitro findings are contradictory re: potentiation or antagonism of chemotherapy. Our advanced pancreatic cancer (APC) specific experience supports protection against recurrent, established, and expected severe AEs; HDAA reduced moderate dose regimens, GFLIO algorithms, risk of severe AEs to 0- 5% (ASCO 16, AACR 17). More than 20,000 patients resort to combination or single treatment (TX) with HDAA each year in the USA.

Methods: Analyses: Compared, -/+ HDAA, Kaplan-Meier (KM), intent to treat, all users inclusive, computer matched pre-registered for FDA registered research, and for compassionate use of pts with preexisting AEs. Eligible patients had measurable APC; HDAA 75-100 GM 1-2 times a week for any duration; -/+ resistance; any age; palliative objectives; performance 0-2, office ambulatory and met standard organ safety criteria. TX in mg /m^2 was gemzar 500, fluorouracil 1200-1500 over 24 hrs; leucovorin 180; irinotecan 80 and on day 2: oxaliplatin 40 (GFLIO), every 2 wks. (Anti Ca Res 16). Standard blood tests and A.L.A.N. score (AS) examined S in subsets defined by the tests (Salati EJC 2019).

Results: Data from 106 pts., resistant (R) 53 and naive 53, include HDAA 30 pts in formal trial (AACR 17) and 31 given compassionate HDAA to prevent recurrence or for prevention of AEs- because of patient's concerns (total 61) and 45 with no HDAA. All survival (S) curves crossed at multiple points over two years. Survival (CI 8-10%) was 76-80% at 6 mos.; 50-58% at 12; 25-42% at 18 and 22-26% at 24 mos. Median and 25th percentile survival were 10.5 -14.5 and 16.5 - 22.5 mos. AS 0, AS 1-2 and normal

individuals prognostic tests identified overall, -/+ HDAA, groups with median survivals of 15.5 -24 mos. HDAA did not significantly reduce survival. Severe AEs range from 0- < 5% in HDAA groups. Favorable S trends were attributable to Taxanes, % females and A.L.A.N. cell ratios. The latter are putative surrogate markers of immune function. Unexpectedly, contrary to clinical characteristics, and referring physician expectations, the majority of patients had up to 75% favorable prognostic tests.

Conclusion: All comparisons, -/+ HDAA, found no decrease in palliative S. All S end points results: median, 25th percentile, 12 and 24 mos, encourage broad treatment, regardless of resistance and age. The A.L.A.N. score and its elements defined S subsets. HDAA is safe with the GFLIO drugs in moderate dosages. Further phase II/III clinical trials are recommended.

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P-384 Quality of life and the systemic pharmacokinetics of oxaliplatin in patients with unresectable peritoneal metastases from colorectal cancer treated with repetitive electrostatic pressurized intraperitoneal aerosol chemotherapy (ePIPAC): The CRC-PIPAC trial

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Background: Repetitive (electrostatic) Pressurized Intraperitoneal Aerosol Chemotherapy ((e)PIPAC) is an emerging palliative treatment for patients with unresectable peritoneal metastases. This manuscript focuses on quality of life and the systemic pharmacokinetics of oxaliplatin of patients treated with repetitive ePIPAC as part of the CRC-PIPAC trial.

Methods: This prospective, single-arm, open-label, multicenter, phase II study treated 20 patients with unresectable peritoneal metastases from colorectal cancer with repetitive ePIPAC with oxaliplatin (92 mg/m^2). Quality of life (QoL) was assessed with the EQ-5D-5L and the EORTC QLQ C30 and CR29, filled out at baseline and at one and four weeks after each ePIPAC. Whole blood samples were collected at t=0, t=5, t=10, t=20, t=30, t=60, t=120, t=240, t=360 and t=1080 minutes. Urine samples were collected at t=0, t=1, t=3, t=5 and t=7 days. All samples were analyzed using atomic absorption spectrometry.

Results: Significant QoL deteriorations were observed in the following scales: Index value, Physical Functioning, Role Functioning, EORTC QLQ C30 Summary score, Fatigue, Pain, and Abdominal Pain, mainly present at one week after ePIPAC but recovered at four weeks after ePIPAC. None of the scores at four weeks after the third ePIPAC significantly differed with baseline scores. Plasma ultrafiltrate Cmax of oxaliplatin reached 1.36-1.90 μg/mL after 30 minutes with an AUC0-24h of 9.6-11.7 μg /mL*h. Plasma Cmax reached 2.67-3.28 μg/mL after 90 minutes with an AUC0-24h of 49.0-59.5 μg /mL*h. The absorption rate constant (Ka) was 1.13/h. Urine concentrations of oxaliplatin rapidly decreased to less than 3.60 μg/mL in 90% of the samples at day 7.

Conclusion: Repetitive treatment with ePIPAC resulted in short-term deteriorations in quality of life, which should be considered given the palliative nature of the treatment. Systemic exposure to oxaliplatin after ePIPAC was considerably higher than expected. A direct comparison with a systemic administration could provide more insight into the systemic exposure after ePIPAC.

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P-385 A phase 1/2 study of combination therapy of ivaltinostat, gemcitabine, and erlotinib in patients with unresectable, locally advanced and metastatic pancreatic adenocarcinoma

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Background: Pancreatic ductal adenocarcinoma (PDAC) is one of the leading causes of cancer mortality with poor overall survival. The 5-year survival rate for advanced PDAC has remained about 3%, even with the recent improvement in combination therapies of FOLFIRINOX, gemcitabine/nab-paclitaxel, and gemcitabine/erlotinib. The objective of the current study was to evaluate the safety and efficacy of the combination of ivaltinostat, a novel HDAC inhibitor, with gemcitabine and erlotinib.

Methods: Patients who were diagnosed with unresectable, locally advanced, metastatic, histologically and cytologically confirmed PDAC were eligible. Patients who had previous histories of anticancer chemotherapy, radiation, or biologics were not eligible. The study was conducted in two parts. Part 1 was a 3+3 dose escalation design to determine the maximum tolerable dose of ivaltinostat in combination with gemcitabine and erlotinib. A total of 24 patients were enrolled in Part 2, which utilized Simon's two-stage design. Patients were treated for 6 cycles with ivaltinostat (250 mg/m^2 IV infusion), gemcitabine (1000 mg/m^2 IV infusion) and erlotinib (100 mg per day taken orally). Both ivaltinostat and gemcitabine were administered on Day 1, 8, and 15 of each 28-day cycle. The primary endpoint was the objective response rate (ORR, %). Secondary endpoints included overall survival, disease control rate (DCR, %), progression-free survival (PFS), time to progression (TTP), change in CA 19-9 from baseline, and quality of life. Safety evaluation included vital signs, adverse events, adverse drug reactions, serious adverse events, ECG, and clinical laboratory tests.

Results: A total of 34 patients, including 10 patients in Part 1, were enrolled and completed the combination therapy. Currently, the data are being analyzed, and the results, including the best overall response rate, median overall survival time, will be presented using descriptive statistics.

Legal entity responsible for the study: The authors.

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P-386 Transcriptome analysis of miR181 target genes and pathways in esophageal squamous cell carcinoma

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Background: MicroRNAs are small non-coding RNA molecules that posttranscriptionally regulate the expression of target genes and have been implicated in the progress of cancer proliferation, differentiation, and apoptosis. Studies have shown that miR-181b is highly expressed in gastric cancer, breast cancer, and other tumors, but its expression in esophageal squamous cell carcinoma (ESCC) has not been reported. This study was conducted to find the differentially expressed genes and pathways related to miR-181b by high-throughput sequencing and bioinformatics techniques in ESCC cells and to explore its clinical application value.

Methods: miR-181b mimics and miR-181b inhibitors were transfected into ECA109 cells, respectively. The expression of miR-181b in the cells was detected by fluorescence quantitative PCR, and the differential genes were detected by high-throughput sequencing. The enrichment analysis of GO, KEGG, and reactome was carried out by Cluster Profiles 3.0.5 software.

Results: After successful transfection, the expression of 149 genes in the cells transfected with miR-181b mimics was increased compared with cells transfected with blank mimics by sequencing detection (fold change >2 and P <.05), whereas the expression level of 416 genes decreased (fold change >2 and P <.05). GO, KEGG, and reactome pathway enrichment analysis showed that 416 genes that were down-regulated in cells transfected with miR-181b mimics, which were mainly enriched in leukotriene biosynthetic and metabolic processes compared with cells transfected with blank mimics (P <.05). The expression of SYK protein in the miR-181b mimics was significantly reduced by Western blotting (P <.05).

Conclusion: The high expression of miR-181b in ESCC can inhibit the expression of the tumor suppressor gene SYK, which further affects the metabolism of leukotrienes, thereby promoting the occurrence and development of ESCC. miR-181b is a potential diagnostic and therapeutic target for ESCC.

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POSTER DISCUSSIONS

PD-1 Systematic review and meta-analysis of the efficacy of chemotherapeutic regimens in advanced gallbladder cancer: Assessing current practice and treatment benefit

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Background: Biliary tract cancers (BTC) are a heterogeneous group of malignancies, including gallbladder cancer (GBC). Treatment for GBC is based on studies recruiting patients with all BTC primary sites rather than GBC alone. GBC represents a different molecular entity to other BTCs, which may impact the response to treatment. The benefit of chemotherapeutic regimens specifically for the treatment of patients with GBC, including the current standard first- and second-line regimens for BTC, is poorly understood. This study explored the benefit derived from palliative cytotoxic chemotherapeutic regimens in GBC.

Methods: A systematic review and meta-analysis were designed and registered with the PROSPERO database prior to commencement (CRD42019155745). A systematic search was conducted on MEDLINE; key bibliographies were reviewed and selected annual conferences were used to identify articles. Eligible studies reported data on patients with advanced GBC treated with systemic chemotherapeutic regimens. Phase II and III trials, case series, and cohort studies were eligible; phase I studies and small cohorts (< 10 in the first line, < 5 in second/third line) were excluded. Data were pooled using random effects models.

Results: 3,035 studies were identified; 58 studies with 66 study arms (n= 1,986 patients with GBC) were eligible for meta-analysis. In patients with GBC, estimated pooled radiological overall response rates (ORR), mean progression-free survival (PFS) and overall survival (OS) were 23.2% [95% confidence interval (CI), 20.0-26.5], 4.8 months (95% CI, 4.3-5.2) and 8.3 months (95% CI, 7.6-8.9), respectively. In patients with GBC, the use of $\geq$3 chemotherapy agents in combination was associated with increased ORR [35.8% (95% CI, 25.4-46.8)], mean PFS [5.9 months (95% CI 5.2-6.7)] and OS [9.9 months (95% CI, 8.5-11.3). There was a significant improvement in ORR, disease-free survival (DFS), mean PFS and OS with increasing numbers of chemotherapeutic agents (all spearman rho coefficients=1; $P< 0.001$). Patients with GBC had a lower ORR than non-GBC BTC [odds ratio (OR) 0.65 (95% CI, 0.50-0.84)]; specifically, patients with GBC have lower ORR when compared with the individual subgroups of BTC: cholangiocarcinoma (not otherwise specified) [OR 0.63 (95% CI, 0.48-0.83)], intrahepatic cholangiocarcinoma [OR 0.51 (95% CI 0.32-0.83)] and extrahepatic cholangiocarcinoma [OR 0.64 (95% CI, 0.40-1.00)].

Conclusion: Patients with GBC respond differently to systemic therapy compared with other BTC primary sites; they achieve lower ORR. In GBC, increasing numbers of chemotherapy agents are associated with better outcomes. Although differences may be due to selection bias, intensification of chemotherapy in fitter patients may be investigated either in a GBC-specific trial or (with a planned statistical and reporting approach) within a large randomised BTC trial.

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PD-2 Role of pretreatment SUVmax on 18F-FDG PET and clinicopathological features in the prognostic stratification of newly diagnosed intrahepatic cholangiocarcinoma

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Background: Cholangiocarcinoma (CCA) is the second most common primary liver cancer, following hepatocellular carcinoma, and it accounts for approximately 3% of all gastrointestinal cancers. CCAs are usually grouped in intrahepatic CCA (iCCA), perihilar CCA (pCCA) and distal CCA (dCCA), according to anatomical location. Several recent studies have suggested an increase in the incidence of iCCA in both western and eastern countries, and unfortunately, most of the patients with iCCA present with inoperable or metastatic disease. After radical surgical resection, the recurrence rate is high and prognosis remains poor, with a median overall survival (mOS) of 10-12 months in metastatic iCCA. Currently, no reliable prognostic factors are available in newly diagnosed iCCA. In this study, we aimed to investigate the correlation between maximum standardized uptake value (SUVmax) in 18F-FDG PET, clinicopathological features at diagnosis and clinical outcomes in newly diagnosed iCCAs.

Methods: We retrospectively collected data from medical records, laboratory tests, clinicopathological features and baseline SUVmax in newly diagnosed iCCA patients attending the medical oncology department of Bologna Sant'Orsola Malpighi Hospital from November 2005 to January 2020. All patients with a previous history of other malignancies were excluded. Clinicopathological factors at diagnosis included: histologic grade, stage, tumor size, cirrhosis, multifocal disease, vascular invasion, perineural invasion, bilirubin levels, serum CA19-9, ECOG-PS, radical surgery (R0). Survival analyses were performed using the Kaplan-Meier method; ROC curve was used to find the best cut-off value for SUVmax at diagnosis (SUVmax $=$ 8.5). Univariate analysis and Cox proportional hazards regression were used to examine the independent effects of each significant variable.

Results: A total of 172 patients (87 males and 85 females; mean age 66 $\pm$ 8) were included in our analysis. The univariate analysis revealed that mOS was significantly related to tumor size < 5 cm ($P < 0.001$), stage I-II ($P < 0.001$), R0 surgery ($P = 0.003$), multifocal disease ($P = 0.002$), cirrhosis ($P = 0.011$), vascular invasion ($P = 0.0013$), perineural invasion ($P = 0.002$), ECOG-PS ($P = 0.0019$), bilirubin levels < 1.5 mg/dL ($P < 0.001$) and serum CA19-9 ($P = 0.018$). Morphology subclassification ($P = 0.8$) and SUVmax ($P = 0.24$) did not significantly affect mOS at univariate analysis. Multivariate analysis identified vascular invasion ($P < 0.001$), perineural invasion ($P = 0.06$), bilirubin levels < 1.5 mg/dL ($P < 0.001$) and ECOG-PS 0-1 ($P = 0.004$) as independent prognostic factors for survival in newly diagnosed iCCA. Tumor grade ($P = 0.075$), stage I-II ($P = 0.076$) and R0 surgery ($P = 0.68$) were not significantly correlated with mOS, but a trend was observed.

Conclusion: Although 18F-FDG PET is undoubtedly an important imaging tool for diagnosis, staging, and re-evaluation in iCCA, in our 15-year single-center experience of 172 cases, metabolic activity detected via pretreatment SUVmax was not associated with patient survival. Conversely, several clinicopathological features were significantly correlated with survival in iCCA, according to our study. Further studies are needed to confirm our results and to clarify the prognostic role of baseline SUVmax in patients affected by iCCA.

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PD-3 Hepatocellular carcinoma in HIV-infected patients: Clinical presentation and outcomes in a racially diverse urban population

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Background: As life expectancy for HIV patients improves in the highly active antiretroviral treatment (HAART) era, hepatocellular carcinoma (HCC) has become a non-AIDS-defining illness with a high impact on morbidity and mortality of HIV-infected patients. We sought to compare outcomes in HIV versus non-HIV patients diagnosed with and treated for HCC at a multiethnic urban academic medical center.

Methods: A retrospective chart review of patients diagnosed with HCC from 1/1/2005 to 12/31/2016 was performed. Subjects included had at least one-week of follow-up and were censored at last point of contact. Variables collected included HIV status, HIV viral load, CD4 count, Hepatitis B virus (HBV) and Hepatitis C virus (HCV) infection, TMN stage, ECOG performance status, MELD score, and AFP level at diagnosis, as well as treatments received. Bivariate associations comparing characteristics between HIV and non-HIV subjects were assessed using t-tests or non-parametric equivalents for continuous variables and chi-square tests for categorical variables. Associations between HIV status, viral load and CD4 count, and overall survival (OS) were assessed using Cox proportional hazards regression as well as the Kaplan-Meier method with log-rank test.

Results: We identified 819 non-HIV and 73 HIV-infected subjects. Race was 17.3% white and 26.7% black for non-HIV versus 2.7% white and 43.8% black for HIV subjects (p=0.001). Ethnicity was 34.1% Hispanic in non-HIV versus 26.0% in HIV subjects. Mean age was 64.2 versus 57.2 years in non-HIV versus HIV subjects (p< 0.001). Rates of HBV (6.7 versus 17.8%, p< 0.001), HCV (59.8 versus 75.3%, p=0.022), and alcohol use (17.6 versus 38.4%, p< 0.001) were lower in non-HIV compared to HIV subjects. Of non-HIV subjects, 34.7% had AFP level >100 at diagnosis versus 49.3% of HIV subjects (p=0.015). Stage, MELD, and ECOG score at diagnosis showed no significant associations with HIV status. While rates of resection and regional treatments were similar, transplantation occurred more often in non-HIV compared to HIV subjects (10.4 versus 2.7%, p< 0.022). Median follow-up was 18.2 months. The 3-year actuarial OS for all patients was 49.7%, and significantly worse for those with HIV infection (37.0 vs. 50.9%, p=0.024). Patients with HIV also had worse OS on multivariable analysis (HR=1.90, p=0.001) when adjusting for age, MELD, AFP, stage and performance status. Viral load, but not CD4 count showed a significant association with survival (p=0.017 and p=0.070, respectively by log-rank test).

Conclusion: HIV-infected HCC subjects have lower survival rates compared with those without HIV. Despite younger age and similar MELD, ECOG, and stage at diagnosis, HCC subjects with HIV have worse outcomes compared to non-HIV counterparts. In our study, HIV-infected subjects had significantly higher rates of HBV, HCV, alcohol use, and lower rates of transplantation–all factors that could mediate the increased mortality observed in these subjects. While the etiology of survival differences between HIV and non-HIV patients with HCC remains unclear, robust efforts should be made to offer the subset of those with HIV not only transplants but also novel systemic therapies, given the profound potential for benefit.

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PD-4 Adjuvant chemotherapy and chemoradiation therapy after R0 resection for pancreatic ductal adenocarcinoma

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Background: Adjuvant therapy is a standard treatment for resected pancreatic cancer, and a variety of regimens are now used in clinical practice. We aimed to compare the efficacy of chemotherapy and chemoradiation therapy in patients with pancreatic cancer treated with R0 resection.

Methods: A total of 335 patients who underwent complete microscopic resection and subsequent adjuvant treatment for pancreatic ductal adenocarcinoma at Seoul National University Hospital from September 2005 to December 2017 were included. Patients were divided into three groups; chemoradiation therapy (CRT) group, systemic chemotherapy (SCT) group, and combined treatment of chemoradiation plus chemotherapy therapy (CRT-SCT) group. The primary outcomes were differences in recurrence-free survival (RFS) and overall survival (OS) between the three groups, and the secondary outcomes were differences in the recurrence pattern and adverse events between the three groups. Survival analysis was based on Kaplan−Meier method with median and 95% confidence interval, and survival differences were compared using log-rank test.

Results: Patients received CRT (n=65), SCT (n=62), and CRT-SCT (n=208). The duration from the surgery to the first adjuvant therapy was 47.6±17.9 days. American Joint Committee on Cancer (AJCC) stage was not significantly different between the three groups (P=0.080). Median RFS and OS in the CRT-SCT group were significantly longer than those in the CRT group (P=0.003 and P=0.042, respectively). In 59 patients with AJCC stage III, median RFS and OS in SCT group (8.9 [95% CI 8.0-NA] and 19.0 [95% CI 12.6-NA] months) and CRT-SCT group (10.9 [95% CI 9.2-15.9] and 23.4 [95% CI 22.0-44.4] months) were significantly longer than those in the CRT group (3.7 [95% CI 3.3-NA)] and 11.8 [95% CI 9.73-NA]). Hematologic adverse events greater than or equal to moderate grade occurred more frequently in SCT and CRT-SCT groups than in CRT group.

Conclusion: SCT with or without CRT is a reasonable choice preferentially over CRT in pancreatic cancer treated with R0 resection, especially in patients with AJCC stage III.

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PD-5 Impact of biliary drainage for unresectable pancreatic cancer treated with FOLFIRINOX or gemcitabine plus nab-paclitaxel: Results from the NAPOLEON study

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Background: Biliary obstruction can arise in patients with unresectable pancreatic cancer (UPC), which leads to delayed initiation of chemotherapy (CTx). Biliary drainage (BD) is essential for these patients, however, re-obstruction could be frequently observed after BD and impair maintenance of CTx. Whereas, we have no established data comparing prognosis between BD and non-BD patients. Also, there has been no data comparing efficacy between first-line FOLFININOX (FFX) or Gemcitabine plus nab-PTX (GnP) after BD. We, therefore, performed a retrospective study to validate the two clinical questions in the real world.

Methods: This retrospective study named NAPOLEON collected the data from CTx-naive UPC patients treated with FFX or GnP as first-line CTx from 14 hospitals in Japan during the period from December 2013 to June 2018. Recurrent patients after curative surgery were excluded in this analysis. Patient characteristics, treatment efficacy, relative dose intensity (RDI), and adverse events were analyzed and compared between BD cases and non-BD (NBD) ones. Among BD cases, those of FFX group and GnP group were also compared. Overall survival (OS) was estimated by Kaplan-Meier analysis, and a Cox proportional hazard model was employed to compare OS. We also conducted a Cox regression-adjusted analysis between BD and NBD cases and first-line treatment regimens to control potential difference or bias.

Results: A total of 274 patients received FFX (108 patients) or GnP (166 patients). Of these, 91 patients had already received BD, and FFX or GnP was administered to 30 and 61 patients, respectively. There was no significant difference in the median OS (11.1 vs. 11.5 months; hazard ratio [HR] 0.90; 95% confidence interval [CI] 0.68-1.21; p=0.50) between the BD and NBD cases, respectively. Moreover, no significant difference in the adjusted median OS (10.6 vs. 12.2 months; HR 1.17; 95% CI 0.86-1.59; p=0.33) was seen. Also, there were no significant difference in RDI between the two cases. The median OS in the FFX group was not significantly longer than that in the GnP group (10.9 vs. 11.1 months; HR 1.09; 95% CI 0.66-1.80; p=0.74 and 10.9 vs. 11.1 months; adjusted HR 1.09; 95% CI 0.63-1.90; p=0.75). There were no significant differences in all-grade adverse events in the two regimens, except that liver dysfunction was more frequent with FFX (30% vs. 11%) and rash was more frequent with GnP (3% vs. 26%). Thirteen percent of the patients with FFX received best supportive care (BSC) as second-line, otherwise, the rate of patients with GnP followed by BSC was 33% (p=0.02).

Conclusion: BD did not affect prognosis in UPC patients treated with FFX or GnP. Also, there were no statistically significant differences in effectiveness or safety between BD-performed FFX and BD-performed GnP.

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PD-6 Gemcitabine + nab-paclitaxel or gemcitabine alone after FOLFIRINOX failure in patients with metastatic pancreatic adenocarcinoma: A population-based, multicenter AGEO study

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Background: FOLFIRINOX (FFX) is a standard first-line treatment in metastatic pancreatic adenocarcinoma (MPA). Because there is no standard second-line treatment after FFX, evaluation of clinical practice shows frequent use of gemcitabine (Gem) alone or in association with nab-paclitaxel (Gem-Nab) without any comparative

prospective study for both treatments. For fit patients, the choice is often guided by nab-paclitaxel availability, as nab-paclitaxel is not publicly founded in France, although it is funded by some hospitals and not others. The aim of this study is to evaluate the impact of nab-paclitaxel in association with gemcitabine in this situation.

Methods: Patients with metastatic pancreatic adenocarcinoma (MPA) were retrospectively included in 19 French centers after failure with FFX. Patients received Gem-Nab (Gem 1000 mg/m^2 + Nab 125 mg/m^2, 3 out of 4 weeks) or Gem alone (1000 mg/m^2, 3 out of 4 weeks). Treatment was administered between September 2010 and July 2019 until progressive disease, death, or unacceptable toxicity. Patients receiving Gem were included in centers where Nab was unavailable at time of treatment.

Results: Overall, 445 patients were included, 228 patients in the Gem-Nab group out of 14 centers and 217 in the Gem group out of 8 centers. Four centers included patients in both groups because Nab became available during the study period. Patients had a median age of 63 (30-92) years and Performance Status (PS) of 0 /1/2/3 in 12%/55%/28%/4%. Age, sex, initial tumor localization, and the number of metastatic sites were comparable in both groups. Patients with PS $\geq$2 were less frequent in Gem-Nab (26% vs 39%; P = .05). Peritoneal metastasis were more frequent in the Gem-Nab group (41% vs 20%; P < .001). Initial disease control rate under FFX was lower in the Gem-Nab group (58% vs 70%; P < .001).

After a median follow-up of 22 months (95% CI, 14.9-NA), Gem-Nab significantly improved the disease control rate (56% vs 31%; P < .001), PFS (3.3 months vs 2.1 months; HR = 0.56; 95% CI. 0.46-0.68; P < .0001), and OS (6.8 months vs 4.3 months; HR = 0.64; 95% CI, 0.52-0.79; P < .0001) compared with Gem alone. The benefit was observed in all analyzed subgroups, including PS $\geq$2, >65 years of age, and patients with immediate progressive disease under FFX. After multivariate analysis, Gem-Nab and PS of 0/1 remained independently associated with better survival. Grade 3/4 toxicity was more frequent in Gem-Nab (43% vs 29%), particularly neutropenia (15% vs 10%) and neuropathy (10% vs 0%).

Conclusion: This is the first comparative study showing an advantage of Gem-Nab as second-line treatment. The retrospective nature of the study could have brought bias by the inclusion of more patients with worse outcomes in the Gem group, with an imbalance in PS. However, a significant effect was still present in all subgroups and in multivariate analysis, limiting this bias. Adjunction of nab-paclitaxel to gemcitabine increases PFS, OS, and ORR at the cost of more toxicity, but is still tolerable in patients with MPA as second-line treatment after FFX failure. These findings must be confirmed by a prospective study.

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PD-7 Updated survival analysis of the Danish randomized study comparing trifluridine/tipiracil with or without bevacizumab in patients with chemo-refractory metastatic colorectal cancer

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Background: Our investigator-initiated randomized trial in patients with chemo-refractory metastatic colorectal cancer (mCRC) patients demonstrated improved PFS and OS in patients receiving bevacizumab combined with trifluridine/tipiracil (FTD/TPI) as compared with patients treated with FTD/TPI alone (Pfeiffer et al, Lancet Oncol 2020). In the present study, we have updated PFS and OS per February 1st, 2020. Furthermore, will evaluate markers for no benefit (1 month CT scan and increase in CEA), look for time to deterioration of performance status, and details regarding treatment-related hospitalization.

Methods: The main inclusion criteria were as follows: histologically confirmed mCRC; PD during or after therapy with FU, irinotecan, oxaliplatin, and EGFR-inhibitor (only RASwt); prior treatment with bevacizumab was optional; performance status 0-1. In arm A: FTD/TPI 35 mg/m^2/dose bid from days 1-5 and 8-12; in arm B the same dose of FTD/TPI with bevacizumab (5 mg/kg), days 1 and 15 of a 28-day cycle. Efficacy (CT scan and CEA) was evaluated at 4 weeks, 8 weeks, and then every 8 weeks.

Results: 93 patients with chemo-refractory mCRC were randomized from September 2017 to October 2018 and followed until February 1st, 2020. The median PFS was significantly prolonged from 2.4 months (arm A) to 4.6 months (arm B) with HR 0.52 (95% CI, 0.34-0.80; P = 0.003). Median OS was significantly prolonged from 6.0 months (arm A) to 9.9 months (arm B) with HR 0.54 (95% CI, 0.35-0.84; P = 0.006). Seven patients were hospitalized due to treatment (definite or possibly related): Arm A, n=2 (febrile neutropenia and GI symptoms); Arm B, n=5 (febrile neutropenia, 2 patients with fever, GI hemorrhage, diarrhea). Analyses of markers for no benefit and time to deterioration of performance status are ongoing.

Conclusion: Updated survival analyses confirm that FTD/TPI in combination with bevacizumab prolongs PFS and OS and is a new valuable option in patients with chemo-refractory mCRC. Results on markers for no benefit and time to deterioration of performance status will be presented.

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The good clinical practice units in Denmark monitors the study.

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PD-8 Regorafenib with TAS-102 in metastatic colorectal cancer patients who progressed after at least two standard therapies: Efficacy and safety results of a multicenter phase I study (REMETY)

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Background: The oral fluoropyrimidine TAS-102 (TAS) and the multi-kinase inhibitor regorafenib (REGO) both show efficacy as single agents in the treatment of refractory metastatic CRC patients (pts). The REMETY trial was conducted to determine a recommended phase II dose (RP2D) of their combination and to increase efficacy in this third-line setting.

Methods: Eligible patients with ECOG 0-1, with measurable mCRC not amenable to surgery, who had at least 3rd-line treatment indication. Prior fluoropyrimidine-based and anti-VEGF (R) combinations were mandatory, as well as anti-EGFR for RAS WT tumors. A conventional 3+3 dose finding strategy was used. TAS was given on days 1-5 and 8-12 (28-days cycle); REGO on days 2-22. Starting dose level (DL 1) was TAS at 25 mg/m 2 BID plus REGO at 120 mg/d. First escalated dose (DL 2) was TAS at 35 mg/m 2 BID plus REGO at 120 mg/d. Planned next escalated dose was TAS at 35 mg/m 2 BID plus REGO at 160 mg/d (DL 3). The following major AE categories were used to define DLTs if they occurred during the first two treatment cycles: any grade $\geq$3 non-hematologic toxicity (with exceptions for vomiting, nausea, non-significant lab abnormalities), grade $\geq$3 hematological toxicities, grade $\geq$3 bleeding. Tumor response was assessed Q8W as per RECIST1.1.

Results: All observed toxicities were consistent with the safety profile of individual IMPs. 6 pts were enrolled into each DL 1 and 2 (n=12 in total). One DLT was observed in 1/6 pts in DL 1; 2 DLTs in 2/6 pts in DL 2. All DLTs were only grade 3 hypertension and causality was attributed to REGO. No DLT resulted in treatment discontinuation. In total, 152 adverse events (AE) were reported. Only 5 of these were serious. AEs affecting the highest proportion of patients were hypertension (5 pts), decreased neutrophil count (5 pts), diarrhea (4 pts), fatigue (4 pts) and nausea (4 pts). Results indicated a RP2D of 25mg/m^2 TAS-102 BID + 120mg REGO daily. No remissions were observed; the disease control rate (DCR) as per investigators' assessment was 58.3% (DCR of 33.3 % in DL 1 and 83.3% in DL 2). Median progression-free survival (PFS) was 3.8 months [95% CI: 1.51 - 5.29]. Preliminary OS analysis: All patients had been followed for >12 months. OS rate was 67% [95% CI: 0.40 - 0.93] at 6 months and 50% [95% CI: 0.22 - 0.78] at 12 months. Mature OS will be presented at the meeting.

Conclusion: All toxicities were consistent with the safety profiles of REGO and TAS. So far, the risk-benefit assessment of the combination is positive taking into consideration that hypertension is clinically well manageable and no additional DLT was attributed to TAS-102. The clinical efficacy is promising.

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PD-9 Universal screening for Lynch syndrome: Reflex testing to improve appropriateness of genetic counseling and diagnosis

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Background: Universal Screening (US) for Lynch Syndrome (LS) in colorectal cancer (CRC) patients through DNA Mismatch Repair deficiency (dMMR) testing is widely endorsed. However, LS is still largely underdiagnosed mainly because of the low adherence to guidelines among oncologists. Genetic counseling (GC) and testing (GT)

are always recommended for CRC patients with MSH2, MSH6 or PMS2 expression loss. However, approximately 80% of all dMMR cases have MLH1 expression loss which is not caused by a germline mutation, but rather by epigenetic methylation of the MLH1 promoter. As BRAF mutation and hypermethylation of the MLH1 promoter (reflex testing) rule out LS in these patients, we estimated the increased rate of LS diagnosis from GC/GT which is obtained by selecting candidates for GC through reflex testing.

Methods: From April 2011 to February 2020, all consecutive stage I-IV CRC surgical patients at our hospital, underwent immunohistochemistry (IHC) for dMMR using anti MLH1, MSH2, MSH6, and PMS2 antibodies. Oncologists were asked to refer all dMMR patients to GC/GT. Starting in 2019, reflex testing was implemented for all patients with MLH1 protein loss at IHC, therefore oncologists were asked to refer only the patients with wild-type BRAF who had no hypermethylation of the MLH1 promoter. BRAFV600E was tested using both IHC and real-time PCR Easy BRAF kit or Sanger sequencing.

Results: Overall, 2532 CRCs were analyzed and dMMR was found in 340 (13%), with 302 showing loss of MLH1 expression (89%). Oncologists referred 47 of the patients (14%) to GC. Among the 38 dMMR patients with loss of expression of MSH2, MSH6 or PMS2 (≠MLH1), oncologists referred seven to GC (18%), three of whom were diagnosed with LS (43%). Among 302 dMMR patients with loss of MLH1 expression, oncologists referred 40 to GC (13%), 8 of whom were LS (20%). Between February 2019 and February 2020, a total of 37 dMMR patients were identified. Their median age was 77 (range 44-100). Only one had loss of MSH6 and underwent GC and GT is ongoing. Reflex testing was therefore carried out in 36 with loss of MLH1 (97%). Among these, 30 showed BRAFV600E mutation (83%). Those with wild-type BRAF were tested for hypermethylation of the MLH1 promoter: two showed hypermethylation and were not referred to GC; two were not hypermethylated and were referred to GC/GT, one of whom was diagnosed with LS; the other two are ongoing. Therefore, by implementing reflex testing, we greatly improved the appropriateness of our referrals to GC, avoiding unnecessary sessions (32/36, 89%) and increasing the yield of LS diagnosis from 1/34 (3%) to 1/2 (50%).

Conclusion: Reflex testing can drastically improve the appropriateness of GC referrals, decreasing the number of unnecessary GC sessions and significantly increasing the diagnostic yield of GC/GT. As stepwise patient selection by oncologists may be impractical in routine clinical practice, patients with MLH1 loss at IHC should undergo reflex testing and an 'LS suspicion alert' on the pathology report could improve oncologists' awareness of LS and their compliance with guidelines.

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PD-10 Improvement of Asia-Pacific colorectal screening score combined with fecal immunochemical testing at adjusted thresholds in colorectal cancer screening

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Background: The Asia-Pacific colorectal screening (APCS) score was developed in identifying the potential high-risk population of colorectal cancer (CRC). However, the clinical utility of such a risk score has not been fully elucidated. We aimed to evaluate the diagnostic accuracy and cost to detect one advanced neoplasia (AN) of the APCS score combined with fecal immunochemical testing (FIT) at various scenarios versus FIT alone in detecting AN.

Methods: Based on an ongoing randomized controlled trial comparing colorectal cancer screening strategies (June 2018 - May 2019), 3407 participants aged 50-74 years who underwent colonoscopies were included in this study. All the participants had available colonoscopy and/or pathology reports. In addition, we prospectively collected fecal samples before the colonoscopy examination. The fecal samples were used for FIT (OC-Sensor, Eiken Chemical, Japan) following a standardized operation process. We collected detailed epidemiological questionnaire data which was further used for the calculation of the ACPS score (based on age, sex, BMI, family history of CRC in first-degree relatives and smoking, yielding risk scores of 0 to 6). For the strategy of the APCS score combined with FIT, the participants were recommended to undergo colonoscopy if they were assessed as high risk of CRC or had FIT-positive results. Diagnostic accuracy for AN was estimated based on FIT or the strategy of the APCS score combined with FIT at multiple adjusted thresholds, respectively. The cost to detect one AN per 100,000 invitees was evaluated. Indicators such as participation and compliance were modeled by summarizing up-to-date evidence from published studies.

Results: Among the 3407 included participants, 1753 (51.5%) were men and the mean age (SD) was 60.5 (6.3) years. The participants included 28 (0.8%) CRC, 255 (7.5%) advanced adenomas, 677 (19.9%) nonadvanced adenomas, and 2447 (71.9%) benign or negative findings. The sensitivity of the combination of the APCS score and FIT for AN ranged from 27.6% (95%CI, 22.4%-33.2%) to 76.3% (95%CI, 70.9%-81.2%) at the positive threshold of 3 or higher for APCS score and of 10 μg Hb/g or higher for FIT, which was higher overall than FIT alone (ranging from 13.8%, 95% CI, 10.2%-18.3% to 17.3%, 95% CI, 13.1%-22.2%). Compared with FIT at the conventional threshold of 20 μg Hb/g alone, the strategy of APCS at the positive threshold of 4 combined with FIT at 20 μg Hb/g improved the detection rate of AN per 100,000 invitees from 1231 to 2562, with numbers of colonoscopies needed to be scoped per 100,000 invitees increasing from 2736 to 17274. Further reducing the positive threshold of APCS from 4 to 3 would detect 24.6% more AN and require 60% more colonoscopies. Costs per AN detected by the strategy of APCS at the positive threshold of 4 combined with FIT at 20 μg Hb/g and FIT (20 μg Hb/g) alone were CNY¥ 4095 to CNY¥ 3550, respectively.

Conclusion: The combination of APCS score and FIT showed high sensitivity to detect AN. Tailored thresholds of the APCS combined with FIT may provide better screening yield at comparable costs compared with FIT-based screening.

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PD-11 Impact of baseline symptom burden as assessed by patient-reported outcomes on overall survival of patients with metastatic gastrointestinal cancer

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Background: Patients diagnosed with metastatic gastrointestinal (GI) cancer have variable symptom burden. However, serial symptom assessments are time-consuming and may be challenging to implement in routine clinical practice. We aimed to determine if a single measurement of symptom burden at the time of diagnosis of metastatic GI cancer is associated with survival outcome.

Methods: We examined prospectively collected baseline patient-reported outcomes (PROs) of patients diagnosed with metastatic esophageal, stomach, pancreatic, and colorectal cancer using the revised Edmonton Symptom Assessment System (ESASr) questionnaire from a large Canadian province between 2016 and 2019. The ESASr was categorized into physical (PH), psychosocial (PS), and total symptom (TS) domains. While PH score included six individual domains- pain, tiredness, drowsiness, nausea, loss of appetite, and shortness of breath, PS score consisted of two domains- anxiety and depression. The TS was derived from the domains in PH, PS, and a domain of overall well being. Each domain was scored from 0-10 by the patient and the scores were classified as mild (0-3), moderate (4-6), and severe (7-10). PS, PH, and TS were calculated by averaging the sum of all the individual domains. Multivariable Cox proportional hazards models were constructed to evaluate the effect of baseline symptom scores on OS to account for the baseline confounding factors.

Results: We identified 810 patients, of whom 63% were men and median age was 67 (interquartile range, 29-91) years. There were 146, 142, 207, and 315 patients with esophageal, gastric, pancreatic, and colorectal cancer, respectively. Approximately one-third of all patients reported moderate to severe PH, PS, and TS scores, with pancreatic cancer patients experiencing the highest symptom intensity across all domains ($P < 0.0001$). The lowest symptom scores were observed in patients with colorectal cancer, and those with gastric and esophageal cancer had similar symptom scores. While age did not affect the symptom scores, females were more likely to report severe PH, PS, and TS scores ($P=0.03$, 0.02, and 0.03, respectively). On multivariable Cox regression analysis, while severe PH and TS scores, older age (hazard ratio [HR], 1.05; 95% confidence interval [CI], 1.03-1.08; $P < 0.0001$), and female sex (HR, 1.78; 95% CI, 1.49-2.06; $P < 0.0001$) were predictive of worse OS, PS scores were not related to outcomes.

Conclusion: A single assessment of baseline symptom burden using the ESASr in patients with metastatic cancer has significant prognostic value. This may represent a feasible first step toward PRO collection for settings in which serial measurements have been challenging to implement.

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PD-12 Clinical, pathological and molecular profiles of G3 neuroendocrine tumors and neuroendocrine carcinomas

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Background: In 2019, WHO subclassified grade 3 (G3) gastroenteropancreatic (GEP) neuroendocrine neoplasms (NEN) into neuroendocrine carcinoma (NEC) or tumors (G3 NET). Yet, few data exist on clinical and molecular profiles for G3 NEN. We aimed to compare the clinicopathological and molecular characteristics of G3 GEP NET and GEP NEC.

Methods: We retrospectively collected data of all G3 GEP NEN patients (pts) diagnosed and treated at our cancer center from 2000 to 2019. Cases with available tumor tissues were reviewed and reclassified according to the WHO 2019 classification. Formalin-fixed, paraffin-embedded NEN tissues had DNA extracted for genomic profiling through next-generation sequencing (NGS), which evaluated mutations profiles, tumor mutation burden (TMB) and the presence of microsatellite instability. Survival from treatment start was the primary endpoint.

Results: Seventy-seven pts were included: median age at the diagnosis was 56 (26-91) years and 62% (48/77) were males. The most common primary sites were gastric (27%, 21/77), pancreas (23%, 18/77) and unknown primary NEN (23%, 18/77). Metastatic disease was present in 69% at diagnosis and 91% developed metastasis. Out of 77, 43 (56%) had pathology revision: 29 cases were NEC (67%) and 14 were reclassified as G3 NET (33%), with a change in diagnosis of 23%. In a median follow-up of 44 months, median OS in non-pancreatic digestive G3 NET, pancreatic G3 NET, and GEP NEC were 23.7, 55.6 and 10.8 months, respectively (non-pancreatic G3 NET vs NEC, p=0.01). Median OS in G3 NET with ki67 $>$ 55%, NEC 55% was 19, 25 and 8 months, respectively. In Cox regression multivariate analysis, only cell differentiation sustained as a risk of death (HR 3.14 NEC vs G3 NET; P $=$ 0.025). NGS was performed in 42% (32/77) cases: 21 NEC and 11 G3 NET. Median tumour mutational burden was 5.67 (0 $-$ 66.82) mutations per megabase among NEC and 4.52 (0 $-$ 8.83) among G3 NET. Tumors were microsatellite unstable in 3 (14.3%) NEC cases but zero among G3 NET pts. The most commonly mutated genes in G3 NET were TP53 (N=3; 27.3%), CDKN2A (N=3; 27.3%) and KRAS (2/11, 18.2%) and TP53 (N=15; 71.4%), Rb1 (N=7; 33.3%), PTEN (N=6; 28.6%) and APC (N=4; 19%) among NEC.

Conclusion: Non-pancreatic digestive G3 NET is associated with increased survival compared to NEC. Pathology revision is essential to estimate prognosis and consequently therapeutic plan, as some of G3 NET can be treated as G2 NET. While G3 GEP NEN generally harbours low TMB and fewer actionable mutations, 14% of NEC cases were microsatellite unstable and could benefit from immune checkpoint inhibitors.

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