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