POSTER PRESENTATIONS

P1 - MELENA CAUSED BY GASTRIC LIPOMA

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Introduction: Gastric lipomas are rare tumors, accounting for about 1-3% of all benign gastric tumors. Most gastric lipomas are asymptomatic and detected accidentally, if they are larger (larger than 3 cm) they can be symptomatic, causing abdominal pain, dyspeptic symptoms, hemorrhage or obstruction. Mostly these are well-limited formations, homogeneous in appearance, adipose tissue density. They are most often located submucosally, but can also be located subserously. The most common localization in the stomach is the antrum. Computed tomography (CT) has a high specificity and sensitivity in diagnosing lipomas of all localizations in the body, including gastric lipomas, which is presented as a well-limited structure of low density (negative values of Hounsfield units), with sharp contours, often with capsule, without infiltration of surrounding structures.

Case report: We present the case of a 57-year-old man who visited the emergency department because of a melena. He had pressure and occasional sharp stabbing epigastric pain for a month until he reported to the emergency department. Laboratory tests revealed a decrease hematocrit, ultrasound of the abdomen was performed and was normal, the patient was referred for gastroscopy, which revealed a polypoid formation in the antrum of the stomach that bleeds sparingly in a small segment, and biopsy samples were taken. The patient was sent for a CT of the abdomen, a submucosal formation was found in the antrum of the stomach measuring 45x20 mm. Mass in the antrum have the coefficient absorption of adipose tissue corresponding to lipoma. Endoscopic biopsy revealed histologically small samples of fibrin corresponding vascularized adipose tissue with fibrin.

Conclusion: CT is the method of choice in the diagnosis of gastric lipomas with the exception of the pediatric population where magnetic resonance imaging is recommended due to ionizing radiation. Endoscopic ultrasound is also an option in the diagnosis. Surgical excision is required in the case of larger symptomatic tumors. In the case of smaller lipomas, endoscopic polypectomy is the method of choice.

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P2 - MULTINATIONAL SURVEY OF BURNOUT SYNDROME IN EASTERN EUROPEAN ONCOLOGISTS

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Purpose: Burnout is defined as a three-dimensional syndrome—emotional exhaustion (EE), depersonalization (DP), and reduced personal accomplishment (PA)—caused by chronic occupational stress. The aim of the current study was to investigate the prevalence of burnout among oncologists in Eastern Europe and to identify the contributing factors.

Methods: The study was conducted as an online survey between October 2017 and March 2018. Oncologists (including medical, radiation, clinical, and surgical oncologists) from 19 countries were invited to participate. The survey consisted of 30 questions, including the standardized burnout instrument, Maslach Burnout Inventory, and eight demographic questions. Burnout risk was scored according to the scoring manual for health care workers.

Results: The study included 637 oncologists. Overall, 28% were at low or intermediate risk and 72% were at high risk for burnout. Forty-four percent of participants were at high risk for EE, 28.7% for DP, and

47.3% for PA. EE risk was associated with female sex. DP risk was highest among clinical and radiation oncologists, whereas PA risk was positively correlated with years of service, percentage of cancer deaths, and availability of the number of oncologists. In multivariate logistic regression analysis, burnout was significantly associated with standardized cancer mortality and fewer years of practice.

Conclusion: Burnout among oncologists in Eastern Europe is high, and younger oncologists are the most vulnerable group. Preventive measures should be taken to address this issue, which negatively affects optimal care delivery and poses a threat to oncologists' health and well-being.

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P3 - RESPONSE TO NEOADJUVANT CHEMORADIOTHERAPY FOR RECTAL ADENOCARCINOMA: A SINGLE CENTER EXPERIENCE

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Introduction: Thirty percent of all tumors of the colon develop in rectum. Neoadjuvant therapy is nowadays the standard of care for most patients with locally advanced rectal cancer. Neoadjuvant treatment can be carried out as short course of radiotherapy or a long course of combined chemoradiotherapy (CRT). The European Society of Medical Oncology recommends neoadjuvant treatment for advanced disease (≥ T3) and lymph node or circumferential margin involvement (where the adequacy of TME surgery is questionable) on imaging. The aim of CRT is to downsize and downstage the tumor to increase the chance of complete resection and to reduce the risk of local recurrence. Until recently, patients were routinely proceeded to surgical resection after CRT, regardless of the response. Nowadays, treatment is tailored depending on the response to CRT. Organ-preserving treatment strategies (local excision or 'watch-and-wait') are a potential option for patients with complete response to CRT (13-15% according to available data). To facilitate such personalized treatment planning, there is now an increased demand for more detailed radiological response evaluation after chemoradiation. MRI is one of the main tools used to assess response, but has difficulties in assessing response within areas of post-radiation fibrosis.

Patients and methods: We retrospectively analyzed 37 patients (25 males and 12 females) treated with neoadjuvant CRT in our institution between January 2017 and December 2019. The indication for neoadjuvant treatment was confirmed by multidisciplinary tumor board. The neoadjuvant regime included radiotherapy (total tumor dose of 5040 cGy in 28 fractions delivered to pelvis and primary tumor) with concurrent chemotherapy (capecitabine, 1650 mg/m2, BID). Evaluation of response was performed by MRI 6-8 weeks after the end of CRT, and the patients were proceeded to surgery approximately 10 weeks after completion of CRT.

Results: After CRT, 33 (89%) patients had MRI- confirmed regression of the primary tumor and 23 patients (62%) had lymph- node regression. In 14 patients (40%) it was possible to establish colorectal anastomosis, but 21 patients (60%) got permanent colostoma. According to Ryan criteria, complete- and near- complete pathologic response (Ryan 1) was achieved in 11 (32%), moderate regression (Ryan 2) in 17 (48%), and minimal regression (Ryan 3) in 7 (20%) patients, respectively. Five patiens (13%) had MRI- confirmed complete response, out of which 3 had complete patologic response after surgery. Two patients with complete radiological response refused surgery and have been rigorously followed up.

Conclusion: In our cohort of patients, neoadjuvant CRT has proven to be effective in achieving tumor response. The percentage of patients with complete response is consistent with literature data.

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P4 - IMPACT OF FIRST-LINE TYROSINE KINASE INHIBITORS DOSE REDUCTION ON CLINICAL OUTCOMES IN PATIENTS WITH METASTATIC KIDNEY CANCER: A SINGLE INSTITUTION EXPERIENCE

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Introduction: Tyrosine kinase inhibitors (TKI) have been the standard first line therapy for advanced kidney cancer over the last 15 years. Even though TKIs prolong survival, these agents bring along significant toxicity that often require dose modifications or treatment interruptions. However, for treatment success it is equally important to achieve sufficient drug exposure for optimal vascular endothelial growth factor (VEGF) suppression and to carefully manage therapy side-effects, what often remains challenging in busy clinical schedule. One way of improving tolerability of VEGF-targeted TKIs is dose reduction. There is gap in knowledge whether such dose reductions of first line TKI compromise patients' oncologic outcomes.

Patients and methodss: From our institution's retrospectively collated database all patients who received first line TKI for treatment of advanced or metastatic clear cell kidney cancer were identified. Data on TKI dose and treatment schedule were retrieved. Progression-free survival (PFS) and overall survival (OS) was estimated by the Kaplan-Meier log-rank method for patients with TKI standard dose and reduced dose, respectively.

Results: A total of 154 patients were included in the study. One hundred ten, 39, and 5 patients were treated with first line sunitinib, pazopanib, and sorafenib, respectively. In total, 40 patients (26%) received a reduced TKI dose during the course of the first-line treatment. From those, 24 patients, 15 patients, and 1 patient were treated with sunitinib, pazopanib, and sorafenib, respectively. Dose reductions occurred after the median of 6 cycles of the TKI treatment at the standard dose. In integral cohort, after median follow-up time of 40 months (range 1-116 months) for living patients, 80% patients experienced disease progression and 66% patients died. PFS and OS for all cohort (N=154) was 9 months (95%CI: 7-96 months), and 22 months (95%CI: 14-116 months), respectively. The median PFS in the patients who continued to receive the standard TKI dose was 7 months compared to 17 months for those who received a reduced dose (hazard ratio=2.33; 95%CI: 1.62–3.37, p=0.001). The median OS in the patients who continued to receive the standard TKI dose was 16 months compared to 43 months for those who received a reduced dose (hazard ratio=2.25; 95%CI: 1.48–3.42, p=0.002).

Conclusions: Toxicity-related TKI dose reduction affects almost one third of patients receiving first-line treatment. Toxicity management strategy which incorporates TKI dose reduction is associated with improved oncologic outcomes.

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P5 - TREATMENT OUTCOMES OF TARGETED THERAPY WITH BRAF AND MEK INHIBITORS IN PATIENTS WITH METASTATIC MELANOMA AT SESTRE MILOSRDNICE UNIVERSITY HOSPITAL CENTER, ZAGREB

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Introduction: Rising incidence rates of cutaneous melanoma have been observed during the last four decades in white populations worldwide. Melanoma incidence peaks at 65 years, though it can appear at any age. According to Croatian National Cancer Registry there were 775 new melanoma cases in 2017, with 219 deaths reported. Melanoma is the most aggressive type of skin cancer and is responsible for more than 75% of skin cancer deaths. Approximately 40-60% of melanoma patients harbor activating (V600) mutation in the serine-threonine kinase B-RAF. The patients with BRAF mutation have worse survival prognosis. Therapy options for BRAF mutated melanomas are immunotherapy and combination targeted therapy with BRAF&MEK inhibitors. Combination targeted therapy options available for metastatic BRAF mutated melanomas in the Republic of Croatia (BRAF&MEK inhibitors) are: vemurafenib+cobimetinib and dabrafenib+trametinib.

Aim, patients and methods: The aim of this single institution retrospective analysis was to determine the time to disease progression (PFS - progression free survival) in patients treated with BRAF&MEK inhibitors as the first line therapy.

In this retrospectiveanalysis, metastatic and unresectable melanoma patients with detected BRAF V600 (either E or K) mutation were included, treated with combination targeted therapy (BRAF&MEK inhibitors) between November 2016 and January 2020. Patients were classified according to gender, age at the time of diagnosis of metastatic disease, ECOG performance status, number of organ sites with metastases, LDH level, diameter of primary tumor, and presence/absence of CNS metastases.

Results: A total of73 patients with detected BRAF V600 mutation were included in the study. Medianpatients' age was 57 years. The most common sites of metastases were lymph nodes in multiple regions, and 51% of patients had 3 or more organs with metastatic sites involved. In 27 patients (37%) LDH value was elevated. Fourteen patients (19%) presented with CNS metastases at the time of diagnosis. Thirty nine patients (63%) were ECOG performance status 0, and 34 patients (47%) were ECOG PS 1 or 2. In 33 patients (45%), diameter of primary tumor was larger than 4 mm, in 23 patients (33%) between 4 and 1.5 mm, in 7 patients (9%) between 1.5 and 0.7 mm. Only 3 patients (4%) had primary tumor smaller than 0.7 mm. Median PFS in the first line treatment in this patient population was 10 months (95% CI 8-38 months).

Conclusion: This single institution results of BRAF&MEK inhibitors in the first line therapy of metastatic melanomashow somewhatworse outcomes according to the PFS in comparison to clinical trials' results, but correspond with other real-world experiences. This is probably due to the fact that BRAF&MEK inhibitors are used as first line therapy option primarily in the patients in need for rapid therapy response because of their poor disease characteristics, resulting in higher proportion of patients with poor prognostic criteria in this patient cohort.

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P6 - MUCOSITIS DURING THE TREATMENT OF HEAD AND NECK CANCER PATIENTS WITH RADIOTHERAPY +/- CHEMOTHERAPY – REAL CLINICAL PRACTICE EXPERIENCE

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Introduction: Radiotherapy is one of the basic treatment methods for patients with head and neck cancer, with or without the addition of chemotherapy. It is used either as a primary treatment modality or as adjuvant therapy. The main side effect during treatment is mucositis. It is manifested by a pronounced head and neck mucosal erythema, appearance of ulceration, severe pain, all that complicates the intake of food and fluid, leads to weight loss, and impairs the patient's quality of life. Pronounced mucositis may be the reason for discontinuation of radiotherapy (+/- chemotherapy) treatment and thus affects treatment outcomes. According to published data, around 80% of patients have pronounced mucositis during radiochemotherapy treatment.

The aim of the study was to present the incidence of mucositis during the radiotherapy treatment of patients with head and neck cancer with or without concomitant chemotherapy administration in real clinical practice.

Patients and methods: Retrospective review of data from the Hospital Information System (BIS) of the Clinic of Oncology at the University Clinical Hospital (SKB) Mostar from January 2014 to the end of December 2019. Patients treated for head and neck cancers with high radiotherapy doses of 5000 – 7000 cGy, either as primary or adjuvant therapy, with or without concomitant administration of chemotherapy, were included. Patients treated with lower doses of radiotherapy and palliative intent were excluded. Mucositis was graded according to NCI CTCAE v.4.03 criteria.

Results: Total number of patients treated with radiotherapy was 131. There were 19 women (14.5%) and 112 men (85.5%). The median age was 61 years (range from 27 to 87 years). Concomitant chemotherapy was administered to 70 of them (53.4%). Mucositis was reported in 121 patients (92.4%), while there was no mucositis reported in 10 patients (7.6%). Distribution of mucositis by grades was: Grade 1 - 20 patients (15.3%), Grade 2 - 31 (23.7%), Grade 3 - 61 (46.6%) and Grade 4 - 9 patients (6.9%).

Conclusions: Results in real clinical practice confirm the high incidence of mucositis during radiotherapy (+/- chemotherapy) treatment of patients with head and neck cancer. Given that pronounced mucositis (especially Grades 3 and 4) is a leading cause of discontinuation in planned treatment, its high incidence requires the improvement of mucositis prevention and treatment measures to improve patients' quality of life and expected treatment outcomes.

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P7 - NIVOLUMAB IMMUNOTHERAPY AS A PART OF THE EXPANDED ACCESS PROGRAMS FOR THE TREATMENT OF PATIENTS WITH LUNG CARCINOMA

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Introduction: Due to the small progress in the treatment of advanced/metastatic lung cancer after progression to platinum-based chemotherapy, the successful results were achieved with immunotherapy in the second-line treatment of patients with non-small cell lung cancer (NSCLC) has been met with high expectations (1,2). Because of limited therapeutic options, following progression to platinum-based chemotherapy and chemotherapy toxicity, the opportunity to enroll patients in Nivolumab Expanded Access Program represented a great opportunity for patients to receive therapy, which extends overall survival and has a favorable toxicity profile.

Methods: Data was retrospectively analyzed in 12 patients with relapsing locally advanced or metastatic NSCLC lung cancer, after progression of disease on platinum-based chemotherapy from Department of Oncology, University Hospital Mostar. They were treated with immunotherapy Nivolumab 3mg/kg or fixed dose 240 mg every 2 weeks as part of Expanded Access Programs which started in 2016 at the Department of Oncology, University Hospital Split.

Results: Twelve patients included, all male, median age was 59.5 years (range 55-64), all patients were former/current smokers. According to the general condition ECOG status 0 had (58.3%) patients and ECOG status 1 (41.7%) patients. According to the histopathological findings, the majority of patients had squamous cell lung cancer (66.7%) and the other patients had adenocarcinoma (33.3%). All patients had progression to chemotherapy prior to initiation of Nivolumab immunotherapy. The median time to disease progression was 11 months. Nine out of 12 patients died, with a median overall survival of 18 months. In 3 patients who are alive immunotherapy was administered for 2 years, one patient has a stable lung disease, another patient has progresses of lung disease and the third patient is monitored clinically and has stable disease, after undergoing oncology treatment, due to progression in the lungs and the brain. Treatment-related adverse events of any grade were reported in 83% patients, and none had grade 3 or 4 event. The most frequently reported treatment-related adverse events were fatigue in 25% patients, decreased appetite (25%), rash (25%), asthenia (16%); pyrexia (16%) and anemia (16%). Treatment-related select adverse events were nausea (8%), thrombocytopenia (8%), arthralgia (8%) and hypothyroidism (8%).

Conclusion: Treatment with Nivolumab, as a part of the Expanded Access Programs in real clinical practice is effective, well-tolerated and in lower-middle-income economies countries is almost the only way to enable therapy that is not otherwise available as a therapeutic option, because of its high cost.

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P8 - LOCAL CONTROL OF LOCALLY ADVANCED CERVICAL CANCER IN PATIENTS TREATED WITH PRIMARY CONCOMITANT CHEMOBRACHYRADIOTHERAPY IN DEPARTMENT OF ONCOLOGY, UNIVERSITY HOSPITAL MOSTAR

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Introduction: Approximately 500,000 women are diagnosed with cervical cancer annually and cervical cancer is number one cause of cancer-related death in most developing countries (1). The achieved results of the Split Protocol using primary concomitant chemobrachyradiotherapy in the treatment of locally advanced cervical cancer (LACC) showed excellent results in local disease control and overall survival with acceptable treatment side effects (2). The results of local disease control obtained by primary concomitant chemobrachyradiotherapy at the Department of Oncology, University Hospital Mostar are presented.

Methods: We treated 46 patients with LACC (International Federation of Gynecology and Obstetrics stages IB2-IVA) with primary concomitant chemobrachyradiotherapy. Patients treated over a period 2013-2019 were included in the analysis. External radiotherapy was administered in 50 Gy in 25 fractions and concomitant chemobrachytherapy administered through 2 applications of low-dose rate brachytherapy with 2 cycles of chemotherapy per IC protocol (cisplatin on day 1 in combination with 24-hour infusion of ifosfamide) and then continued treatment with consolidation chemotherapy per IC protocol starting 4 weeks after the second concomitant chemobrachyradiotherapy cycle.

Results: The median age of the patients was 60 years and the majority of patients had squamous cell carcinoma (97.8%). FIGO stage IB2 was in (2.2%) patients, FIGO II (71.7%), FIGO III (26.1%) and none of the patients had FIGO IVA disease stage. Local disease control was 97.8%, only one patient had a local recurrence of the disease that developed 2 years after completing oncological treatment with regional pelvic lymph node metastases and bone disease metastasis.

Conclusion: Treatment of patients with cervical cancer with primary concomitant chemobrachyradiotherapy according to the Split Protocol has achieved excellent results in local disease control.

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P9 - A RARE HER-2 POSITIVE NEUROENDOCRINE CARCINOMA OF THE BREAST: A 9-YEAR FOLLOW-UP CASE REPORT

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Primary location of neuroendocrine carcinoma of the breast (NECB) is extremely rare and it is believed that their incidence ranges from 1% to 5% of breast carcinomas, accounting for less than 1% of all neuroendocrine tumors (1,2). The most sensitive and specific neuroendocrine markers are chromogranin A or B and synaptophysin (3). Sometimes neuron specific enolase (NSE) can also be found in NECB. NECB mostly have positive hormone receptors, human epidermal growth factor receptor 2 (HER-2) status is almost always negative and more than 50% of the tumor has luminal B subtype. NECB treatment is due to the lack of prospective studies the same as for the typical breast tumor (2).

A 70-year-old woman was diagnosed with neuroendocrine carcinoma of the breast in February 2011. Screening mammography detected a well defined mass in the upper inner quadrant of the right breast. No microcalcifications were identified. Ultrasonography showed a hypoechogenic mass measuring 30 mm in its greatest diameter. No carcinoid associated syndrome was presented. Further diagnostic examinations were negative for metastatic disease. She underwent right tumorectomy. After that she underwent right radical mastectomy and right axillary node dissection. Patient wasn`t subjected to a core-biopsy before surgery. Macroscopically, the resected tumor measured 3x2x2 cm (pT2). Number of positive axillary lymph nodes was 1/8 (pN1). Microscopically, tumor cells contained polymorphic vesicular nuclei, prominent nucleoli. Also, rosette-like spaces were evident. Histopathological examination revealed NECB (well differentiated neuroendocrine tumor of the breast according to the World Health Organization 2012 classification). The tumor histologic grade was 2. Immunohistochemical analysis showed that tumor cells were positive for chromogranin A and also for NSE. Immunohistochemical staining for synapthophysin was non-specific. Estrogen receptors (ER) were positive in 100% of the tumor cells, progesterone receptors (PR) were positive in 10% of the tumor cells and HER-2 status was 3+. According to the Tumor, Node, Metastasis (TNM) Classification of Malignant Tumors, pathologic stage was IIB - pT2pN1cM0. Ki-67 proliferation index was 5,7%. After surgery patient received adjuvant chemotherapy: 5-fluorouracil plus doxorubicin plus cyclophosphamide (FAC protocol) on day 1 every 3 weeks for six cycles. Further treatment plan was: adjuvant radiotherapy to the chest wall and regional lymphatics plus intravenous trastuzumab every 3 weeks up to 1 year and endocrine treatment with aromatase inhibitor – letrozole for 5 years. She finished adjuvant endocrine treatment in September 2017. She is still on clinical monitoring, with no signs of local recurrence or distant metastasis after 9 years of surveillance.

To our knowledge this is the second described case of HER-2 positive NECB being treated with trastuzumab. Literature review revealed that this is the first described case of HER-2 positive primary NECB being treated with adjuvant trastuzumab (4,5). Prognosis of NECB is not different from that of other invasive breast carcinomas and it seems to correlate with the stage of disease (6). Long-term follow-up is recommended because NECB can metastasize to multiple sites even years after the adjuvant treatment (2).

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P10 - ANALYSIS OF THE APPLICATION OF DIFFERENT CLINICAL CT IMAGING PROTOCOLS AS FACTORS IN THE CALCULATION OF ABSORBED DOSE DISTRIBUTIONS USING THE ELEKTA MONACO RADIOTHERAPY PLANNING SYSTEM

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Introduction: The Monte Carlo based Elekta Monaco treatment planning system (TPS) is used to calculate absorbed dose distributions for intensity modulated radiotherapy (IMRT).

The application of IMRT technique requires high accuracy of dose calculation and according to international guidelines a maximum error of up to 3% is recomended**1**.

To calculate dose distributions, the TPS uses patient/phantom image data sets obtained from CT data translated into voxel geometry where relative electron density (RED) is assigned to the associated Hounsfield number (HU) of each voxel using a calibration curve. Therefore, the application of different imaging protocols (different U_{tube} and FOV) can affect the accuracy of the dose calculation**2**.

Materials and methods: A study was conducted to investigate the effect of CT imaging protocols and their associated HU-RED curves on the accuracy of the calculation of absorbed dose distributions using the Elekta Monaco 5.10.02 TPS. Siemens Somatom Open CT simulator and CIRS Thorax semi-anthropomorphic phantom were also used.

Two different CT protocols were applied for the acquisition of the phantom data sets using different voltages (U_{tube}= 80,100,120,140kVp) with standard (FOV=438mm) and extended field of view (eFOV= 650mm)3.

Simple 15x15cm^2 field, 3DCRT and IMRT plan were calculated using the 6MV X-ray beam on 8 phantom data sets creating 24 absorbed dose distributions in total.

Dose distributions obtained using 120 kVp voltage and standard FOV were defined as reference (using the optimal protocol) and were compared with the others. The analysis was performed using the gamma index to calculate differences between the 3 reference and 21 corresponding absorbed dose distributions comparing dose and distance to agreement differences with 95% confidence level.

Results: Comparison of reference dose distributions with the others shows that for simple fields, more than 95% of the analysed points have a dose difference of less than 2% for all fields and all compared protocols irrespective of the U_{tube} and FOV/eFOV used.

For the 3DCRT plan, the analysis shows different behaviour when compared to protocols with standard FOV applied (95% of the analysed points have a dose difference of less than 3%) versus those using eFOV that exhibit larger differences (95% of the analysed points have a dose difference of less than 4%).

IMRT plan analysis also shows different behaviour when compared to protocols with standard FOV applied (95% of points analysed have a dose difference of less than 1%) versus those using eFOV (95% of points have a dose difference of less than 7%).

Conclusion: Evaluation of the differences in dose calculated by the Elekta Monaco system on a phantom imaged using different clinical CT protocols shows an impact of using different tube voltages and high dependence on whether standard or eFOV are applied4.

The use of different CT protocols can lead to an increase in the differences in calculated absorbed dose distributions with increasing complexity of the radiotherapy planning techniques used. In order to preserve the accuracy of the clinical dose distribution calculations, it is important to use HU-RED curves that exactly match the CT protocols used for patient data set acquisition.

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P11 - COMPARISON OF TWO PLANNING TECHNIQUES (F-IMRT/I-IMRT) FOR POST-OPERATIVE RADIOTHERAPY TREATMENT OF PROSTATE CANCER

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Introduction: With the development of medical linear accelerator and algorithms for absorbed dose calculation and optimization, a great progress has been made in radiotherapy treatment of prostate cancer [1]. At UH Rijeka, since 2016, when the system for dose distribution optimisation based on Monte Carlo calculation has been clinically implemented, IMRT technique (inverse IMRT, I-IMRT) became the technique of choice for radiotherapy treatment following radical prostatectomy [2]. Previously, advanced 3-DCRT technique using field-in-field method was used for dose distribution optimisation around target volumes and organs-at-risk (forward IMRT, F-IMRT). This research has been performed with purpose of investigating how choice of planning technique (F-IMRT or I-IMRT) affects coverage of target volumes with prescribed dose and organs-at-risk sparing.

Methods and materials: Comparison of dose distributions calculated using F-IMRT and I-IMRT techniques was done for 10 patients with indicated post-operative radiotherapy, and whose treatment was carried out at the Clinic for Radiotherapy and Oncology at UH Rijeka. Prescribed dose for all patients was delivered using I-IMRT technique, and for purpose of this research, dose distributions using F-IMRT technique were calculated. Absorbed dose of 46Gy was delivered to target volume PTV_1, created by adding a 0.7cm margin around lymph nodes (CTV) and 1.0cm around prostate bed (GTV). Additional 22Gy were delivered to target volume PTV_2 with 1.0cm margin around prostate bed [2]. For I-IMRT and F-IMRT techniques, photon beams of linear accelerator equipped with a 160 leaf MLC were used. To determine the influence of planning technique on dose distribution, parameters related to target volumes (GTV, CTV, PTV_1, PTV_2) were analysed. For organs-at-risk sparing (rectum, bladder, femoral heads), three dose-volume constraints were used.

Results and discussion: By analysing parameters related to target volumes, most of them shown no statistical significance ($V_{100\%}$(GTV), $V_{100\%}$(CTV), $V_{95\%}$(PTV_2), $V_{95\%}$(PTV_1), $D_{2\%}$). For both planning techniques, internationally set [3] dose constraints were achieved: for GTV, $V_{100\%}$=98,8±1,3 (F-IMRT) and $V_{100\%}$=99,9±0,2 (I-IMRT), for CTV, $V_{100\%}$=99,4±0,9 (F-IMRT) and $V_{100\%}$=99,4±0,8 (I-IMRT), for PTV_2, $V_{95\%}$=99,9±0,2 (F-IMRT) and $V_{95\%}$=99,7±0,4 (I-IMRT), and for PTV_1, $V_{95\%}$=99,3±0,6 (F-IMRT) and $V_{95\%}$=99,9±0,1(I-IMRT). Statistically significant difference was found for $V_{100\%}$(PTV_2), p=0,000534 and $V_{100\%}$(PTV_1), p=0,042944 in favour of I-IMRT technique. For PTV_2, $V_{100\%}$=91,6±3,8 for F-IMRT and $V_{100\%}$=97,9±1,4 for I-IMRT and for PTV_1, $V_{100\%}$=93,3±2,0 for F-IMRT and $V_{100\%}$=95,8±2,5 for I-IMRT. Comparing the effect of planning technique to organs-at-risk sparing, statistically significant difference (p=0,045966) was found for V_{40Gy} for rectum where the sparing is better for I-IMRT technique. For dose-volume constraints related to bladder and femoral heads, no statistically significant difference was found.

Conclusion: Results of this research show statistically significant difference for minimal absorbed dose delivered to target volumes PTV_1 and PTV_2, with better dose coverage in favour of I-IMRT. Concern-

ing organs-at-risk sparing, statistically significant difference in favour of I-IMRT was found for V_{40Gy} for rectum. Expectedly, I-IMRT technique provided better results [4]. However, differences for two planning techniques (F-IMRT and I-IMRT) for analysed parameters are rather small which points to the fact that well-executed radiotherapy planning by using F-IMRT technique can be used as a technique of choice as well.

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P12 - CAN OPTIMALLY ORGANIZED CANCER CARE HAVE AN IMPACT ON THE TRANSITION OF PATIENTS WITH METASTATIC COLORECTAL CANCER THROUGH TREATMENT LINES? - A RETROSPECTIVE OBSERVATIONAL STUDY AT THE DEPARTMENT OF ONCOLOGY AND RADIOTHERAPY, UNIVERSITY HOSPITAL OF SPLIT

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Backround: In Croatia, colorectal cancer (CRC) presents a significant public health problem due, among other things, to lack of true multidisciplinary work and *poor quality control,* leading to one of the worst outcomes in Europe and a 5-year survival of 48%, according to the Concord 3 study[1]. When compared to the Western countries, most drugs are available in Croatia but unfortunately without any knowledge about their impact on treatment outcomes as there has been no data published about those particular issues. Defining optimal reporting and monitoring of metastatic colorectal cancar (mCRC) treatment is one of the key points in our quest to improve outcomes. One of the examples about the importance of organized cancer care with continuous quality control is presented in a recent study about the expenditures on oncology drugs and cancer mortality-to-incidence ratio in Central and Eastern Europe[2]. Their results have shown that study outcomes in a form of mortality-to-incidence ratio were significantly better in the Czech Republic as opposed to Slovakia although Slovakia spent almost twice as much per newly diagnosed cancer patient. The proportion of mCRC patients continuing treatment after first line could definitely be increased so finding the ideal strategy that will offer multiple lines of treatment is essential for the improvement of mCRC outcomes[3,4.]

Materials and methods: We retrospectively evaluated health charts of 107 patients with mCRC who were presented at our Multidisciplinary gastrointestinal tumor board at the Department of Oncology and Radiotherapy, University Hospital Split during 2017. The data was analyzed with methods of descriptive statistics by using Microsoft Excel tools.

Results: A total of 107 patients with mCRC were presented at our Multidisciplinary gastrointestinal tumor board in 2017. 17 patients (16%) did not receive any specific treatment as they were provided with best supportive care whereas 7 patients (6%) were treated with semiadjuvant FOLFOX regimen after liver metastasectomy. First line treatment for inoperable mCRC was initiated in 83 patients (78%). The most common first line treatment regimen was FOLFIRI and bevacizumab combination, reported in 37 patients (45%). Other first line regimens include FOLFIRI and EGFR inhibitor combination, FOLFIRI regimen and capecitabine, reported in 18 (22%), 12 (14%) and 16 (19%) patients, respectively. Of the 83 patients who started first line treatment, 50 patients (60%) entered second line treatment whereas 27 (33%) and 10 (12%) patients were treated in the third and fourth line, respectively. The median progression-free survival (mPFS) in the first line was 12.62 months, whereas for the second, third and fourth line it was 2.35, 1.73 and 2.25 months, respectively.

Conclusion: The results of our retrospective analysis show a significant decrease in the proportion of patients with mCRC represented in later lines of treatment which is comparable to previously published studies. The transition of patients across treatment lines could be a potential indicator of the quality of

cancer care organization and could be related to the outcomes of not only mCRC patients but all cancer patients in general.

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P13 - TREATMENT OUTCOMES BY PRIMARY TUMOR LOCATION IN PATIENTS WITH METASTATIC COLORECTAL CANCER AT THE DEPARTMENT OF ONCOLOGY AND RADIOTHERAPY, UNIVERSITY HOSPITAL OF SPLIT DURING 2017 - A RETROSPECTIVE ANALYSIS.

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Backround: Worldwide, colorectal cancer (CRC) is the second leading cause of death[1]. Due to its poor treatment outcome and a 5-year relative survival of only 14.2%, stage IV disease remains our biggest challenge[2]. However, in the last decade there have been significant improvements in mCRC treatment. One of the reasons for such advances is the increasing number of available chemotherapeutic and biologic agents but also the growing importance of molecular biology highlighted by the predictive and prognostic value of RAS/BRAF and HER2 status, microsatellite instability (MSI) and primary tumor location[3,4,5]. The aim of this abstract is to present our results regarding the treatment patterns used at our Department and outcomes by primary tumor location.

Materials and methods: We conducted a retrospective health chart analysis of 107 patients with mCRC who were referred to the Department of Oncology and Radiotherapy, University Hospital Split during 2017. First line treatment regimens being used at that time included FOLFIRI and bevacizumab combination for patients with RAS mutated tumors, FOLFIRI and EGFR inhibitor combination for patients with RAS "wild type" tumors. The data was analyzed with methods of descriptive statistics by using Microsoft Excel tools. P values were calculated with t-test for small independent values.

Results: The median age at diagnosis was 67 years. The primary tumor was left-sided in 81 (75.7%) and right-sided in 26 (24.3%) patients. A total of 83 patients out of 107 entered first line treatment. The median follow-up was 17.13 months with a median progression free survival (mPFS) and overall survival (mOS) being 12.62 and 20.57 months, respectively. When divided by primary tumor location the mPFS did not show significant difference between left and right-sided tumors (12.73 vs 10.22 months, $p>0.05$), whereas the mOS was significantly longer for the left sided tumors (25.43 vs 12.67 months, $p<0.05$). Considering the main treatment regimens, left-sided tumors treated with FOLFIRI and bevacizumab showed significantly better results in comparison to the right-sided tumors (mPFS 12.67 vs 6.97 months, $p > 0.05$ and mOS 28.07 vs 13.02 months, $p<0.05$). On the other hand, left-sided tumors treated with FOLFIRI and EGFR inhibitors showed similar results as opposed with right-sided tumors (mPFS 15.97 vs 13.93 months, $p > 0.05$ and mOS 22.2 vs 21.07 months, $p > 0.05$).

Conclusion: The results of our retrospective analysis show treatment outcomes similar to those of previously published relevant clinical studies. Right-sided primary tumors were related with poorer outcomes as opposed to the left-sided tumors. However, there was no significant difference in outcomes by primary tumor location in patients treated with EGFR inhibitors whereas bevacizumab showed significantly worse results in right-sided tumors.

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P14 - THE IMPACT OF LIVER RESECTION ON TRETMENT OUTCOMES OF METASTATIC COLORECTAL CANCER PATIENTS AT THE DEPARTMENT OF ONCOLOGY AND RADIOTHERAPY, UNIVERSITY HOSPITAL OF SPLIT DURING 2017 - A RETROSPECTIVE ANALYSIS

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Backround: Approximately 20-25% of colorectal cancer (CRC) patients are initially diagnosed with metastatic disease in which liver metastases are being presented synchronously with the primary tumor at the time of diagnosis in 20 to 30% of cases[1]. Unfortunately, the majority patients with liver metastases are unresectable with only about 20 to 25% of them declared resectable at initial diagnosis and therefore potentially curable, according to relevant studies[1,2]. Median 5-year survival rates in mCRC patients with "liver-limited" disease who underwent liver resection range from 38 to above 50% according to recent reviews and meta-analysis[2,3]. Lately, there have been significant improvements in the management of initially unresectable or borderline resectable mCRC patients and the impact of doublet or triplet chemotherapy regimens in combination with biological agents have on conversion to resectability and survival rates[4]. Today,multimodal treatment of mCRC patients based on true multidisciplinarity is essential in our goal to improve outcomes. The aim of this study was to retrospectively investigate outcomes in consecutive patients undergoing liver metastasectomy in our institution.

Materials and methods: A retrospectively-based analysis was performed on a cohort of mCRC patients diagnosed with liver-limited disease who were referred to the Department of Oncology and Radiotherapy, University Hospital Split from January 2017 to December 2017. The information about the patients was identified through patient`s records. The data was analyzed with methods of descriptive statistics by using Microsoft Excel tools.

Results: Among 107 patients with newly diagnosed mCRC, 22 (20.5%) underwent liver resection for metastatic *liver-limited* disease. The median overall survival (mOS) for all resected patients was 28.23 months. Due to extensive progression of the disease in the liver on the postoperative CT scan as well as very poor performance status after surgery, 2 patients (9%) were provided with best supportive care as no specific systemic therapy was given. In 13 patients (60%) there was either a residual disease at the postoperative CT scan or newly diagnosed multiple liver metastases so they were treated with first line treatment regimens for unresectable metastatic disease. The mOS for those patients with residual disease was 26.07 months. 7 patients (31%) with no residual disease at the postoperative CT scans were treated with the Folfox regimen in the semiadjuvant setting for 6 months. The disease-free survival and OS for patients with no residual disease after undergoing metastasectomy was 19.5 and 30.87 months, respectively (medians not reached).

Conclusions: Although a small sample size, the results of this retrospective analysis confirm the impact careful patient selection, optimally performed liver metastasectomy and semiadjuvant systemic chemotherapy have on treatment outcomes, especially in patients with no residual disease on the postoperative CT scan. However, there are still significant issues needed to be adressed in order to achieve better outcomes, one of them being better collaboration with surgeons and a multidisciplinary approach in the assessment of resectability.

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P15 - EXPERIENCES WITH NEOADJUVANT THERAPY FOR BREAST CANCER IN OUR CLINIC IN 2018

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Introduction: Neoadjuvant therapy is defined as systemic treatment of cancer prior to definitive local therapy. Typically, in breast cancer, neoadjuvant treatment is in form of chemotherapy, although, in luminal tumours, neoadjuvant endocrine therapy is equally valuable option. Neoadjuvant chemotherapy should be considered whenever adjuvant chemotherapy is indicated. It offers advantages such as early treatment of micrometastatic disease, *in vivo* assessment of tumour response, and tumour down staging that leads to improvement in its resectability (increased rate of surgery with better cosmetic outcomes). Recent studies showed that achieving a pathological complete response (pCR) is associated with better outcomes, and that correlation is strongest for triple negative breast cancer (TNBC) and HER2 positive disease. In those patients that don't achieve pCR, there are post-neoadjuvant treatment options now (TDM1 for HER2 positive disease based on KATHERINE trial; capecitabine for triple negative disease based on CREATE-X trial). In comparison to previous years, the number of early breast cancer treated with neoadjuvant therapy in our clinic is increasing as also as number of pCR. This could be related to better diagnostic approach, better therapeutic approaches, stage migration as well as better multidisciplinary organization.

Matherials and methods: A retrospective analysis of data collected from the case history of breast cancer patients treated with neoadjuvant therapy in 2018 was performed. A total of 29 patients were treated. Seven patients were treated with hormone therapy and the remaining twenty-two patients received chemotherapy with or without hormone and immunotherapy.

Results: Median age of the analyzed patients is 62 years (n=29). By excluding patients treated with neoadjuvant hormone therapy, the median is 60 years (n=22). Nine patients had stage II cancer and the remaining 20 had stage III cancer. Of the 22 patients treated with neoadjuvant chemotherapy, 9 (40.9%) of them achieved pCR (pCR for TNBC was 5/5 (100%), 2/2 (100%) for HER2 positive and 2/3 (66.6%) for LUM B HER2 positive). The results reported are in line with studies. Of the 7 patients treated with neoadjuvant hormone therapy, only one was operated (residual cancer burden III (RCB III), while the other patients declined surgery. The median time from completion of neoadjuvant therapy to surgery was 37 days. 6 patients (27%) have not received planned neoadjuvant chemotherapy completely: 4 interruptions of therapy were caused by peripheral neuropathy (18%), 1 cardiac decompensation (4.5%), 1 hematologic toxicity (4.5%).

Discussion: The results of our analysis are consistent with those of the relevant studies in the aforementioned area. Our pCR rate of 40.9% could be explained by the fact that all our patients were administrated "dose dense" therapy, that the median time from diagnosis to presentation on multidisciplinary team was 18 days, and that all HER2 positive patients have received dual anti HER2 therapy. Despite the high rate of pCR, almost no patients underwent conservative surgery, which is one of the goals of neoadjuvant treatment. Therefore, additional efforts should be made to improve multidisciplinarity when discussing treatment options.

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P16 - IMMUNE CHECKPOINT INHIBITORS COMBINED WITH CHEMOTHERAPY IN EXTENSIVE-STAGE SMALL-CELL LUNG CANCER – SINGLE CENTER EXPERIENCE

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Background: In extensive-stage small-cell lung cancer (ES-SCLC) immune checkpoint inhibitors when combined with chemotherapy in the first line setting show better efficacy than chemotherapy alone. Safety profile of the combined therapy is the same as the adverse events of individual agents.

Methods: We administered atezolizumab with platinum doublet (cisplatin or carboplatin and etoposide) in the first line treatment in 24 patients diagnosed with ES-SCLC. Patients were treated until disease progression or unacceptable toxicity. At the time of data cutoff, the median follow-up was 8.8 months.

Results: 24 patients were treated from December 2018 until September 2019. 13 were males and 11 were females with median age 61 (ranging from 44 to 80). Majority of patients were ECOG 1 and only few were ECOG 2. Median number of applied atezolizumab doses was 8.5 (ranging from 2 to 11). We observed median progression free survival of 6 months (95%CI 4,28-7,72), while median overall survival was not reached. There was no difference in PFS or immune-realted adverse events in patients receiving carbolatin (8 patients) and cisplatin (16 patients). 10 patients (41%) are still undergoing treatment and 9 patients (37%) have died. Immune-related adverse events occurred in 6 patients (25%). Four patients developed pneumonitis (all of them CTCAE grade 2), two patients colitis (CTCAE grade 2 and 3) and one patient rash (and later on pneumonitis), CTCAE grade 3. Patients were treated with oral corticosteroids and median treatment pause was 5 weeks (ranging from 3 to 12 weeks). There were no treatment discontinuations because of adverse events.

Conclusions: Atezolizumab combined with chemotherapy in ES-SCLC showed good tolerability and effectiveness and it is new standard of care for these patients. Our data are consistent with published clinical trial data. Limitations of our report are small sample size and short follow-up time.

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P17 - HEMATOLOGIC TOXICITY OF CYCLIN DEPENDENT KINASE 4/6 (CDK4/6) INHIBITORS PALBOCICLIB AND RIBOCICLIB DURING FIRST THREE CYCLES OF 1ST LINE TREATMENT OF METASTATIC BREAST CANCER - RETROSPECTIVE ANALYSIS IN SINGLE CENTRE

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Introduction: Approximately 6-10% of new breast cancer cases are initially metastatic, and 20-30% of patients diagnosed with early breast cancer develop disease recurrence. Up to 70% of breast cancers are hormone receptor (HR) positive. According to current guidelines, endocrine therapy (ET) in combination with CDK4/6 inhibitors is the mainstay of the 1st line treatment of luminal metastatic breast cancer. With similar efficacy obtained in clinical trials, the most important difference based upon we could choose between CDK4/6 inhibitors could be their toxicity profile. That is the reason why we have initiated analysis of hematologic toxicity profiles of our mBC patients treated with palbociclib and ribociclib.

Methods: We did retrospective analysis of 32 consecutive patients treated with ribocicib or palbociclib in combination with ET as the 1st line treatment for metastatic breast cancer. Patients have signed informed consent and medical data was analyzed. Laboratory tests were analyzed at day 1 and 15 of the 1st and 2nd cycle and on day 1 of the 3rd cycle.

Results: Analysis included 32 consecutive postmenopausal patients, with median age of 63 years. Bone only disease was observed in 44% (14/32) of patients, visceral disease in 22% (7/32) and both visceral and bone disease in 34% (11/32) of patients. 10 (31%) patients received palbociclib, and 22 (69%) received ribociclib. Neutropenia of any grade occurred in 87% (28/32) of all patients. Grade 3 or 4 neutropenia occurred in 16/32 (50%) of patients. There were no cases of febrile neutropenia. Anemia and thrombocytopenia of any grade were not reported. All grades of neutropenia were observed in 90% (9/10) patients treated with palbociclib plus ET; 30% (3/10) experienced grade 3 and 20% (2/10) grade 4 neutropenia. In ribociclib group 86% (19/22) of patients developed any grade of neutropenia. Grade 3 neutropenia was reported in 54% (12/22) of patients. There was no grade 4 neutropenia. Temporary treatment discontinuation due to hematological toxicity has been observed in 43% (14/32) of all patients. In palbociclib group in 30% (3/10) patients and in ribociclib group in 11/22 (50%). Dose reduction was required in one patient in palbociclib group and in one patient in ribociclib group due to repeating neutropenia. One patient in ribociclib group stopped therapy due to grade 3 hepatotoxicity.

Conclusion: This retrospective analysis shown hematological toxicity profile similar to registration trials results. The aim was to learn how to deal with relatively new group of anticancer drugs toxicity. Larger number of patients, longer follow up and inclusion of non haematological toxicity is needed for more adequate comparisment of toxicity profiles of this two drugs.

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P18 - THE ROLE OF GENETIC TESTING IN BREAST CANCER PATIENTS UNDERGOING NEOADJUVANT TREATMENT

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Introduction: Pathologic complete response (pCR) after neoadjuvant systemic treatment appears to be a valid surrogate for better overall survival in breast cancer patients. Together with standard clinicopathologic assessment novel molecular biomarkers and genetic mutations are being tested in order to look into the heterogeneity of breast cancer. Advances in molecular genetics have identified a number of genes associated with inherited susceptibility to breast and ovarian cancer (BRCA1/2, TP53, PALB2, CHECK2, ATM, LZTR1, MSH6, BRIP1, AIP). Breast cancer in BRCA mutation carriers shows different biological behaviour and clinical course than in non-BRCA breast cancer. BRCA status is being studied as predictive biomarker of response to platinum agents and the key factor in surgical decision-making regarding the risk-reducing bilateral mastectomy. The aim of our study was to find pathogenic mutations before making a treatment plan for patients undergoing neoadjuvant treatment.

Materials and methods: Genetic counseling was conducted on 161 patients from 1st of February 2019 until 31st of January 2020 in the Department of Oncology in University Hospital Center Zagreb. We genetically tested 101 participants of which 73 of them (72.28%) were diagnosed with breast cancer, 23 (22.77%) were healthy relatives, 4 (3.96%) had other types of cancer and 1 (0.99%) had unknown diagnosis. In this study we analysed clinical data and results of genetic testing for 11 patients with early and locally advanced breast cancer who started neoadjuvant chemotherapy. We used a panel for hereditary cancer that includes 113 genes. DNA was isolated from peripheral blood using a commercial DNA isolation reagent kit and the sequencing was performed on a MiniSeq sequencing device (Illumina).

Results: Median age at the time of diagnosis was 38 years. The most common surrogate subtype of breast cancer was triple negative breast cancer (TNBC) that was found in 7 patients (63.64%). Other 4 patients (36.36%) had Luminal B HER2 negative breast cancer. During evaluation of personal and family history we found that 8 patients (72.73%) had an affected relative in their close family, 6 of them (54.55%) with breast cancer and 2 (18.18%) with ovarian cancer. In 6 patients (54.55%) we found pathogenic variants, 4 of them (36.36%) had BRCA1 mutation, 1 patient (9.09%) had BRCA2 mutation and 1 patient (9.09%) ATM mutation. 4 out of 5 patients with BRCA mutations had triple negative breast cancer. Likely pathogenic variant was determined in 2 patients (18.18%) and variants of uncertain significance (VUS) were detected in 6 patients (54.55%).

Conclusion: On a small number of patients we found a significant number of pathogenic and likely pathogenic variants with high clinical relevance. Germline BRCA1 and BRCA2 mutations are frequently detected among patients with TNBC, a subgroup that can benefit most from a new therapeutic options.

Small, pivotal trial has shown promising results of pathologic complete reponse with talazoparib monotherapy as a neoadjuant treatment in germline BRCA mutation carriers. In our small subset of patients with BRCA1 and BRCA2 mutations, all patients were subjected to radical mastectomy instead of breast-conserving surgery, regardless of good response to neoadjuvant chemotherapy.

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P19 - NON-BRCA GERMLINE PATHOGENIC VARIANTS IN BREAST CANCER PATIENTS TESTED AT THE UNIVERSITY HOSPITAL CENTER ZAGREB

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Genetic testing is a powerful tool that allows detection of BRCA and non-BRCA germline pathogenic variants in breast cancer (BC) patients or in individuals at high risk of BC. Inherited pathogenic variants (PV) in genes related with moderate to high risk of BC may explain up to 50% of familial BC. Germline BRCA1 and BRCA2 pathogenic variants are responsible for up to 30% of inheritable BC and are the most common assessed pathogenic variants. Non-BRCA pathogenic variants are less common but have been identified and known to contribute hereditary BC syndromes. Although established for BRCA pathogenic variants, indications and interpretations of genetic testing in non-BRCA pathogenic variants are not well defined. Significant progress has been made in the identification of inherited genetic factors underlying hereditary cancers. Pathogenic variants in PTEN, TP53, CHEK2, ATM, NBS1, RAD50, BRIP1 and PALB2, amongst others, have also been shown to contribute moderate to high risk of breast cancer.

The aim of the study was identification of inherited PV of non-BRCA pathogenic variants in BC patients tested at the University Hospital Center (UHC) Zagreb.

Materials and methods: Clinical and demographic data of 161 participants who underwent genetic counseling at the UHC Zagreb during the period of one year (February 2019 - January 2020) were analyzed. 101 of them underwent expedited panel testing. DNA was isolated from peripheral blood using a commercial DNA isolation reagent kit. Sequencing libraries were prepared using a Nexter Flex for enrichment reagent kit using an optimized DNA tagging method (Illumina). Data analysis was performed using the Variant Studio software package. For genetic testing, a hereditary cancer panel including 113 genes, was used.

Analysis of 80 participants who met clinical criteria for genetic testing but were not carriers of BRCA pathogenic variants, was done.

Results: In 31.25% (25/80) of analyzed BRCA-negative participants, expedited panel testing revealed pathogenic variants (PV) or likely pathogenic variants (LPV) of the tested genes. PV were found in HNF1A (in two participants), AIP (in two participants), CHEK2 (in two participants), MUTYH and ATM genes in overall 10% (10/80) of participants and LPV were identified in MSH6 (in six participants), CHEK 2 (in three participants), PALB 2 (in two participants), TP53, BRIP1, MUTYH, BARD1, FANCI and NTHL1 gene in overall 21.25% (17/80) of participants.

This study revealed an unmet clinical need of genetic testing that could benefit a significant proportion of at-risk individuals.

Conclusion: Identifying germline pathogenic variants in women with BC is important because it can influence their immediate and long-term management and has important implications on other family members. Multigene panel findings are likely to change clinical practice for substantially more patients than BRCA1/2 testing alone. For a large proportion of the genes included in hereditary cancer gene panels, clinical guidelines are to be established.

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P20 - GENETIC ASSESSMENT AND TREATMENT DECISION-MAKING IN PATIENTS WITH METASTATIC BREAST CANCER IN UNIVERSITY HOSPITAL CENTER ZAGREB

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Introduction: Metastatic breast cancer is an incurable disease with highly variable clinical course and outcome. Intrinsic genetic heterogeneity of the primary breast tumor may play a role in this variability and may explain it in part. The aim of the study was to determine pathogenic and likely pathogenic variants in a set of highly penetrance genes which can provide new information in the process of treatment decision-making. By genetic testing we can detect patients with BRCA mutations who can benefit from the poly ADP-ribose inhibitors (PARPi) that represent a potentially important therapeutic option directed at targeting cancers with defective DNA-damage repair mechanisms.

Materials and methods: In the Department of Oncology in University Hospital Center Zagreb during the period from February 1, 2019 until January 31, 2020, genetic counseling attended 161 clients and multigene panel testing was performed on 101 participants. Among 101 tested participants, 23 were healthy relatives, 73 were diagnosed with breast cancer, 4 were diagnosed with other types of carcinoma and 1 had unknown diagnosis. In this study we retrospectively analyzed clinical data for 24 patients with metastatic breast cancer obtained from our hospital infomation system and also analyzed the results of previous genetic testing. For genetic testing we used a panel for hereditary cancer that includes 113 genes. DNA was isolated from peripheral blood using a commercial DNA isolation reagent kit. The sequencing was performed on a MiniSeq sequencing device (Illumina).

Results: In our cohort of 24 women with metastatic breast cancer, median age at the time of diagnosis was 46. Pathohistological specimens obtained by breast cancer biopsy showed that 15 patients (62.50%) had triple negative breast cancer (TNBC), 4 patiens (16.67%) had Luminal B HER2-negative breast cancer, 3 patiens (12.50%) had Luminal A breast cancer and there was 1 patient (4.17%) with two malignant tumours, breast cancer and sarcoma and 1 patient (4.17%) with lobular carcinoma. Out of 15 patients (62.50%) with positive family history among first- and second- degree relatives, 10 family members had breast cancer and 3 family members had ovarian cancer. Mutation was not found in only 1 individual. There were 8 patients (33.33%) with true-positive test results and 20 patients (83.33%) with inconclusive test results (or variants of unknown signifacance [VUS]). Pathogenic variants were detected in 3 patients (12.50%), one variant in AIP, one in BRCA1 and one in CHEK2 gene. Furthermore, 5 patients (20.83%) had likely pathogenic variants in the TP53, CHEK2, BRIP1, BRCA1 and PALB2 genes. Based on these genetic test results, 2 women with BRCA1 and PALB2 likely pathogenic variants were assigned to receive talazoparib through a compassionate use programme. Small number of patients with detected BRCA mutation during neoadjuvant treatment progressed to metastatic stage and consequently received talazoparib.

Conclusion: There is still an insufficient number of metastatic patients in our genetic assessment group because of limited resources. Nevertheless, multi-gene testing provided a substantial benefit in clinical management of breast cancer because the small subset of patients were found suitable for the PARP-inhibitor therapy.

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P21 - MAKING OF A CLINICALLY USEFUL QUESTIONNAIRE FOR ASSESSMENT OF EMOTIONAL DISTRESS IN PATIENTS WITH CANCER

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Introduction: The diagnosis of malignant disease, together with the disturbance of physical health caused by cancer pose emotional and psychological challenge for the individual. Patients undergoing active oncological treatment find themselves in new stressful situations that profoundly change their way of life. Anxiety and depression in patients with cancer are associated with poor health-related quality of life, disease-related morbidity, poor treatment adherence, and prognosis. Screening for emotional distress is becoming increasingly common; it helps to detect psychological distress early and thus enable timely provision of adequate treatment. Validated questionnaires are generally used for that purpose in clinical trials, but their clinical acceptance is low. The Emotion Thermometer (ET) is a validated screening tool comprising five dimensions (distress, anxiety, depression, anger, and need-for-help).

Aim: The aim of this study is to make a Croatian version of ET for measurement of emotional distress in patients with cancer and to evaluate the patients' needs for psychological support during anticancer treatment. Once validated, the Croatian version of the Emotional Thermometer will be a short, reliable and effective tool for emotional distress screening and follow- up, useful in everyday clinical practice as a part of a structured program of cancer care.

Patients and methods: Approximately 450 patients (female and male) receiving treatment (radiotherapy or systemic therapy) for breast cancer and colorectal cancer will be included. The study will be conducted in all university hospital centers in Croatia. All patients will be given the Information Letter and should sign the Informed Consent Form. The participants will be asked to fill in 3 questionnaires: a quesstionaire with general information about the patient, HADS (Hospital Anxiety and Depression Scale) questionnaire used as a gold standard against which the third administered instrument, the Emotion Thermometer, will be validated. Questionnaires will be collected from January to April 2020. The results of the study are expected in June 2020.

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P22 - PRETREATMENT KI67 AND THE EFFICACY OF NEOADJUVANT CHEMOTHERAPY IN BREAST CANCER

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Nowadays neoadjuvant chemotherapy (NAC) is the standard treatment for advanced breast cancer (BC) decreasing the extent of surgery. After surgery, pathologists evaluate tumor response to treatment based on pathological yTNM-stage and by residual cancer burden (RCB) scoring using MD Anderson Cancer Center online calculator. Many studies showed that the Ki67 proliferation marker could predict response to NAC[1]. Cabrera-Galeana et al.[2] found that patients without a decrease in Ki67 expression after NAC had worse DFS and OS, while Billgren et al.[3] reported that a decrease of more than 25% significantly predicted a reduced risk of recurrence. Other studies reported that only Ki67 at 30% threshold were independently linked to OS[4, 5].

Results: 249 BC patients have undergone NAC and RCB group was evaluated on surgical specimens. We compared Ki67 expression on pre-treatment biopsy and post-treatment surgical specimens with NAC efficacy. Tumors achieved a complete pathological response (RCB-0) in 28.1%, RCB-I in 6.4%, RCB-II in 38.6%, and RCB-III in 26.9% of BC patients. The overall median of Ki67 expression before treatment was 36.5%, and after treatment, 25% (overall decrease of 31.5%). The median Ki67 before NAC for tumors achieved RCB-0 and RCB-I was 38%, and on surgical specimen, it was 19% for RCB-I (50% decrease). Tumors that recorded only a partial response to NAC (RCB-II) had a decrease in Ki67 expression by 32.4% (from 37% to 25%) and those without a response to NAC (RCB-III) had a decrease of only 23.4% (from 32% to 24.5%). Luminal B tumors had the worst response to NAC with only 8.8% RCB-0 or 1, despite the fact that the median Ki67 expression was 33%. Those who achieved RCB-0 had a median Ki67 of over 40%. Luminal B tumors more frequently (59.8%) than other intrinsic subtypes had positive lymph nodes (59.8%). Ki67 expression decreased in intrinsic subtypes as follows: 66.7% in Luminal B/HER2positive, 32.5% in HER2 positive, and 24.2% in Luminal B while triple negative BC tumors either responded very well (34.8%) or did not have almost any reduction in Ki-67 expression. Spearman's analysis showed that higher Ki67 expression before NAC indicated a sensibility to therapy resulting with smaller residual tumor (P =.05), and lower RCB (P =.02). Interestingly, biopsy tumors had a slight decrease in Ki67 expression as the number of positive lymph nodes increased (P =.03). However, high expression of Ki67 after NAC indicates poor response to therapy and a higher residual tumor (yT) and positive lymph node (yN) status (P <.001).

According to our results, high expression of Ki67 in biopsy and a decrease in surgical specimens suggests a sensibility to neoadjuvant chemotherapy. Patients follow-up will give us more information about the DFS and OS. Our results suggest that tumors with Ki67 over 40% have better response to NAC, but we cannot state that Ki67 is a predictor of NAC, especially not for all intrinsic subtypes equally.

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P23 - ASSESSMENT OF CREATININE LEVEL RISE IN CANCER PATIENTS TREATED WITH RIBOCICLIB AND ANTIHORMONAL THERAPY AT THE UNIVERSITY HOSPITAL FOR TUMORS

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Selective cyclin-dependent kinases 4/6 (CDK 4/6) inhibitors, in addition to antihormonal therapy, are now standard of care for metastatic hormone receptor (HR) positive Her-2 negative breast cancer. Based on the research of Wilson et al. (2019), our study aims to discuss and evaluate a correlation between ribociclib and changes in creatinine level in patients with HR-positive Her-2 negative metastatic disease. According to the Summary of Product Characteristic for ribociclib, an elevation of plasma creatinine level is a common side effect. Abnormal kidney blood test result is described in around 98% of patients treated with abemaciclib. Neither one of three selective CDK 4/6 inhibitors requires dose adjustment for patients with mild to moderate renal impairment, based on estimated glomerular filtration rate. Therefore, we can define it as a drug class effect.

We obtained the data from 58 patients with HR-positive Her-2 negative breast cancer who were treated at the Department of Medical Oncology with ribociclib and antihormonal therapy, in the period from 08/2018 to 1/2020. Patients had to complete at least one four-week cycle of therapy and had to have baseline serum creatinine level in normal range. Fifty four female patients were eligible for further analysis and their median age was 66. Patients with baseline creatinine level >90 μmol/l were excluded. During the therapy with ribociclib, around 40% of included patients had an elevation of plasma creatinine level above normal ranges (which for our laboratory is less than 90 μmol/l). Three patients developed a grade II acute kidney injury according to Common Terminology Criteria for Adverse Events version 4.0, and at this moment none of them ceased therapy. None of the patients, from an analysed group, had a dose reduction due to this reason.

Elevation in plasma creatinine level during the therapy with ribociclib is already reported as common in routine clinical practice. Clinicians should be aware of the possibility and the incidence of this side effect and interpret it with the respect to patients' comorbidities and chronic therapy, and thus elude termination of treatment or excessive further diagnostics. Further studies should evaluate the etiology of plasma creatinine level rise due to ribociclib use.

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P24 - HOW TO DISTINGUISH PRIMARY FROM ACQUIRED ACHALASIA?: A PATIENT WITH ACHALASIA AND CANCER OF BOTH KIDNEYS

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Introduction: Achalasia is a motor disorder of the esophageal smooth muscle that results because of the loss of ganglion cells in the myenteric plexus of the distal esophagus. The most common symptoms of the the disorder are dysphagia, regurgitation, chest pain, heartburn, weight loss, and aspiration pneumonia. Etiologically, primary (idiopathic) should be distinguished from acquired achalasia resulting from tumor infiltration of the lower esophageal sphincter (LES), viral infections, or neurodegenerative diseases.

Case report: This is the case of a 39-year-old patient who was initially referred from another health center due to dysphagic problems and vomiting of food. Since the onset of the dissease (6 months), he has lost about 20 pounds. Esophagogastroduodenoscopy (EGDs) showed a dilated esophagus with retention of food in the lumen, without peristalsis and with narrowing in the distal part of the esophagus that could be passed only with considerable resistance (biopsies taken for PHD were not specific). Esophageal manometry findings are characteristic of achalasia (type II): aperistatic activity of the esophagus body, elevated pressure of the DJS at rest and no relaxation upon swallowing (integrated relaxation pressure-IRP is elevated). The additional work up (ultrasound and MSCT of the abdomen and thorax) was performed and it verified the large expansive process of the distal third of the left kidney and the hypoplastic right kidney ectopically located in a small pelvis with an expansive process in the middle of it. The patient was presented at the gastro-urological-oncology meeting and the endoscopic balloon dilation of the DJS was first performed. Subsequently, a radical left-sided nephrectomy (PHD: Adenocarcinoma renis. PT1b-NXMX.G3) was performed and then, according to the patient's wish, enucleation of the ectopic right kidney tumor (PHD: Adenocarcinoma renis). In the meantime, another endoscopic balloon dilation of the DJS was performed: Significant clinical improvement was achieved (the patient was swallowing food properly) and he gained significantly on weight. Endoscopically, there is no longer any retention of food in the lumen of the esophagus and the distal part undergoes less resistance and at the last manometric finding the pressure of the DJS at rest is not increased. Further monitoring of the patient is required.

Conclusion: When treating dysphagia and suspected achalasia, it is important to determine whether it is primary (loss of ganglion cells in the myenteric plexus of the distal esophagus) or acquired achalasia (most commonly due to DJS tumor infiltration). A characteristic finding for achalasia is complete absence or partial relaxation of the DJS when swallowed, which was the case in our patient with adenocarcinoma of both kidneys.

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P25 - TOLERABILITY OF BEVACIZUMAB IN ELDERLY PATIENTS WITH OVARIAN CANCER: AN EXPERIENCE FROM THE DEPARTMENT OF GYNECOLOGIC ONCOLOGY IN THE UNIVERSITY HOSPITAL CENTRE ZAGREB

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Introduction: Bevacizumab is a recombinant humanized anti-VEGF monoclonal antibody. It is an effective treatment for epithelial ovarian cancer, both in primary and recurrent disease. The incidence of ovarian cancer increases with advancing age. Despite the high prevalence of the ovarian cancer in elderly, the management of these patients is often less aggressive than that in younger patients. Our aim was to investigate the safety of bevacizumab administration in patients older than 65 years.

Methods: We have analysed the medical data of 65 patients with epithelial ovarian, fallopian tube, or primary peritoneal cancer who started treatment with bevacizumab in primary advanced and in first relapse of the disease at the Department of Gynecologic Oncology in the University Hospital Centre Zagreb in the period from April 2017 to December 2018. Patients were divided in two categories according to age: group 1 (>65 years) and group 2 (≤65 years).

Result: Our analysis included 65 patients:18 (27,7%) patients in group 1 compared with 47 (72.3%) in group 2. Bevacizumab have been administered to 38 (58.5%) patients as first-line treatment and to 27 (41.5%) patients as second -treatment. The median age was 70 years (range 66-76 years) in group 1 and 55 years (range 35-65 years) in group 2. ECOG status 0 had 44.7% of patients in group 2 compared with only 33.3% in group 1. At the time of diagnosis, elderly patients had presented with at least one comorbidity in 66.6% of the cases, compared with 40.4% in group 2. The median number of cycles of bevacizumab was 9 in elderly patients and 17 cycles in group 2. Among those patients receiving bevacizumab in the first-line setting, median progression free interval (PFI) was 12 months in younger patients versus 7 months in elderly patients. Similarly, among those receiving bevacizumab in the second-line setting PFI was 9 months in younger patients versus 1 months in elderly patients. The occurrence of non-haematological toxicity did not increase in elderly patients; 51.1% of patients in group 2 reported some of non-haematological adverse events versus only 27.8% in elderly patients.

Conclusion: In Croatia, from February 2017 we have opportunity to treat patients with epithelial ovarian, fallopian tube, or primary peritoneal cancer with bevacizumab in the first-line and second-line settings. Our experience in treating patients with bevacizumab showed good results with acceptable toxicity and our findings suggest that its use in the elderly population should be considered as safe and manageable.

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P26 - THE EFFICACY AND SAFETY OF CONCURRENT CHEMORADIOTHERAPY IN PATIENTS WITH NON-SMALL CELL LUNG CANCER - SINGLE INSTITUTION STUDY AT DEPARTMENT OF ONCOLOGY AND RADIOTHERAPY, UNIVERSITY HOSPITAL OF SPLIT

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Backround: Lung cancer is most frequently diagnosed cancer and leading cause of cancer death worldwide. Concomitant chemoradiotherapy is the treatment of choice for patients with non-small cell lung cancer, who are in good condition, with stage IIIB, IIIC and selected patients with earlier stages of the disease that is inoperable. Although randomised clinical trials have proved the benefit of this approach, in everyday clinical practice, due to multiple reasons, it is still underutilised. Based on survival benefit with consolidation immunotherapy with durvalumab after concomitant chemoradiotherapy, this has become new standard of treatment in western countries. The prerequisite for optimal results of this new strategy, that is still not reimbursed in Croatia, is properly conducted chemoradiotherapy part of the treatment.

Objectives: Our goal was to examine the efficacy and safety of concurrent chemoradiotherapy as primary therapy in patients with non-small cell lung cancer stages I-III, treated at the Department of Oncology, University Hospital of Split from 2011. till 2018.

Patients and metods: In a retrospective study conducted at Department of Oncology and Radiotherapy, University Hospital of Split, the comprehensive demographic and clinical data was collected on a total of 84 patients, treated with concurrent chemoradiotherapy as a primary treatment, in period between 2011., when we introduced 3D conformal radiotherapy, and 2018. Study protocol was approved by University Hospital of Split Ethics' Committee.

Results: The median age of patients was 61 years, 75% being male. The most common histological types where squamous cell carcinoma (56%) and adenocarcinoma (32%). The median dose of applied radiotherapy was 55 Gy, with 30% of patients receiving 60 Gy or more. All patients got concurrent platinum and etoposide (PE) chemotherapy, five or three-day regimens, and 69% got both cycles.The median follow-up time of our patients was 15 months. Objective response rate was 69%. The median progression free survival (PFS) was 9 months (95% CI: 7.27-12.57) and median overall survival (OS) was 17 months (95% CI: 13.47-27.43). The treatment was relatively well tolerated. The most common acute toxicity was leukopenia, observed in 65% of patients. Radiation esophagitis, with a 39% occurrence, was the most common acute toxicity of grade 1 and 2, while the most common grade 3 and 4 toxicity was neutropenia (38% of patients).

Conclusion: This retrospective analysis on treatment outcomes of patients with locally advanced lung cancer treated with concomitant chemoradiotherapy showed comparable results in clinical efficacy and toxicity with older randomised clinical trials that positioned the role of concurrent chemoradiotherapy in this disease, but are slightly inferior to the most recent trials. Possible explanations are: retrospective nature of the study, treatment in every day setting that differs significantly from clinical trials conditions, mainly by inclusion of patients with worse demographic and clinical characteristics. Nevertheless,

these results are the first one reported on treatment outcomes of this approach in Croatia, and are again pointing out on importance of real multidisciplinary approach to lung cancer patients.

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P27 - V50 – PREDICTIVE MARKER IN RADIOTHERAPY INDUCED HYPOTHYROIDISM IN HEAD AND NECK CANCER PATIENTS

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Patients with head and neck squamous cell carcinoma (HNSCC) are often treated with radiation therapy at some point during their disease. Up to 50% of patients that undergo neck irradiation are affected by hypothyroidism, which usually develops between 6 and 24 months after treatment. Although thyroid gland, as an OAR, is frequently involved in the treatment field due to its midline neck position and the dose it receives often exceeds 50 Gy, it remains a gray zone in radiotherapy. Previous studies have shown the association between higher radiation doses and higher HT rate, but no clear threshold has been defined and we lack accepted consensus on dose-volume parameters and constraints.

A study was conducted to determine the predictive value of various dosimetric parameters and clinical characteristics on the development of HT and to identify a subgroup of patients at high risk for developing HT. A total of 156 clinically euthyroid patients with HNSCC, who were treated with (chemo) radiotherapy in a primary or postoperative setting between August 2012 and September 2017, were included in the study.

Dose-volume parameters as well as V10 toV70, D02 to D98, and the VS10 to VS70 were evaluated. The patients' hormone status was regularly assessed and after a median follow-up of 23.0 (12.0–38.5) months, 70 (44.9%) patients developed HT. In univariate analysis, VS65, Dmin, V50, and total thyroid volume (TTV) had the highest accuracy in predicting HT. Hypothyroidism risk score (HRS) was constructed as a regression equation and comprised TTV and Dmin. HRS had an AUC of 0.709 (95% CI 0.627–0.791). HT occurred in 13 (20.0%) patients with a score < 7.1 and in 57 (62.6%) patients with a score > 7.1.

Among the VX parameters, V50 was found to be the best predictive factor for the development of HT. In the literature V50 has been previously reported as the most valuable parameter in this setting, but between studies its threshold levels significantly varies. A study by Ling et al., showed that HT was reduced when achieving D50 < 50 Gy, V50 <50%, and a mean dose of < 54.58 Gy. To avoid HT, Lin et al. proposed V50 threshold of <75%. Another study by Sachdev et al. reported that after a 50-month follow-up, the total rate of HT was 33%, with the proposed threshold V50 >60%. When all these results are analyzed collectively, it can be concluded that the rate of HT is small in patients receiving <50 Gy. In our cohort of patients V50 was capable of delineating 14 patients with V50 < 60% as those with a lower risk of HT, but when we employed HRS in patients with V50 > 60%, additional 52 patients were categorized as those with lower risk.

Although thyroid sparing should never compromise tumor coverage, it may be optimized by using V50 < 60% as a dose-volumetric threshold when possible. When V50 > 60% HRS may be helpful in predicting HT risk more precisely and patients should be closely monitored even during follow-up period.

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P28 - TREATMENT WITH CDK 4/6 INHIBITORS IN METASTATIC HORMON RECEPTOR POSITIVE, HER-2 NEGATIVE BREAST CANCER – A SINGLE CENTER EXPERIENCE

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Introduction: Worldwide, breast cancer is the leading cause of cancer-related death in women. According to Croatian National Cancer Registry, in 2017 breast cancer was the most common cancer site in women (25% of all cancers in women) with the incidence of 129,7/100000. Approximately 65% of metastatic breast cancer are hormon receptor (HR) positive, HER-2 negative, median duration of survival for these patients is approximately 40 months with no dramatic improvement over the past decade. Endocrine therapy (ET) is the preferred option for hormon receptor positive disease, unless there is a visceral crisis. The addition of a cyclin-dependent kinase 4/6 (CDK 4/6) inhibitor to an aromatase inhibitor or fulvestrant, in patients naïve or pre-exposed to ET is one of the preffered treatment option. To date there are three CDK 4/6 inhibitors approved by European Medicines Agency (EMA) in this indication: palbociclib ribociclib and abemaciclib.

Patients and methods: We treated 27 women with HR-positive, HER-2 negative metastatic breast cancer in our Department from October 2018 to January 2020. Median age was 62.8 years at the time of diagnosis of metastatic disease (range 42-89 years), 12 patients (33%) previously received adjuvant therapy and 15 (67%) were "de novo" metastatic. Two thirds of patients received the combination of CDK 4/6 inhibitors and ET in first line (CKD 4/6 inhibitor with letrozole), and one third in second line (CKD 4/6 inhibitor with fulvestrant). Two thirds received palbociclib as the CDK 4/6 inhibitor partner either in first or second line, the rest received ribociclib, at the time of the analysis abemaciclib was not used. Regarding endocrine sensitivity, 18 women were endocrine sensitive, 9 were resistant of which three progressed after first evaluation.

Results: At the time of the analysis 13 (48%) women are still in treatment, 6 (22%) had progressive disease, 6 (22%) are in treatment evaluation, one patient died due to sepsis and one was lost in follow up. Approximately 40% of patients remain progression-free on treatment 2.2 years after initiating treatment with ET and a CDK4/6 inhibitor. Median progression free survival was not reached at the time of the analysis. Most common adverse event was neutropenia. A total of 20 patients (74%) had neutropenia (11 (41%) grade 3), there was no documented febrile neutropenia, and we had to reduce the dose of the CDK 4/6 inhibitor in one patient. There were no severe adverse events documented and the therapy was well tolerated.

Conclusions: The optimal sequence of endocrine based therapy is uncertain, therefore there is a need for new effective drugs in HR positive, HER-2 negative advanced breast cancer sensitive and (even more) resistant to ET. Ongoing and upcoming trials will hopefully provide more data in both groups.

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P29 - MULTIDISCIPLINARY TEAM FOR THORACIC TUMORS AT UNIVERSITY HOSPITAL CENTER SESTRE MILOSRDNICE IN 2019

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Lung cancer is among the top five most commonly diagnosed cancers. It is by far the leading cause of cancer death among both men and women, making up almost 25% of all cancer deaths. According to the latest Croatian National Cancer Registry lung cancer is the second most common cancer in both sexes and represents a major health problem. Multidisciplinary team (MDT) management has emerged as the standard of care and is being implemented in everyday practice to evaluate, treat and monitor cancer patients (pts). Overall evidence suggests that multidisciplinary care may result in improved survival, guideline-based treatment and increased quality of life for lung cancer patients.

Here we present the work of our MDT for thoracic tumors in the year 2019. The team has been active since April 2018. It consists of 19 medical members of various specialities: oncologists (5), pulmonologists (2), pathologists (2), radiologists (4), thoracic surgeons (3), cytologists (3) and molecular biologist. From January to December 2019 a total of 239 patients were presented, 156 men and 81 women, aged 39-86 years with median age of 65 years.

Through 2019 a total of 56 transthoracic needle biopsies and 89 bronchoscopies were preformed. In some patients lymph node extirpation, endobronchial ultrasound or surgery were preformed to establish the diagnosis. Altogether 76 patients either had no evidence of malignant disease or had metastasis from other primary tumor. When looking at histology pattern of our represented patients, distribution was as expected in literature: small cell lung carcinoma (SCLC) - 19,0% (31 pts), non-SCLC (NSCLC) - 79,7% (130 pts) and mesothelioma - 1,2% (2 pts), as well as the distribution of histologic subtypes of NSCLC: adenocarcinoma - 63,2% (81 pts), squamous cell carcinoma - 30,7% (40 pts), large cell carcinoma - 1,6% (4 pts) and carcinoma not otherwise specified (NOS) - 4% (5 pts).

Turning point for our MDT was establishing of molecular profiling for biomarkers (EGFR, ALK, PD-L1) from tissue samples at our hospital in March 2019, which significantly reduced time to treatment. Soon we will be able to analyze biomarkers from cytology samples as well.

In all 73 tested patients, molecular analysis showed PD-L1 >50% in 27,3%, PD-L1 1-49% in 35,6% and PD-L1 <1% or negative in 30,1% of patients, respectively. One patient tested positive for EGFR mutation and 4 patients had ALK positive tumors.

A total of 11 (6,7%) patients were referred for surgery and 6 (3,6%) to stereotactic ablative radiotherapy (SABR), 23 (14,1%) patient had indication for sequential or concurrent chemo- and radiotherapy, and 61 (37,4%) patients started therapy for stage IV disease. Due to poor performance status, 35 (21,4%) patients were reffered to palliative care, with no active oncological treatment. We lost 15 (9.2%) patients to follow –up, and 12 patients (7,3%) decided to continue treatment in other hospitals.

Our data shows a significant increase in the number of patients diagnosed and treated for lung cancer (in comparison, in the year 2018 there were approximately 120 patients presented on the team).

Barriers to effective MDT working include poor attendance by some specialists, inadequate or poor quality information presented about the patient. We all have to aspire to cross these barriers in order to give optimal care to our patients.

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P30 - FIRST EXPERIENCES OF ALPELISIB TREATMENT OF HR + HER2- METASTATIC BREAST CARCINOMA IN CROATIA

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Introduction: Breast cancer is the most common cancer among women. It is estimated that worldwide over 600 000 women died in 2018 due to breast cancer. About 65% of metastatic breast cancers are HR+ HER2 negative. In the last few years the combination of standard endocrine agents with cyclin-dependent kinases inhibitors (CDKi) has significantly improved progression free survival (PFS) in endocrine sensitive as well in resistant population (HR: 0.53 - 0.57, median PFS of 22 to 34 months for sensitive and HR: 0.55 – 0.59, median PFS 11.2 – 20.5 for resistant population). Phosphatidylinositol 3 kinase (PIK3CA) mutations occur in approximately 40% of patients with HR+ HER2neg breast cancer. New therapeutic approaches in that subgroup of patients showed clinically significant efficiency in respect to the standard therapeutic approaches: PFS at a median follow-up of 20 months was 11.0 months in the alpelisib–fulvestrant group, as compared with 5.7 months in the placebo–fulvestrant group (HR 0.65; 95% CI; P<0.001).

Due to the open managed access program available in our clinic, patients diagnosed with HR+ HER2neg advanced breast cancer with mutated PIK3CA, may have access to the alpelisib treatment if eligible. Since the most common adverse event in SOLAR I study was hyperglycemia (63.7%), we tried to downsize and prevent hyperglycemia and consequently hyperinsulinemia by taking alpelisib in the evening (at least five hours after the last meal low in carbohydrates) instead as commonly in the morning. Doing this would potentially increase alpelisib efficiency, decrease incidence of adverse events and improve quality of life (QoL) of our patients.

Materials and methods: Retrospective - prospective analysis of data from patients who started aleplisib therapy in our clinic until February 2020. Twenty-four patients were tested, of which 10 were found to have a PIK3CA mutation. Analysis were performed using RT-PCR technique. All but one was made from the primary tumour. Three patients started treatment on 28 November 2019. Three days before the start of alpelisib treatment and three days after, a 7-point glycemic profile was made. Blood glucose levels continued to be measured daily: in the morning before eating and in the evening before taking alpelisib, five hours after last meal. Values of C peptides and total cortisol were regularly measured at the beginning of every cycle of therapy.

Results: The median age of patients is 67 years. All three patients received numerous (min 4, max 11) therapies for metastatic breast cancer. All three of them previously received CDKi + hormone therapy (HT). Patients have recived alpelisib therapy for medium time of 4 months. Only one patient, who was prediabetic before the start of alpelisib, developed hyperglycaemia gr 3. With the introduction of antidiabetic therapy (SGLT2 inhibitor, pioglitazone and diabetic diet), blood glucose levels were reduced. A decrease of the Ca 15.3 tumour marker was noted in all three patients. Two patients reported weight loss of gr I. There were no other side effects.

Discussion: By adjusting diet habits in our patients and dosing alpelisib in the evening, alpelisib therapy did not cause serious side effects and did not require discontinuation or dose reduction. To potentially confirm our hypothesis, phase II study is planned: usual ordination of alpelisib in the morning without dietary restrictions will be compared with evening ordination with dietary restrictions and 5 hour fasting period.

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P31 - PROSTATE CANCER TREATMENT DECISION SUPPORT TOOL FOR PATIENTS: DEVELOPMENT AND TRANSLATION OF SMART PHONE APP TO THE CLINIC. RESULTS OF THE PROSPECTIVE PILOT STUDY

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Introduction: Treatment decisions for men with localized prostate cancer are complex and are often plagued with lack of high-quality evidence to guide the decision. We hypothesized that simple decision-making educative mobile device-based tool could potentially have positive impact on patient informed decision making and education on different treatment options with potentially improved patients' satisfaction, better quality of life and closer physician-patient interaction. Therefore, we have created an APP and conducted prospective pilot study with primary endpoint of feasibility of such novel approach.

Patients and methods: Created APP for newly diagnosed PCa patients can be used on smart phone and tablet platform and has 32 questions covering following areas: patients' personal values and health/treatment emphasis, general health, prostate cancer data, urinary function, rectal function, family history, and personal priorities. Validated EPIC-26 questionnaire was incorporated as quality-of-life assessment tool. Background patient demographic and clinical data clustering and machine learning were integrated and optimized using cloud technology to provide customized treatment options. At the end APP offers extensive explanation and side-effects of radiotherapy, radical prostatectomy, hormonal therapy and active surveillance management. APP allows prospective determination of quality of life and treatment satisfaction using email prompts sent to patients where they can answer questionnaires from the comfort of their homes.

Results: During 2018-2019, after screening of more than 134 patients, twenty patients (15%) were included in this feasibility trial. Main reasons for failed inclusion were lack of patient interest or time, lack of understanding of the project, impaired cognitive issues, vision issues (inability to read small letter on tablet screen), mistrust in modern technology, lack of space, and low level of basic IT literacy. All included patients had newly diagnosed prostate cancer. Median patient age was 65 years, 75% patients had Gleason score 7 prostate cancer, median PSA level was 10.5 ng/mL, all had localized prostate cancer, and majority of patients were referred by urologist for radiotherapy consultation. Average time to fulfill APP questions was 11 minutes (range 9-16 minutes). In first phase of the APP development we noticed issues with understanding of certain questions or items therefore we amended APP to improve clarity and avoid redundancy. From 20 patients, after using APP educational tool, 13 patients underwent radical prostatectomy, 6 patients underwent radiotherapy and 1 patient underwent active surveillance. Only 8 patients (40%) could fulfill and handle APP alone, without help. On survey, eighteen patients (90%) were satisfied with information provided by the APP saying they had learned significant new information on treatment options for prostate cancer. Unfortunately, due to patient's low compliance and lack of IT support and skills, we were unable to collect prospective quality-of-life and treatment satisfaction data using email prompt system.

Conclusions: Although majority of patients were satisfied with information provided through APP-based educational tool, practical adoption of such intervention in busy clinic was challenging. However,

with additional support from study nurse or immediate family member provision of IT-based solutions might be more feasible.

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P32 - NEOADJUVANT THERAPY IN BREAST CANCER – A SINGLE CENTER EXPERIENCE

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Introduction: Breast cancer is the most common cancer in women and leading cause of cancer death in women worldwide. In order to improve outcome and survival, early detection and optimal treatment is critical. Neoadjuvant treatment (NAT) offers several potential advantages. It can facilitate breast and axillary conservation, render inoperable tumors operable, allows for early evaluation of clinical efficacy and tailoring of adjuvant therapy to the individual based on response to neoadjuvant treatment (pathologic complete response (pCR) vs residual disease (RD)). NAT can be considered in patients with inoperable disease (inflammatory breast cancer, bulky or extensive nodal disease, tumors invading the chest wall or skin) and those with operable disease but certain high-risk features including HER2-positive or triple-negative disease with tumors larger than 2 cm and positive nodal disease. Obtaining pCR to neoadjuvant therapy is associated with favorable outcomes. The correlation between pathologic response and long-term outcomes is strongest for patients with triple-negative breast cancer (TNBC), less so for HER2-positive disease, and least for luminal disease.

Patients and methods: We retrospectively analyzed patients with high risk early-stage or locally advanced breast cancer treated with neoadjuvant therapy at our institution from January 2016 to January 2020. In total, 46 female patients were treated. Median age at time of diagnosis was 52 (ranging from 26-74 years). All patients were presented at the Multidisciplinary Tumor Board for Breast Cancer before start of NAT and after surgery. Patients received anthracycline-based chemotherapy (ACx4) administered sequentially with paclitaxel weekly x12, with or without anti-HER2 targeted therapy (trastuzumab or pertuzumab plus trastuzumab). According to disease subtypes, 33% of patients were luminal B HER2-negative, 30% Luminal B HER2-positive, 13% HER2-positive and 24% were triple-negative.

Results: A majority of patients (85%) completed NAT, four are still on treatment as of January 2020 and treatment was discontinued in three patients (one progressed during NAT, one refused further treatment after 3 cycles of AC chemotherapy and treatment was discontinued in one patient due to adverse effects). Of the 39 patients that completed NAT, 37 underwent surgery and two patients were lost to follow up. Of these, twenty-eight patients (76%) had radical surgery and only 9 breast conserving surgery. PCR was achieved in 12 patients (32%), 5 of which had TNBC and 4 that were HER2-positive.

Conclusions: The results of neoadjuvant treatment at our institution are mostly in accordance to similar studies reported in the literature. They confirm that NAT is in particular useful for breast cancer patients with TNBC and HER2-positive tumors. Our results suggest the need to modify surgical approach considering the relatively large number of patients who have undergone radical surgery. Also, they emphasize the responsibility of multidisciplinary teams (MDT) to adequately screen patients for NAT and ensure that treatment is performed within the best possible timeframe.

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P33 - ANGIOMYXOMA TESTIS: A RARE CASE

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Aggressive angiomyxoma (AAM) particularly testicular origin is a rare benign mesenchymal myxoid tumor which is locally aggressive, blatant for local recurrence, and may metastasize. It occurs mostly in females of a childbearing age and extremely rare in males. We report a very rare case of paratesticular AAM which presented as a scrotal swelling.

Case report: A 58-year-old man presented with the right scrotal mass. Physical examination revealed a nontender right scrotal swelling measuring 5×3 cm, soft in consistency. Transillumination examination was positive. Ultrasonography (USG) examination demonstrated a well-defined hypervasculary mass seen within the right scrotum measuring 45 mm × 25 mm Right testis was visualizing the normal. A radical right orchidectomy was done. Tumors marker was negative. Histologically, the lesion was hypocellular, composed of uniform and bland-looking spindle to stellate shaped neoplastic cells embedded within the loose myxoid stroma. Numerous small- and medium-sized thick walled vessels are also seen. No nuclear atypia or mitosis is found. Immunohistochemically, the neoplastic cells showed diffuse smooth muscle actin (SMA) and desmin immunoreactivity. Progesterone receptor, however, was negative. CD34 and S100 were also negative. The patient was followed up regularly with USG and computed tomography (CT) scan. He did not have local recurrence or distant metastasis two years postsurgical resection.

Discussion: Surgery remains the mainstay of treatment to date. Other treatment modalities such as radiotherapy and hormonal manipulation using tamoxifen, raloxifene, and gonadotropin-releasing hormone analogs were reported. Long-term follow-up with either USG or CT scan is recommended due to its local aggressiveness. AAM in the scrotal region may present as a scrotal mass, often wrongly a diagnosed as a hernia, hydrocele, spermatocele, ot testicular neoplasm as in the current case. Three types have been identified: AAM, angiomyofibroblastoma, and superficial angiomyxoma. Detailed radiological workup such as USG, CT scans, and magnetic resonance imaging may be helpful in the diagnosis, but histological examination of the excisional specimen is the gold standard for establishing the diagnosis. We encountered the first case of paratesticular AAM presented as a scrotal mass after reviewing the final histological examination. Histologically, the tumor appears poorly circumscribed with infiltrative border and consists of uniform and bland-looking spindle to stellate shaped neoplastic cells arranged in a loose myxoid background. Numerous small- and medium-sized thick walled vessels are usually present diagnosis. Immunohistochemically, the neoplastic spindle cells are typically immunoreactive for SMA, desmin, and vimentin. Estrogen and progesterone receptors maybe positive in some cases. Classically, the tumor cells are immunonegative for S100 protein and CD34.

Conclusion: Paratesticular AAM is a very rare benign neoplasm which is locally aggressive, blatant for local recurrence, and may metastasize. Surgery is the mainstay of treatmentand subsequent long-term radiological follow-up is recommended.

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P34 - MULTIDISCIPLINARY SURGICAL APPROACH TO THE TREATMENT OF RENAL CELL CANCER STAGE T3C

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Introduction and objectives: Renal malignancies account for 3% of all malignancies. Histologically the most common type are adenocarcinomas. Renal cell cancer primarily metastasizes via lymphatic and hematogenic pathways, but also through the creation of tumor thrombus that spreads into the renal vein then into inferior vena cava and from there into the right atrium. Aim is to present our case series documenting our experience and results with surgical management of T3c renal cell cancer(RCC).

Material and methods: From database of patients operated in our hospital we have identified patients who were treated for T3c RCC. We performed analysis of patients medical records.

Results: In the period from 2008 to 2019, at the Department of Urology, University Hospital Center Zagreb, 12 patients were treated for T3c RCC. Average age of patients was 57,3 (29-77) years. All operations were performed in cooperation with cardiac surgeons. Surgical procedures were performed in hypothermia using extracorporeal circulation. In this moment eight patients are being monitored. Of the 12 operated, three patients are alive more then five years and seven are more than two years old. Extracorporeal circulation averaged 73-140 minutes and cardiac arrest 7 – 56 minutes. In all cases pathology report was clear cell renal cancer. Postoperatively, two patients have had pulmonary embolism and one patient have had partial kidney embolism and infrarenal aortic dissection that was treated conservatively. During average follow up period of 42,9 (8-106) months 4 patients have died (two because of RCC).

Conclusion: Surgical treatment of advanced RCC involving the IVC is feasible with acceptable morbidity and mortality. Our series is comparable to other reported series. Long-term survival can be expected in non-metastatic patients. These cases benefit from a multidisciplinary surgical approach.

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P35 - EARLY EXPERIENCE WITH NEOADJUVANT CHEMOTHERAPY IN MUSLE-INVASIVE BLADDER CANCER: RESULTS FROM SINGLE INSTITUTION RETROSPECTIVE EVALUATION

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Introduction: The survival benefit of neoadjuvant chemotherapy (NAC) in the treatment of muscle-invasive bladder cancer is well established. Large meta-analysis of 11 trials involving 3005 patients showed that cisplatin-based multiagent neoadjuvant chemotherapy was associated with improved 5-year overall and disease-free survival. However, despite supporting evidence, the uptake of NAC remains globally low. In Croatia NAK has only been sporadically used. The aim of this analysis was to evaluate our initial experience with systematic use of NAC in MIBC, in terms of pathologic efficacy and toxicity. We also provide early data on potential predictive role of immunohistochemically assessed bladder cancer molecular tumor subtypes in response to NAK.

Patients and methods: We retrospectively evaluated patients who underwent neoadjuvant chemotherapy from April 2018 through February 2020 at single institution. The decision to offer NAK was made on uro-oncology multidisciplinay meeting, where findings from pathology report of transurethral bladder tumor resection (TURBT) and computed tomography staging scans were discussed. The efficacy of NAC was assessed based on pathological T0 rate in radical cystectomy specimen. Treatment-related toxicity was assessed using Common Toxicity Criteria version 4. Tumor immunophenotype (luminal vs basal subtype) was assessed on retrieved archived formalin-fixed paraffin-embedded tissue from TURBT specimen using following urothelial markers: CK5/6, CK20, CD44, GATA-3, and p53.

Results: Untill February 2020, 19 patients completed NAK, with two patients still under treatment. Median age was 62 years (range 48-73 years). Fiveteen patients (71%) were males. Distribution of clinical T stages (based on TURBT and CT investigations) was following: cT2, cT3, and cT4 in 14, 5, 2 patients, resepctively. Eleven patients had presumable metastatic pelvic lymph nodes on CT scans. Twenty patients (95.2%) recieved dose-dense (dd) metothrexate-vinblastin-doxorubycine-cisplatin (MVAC) protocol, and 1 patient (4.8%) recieved gemcitabine-cisplatin (GP) protocol. Granulocyte colony stimulating factor profilaxis was given in all patients receiving ddMVAC regimen. Median duration of NAC was 7 weeks (range 4-18 weeks). Distribution of NAK cycles was following: 4, 3, 2, and 1 cycles were given in 11, 5, 2, and 1 patients, resepctively. Median time from last chemotherapy cycle to cystectomy was 10 weeks (range 8-17 weeks). All patients had re-staging CT scans following completion NAK. Thirteen patients (61.9%) underwent radical cystectomy with no major surgery-related complications. Two patients declined cystectomy, one of them underwent bladder preservation chemoradiotherapy. In two patients disease progressed during NAK (bone et liver disemination) and they were not eligible for cystectomy. We observed grade 3 toxicity events in 10 patients (febrile neutropenia, anemia, stomatitis). In patients that underwent cystectomy, 4 patients (19%) achieved complete pathological response (pT0 pN0 on cystectomy specimen). Immunophenotype analysis was performed in central pathology lab in 10 patients (47.6%). Molecular

features suggesting luminal and basal subtype was found in 6 and 3 patients, respectively. From patients achieving complete response, 3 patients and 1 patient had tumors categorized as luminal subtype, and basal subtype, respectively. Both patients who progressed during NAK had tumors categorized as luminal subtype.

Conclusions: Initial experience with NAK at our institution is encouraging. We were able to complete NAK within 2 months in majority of patients. Toxicity profile is acceptable and improving, while pathologic complete response rate is similar to published landmark studies. More work is needed to improve baseline tumor extent assessment and streamline whole NAK-restaging scans-cystectomy workflow. Early data on potential predictive role of immunohistochemically assessed bladder cancer molecular subtypes are limited, inconclusive and conflicting and require further validation.

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P36 - COULD RATIO OF UNTREATED/TREATED PATIENTS WITH METASTATIC COLORECTAL CARCINOMA INDICATE IT`S QUALITY OF CARE?

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Background: Colorectal carcinoma (CRC) is the second most commonly diagnosed and second leading cause of death by malignant disease in Croatia[1]. According to CONCORD 3 study, 5-year survival of 50% in Croatia, in comparison to up to 71% for the developed countries worldwide, is making it as one of the major health care priorities[2]. Also, despite knowing underlying risk factors and population-based screening methods, almost 20% of patients presents with metastatic disease at the time of diagnosis[1]. Development of new drugs and therapy modalities as well as multidisciplinary approach resulted in significant increase of median time of overall survival, from 12 months when 5 fluorouracil was only drug used, to about 24-30 months recently, when multiple drugs, biological included, have been used[3]. Unfortunately, significant minority of patients do not receive any treatment most usually due to bad performance status, significant comorbidities, or some other organizational reasons with expected median overall survival (mOS) less than 5 months[4]. One of the potential ways to improve further existing outcomes of patients with mCRC is to analyze such patient population in every day clinical practice and, based on the results of such analysis, improve existing infrastructure and decrease number of patients treated with palliative care therapy only. The purpose of this study was to describe more closely characteristics and outcomes of patients who were not administered systemic oncological therapy.

Methods: The retrospective cohort study was conducted at the Department of Oncology and Radiotherapy, University Hospital of Split. It included patients who were either newly diagnosed with stage IV CRC or whose initially early staged disease has progressed during 2017 and were only provided with best supportive care (BSC). The data were analysed with methods of descriptive statistics using Microsoft Excel tools.

Results: In total, 17 (16%) out of 107 patients diagnosed with mCRC in 2017 have received BSC only. All of them were presented to multidisciplinary team and have received BSC which consisted mostly of parenteral hydration, analgesics, nutritional support and/or blood transfusion and palliative radiotherapy. Minority of patients (23,5%) lived in Split, while the rest (76,5%) lived in the surrounding area without everyday hospital care available. Median age was 81 year (range 61-90) with 76% having ≥70 years. At the time of diagnosis, 59% of patients had Eastern Cooperative Oncology Group Performance Status (ECOG PS) either 3 or 4. Most of the patients cited inappetence and fatigue and 71% had an averrage of 10 kg of the body weight loss which by cahexia staging score (CSS) corresponds to cahexia[5]. Furthermore, majority of patients (13, 76%) were already receiving concomitant medications for coexisting comorbidities and for the rest (4, 24%) the data was unknown. All patients, except one, had patohistologically confirmed adenocarcinoma without further molecular profiling. Most common site of metastases was liver with 59% of patients who had liver-only metastasis and 35% had multi-organ metastases. Median OS for our cohort of untreated patients was 3,7 months. It is of an importance to emphasize that for 3 patients observed mOS was ≥20 months.

Conclusion: One of the indicators of quality of mCRC care is ratio of untreated and treated patients. More untreated patients are expected in less organized systems where less educated population exists.

Therefore, there is potential to improve further existing outcomes of patients with mCRC with decreasing number of untreated patients. Considering 3 patients whose mOS was more than expected, the arising questions are whether these patients could have benefit from the treatment or has the avoidance of severe consequences of the treatment caused longer mOS. Even though studies suggest the benefit of oncological treatment for elderly and some for patients with poor performance status (6,7), only tackling mCRC multidisciplinary and in accordance with clinical presentation of every patient individually will result in administration of the optimal therapy of choice and improved outcomes for every individual patient.

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P37 - MOLECULAR PROFILING FREQUENCY OF METASTATIC COLORECTAL CARCINOMA AND IT`S IMPACT ON THE OUTCOMES: A SINGLE INSTITUTION STATUS REPORT IN 2017

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Background: Acchievements in the field of genetic research and molecular profiling such as RAS, BRAF and dMMR/MSI status of colorectal carcinoma (CRC) have yielded new therapy approaches and have increased median survival of metastatic CRC (mCRC) to up to 30 months[1]. In general, patients with mCRC are in medically rather deprived position beacuse the outcomes of their treatment depend more on the oncological organizational infrastructure and multidisciplinarity. Croatia is unfortunately among countries with lowest median overall survival for CRC in Europe[2]. As such, it is of essential importance to monitor and define omission points of health care and it`s quality control, in order to improve existing outcomes. One of the potential ways to do so, is to consolidate diagnostics through molecular profiling for every patient, consequently leading to therapy personalization and greater impact on the survival. The main purpose of this study was to asses testing rates for mCRC guideline-recommended biomarkers in 2017 in a single academical institution in Croatia[3].

Methods: The observational retrospective study was conducted at the Department of Oncology and Radiotherapy, University Hospital of Split. It included results of either RAS, BRAF or dMMR/MSI profile for patients who were either newly diagnosed with mCRC or whose initially early staged disease has progressed during 2017. The data were analysed with methods of descriptive statistics using Microsoft Excel tools.

Results: A total of 107 patients were identified, of whom 81 (75,7%) patient was newly diagnosed with mCRC and 26 (24,3%) patients, who were primarly diagnosed with early stage CRC, had disease progression to distant organs in 2017. Median age of the population was 67 years with 63 (59%) being ≤70 years. In total, for 74 (69%) patients either RAS, BRAF, dMMR/MSI or their combination was determined. RAS testing, by any methodology, was completed in 69 (64,5%) patients with 46 (66,6%) of them harbouring mutation. BRAF testing had 18 (17%) patients with 3 (16,6%) harbouring mutation. MSI status was determined for 23 (21,5%) patients with 4 (17,4%) of them showing MSI. Considering patient`s either RAS, BRAF or dMMR/MSI profile, median overall survival (mOS) for tested patients was 25,9 months, whilst for patients with unknown status mOS of 6,5 months was significantly lower ($p<0.05$, CI=0,95). However, it is important to mention that 15 out of 33 patients with unknown status did not receive systemic oncological treatment due to their initially poor performance status.

Conclusion: Our results show that one third of patients have not received guideline-aligned biomarker testing in 2017 contributing to possibly having less chance for optimal treatment decision resulting in lower mOS. Nearly 50% of those patients presented in poor physical condition and were provided only with palliative care, which could be the reason for not ordering further molecular profiling. Testing rate of 69% puts our institution somewhere in-between United States with rate of 40% (2013-2017) and France, where adherence to biomarker testing was 90% in 2014[4,5]. Regardless, results suggest room for improvement in diagnostics through genotyping for recommended biomarkers in order to optimise the treatment and increase existing outcomes. Also, they imply the need of better surveillance and report in years to

come so that real impact on the outcomes and cost effectiveness, with choosing appropriate therapy, could be determined.

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P38 - IMMUNOTHERAPY IN TREATMENT OF METASTATIC MELANOMA AT UNIVERSITY HOSPITAL CENTER SESTRE MILOSRDNICE

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Introduction: According to the latest Croatian National Cancer Registry, melanoma accounts for 3% of all malignant tumors in men and in women, with 805 newly diagnosed patients (439 men, 366 women) and 219 deaths in the year 2017. Fortunately, the long-term survival of patients with metastatic melanoma has improved dramatically over the last decade, with a median overall survival of 32.7 months in patients receiving pembrolizumab in the first line. The current first-line standard of care treatments for unresectable stage III/IV melanoma include immune checkpoint inhibitors (PD-1 inhibitors nivolumab and pembrolizumab, CTLA-4 inhibitor ipilimumab) - single agent or combined PD-1 and CTLA-4 blockade, and combined targeted therapy for BRAF V600-mutated melanoma (BRAF&MEK inhibitors). For patients with BRAF mutated metastatic melanoma, first-line options can be either immunotherapy or BRAF&MEK inhibitors, but choosing optimal sequencing of therapy is still a big challenge. Clinical parameters associated with disease progression, such as lactate dehydrogenase (LDH) level, number of metastatic sites, and performance status, which represent strong negative predictive biomarkers, should be taken into account.

Aim: The aim of our analysis was to determine progression-free survival (PFS) in patients treated with immunotherapy in the 1st line and overall characteristics of our patients.

Patients and methods: We retrospectively analyzed patients with metastatic melanoma treated with immunotherapy (PD-1 inhibitors pembrolizumab and nivolumab) at our institution from March 2017 to January 2020. Patients were classified according to gender, age at the time of diagnosis of metastatic disease, number of metastatic organ sites, ECOG performance status, BRAF status, LDH levels, and presence/absence of brain metastases.

Results: Overall, 109 patients received immunotherapy, of which 62% were male and 38% female. The median age at the time of diagnosis was 61 (19-84). The most common sites of disease were lymph nodes, lungs, and skin, respectively. A total of 81 (74%) had metastases in <3 sites, and 28 (26%) in ≥3 sites. The majority of patients had ECOG PS 0 (83%). BRAF status was defined as wild type in 58 (53%) and mutated in 51 (47%) patients. Initially, 25% of patients had elevated lactate dehydrogenase (LDH) level, and 10% had brain metastases. Seventy-six (70%) patients received immunotherapy as 1st line treatment, 31 (28%) as 2nd line treatment, and 2 patients (2%) as 3rd line treatment. Here we focused on the 76 patients receiving immunotherapy as first-line treatment. Almost 90% of patients were treated with pembrolizumab and the rest with nivolumab. Combination immunotherapy is not available in Croatia. As of January 2020, 35 patients (46%) are still on treatment. Of the remaining 41 patients (54%) who have stopped treatment, 5 have a complete response to therapy, 14 patients had disease progression, 18 patients had died and 2 were lost to follow-up. Only four patients (5%) overall permanently discontinued treatment due to immune-related side effects, two of which still have a durable response, and the remaining two were switched to targeted therapy.

Conclusion: Our analysis showed similar patient characteristics (LDH level, BRAF status, disease burden…) as shown in the literature. Median progression-free survival was not yet reached at the time of

the analysis (less than 50% of patients had progressive disease), probably due to the fact that many of these patients had good prognostic parameters.

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P39 - REGULATION OF PD-1/PD-L1 PATHWAY IN MALIGNANT MELANOMA – A PILOT STUDY

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Backround: Malignant melanoma (MM) is one of the genetically most complex tumors. In modern oncology, emphasis is on immunotherapy and targeted mutation-dependent therapy. It is known that MM craftily avoiding the immune response of the host. Inhibitory molecules on the surface of malignant cells block the cytotoxic effect of T lymphocytes. Lymphocytes in tumor inflammatory cell infiltrate (TIL) show PD-1 (programmed cell death 1) protein expression. Known ligands for PD-1 are PD-L1 and PD-L2. The extrinsic and intrinsic mechanisms of PD-L1 regulation in melanoma require further research because it's crucial for advancement in this type of melanoma patient therapy.

Aim: In order to predict the efficacy and optimization of anti-PD-1 and anti-PD-L1 therapy, alone or in combination with other treatment options, it's important to clarify regulation mechanisms. Our project research is based on role of several types of regulation on PD-1 / PD-L1 signal pathway control proteins. We divided them into three groups: changes in genetic material and signal pathways of melanoma cell, regulation by the immune system, and regulation by tumor-microenvironment enzymes. In this pilot study, we will analyse a small group of patients and examine regulation by the immune system.

Methods: Retrospectively, archive material in basis of the Department of Pathology, Faculty of Medicine in Rijeka, will be used in this research. Primary malignant melanoma biopsies specimens of patients treated with pembrolizumab immunotherapy in Clinic for Radiotherapy and Oncology, Clinical Hospital Centre Rijeka, will be analysed. Preparation and immunohistochemical staining will follow with the determination of PD-L1 immunohistochemical positivity, and presence of $CD3^+$ and $CD20^+$ lymphocytes. Primary melanomas centrally will be reviewed for TIL grade (absent, non-BRISK, or BRISK). The odds of TIL grades associated with clinicopathologic features and melanoma cell PD-L1 expression will be examined.

Results: Since March 2017, a total of 31 patients with metastatic melanoma have been treated with pembrolizumab at our Clinic. In this pilot study, we included some of patients who received at least 3 cycles of pembrolizumab (every 3 weeks). They were divided into two groups: Group 1 (n=6) consisted of patients who received more than 6 cycles of therapy (median of cycles in this group was 19) without signs of disease progression, and Group 2 (n=4) consisted of patients who at the first radiological control (after 5 cycles) had signs of disease progression according to RECIST criteria. Analysis of biopsies of primary melanomas in Group 1 showed that all samples had BRISK type TIL (3 BRISK A and 3 BRISK B). In contrast, in Group 2 we found 1 BRISK B, 2 non-BRISK and 1 absent tumor infiltrating lymphocytes. PD-L1 expression did not statistically significantly correlate with TIL type in either group.

Conclusion: Definition of proteins responsible for immune inhibition and immune cell regulation will contribute to better use of immunotherapy as treatment for metastatic melanoma and possible future use of same treatment in adjuvant therapy. We conclude that TIL grade deserves further prospective investigation to determine whether it should be included in future AJCC staging revisions.

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P40 - HEPATOTOXICITY PROFILES OF BIOSIMILARS VS. GENERIC ANTI-HER2 THERAPY IN EVERYDAY CLINICAL PRACTICE- OBSERVATIONAL STUDY AT THE DEPARTMENT OF ONCOLOGY AND RADIOTHERAPY, UNIVERSITY HOSPITAL OF SPLIT

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Background: Anti-HER2 therapy, consisting of trastuzumab and pertuzumab, is mainly associated with infusion reactions and cardiotoxicity as the most common and dangerous undesirable events[1,2]. Even though hepatotoxicity is not usually anticipated in the therapy with monoclonal antibodies, in the pivotal clinical trials it is listed amongst common side effects[1,2]. Despite aforementioned, trastuzumab is not described as such in the clinical practice, consequently having no significant impact on the course of the treatment[3]. Furthermore, there are no reports of pertuzumab induced hepatotoxicity in the literature, while for trastuzumab there are only four case reports described[4,5,6,7]. However, since the introduction of biosimilar drugs, their approval and expanding list of Herceptin biosimilars in the use, a certain level of alertness should exist for their highly similar but not exactly the same toxicity profile. Hence the aim of this study was to clarify the cause of observed higher level of liver enzymes in a single academical institution in Croatia since the use of approved Herceptin biosimilars Ogivri and Herzuma.

Methods: The observational study was conducted at the Department of Oncology and Radiotherapy, University Hospital of Split. It included HER2 positive breast cancer patients treated with anti-HER2 therapy whether in neoadjuvant, adjuvant or metastatic setting since the introduction of Herceptin biosimilar drugs Ogivri (11. /2019.) and Herzuma (06. /2019.) in everday clinical practice at our Department. Patients were divided in three groups depending on the type of trastuzumab used; patients treated with Herceptin, Herzuma and Ogivri. Considering the fact that there was no observed pertuzumab induced hepatotoxicity in the clinical practice, pertuzumab was excluded as a possible cause of liver enzyme elevation in patients receiving dual anti-HER2 therapy. As for the patients who were receiving taxane based chemotherapy concomitantly with anti-HER2 therapy, there was a control group of patients who were treated only with paclitaxel monochemotherapy. The data were analyzed with methods of descriptive statistics using Microsoft Excel tools.

Results: A total of 64 patients diagnosed with breast cancer were included in the observational study, of which 49 (77%) patients were treated with anti-HER2 therapy and 15 (23%) patients were treated with paclitaxel as monochemotherapy. Out of 49 patients, 17 (35%) were receiving Herceptin, 16 (32.65%) Ogivri and 16 (32.65%) Herzuma. Dual anti-HER2 therapy concomitantly with taxane based chemotherapy was given to 11 (22.44%) patients in the Herceptin group, 11 (22.44%) in Herzuma and 10 (20.40%) in Ogivri group. Furthermore, 4 (8.16%) patients were receiving Herceptin in combination with taxane based chemotherapy, 3 (6.12%) Herzuma with taxane and 1 (2.04%) patient was receiving Ogivri with taxane chemotherapy. Trastuzumab as monotherapy received 2 (4.08%) patients in Herceptin, 2 (4.08%) in Herzuma and 3 (6.12%) patients in Ogivri group, while two patients (4.08%) who were only receiving dual anti-HER therapy were from Ogivri group. Normal levels of liver enzymes at the beginning and throughout the treatment had 16 (32.65%) out of 49 patients (7 (41.17%),2 (12.50%),7 (41.17%) in each of the groups) treated with anti-HER2 therapy and 8 (53.3%) out of 15 patients in paclitaxel control group. Initially elevated and

persistency of higher levels of liver enzymes had 8 (16%) patients (2 (11.76%),5 (31.25%),1 (6.25%) in the groups) and none in the paclitaxel group, while 1 patient in the Ogivri and 1 in the paclitaxel group had normalization of levels. After ordination of the first cycle of immunotherapy or monopaclitaxel, elevation was noticed in the 7 (41%), 9 (56.3%), 7 (43.8%) and 1 (6.7%) patients in the Herceptin, Herzuma, Ogivri and paclitaxel group. From the above mentioned, normalization of levels experienced 5 (71.4%), 4 (44.4%) and 4 (57.14%) patients in Herceptin, Herzuma and Ogivri group. Elevation of levels with normalization was noticed in 1 patient in Herceptin and 2 patients in paclitaxel group, while for the 3 patients in paclitaxel group higher levels persisted throughout the treatment.

Conclusion: Our results showed no significant difference in hepatotoxicity between reference drug Herceptin and two approved biosimilar drugs Herzuma and Ogivri used in our clinic ($p>0.05$ for AST, ALT and GGT levels). Observed hepatotoxicity only included grade I/II elevations of AST, ALT and GGT according to Common Toxicity Criteria (CTC)[8], transitory in nature and without significant impact on the course of the treatment. Our study confirms existance of mild and transient trastuzumab induced hepatotoxicity that should be monitored throughout trastuzumab application.

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P41 - INSTITUTIONAL DATA ON SURVIVAL AND DISEASE CONTROL FOR EARLY AND LOCALLY ADVANCED BREAST CANCER PATIENTS IN THE ERA CONSERVATIVE SURGICAL AND ADJUVANT ONCOLOGICAL APPROACHES

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Background: In the last few decades there is a constant trend of de-escalation in the surgical approach to breast cancer (BC) patients. Following the results of NSABP B-04 and B-32 trials, as well as the ACOSOG Z011 and AMAROS trial, conservative approach is strongly recommended for all early BC patients. In Clinical Hospital Center (CHC) Rijeka all mentioned recommendations were accepted. However, in this era of conservative surgery, we have found that institutional and national follow up data are lacking. The purpose of this retrospective analysis is to report our latest updates on survival and disease control rates. The analysis was approved by the Institutional Ethics Committee.

Patients and methods: Overall 915 female BC patients were surgically treated in CHC Rijeka, in the period from 2011 till 2014. However, we excluded patients older than 80 years or with M1 status at the time of surgery, recurrent, bilateral or in situ disease, patients diagnosed with other malignant conditions and those without any postoperative data. Therefore, 615 patients remained for the analysis. The results were analyzed using Statistica 13 software and interpreted at the level of statistical significance p = 0.05.

Results: All patients were a female, mean age of 59 years at the time of the surgery. Overall local, regional and distant recurrence free survival rates, as well as overall survival and disease-free survival rates in 5 postoperative years, were calculated. As expected, all mentioned rates are proportionally decreasing with the higher T(p=0.00000-0.00112) and N status (p=0.00000-0.00637) as well as with a higher stage of disease (p=0.00000-0.00234). Interestingly, the regional recurrence free survival rates are almost identical between pN0 and pN1 patients (97.97% and 97.84%), but statistically significant different from the pN2 and pN3 patients (p=0.00000). Moreover, in pT1-3 N0-1 subgroup SLNB was not inferior to ALND in terms of local and regional control of the disease (p=0.958, p=0.502).

Conclusion: Development of novel anticancer drugs and increasing trend of neoadjuvant oncological approach for operable BC are reducing the need for radical procedures. Several ongoing trials are aiming for more de-escalation of surgery for early and locally advanced BC. Besides updating our institutional data, our analysis had confirmed that locoregional control of the disease in stage pT1-3 N0-1 is not related to the extent of axillary surgery in the primary surgery era. The prospective observational trial, currently ongoing in CHC Rijeka, is aiming to determine whether omission of ALND after NAT in cN(+)àypN(-) patients affect the locoregional control of the disease, as well as if survival rates for cN2 patients, converted to ypN0 following neoadjuvant treatment (NAT), are remaining the same or would improve to become more alike N0-1 rates.

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