

POSTER PRESENTATIONS

P1 - RADIOLOGICAL AND CLINICAL FINDINGS OF IMMUNOTHERAPY COMPLICATIONS IN PATIENTS TREATED WITH PEMROLIZUMAB IN THE FIRST-LINE TREATMENT OF METASTATIC LUNG CANCER IN PATIENTS WITH PD-L1 EXPRESSION >0%

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The use of immune mediated treatment of cancer is improving dramatically the patient's outcome and comfort, but it also carries new toxicity profiles. While standard antineoplastic therapy is associated with immunosuppression and infections, these new therapies induce overwhelming inflammation and autoimmunity. The vast majority of these adverse events can be classified as mild or moderate, but severe and life-threatening complications requiring ICU admission can also occur.

Methods and results: In this retrospective study, data on the treatment of lung cancer with pembrolizumab were analyzed in 78 patients who started pembrolizumab therapy as first-line treatment for metastatic disease at University Hospital Centre Osijek, from May 15, 2018, until December 31, 2021. November 30, 2022, was set as the last date of data monitoring.

The main objectives of the study were OS (overall survival) and PFS (progression-free survival). The differences in the incidence and type of adverse events between the two groups of patients were also compared.

Kaplan-Meier analysis of the survival determined that the median OS was 20 months and PFS was 13 months. Although OS and PFS are longer in patients with PD-L1 (programmed death-ligand 1) $\geq 50\%$, the differences are not statistically significant.

The most commonly reported adverse events related to pembrolizumab treatment were gastrointestinal adverse events. No significant differences were found in the frequency of occurrence of certain adverse events between the two groups of patients.

Adverse effects related to immunotherapy diagnosed by radiology imaging methods were found (cardiac disorders 4 patients, respiratory, thoracic and mediastinal disorders in 13 patients, pneumonitis in 4 patients, nervous system disorders in 4 patients, hypophysitis in 1 patient, gastrointestinal disorders in 24 patients, myositis in 1 patient, hepatitis in 5 patients).

From the immune-related adverse effects than can be diagnosed by radiology imaging methods, we found cases of: hypophysitis, nervous system disorders, synovitis, hepatitis, different types of pneumonitis and colitis/enteritis that can be diagnosed with computed tomography (CT), magnetic resonance imaging (MRI) and ultrasound.

Discussion: A considerable part of adverse effects related to immunotherapy can be diagnosed by radiology imaging methods. This situation makes the role of the radiologist key when it comes to optimizing treatment individually for each patient, taking into account the risks and benefits of the different therapies.

Conclusion: This review will focus on the radiological approach to the new challenge that is to make an accurate and early diagnosis of these complications to help oncologist and patient when it is needed.

Keywords: computed tomography, hypophysitis, magnetic resonance imaging, PD-L1, pembrolizumab, pneumonitis

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P2 - UPDATED EFFICACY AND SAFETY RESULTS FROM PHASE 3 GLOW STUDY EVALUATING ZOLBETUXIMAB + CAPOX AS FIRST-LINE TREATMENT FOR PATIENTS WITH CLAUDIN 18 ISOFORM 2-POSITIVE, HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR 2-NEGATIVE, LOCALLY ADVANCED UNRESECTABLE OR METASTATIC GASTRIC OR GASTROESOPHAGEAL JUNCTION ADENOCARCINOMA

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Background: The phase 3 GLOW study showed statistically significant improvement with first-line (1L) zolbetuximab + capecitabine + oxaliplatin (CAPOX) vs placebo + CAPOX in progression-free survival (PFS; final; median 8.2 vs 6.8 months; hazard ratio [HR] 0.69, 95% confidence interval [CI] 0.54, 0.87; P =

0.0007) and overall survival (OS; interim; median 14.4 vs 12.2 months; HR 0.77, 95% CI 0.62, 0.97; $P = 0.0118$) in patients with claudin 18 isoform 2-positive (CLDN18.2+), human epidermal growth factor receptor 2-negative (HER2-), locally advanced (LA) unresectable or metastatic gastric or gastroesophageal junction (mG/GEJ) adenocarcinoma. We present an updated efficacy and safety analysis with 8.7 months additional follow-up from the primary analysis.

Methods: Patients were randomly assigned 1:1 to zolbetuximab IV 800 mg/m² (cycle 1, day [D] 1) followed by 600 mg/m² (every 3 weeks) + CAPOX (oral capecitabine twice daily on D1–14 and oxaliplatin IV on D1) for eight 21-day cycles or to placebo + CAPOX; patients without progressive disease (PD) continued beyond cycle 8 with zolbetuximab or placebo, + capecitabine at investigator's discretion, until PD or discontinuation criteria were met. The primary endpoint was PFS per Response Evaluation Criteria in Solid Tumors version 1.1 by independent review committee; OS was a key secondary endpoint.

Results: At data cutoff (June 29, 2023), 507 patients were assigned to zolbetuximab + CAPOX ($n = 254$) or placebo + CAPOX ($n = 253$). In the zolbetuximab vs placebo arms, median follow-up was 17.8 vs 15.1 months for PFS and 26.1 vs 26.2 months for OS, respectively. Median PFS in the zolbetuximab vs placebo arms was 8.3 vs 6.8 months (HR 0.68, 95% CI 0.55, 0.85; $P = 0.0004$). Median OS in the zolbetuximab vs placebo arms was 14.3 vs 12.2 months (HR 0.77, 95% CI 0.62, 0.95; $P = 0.0079$); the 24-month OS rate was 28.3% vs 18.8%, with follow-up ongoing through final analyses. The most common treatment-emergent adverse events (TEAEs) with zolbetuximab + CAPOX were nausea (zolbetuximab arm: 68.9% vs placebo arm: 50.2%), vomiting (66.1% vs 31.3%), and decreased appetite (41.3% vs 34.5%); incidences of serious TEAEs were similar between arms (48.0% vs 50.6%).

Conclusions: Zolbetuximab + CAPOX continued to demonstrate statistically significant improvement in PFS and OS compared with placebo + CAPOX, with no new safety signals, supporting zolbetuximab + CAPOX as a potential new option for 1L treatment of patients with CLDN18.2+, HER2-, LA unresectable or mG/GEJ adenocarcinoma.

Keywords: zolbetuximab, CAPOX, claudin 18 isoform 2- positive, gastric or gastroesophageal junction adenocarcinoma

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P3 - INTENSITY-MODULATED RADIOTHERAPY IN THE TREATMENT OF NASOPHARYNGEAL CARCINOMA: A SINGLE CENTER EXPERIENCE

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Background and Aim: Nasopharyngeal carcinoma (NPC) is an undifferentiated form of squamous cell carcinoma arising from the epithelium of the nasopharynx. It is the most common malignancy of the nasopharynx. Endemic to parts of Asia and Africa but found worldwide, the malignancy shows a variable rate of occurrence. Radiation therapy is the management of choice for primary lesions and cervical metastases. We report our experience with patients with nasopharyngeal carcinoma who were treated by intensity-modulated radiation therapy (IMRT) combined with simultaneous or induction chemotherapy (iCHT).

Methods and Materials: By reviewing patients treated with IMRT in the period from 2019 to 2023, we found 19 patients with NPC out of a total of 376 patients with cancers of the head and neck area. There were 2 females and 17 males, with a mean age of 49 (range 36–78). The disease was Stage II in 2 (10%), Stage III in 3 (15%), and Stage IV in 14 (75%). In this research, Elekta Monaco 5.11 (Elekta, Crawley, UK) treatment planning system (TPS) was used. Radiotherapy plans were performed with a 6MV beam and IMRT delivery technique. The calculation algorithm for IMRT built in the Elekta Monaco TPS is based on Monte Carlo (MC) simulation. All patients received concomitant cisplatinum and 3 patients received iCHT with cisplatinum and 5-FU, while 5 patients received iCHT with cisplatinum and gemcitabine. The prescribed dose was 65–70 Gy to the gross tumor volume (GTV) and positive neck nodes, 60 Gy to the clinical target volume (CTV), 50–60 Gy to the clinically negative neck. The local progression-free, local-regional progression-free, distant metastasis-free rates, and the overall survival were calculated using the Kaplan-Meier method.

Results: With a median follow-up of 26 months (range 7 to 62 months), there has been one local recurrence at the primary site. One patient failed in the neck. Four patients developed distant metastases; 3 of these patients have died. Local progression-free, local-regional progression-free, and distant metastases-free rates were 100%, 98%, and 72% respectively. The average value of the near minimum dose to the tumor (D98% GTV) was 100.56%. The majority of the GTV and CTV actually received more than 105% of the prescribed dose. The percentage of the volume of the PTV covered by 95% of the prescribed dose (D95) was 97.9% in average. There was significant sparing of all critical structures without compromising tumor target coverage. The results of the quantitative analyses of the DVHs for the tumor target and critical structures were consistent with the clinical results of excellent local control.

Conclusion: Excellent local-regional control for NPC was achieved with IMRT. IMRT provided excellent tumor target coverage and allowed the delivery of a high dose to the target with significant sparing of nearby critical normal tissues.

Keywords: Nasopharynx Carcinoma; Intensity-modulated Radiotherapy; Induction chemotherapy

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P4 - POOR DENTAL STATUS AS A FACTOR WHICH PREVENTS PRESCRIPTION OF BONE ANTIRESORPTIVE AGENTS IN PATIENTS WITH METASTATIC CASTRATION-RESISTANT PROSTATIC CANCER- SINGLE CENTER EXPERIENCE

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Introduction: Metastatic castration-resistant prostate cancer (mCRPC) is a type of advanced prostate cancer that has spread to other parts of the body, and does not respond to androgen deprivation therapy (ADT). In patients with bone metastases and CRPC, who are at risk for clinically significant skeletal-related events (SREs), bone antiresorptive agents such as bisphosphonates or denosumab are recommended. Since osteonecrosis of the jaw, as side effect of this therapy can occur, good dental status is a prerequisite for administration of these agents.

Patients and methods: In the present retrospective observational study, conducted at the Department of Internal medicine at the General Hospital od Šibenik-Knin county, we examined the records of patients with mCRPC using locally maintained registry. The patients were treated in our hospital from January 2022.- December 2023. Their dental status, as well as overall oral health, was examined by oncologist and/or dentists. If there was a need for tooth extraction, the eventual decision regarding procedure was made in agreement between the patient and the dentist.

Results: A total of 26 patients with mCRPC, in the age range of 49-88 years, were included in this study. Patients were in good general condition (77% of them were ECOG status 0 or 1). The vast majority of them had metastases in or also in the bones (88%), while a minority (12%) had exclusively extraosseal metastases.

Among the patients who had bone metastases, 83% of them have received medical antiresorptive therapy. In the group of patients who have received antiresorptive therapy bisphosphonates were mostly

prescribed (74%), denosumab received 16% of patients, and 10% of patients has been treated at the beginning with bisphosphonates, but due to the development of renal insufficiency antiresorptive therapy was switched to denosumab.

Due to unsatisfactory dental status in 15% of patients with mCRPC, and bone metastases, treatment with antiresorptive therapy was not indicated. None of patients with unsatisfactory dental condition underwent tooth extraction in order to rehabilitate their condition.

Only for 2% of patients with mCRPC, and bone metastases, medical antiresorptive therapy was not prescribed because it was concluded that the presence of metastases in the bones does not endanger them for possible development of significant unwanted skeletal-related events.

Conclusion: The data obtained in our study indicate that the poor dental status could be a factor that in a significant percentage of patients with mCRPC prevents the prescription of bone antiresorptive agents, which should be carried out in accordance with the guidelines of the European Society for Medical Oncology (ESMO). Further studies are necessary to confirm the results of this single center study.

Keywords: metastatic castration resistant prostate cancer; dental status; bisphosphonates; denosumab

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P5 - IS EAT-10 IN CORRELATION WITH BIA PARAMETERS USEFUL TO ASSESS SWALLOWING DURING THE RADIOTHERAPY IN PATIENTS WITH HEAD AND NECK CANCER? A PILOT STUDY

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Background and Aim: The incidence and prevalence of head and neck cancer (HNC) are increasing rapidly worldwide. Moreover dysphagia is the most frequent side-effect of radiotherapy (RT), reaching 37% at 6-month follow-up. Patients with HNC who receive chemotherapy (CRT) also may perceive changes in swallowing as the disease progresses, mainly during and after the CRT treatment period. The 10-item Eating Assessment Test (EAT-10) has been from unsafe swallowing in amyotrophic lateral sclerosis, stroke, and general populations. Phase angle (PhA), determined by bioelectrical impedance analysis (BIA), detects changes in tissue electrical properties. Lower phase angles suggest cell death or decreased

cell integrity. In daily clinical practice, there is a lack of reliable diagnostic tools for predicting changes in body composition in individuals following radiotherapy (RT). This study was conducted to investigate the prognostic role of PhA and other BIA scale parameters in HNC during radiotherapy. Also, we aimed to examine the relationship of BIA parameters with a possible worsening of dysphagia as well as an increase in the EAT-10 score.

Materials and Methods: Using BIA (TANITA scale), the body composition was measured prior to RT in 42 HNC patients. Body mass index, sarcopenic index, bone mass, muscle mass, percentage of body water and phase angle were analyzed before radiotherapy. The EAT-10 consists of 10 items scored from 0 (no impairment) to 4 (severe impairment). Total scores range from 0 to 40; higher scores indicate greater self-perceived impairment. Patients scoring ≥ 3 are considered at risk of difficulty in swallowing. We considered an increase (> 10) in the EAT-10 score after 3 months as an indicator of an acute side effect of radiotherapy. Patients treated with primary intensity modulated radiotherapy (IMRT), in 2023.

Results: In the analyzed group, 23 patients received definitive chemoradiotherapy, while the others received adjuvant radiotherapy. The oral cavity (37%) was the most frequent anatomical site affected. The most common histopathological type was squamous cell carcinoma (84%). In the analysis of the sarcopenic index, it was evident that patients with laryngeal carcinoma are at a higher risk of development of sarcopenia ($p = 0.002$). There is a statistically significant difference in the value of the phase angle in patients with oropharyngeal cancer (mean 4.2 ± 0.7) compared to other HNC localizations. A statistically significant inverse correlation was found in the value of PhA and EAT-10 before radiotherapy ($p < 0.001$). We did not find a statistically significant correlation between the sarcopenic index and EAT-10 score before radiotherapy ($p = 0.331$). In the group of patients whose EAT-10 score increased by 10 three months after radiotherapy, statistically significantly lower PhA and higher sarcopenic index were confirmed ($p < 0.001$).

Conclusion: PhA prior to RT is a useful marker for selection of individuals with HNC who are at a high risk of dysphagia.

Keywords: Dysphagia Bioimpedance electrical analysis, Radiotherapy, Phase Angle

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P6 - BIOELECTRIC IMPEDANCE ANALYSIS PARAMETERS AS PREDICTORS OF SIDE EFFECTS IN PATIENTS TREATED WITH CHEMOTHERAPY

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Introduction: Using Bioelectrical impedance analysis (BIA), we can determine how much fat (higher resistance) and lean (lower resistance) tissue is in the body at the point where prescribing decisions are made. The electrical properties of the body also provide information on the membrane (the lining or wall of the cells in the body), what appears to indicate frailty and vulnerability to disease and treatment. What we need to know now is whether this approach can help predict which patients are at higher risk of developing side effects related to chemotherapy.

Materials and Methods: This cross-sectional study was conducted in Clinical Hospital Center Rijeka in a group of 40 patients treated with chemotherapy. Before the start of chemotherapy treatment, BIA was performed on each patient, where the following parameters were observed: body mass index (BMI), percentage of fat tissue, percentage of muscle mass, percentage of skeletal mass, sarcopenic index, percentage of body water and phase angle. During the follow up period of 6 months, the patients were monitored for the development of the following side effects: anemia, neutropenia, thrombocytopenia, nausea, vomiting, and diarrhea. Patients were divided into two groups depending on whether they developed side effects or not. The difference in each individual parameter of the BIA analysis between the group of patients who developed a certain side effect and those who did not were statistically analyzed. The program 'Statistica' was used for data processing. All patients received exclusively cytostatic therapy. All patients had never been treated with cytostatic therapy or radiotherapy before the first BIA measurement.

Results: The median age of the patients was 65 years (range 35-81 years). Anemia occurred in 52% of examined patients. Development of anemia was statistically significant more often in patients who had reduced bone mass and who had a higher sarcopenic index. The mean bone mass in kilograms of 2.81 kg and the sarcopenic index of 7.9 compared to 2.57 kg and 7.0 in patients who did not develop anemia were determined in the examined patients who developed anemia ($p=0.04$, $p=0.02$). Nausea and vomiting developed in 27% of patients. Nausea and vomiting occurred statistically significant more often in patients who had a lower phase angle. The mean phase angle in patients who had this side effect was 4.8, while in those who did not it was 5.7 ($p=0.03$). By comparing the parameters of the BIA scale and other investigated side effects, we did not find a statistically significant difference.

Conclusion: The results of our research indicate that certain parameters of the BIA analysis could be predictors of the development of chemotherapy side effects. Good patient conditioning (eg, early nutritional intervention) before the start of chemotherapy treatment could potentially be important to reduce the possibility of developing side effects of chemotherapy. To confirm such conclusions, a prospective study including larger number of patients and a longer follow-up is crucial.

Keywords: BIA, chemotherapy, side effects

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P7 - ABEMACICLIB-ASSOCIATED DIARRHEA AND DOSE MODIFICATION IN PATIENTS WITH EARLY BREAST CANCER

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Background: Abemaciclib is a cyclin-dependent kinase 4/6 inhibitor, used together with endocrine therapy (ET) is approved for treating hormone receptor-positive and HER 2-negative, node-positive early and advanced breast cancer. Abemaciclib safety profile is characterized by frequent gastrointestinal toxicity, in particular diarrhea. Among all patients studied in the monarchE study approximately 1 in 5 patients required a dose modification when treated with abemaciclib and ET. For diarrhea grade ≥ 2 that persists or recurs after the same dose despite maximal supportive measures dose modification is required. Abemaciclib was shown to remain effective at reduced doses.

Method: We conducted an exploratory analysis of the most frequent and clinically relevant adverse events in patients receiving abemaciclib for early-stage breast cancer. The safety population included all patients with early breast cancer who received at least one full dose of abemaciclib in Clinics for Tumors KBCSM from January 2023 till January 2024 (n = 60). Safety analyses included common and clinically relevant adverse events (AEs) and related dose adjustments. Patient-reported outcome questionnaire (PRO) was administered before each cycle.

Results: The most frequently reported AE in the questionnaire was diarrhea, and the median time to onset was during the first cycle. Around 50% of patients assessed diarrhea with grade 2 or 3 after finishing the first cycle (i.e. first two weeks of treatment). With each subsequent cycle, patients reported diarrhea less frequently. Dose adjustment occurred in 15% of patients after finishing the first cycle due to clinically significant diarrhea (grade ≥ 2 , > 4 stools). Similar findings were reported in MonarchE study.

Conclusion: In general, abemaciclib was well tolerated. The dose adjustment strategy appeared to be an effective way to manage toxicity without compromising efficacy. Except for side effect management strategies, clinicians should implement dose adjustments for commonly occurring and serious adverse events to ensure continued treatment and decrease toxicity burden.

Keywords: abemaciclib, diarrhea, toxicity, dose modification

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P8 - AVELUMAB AS MAINTENANCE AFTER PLATINUM-BASED CHEMOTHERAPY FOR ADVANCED UROTHELIAL CANCER (AUC) – UPDATED RESULTS FROM CROATIAN URO-ONCOLOGY COLLABORATIVE GROUP (CUOCG)

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Introduction: Platinum-based chemotherapy followed by avelumab switch maintenance in non-progressors is the standard of care first line treatment for advanced urothelial cancer (aUC). In this study, we describe clinical characteristics and updated outcomes in a ‘real-world’ cohort of patients treated with avelumab maintenance for aUC within Croatian Uro-Oncology Collaborative Group (CUOCG).

Patients and Methods: In this retrospective cohort study we included patients from 9 CUOCG-affiliated institutions who received maintenance avelumab after platinum-based chemotherapy for aUC. Anonymized data were centrally analyzed. We reported toxicity, overall response rate, progression-free survival and overall survival for this cohort of patients, representative for treatment pattern of all aUC patients in Croatia.

Results: Ninety-one (91) patients with aUC who received avelumab maintenance from July 2022 to February 2024 were identified within CUOCG network. Twenty-two percent of patients had subtype histology; median age at avelumab initiation was 68 years (range 41-82 years), 17% had upper tract primary tumor, 70% received prior cisplatin-based chemotherapy (gemcitabine/cisplatin 56%, ddMVAC 14%), 18% had liver metastasis and 65% were ECOG PS 0 at time of chemotherapy initiation. Following chemotherapy, observed complete response was found in 4%, partial response in 63%, and stable disease in 32% of patients, respectively. Seventy-two patients (79%) were available for response assessment. The overall response rate with avelumab maintenance was 20% (complete response [CR] for 5%, partial response [PR] for 14%), stable disease (SD) 29%; progression as the best response was noted in 37% of patients, respectively. After median follow-up time of 10 months (95%CI 8-25 months), 31 patients (34%) experienced disease progression. Fifty-two patients (57%) are still on treatment. Median progression-free survival was 13 months (95%CI 10-18), while median overall survival was not reached. The observed rate of immunotherapy-related side-effects was 15% for grade 2, 3% for grade 3, and 1% for grade 4, respectively. Four patients (4%) required therapy termination due to serious immunotherapy-related side-effects. Given insufficient number of events, analyses based on number of chemotherapy cycles, type of response to chemotherapy and other prognostic variables of interests were all statistically non-significant. Eleven patients (35% of progressing patients) received active treatment post avelumab progression.

Conclusion: Early real-world outcomes with avelumab maintenance, characterized by relatively short follow-up, low number of progression events and surprisingly high progression-free survival, revealed unusually high prevalence of cisplatin-based chemotherapy in our population, relatively high overall response rate (higher than in JavelinBladder100 trial) and lower incidence of immunotherapy-related side-effects compared to registration trial. Limitations include retrospective nature, patient selection, and the lack of central radiology review. Longer follow-up is needed to objectively assess mature oncologic outcomes and toxicity profile.

Keywords: urothelial cancer, avelumab maintenance

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P9 - CANCER PATIENTS IN EMERGENCY DEPARTMENT – SINGLE-INSTITUTION EXPERIENCE

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Aim: With the rising prevalence of cancer along with cancer survival rates, cancer patients' visits to the emergency department (ED) are increasing, regarding cancer itself or various treatment-related complications. The aim was to determine the clinical characteristics of cancer patients visits to the ED at the University Hospital Center Sestre milosrdnice.

Materials and methods: Medical records of all ED visits from December 1st 2023 until February 1st 2024 were reviewed and descriptive retrospective research was performed regarding patients' demographics, cancer characteristics, main symptoms, reasons for admission and outcomes of ED visits.

Results: There were overall 4630 ED visits, and 5,3% were cancer patients (250 visits). Our research included 105 males (42%) and 145 (58%) females with a median age of 70 years (range 30-89). The main symptoms of cancer patients referred to ED were: dyspnea (27,2%), abdominal pain (20,8%), fever (10%), weakness and fatigue (9,6%), peripheral edema (7,6%) and nausea (6%), and other identified symptoms were chest pain (4,8%), hemorrhage of any kind (4,4%), arterial hypertension (2%) and rash (1,6%), in much lower prevalence. Out of a total number of visits, there were 69,2% (173) cancer patients in active treatment, and they were stratified based on the type of treatment – chemotherapy, endocrine therapy, immunotherapy, radiotherapy and other specific therapy subtypes, as well as various combination therapy regimens. Palliative patients visited in 16% of cases, and 14,4% were patients who hadn't yet started active treatment for various reasons. Out of all visits, 70,4% were patients with metastatic disease, 22,8% with early stage, and 4,8% with locally advanced disease. The most common cancer sites were breast cancer (20%), lung cancer (16,4%), colorectal cancer (16,4%), pancreatic cancer (6,4%), ovarian cancer (6,4%), and prostate cancer (6%). Hospitalization rate was 38%, and almost half of those patients eventually died in the hospital (17,8%).

Conclusion: Accurate recognition of cancer-related symptoms and treatment side effects, as well as adequate symptomatic treatment in palliative care, can improve the quality of life of cancer patients and reduce ED visits.

Keywords: emergency department, cancer patients, treatment side effects, palliative care

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P10 - CLINICAL CHARACTERISTICS AND OUTCOMES OF PATIENTS WITH LUMINAL B SUBTYPES OF BREAST CANCER TREATED WITH NEOADJUVANT THERAPY – SINGLE CENTER EXPERIENCES FROM UNIVERSITY HOSPITAL OF SPLIT

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Introduction: Neoadjuvant therapy (NAT) is given systemically in the early stages of treatment to control the tumor size and reduce the risk of postoperative metastasis. Neoadjuvant chemotherapy (NAC) is less effective in luminal breast cancer than in other subtypes. Degree of response is associated with event free survival (EFS) and overall survival (OS).

Aim: The aim of this report was to investigate the clinical characteristics and outcomes of patients with luminal B subtypes of breast cancer treated with NAT in Department of Oncology and Radiotherapy of University hospital of Split.

Methods: Data from the medical history of 41 patients with luminal B subtype of breast cancer treated with NAT in the period from January 1, 2018 to June 1, 2021, were retrospectively collected and processed.

Results: The median age of patients with early stage, luminal B subtype of breast cancer at the time of diagnosis was 62 years (range 31-82). Forty female patients and 1 male patient were included in the study. Two thirds of the diagnosed patients (27 patients) were postmenopausal. Majority of patients were diagnosed with stage IIA (19 patients, 46,3%), IIB (10 patients, 24,4%) and IIIC (6 patients, 14,6%).

All patients received neoadjuvant therapy: 33 patients (80%) were treated with NAC (ACdd-T protocol) and 8 (20%) patients with neoadjuvant endocrine therapy. Median duration of NAT was 5,5 months.

All patients were operated after NAT, mostly with radical mastectomy and axillary lymph node dissection (38 patients, 93%). Complete pathological response (pCR) was recorded in only 3 patients (7%).

Forty patients (97.6%) received adjuvant local/locoregional radiotherapy and endocrine therapy, 35 patients (85,4%) adjuvant bisphosphonates and 10 patients (24%) adjuvant capecitabine.

After 41,5 months of median of follow-up, 1 patient developed local recurrence, 1 patient locoregional recurrence, 5 patients disseminated disease and 2 patients were diagnosed with second primary cancer. At the end of the analysis, 33 patients (78%) were alive without disease, 4 patients (10%) were alive with the disease, 5 patients (12%) died due to breast cancer. Consequently, EFS and OS for this study population has not been reached yet.

Conclusion: Our analysis showed results consistent with data from many clinical reports with luminal B breast cancer treated with NAT. Longer follow-up is needed to define the survival impact of NAT.

Keywords: Luminal B subtype of breast cancer, neoadjuvant therapy

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P11 - CLINICAL OUTCOMES OF PATIENTS WITH METASTATIC NON-SMALL CELL LUNG CANCER TREATED WITH PEMBROLIZUMAB - EXPERIENCE OF ONE CENTER

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Background: The real- world evidence showing the efficacy of immune- checkpoint inhibitors in terms of achieving long-term control in patients with advanced, non- oncogene addicted non- small cell lung cancer (NSCLC) is continuously growing. The aim of this retrospective study was to analyze clinical outcomes in a population of patients (pts) with metastatic NSCLC treated with pembrolizumab at Sestre Milosrdnice University Hospital Center.

Methods: Medical records of 121 (89 male and 41 female) pts with metastatic NSCLC treated with pembrolizumab from March 2018 until September 2023 at Sestre Milosrdnice University Hospital Center were retrospectively reviewed. Patients with programmed- death ligand (PD-L1) expression on tumor cells $\geq 50\%$ received pembrolizumab monotherapy, and pts with tumor PD-L1 expression 0-49% received pembrolizumab in combination with platinum-based chemotherapy. Progression-free survival (PFS) and overall survival (OS) in both groups were calculated using the Kaplan Meier method. Association of clinico-pathological variables with PFS and OS was assessed using Cox regression model.

Results: In the pembrolizumab- monotherapy group (N=73), median age was 69 years. After a median follow-up of 37 months, median PFS was 12 months (95% confidence interval [CI] 6-25 months). The 1-year PFS rate was 48% and the 2-year PFS rate was 40%. Median OS was 27 months (95% CI 13-40 months). The 1-year OS rate was 62% and the 2-year OS rate was 52%. The occurrence of grade ≥ 2 immune- related adverse events was associated with longer PFS (HR 0.48, 95% CI 0.23-0.98, $p=0.03$).

In the chemotherapy + pembrolizumab group (N=48), median age was 65 years. After the median follow-up of 23 months, median PFS was 14 months (95% CI 8-19 months). The one-year PFS rate was 55%, and 2-year PFS rate was 30%. Median OS was 18 months (95% CI 15-31 months), 1-year OS rate was 67%, and 2-year OS rate was 38%. None of the analyzed clinico- pathological variables significantly influenced PFS or OS.

Conclusion: Our results are in line with the real- world data, confirming the efficacy of pembrolizumab in terms of achieving long-term disease control in pts with advanced NSCLC.

Keywords: metastatic non-small cell lung cancer, pembrolizumab, clinical outcomes

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P12 - COMPARISON OF HYPOFRACTIONATION AND STANDARD FRACTIONATION FOR SALVAGE RADIOTHERAPY IN PATIENTS WITH BIOCHEMICAL RECURRENCE OR PSA PERSISTENCE FOLLOWING PROSTATECTOMY: SINGLE INSTITUTION ANALYSIS (N=379)

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Introduction: Hypofractionation for salvage postprostatectomy radiotherapy is an emerging practice but with limited randomized evidence. The purpose of this study was to investigate and report the outcomes and prognostic factors of patients who underwent salvage radiotherapy for biochemical recurrence following radical prostatectomy at a single center with special emphasis on fractionation regimen and pelvic radiotherapy.

Patients and methods: We retrospectively reviewed electronic charts of 379 patients who underwent salvage radiotherapy for biochemically recurrent prostate cancer after radical prostatectomy between May

2012 and January 2021. PSA failure-free and metastasis-free survival were calculated using Kaplan-Meier log-rank method. Cox regression analysis was performed to test the association of fractionation regimen and other clinical factors with treatment outcomes.

Results: Three hundred seventy (370) patients with complete clinical and follow-up data were identified. Median follow-up was 56 months (range, 6-132 months). Forty-one patients (10%) received elective pelvic nodal radiotherapy. Median pre-radiotherapy PSA 0.4 ng/mL (range 0.01-30). Two hundred eighteen (218, 57%) patients received concomitant androgen-deprivation therapy (ADT). In population of 333 patients with prostate bed only radiotherapy, 211 (63%) received conventional fractionated radiotherapy, 66 Gy in 33 fractions, 2 Gy per fraction, and 122 patients (36%) received hypofractionated radiotherapy, 52.5 Gy in 20 fractions, 2.63 Gy per fraction. 5-year PSA failure- and metastasis-free survival rate was 62% and 85%, respectively. One hundred nine (109) patients (28%) experienced biochemical failure after salvage radiotherapy and 46 patients (12%) experienced metastatic relapse. Median PSA failure-free survival was 86 months (95%CI; 69-107 months), while median metastasis-free survival was not reached. On univariate analysis, factors associated with PSA failure-free survival were fractionation regimen, pathologic Gleason score/Grade Group, the presence of seminal vesicle involvement, extracapsular extension and pT stage on prostatectomy specimen, the first post-prostatectomy PSA level (continuous variable), PSA level before the salvage radiotherapy and the use of ADT. After adjusting for inherent imbalances in patients receiving each fractionation scheme, ADT use and ADT duration on the multivariate analysis, the only significant factor associated with PSA failure-free survival was pre-radiotherapy PSA level. On receiver operator curve (ROC) analysis, patients with PSA \geq 0.58 ng/mL have an increased risk of PSA failure post salvage radiotherapy. Eighteen patients (4%) experienced late genitourinary or gastrointestinal grade 3 toxicity with no difference between two fractionation schemes.

Conclusions: Salvage radiotherapy is an effective treatment for biochemical recurrence following radical prostatectomy with tolerable toxicities. Hypofractionation is acceptable resource-sparing option for salvage radiotherapy. Our results supported the current recommendations that salvage radiotherapy should be initiated before PSA reaches 0.5 ng/mL. In future analysis machine learning models will be used to detect PSA threshold which is associated with increased risk of biochemical failure.

Keywords: radical prostatectomy, prostate cancer, salvage radiotherapy, hypofractionation, standard fractionation, biochemical recurrence, androgen deprivation therapy

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P13 - CONSTRAINT DOSE EFFECT ON THE THYROID GLAND IN THE CONTEXT OF DEVELOPMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE IN PATIENTS WITH BREAST CANCER

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Introduction: Nonalcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease and one of the leading causes of death from liver disease in developed Western countries. It is defined by excessive accumulation of fat within >5% of hepatocytes and can be proven by histological and/or imaging methods in combination with laboratory indicators(1).

NAFLD is a complex clinical entity that can be secondary to many other diseases including hypothyroidism, which is characterized by a decrease in thyroid hormone and an increase in thyroid-stimulating hormone(2,3).

Hypothyroidism has been reported as the most common thyroid disease after neck radiotherapy. Based on this experience, the adult thyroid is considered to be a relatively radiation-resistant organ, although the dose range for thyroid ablative radiation appears to be wide at 10-80 Gy. The minimum TD 5/5 thyroid (incidence of clinical hypothyroidism in 5% of patients 5 years after treatment) is considered to be 20 Gy when all or part of the gland is irradiated by conventional fractionation.

Methods: 28 patients treated with adjuvant radiotherapy with 3D conformal radiotherapy of the breast area and lymphatic regions were analyzed. Irradiation of TD 4005cGy in 15 fractions was performed, and the thyroid gland was contoured as a risk organ. Nine patients suffered from cancer of the right breast and the remaining from cancer of the left breast. Fibroscan is an ultrasound method that measures steatosis, i.e. liver fat. Fibroscan analysis divides the condition into four levels according to the degree of steatosis - normal values up to 238 dB/m, the first level from 238 dB/m to 260 dB/m, the second level from 260 dB/m to 290 dB/m, the fourth from 290 dB/m m to 400 dB/m. The examined group of patients was divided into two groups according to the increase in the degree of steatosis six months after the completion of radiotherapy treatment.

Results: Analyzing DVH of radiotherapy plan the average Dmean is 19.43, average V10 Gy 58%, average V20 Gy 46% and average V30 Gy 35%. An increase in the degree of liver steatosis was verified in 10 investigated patients, i.e. 34% of them. In the aforementioned group of patients, a statistically significant increased value of Dmean per thyroid volume was determined, and the average Dmean was 23.4 Gy. According to the above result, V10, V20 and V30 are statistically higher in patients who have increased the grade (average V10 71%, average V20 60%, average V30 48%).

Conclusion: According to our research, Dmean greater than 23 Gy on the contoured volume of the thyroid gland in patients treated with adjuvant radiotherapy may be a risk factor for the development of non-alcoholic fatty liver disease. Further research is needed to confirm the stated thesis.

Keywords: breast cancer, radiotherapy, NAFLD, thyroid gland

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P14 - CORRELATION OF LVEF DROP AND CARDIAC RADIATION DOSES IN PATIENTS WITH LEFT BREAST CANCER UNDERGOING HYPOFRACTIONATED ADJUVANT RADIOTHERAPY WITH CONCURRENT HER2 TARGETED THERAPY

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Background: HER2 targeted therapy and left breast adjuvant radiation therapy (RT) can both result in cardiotoxicity. The aim of this study was to evaluate the influence of radiation dose on cardiac structures on the values left ventricular ejection fraction (LVEF) in patients with HER2- positive left breast cancer undergoing adjuvant concomitant HER2 targeted therapy and radiotherapy, and to establish a correlation between the LVEF drop and cardiac radiation doses.

Methods: Fifty- seven patients underwent left breast hypofractionated radiotherapy in parallel with HER2 targeted therapy: trastuzumab, combined trastuzumab– pertuzumab or trastuzumab emtansine (T-DM1). LVEF values were measured prior to and upon completion of radiotherapy. A significant drop in LVEF was defined as >5% (percentage points) from baseline. Dose volume histograms (DVH) were generated for the heart, left ventricle (LV) and left anterior descending artery (LAD). The LVEF drop was correlated with radiation doses on cardiac structures.

Results: Median LVEF value prior to RT was 64% (IQR 60 – 65). A drop in LVEF values of 5% was observed in 14 patients (Group 1). Patients in Group 1 on DVH had significantly higher AUC (area under curve) for the heart and LV ($p < 0.01$ for both) compared to Group 2 of patients in whom LVEF drop was not observed. Also patients in Group 1 received significantly higher maximal radiation dose on LV than patients in Group 2 ($p < 0.01$). No difference has been observed between patients' groups in terms of radiation doses on LAD.

	Patients with LVEF drop N = 14/57 (25%)	Patients without LVEF drop N = 43/57 (75%)	P Mann-Whitney U
LVEF before RT % (M,Q1,3)	65 (60 – 68)	63 (60 – 65)	0.08
LVEF after RT % (M,Q1,3)	60 (55 – 61)	60 (60 – 65)	<0.01
RT dose heart AUC % (M,Q1,3)	71 (67 – 73)	62 (57 – 62)	<0.01
RT dose LV AUC % (M,Q1,3)	69 (67 – 70)	59 (59 – 60)	<0.01
LV Dmax Gy (M,Q1,3)	38 (36 – 39)	37 (33 – 39)	<0.01

Conclusion: The LVEF drop observed in patients receiving HER2 targeted therapy after adjuvant RT was positively associated with radiation doses on the heart and LV, including Dmax on left ventricle.

Keywords: breast cancer radiotherapy, cardiotoxicity, HER2 targeted therapy

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P15 - EFFECT OF NEOADJUVANT ENDOCRINE THERAPY (NET) DURATION ON CHANGES IN CLINICAL RESPONSE RATE

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Introduction: Over the last ten years, neoadjuvant endocrine therapy (NET) has been increasingly investigated and has gained recognition. International guidelines consider that NET given for 4 to 8 months is a validated treatment in postmenopausal women with hormone receptor-positive HR+/HER2-negative (HER2-) breast cancer to improve surgical outcomes. The duration of NCT ranges from 3.5 to 6 months depending on the number of cycles and/or dose-dense schedules. The optimal duration of NET remains controversial, as the time to best response is longer with endocrine therapy than with chemotherapy. Some studies have suggested the need for longer treatment. (1) It is necessary to establish the optimal duration to attain the maximal response. In our analysis, we evaluated if longer duration of therapy results in better clinical response status.

Methods: We did retrospective analysis of collective data from January 2019 until November 2023 for 46 patients who had been treated with neoadjuvant endocrine therapy with fulvestrant and aromatase inhibitors for a period of at least 6 months. 39 patients were eligible for evaluation of clinical response. Patients have signed informed consent and medical data was analysed.

Results: Our analysis included 46 patients treated with neoadjuvant endocrine therapy with fulvestrant and aromatase inhibitors, with median age of 73. Median duration of therapy was 9.47 months. First morphologic evaluation was performed in median after 3.5months of therapy. Due to late beginning of therapy, 7 patients (15%) still didn't have radiologic evaluation of response at the time of analysis. 21 patients (45%) had partial response, 14 patients had stable disease (30%), 2 patients (5%) had complete response and 2 patients (5%) had progression of disease. Changes in response with longer duration of hormonal therapy was observed in 13 out of 39 evaluated responses. 10/39 of patients had stable disease at first evaluation, and partial response later, and 3/39 patients had partial response at first evaluation, and complete response later. Median time to change in response status was 6 months.

Conclusion: Our analysis showed that longer duration of NET resulted in higher clinical response rates. Our results are consistent with data from clinical trials (TEAM IIA, CARMINA02). (2,3). Due to short duration of endocrine therapy in significant number of patients at the time of analysis, longer follow up will probably result in higher percent of patients with changes in response status according to duration of therapy. The question that remains is whether clinical response will predict long-term outcome when NET continues until maximal response.

Keywords: neoadjuvant therapy, duration of NET, clinical response, fulvestrant and aromatase inhibitor

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P16 - EVALUATION OF THE FACTORS AFFECTING SURVIVAL IN ELDERLY LUNG CANCER PATIENTS TREATED WITH IMMUNOTHERAPY

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Introduction: Immunotherapy has revolutionized the treatment of lung cancer patients. However, most studies did not include elderly patients, who represent a growing population in real-world centers. While age is not a limitation for the initiation of immunotherapy, there is a scarcity of data on immunotherapy efficacy in patients over 70.

Patients and methods: We retrospectively analyzed data on 93 consecutive patients over 70 treated with at least 1 cycle of immunotherapy for metastatic or inoperable lung cancer from June 2017 until June 2023, using descriptive statistics, Kaplan-Meier analysis, and Cox proportional hazards.

Results: The majority of patients were male (N=69, 74.2%), ECOG 1 (N=84, 90.3%), and treated in the first-line setting (N=54, 58.1%) for lung adenocarcinoma (N=62, 66.7%). The median age was 73 (95% CI 73-74, range 70-83).

The median progression-free survival (PFS) for the whole group was 9.9 months (95% CI 7.5-13.7), with 66.7% of patients progressing in the follow-up (N=62).

Treatment in the first-line setting was associated with a longer PFS (15.5 months (95% CI 10.7-22.7) vs. 4.9 months (95% CI 2.0-8.8), HR 0.37 (p<0.0001). Similarly, female gender (N=24) was associated with longer survival compared to males (N=69) (14.2 months (95% CI 9.8-15.1 vs. 8.8 months (95% CI 5.8-11.9), p=0.037 (HR 0.52 (95% CI 0.30-0.89)). There was a trend towards longer PFS for patients with ECOG 0 compared to ECOG 1 (p=0.17) and for patients with adenocarcinoma (p=0.16), with no PFS difference based on the use of corticosteroids (p=0.39).

There was no difference in PFS between patients younger vs. older than 80 (p=0.09). When dividing patients into three age subgroups, we found no difference in PFS between patients aged 70-74 and 75-79 (HR 1.6 (95% CI 0.90-2.98)); however, a longer PFS was registered in patients older than 80 compared to both youngest (HR 0.45 (95% CI 0.20-0.98)) and the middle age group (HR 0.27 (95% CI 0.11-0.67), p=0.034.

Similar results were registered for overall survival (OS), where a median for the whole group was 17.2 months (95% CI 12.3-31.6), with 53 patients dying in the follow-up (57.0%). We found a significant difference in OS for female patients (HR 0.36 (95% CI 0.19-0.65), $p=0.008$) and first-line setting (HR 0.39 (95% CI 0.22-0.69), $p=0.0004$). A numerical trend towards a longer OS was found for patients with ECOG 0 vs. 1 ($p=0.12$), for the adenocarcinoma subtype compared to other subtypes ($p=0.10$), and for the use of corticosteroids ($p=0.10$).

Patients older than 80 did not exhibit shorter survival compared to the younger ones (n/r vs. 17.2 months (95% CI 9.9-24.9), $p=0.26$). There was no difference in OS even when dividing patients into different age groups ($p=0.08$).

Conclusion: Female gender and treatment in the first-line setting were associated with significantly longer PFS and OS in elderly lung cancer patients, while ECOG status 0 and adenocarcinoma subtype exhibited a trend towards a longer survival. There was no detrimental effect of older age on survival during immunotherapy treatment.

Keywords: lung cancer, elderly patients, immunotherapy

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P17 - EVOLUTION OF BREAST CANCER MANAGEMENT AND SURVIVAL OUTCOMES: TWO DECADES OF CHANGE IN LARGE TERTIARY INSTITUTION

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Introduction: Over the last two decades, numerous studies have emerged on the optimal treatment of breast cancer. The collected data has been influencing and shaping breast cancer practice. However, little is known about contemporary trends in clinical features, management patterns, and stage-based survival of breast cancer patients in Croatia. The aim of this study was to investigate trends in presenting clinical features, type of surgery, and mature survival outcomes observed over a 20-year period in a large breast cancer referral center.

Methods: A retrospective review was conducted on the radiotherapy charts of breast cancer patients referred to postoperative radiotherapy at a major academic hospital between 2000 and 2009. The collected data included clinical and histopathological factors, type of breast primary surgery, and UICC stage of disease. The data was analyzed using the Jonckheere trend test or univariate linear regression. Univariate and multivariate analysis were performed to identify predictors of the surgery type received. The Kaplan-Meier method was used to assess breast cancer-specific survival (BCSS). The data on survival were obtained from the Croatian National Cancer Registry.

Results: Total of 895 breast cancer patients received postoperative radiotherapy, with data complete for 879 patients. In total, 275 (57%) breast cancer-related deaths and 201 (43%) non-breast cancer related deaths were observed. Median follow-up for patients alive was 16 years (95% CI 16-23 years). Median of overall survival (OS) was 15 years (95% CI 13-17 years). Median overall breast cancer-specific survival (BCSS) was not reached. An increase in annual incidence, increase in proportion of older patients, increase in proportion of stage 1 tumors (tumors <2 cm and negative axillary lymph nodes) and an increase in reduced volume of radiotherapy were observed. There has been a sharp decrease in mastectomy rates and a proportional increase in breast-conserving surgery rates ($p < 0.001$). On multivariate analysis factors that remained significantly associated with mastectomy were increasing primary tumor size ($p < 0.001$) and receipt of adjuvant chemotherapy ($p < 0.044$). On univariate analysis, factors significantly prognostic for worse BCSS were T stage, N stage, IUCC stage, volume of radiotherapy, mastectomy, adjuvant chemotherapy and negative hormone receptors.

Ten and sixteen-year BCSS rates for UICC stages 0, 1, 2, 3, and 4, respectively, were 86% and 86%; 91% and 89%; 73% and 64%; 41% and 35%; 36% and 35%, respectively. On multivariate analysis, factors significantly prognostic for worse BCSS were, T stage ($p = 0.01$), N stage ($p = 0.02$), UICC stage ($p = 0.01$), negative hormone receptors ($p = 0.04$).

In additional analysis we found no difference in heart-related mortality between left and right sided breast cancer.

Conclusions: Significant improvements have been made in the management of breast cancer over the past two decades, largely due to the adoption of international studies that have led to changes in practice. National clinical data has shown that breast cancer survival rates are comparable to those in developed countries.

Keywords: breast cancer, survival outcomes

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P18 - EXPERIENCES OF KBC OSIJEK WITH PATIENTS WHO WERE DIAGNOSED WITH BREAST CANCER IN 2021 AND 2022 AND THEIR RESPONSE BASED ON THE TYPE OF TUMOUR AFTER RECEIVING NEOADJUVANT THERAPY

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Introduction: Breast cancer, a heterogeneous disease with diverse presentations, prompts varied treatment approaches. Neoadjuvant therapy, involving systemic treatment before surgery, encompasses hormone therapy, targeted therapy, or chemotherapy. In order to increase the efficacy of the tumor's future surgical removal, this strategy is used to reduce the tumor's size or eradicate any micrometastases within the body. Decisions on neoadjuvant therapy hinge on factors like tumor features, size, HER2/neu status, positive axillary nodes and overall health. Evaluating therapy response based on tumor type becomes pivotal for optimizing neoadjuvant treatment efficacy. To address this, we analyzed patient data from our center, focusing on those undergoing neoadjuvant therapy.

Methods: All patients diagnosed and treated (undergoing neoadjuvant therapy) at KBC Osijek in 2021 and 2022 were included in this retrospective study, in which data about the pathohistological response to different tumour types were analysed. The aim was to compare the complete pathological response (pCR) depending on the specific tumor types, mainly the HER2/neu receptor status.

Results: A total of 73 patients were diagnosed and treated (with neoadjuvant therapy) in 2021 and 2022 at KBC Osijek. Out of a total of 73 patients, 28.77% had a pCR. We divided them into 5 subtypes depending on hormone receptor status and HER2/neu status and compared their frequency and response to neoadjuvant therapy (pCR). The first group were patients who are triple negative/HER2/neu 0 and make up 13.7% of the total number, in that group pCR was observed in 30% of patients. The second group was triple negative/HER2/neu 1+ and 2+ which made up of only 5.48% of patients but 50% of pCR was observed. The third group (Luminal – HER2/neu 0) makes up 24.66% of the total number and the fourth group (Luminal – HER2/neu 1 + and 2 +) makes up 15.07% and did not have a single pCR. The fifth group is the HER2/neu 3+ group, which included 30 patients, or 41.1% of the total number of patients, and exhibited highest pCR of 53.33%.

Conclusion: A significant association was observed between HER2/neu expression and the probability to achieve pCR. We found that the group of HER2/neu positive tumours had recorded the highest rate of pCR. Additionally, we discovered that triple negative breast tumours, a far more aggressive form of the disease, had an acceptable amount of pCRs identified, but luminal breast cancers had much fewer. Long recognised, neoadjuvant therapy increases the probability of pCR in patients with triple-negative and HER2-positive disease. Given their worse prognosis and potential benefit from extra adjuvant treatment, individuals who do not respond to neoadjuvant therapy should be identified. More research should be conducted to identify the reasons behind some tumours' inferior response to neoadjuvant therapy. This will allow for a more focused investigation of neoadjuvant therapy's potential modifications, the identification of distinct tumour types that benefit most from it, the establishment and addition of adjuvant therapy, and prompt response and surgery.

Keywords: breast cancer, neoadjuvant therapy, complete pathological response

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P19 - FEASIBILITY OF COMPREHENSIVE GENOMIC PROFILING (CGP) IN PERSONALIZED APPROACH TO PATIENTS WITH METASTATIC COLORECTAL CANCER – RESULTS FROM THE FIRST TWO YEARS OF TESTING IN CROATIA.

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Background: Colorectal cancer is the most common diagnosed malign disease in Croatia with over 3000 newly diagnosed patients each year. Also, it ranks third in mortality with almost 2000 patients who succumb to the extent of the disease every year and with that represents challenge to nowadays precision oncology which goal is improvement of the outcomes (1). Precision medicine has already paved its way into everyday clinical work of diagnostic and therapeutic management of colorectal cancer with affirmation of the comprehensive genomic profiling (CGP) and targeted therapy and immunotherapy becoming the standard treatment (2-4). The aim of this study is to present potential utility of CGP in everyday work and to analyze its implementation in the first two years since it became available in Croatia.

Methods: This cross-sectional retrospective study was conducted in six Croatian institutions from January 1, 2020 to December 31, 2021. It included patients diagnosed with metastatic colorectal cancer on whose tumors CGP was performed after decision from multidisciplinary teams inherent to each institution and in accordance with criteria for testing (5). The data was analyzed using Microsoft Excel descriptive statistics tools.

Results: There was 89 patients in total. CGP was performed through FoundationOne CDx test for tissue specimens for majority of patients (91%) and most of them had profiling done on the tissue from primary tumor (76%). Median age was 55 years (IQR 45-64). CGP results revealed clinically relevant genomic alteration in 68 (76%) patients and the most common were KRAS, PIK3CA and PTEN mutations in 40 (59%), 12 (18%) and 6 (8%) patients. Genomic alterations with unknown significance were found in 87 (98%) patients with APC and TP53 mutations as the most common in 62 (71%) patients. Most of the patients had microsatellite stable tumor (81%), while 6 (7%) patients had highly instable tumor and for 11 (12%) patients status was not determined. Median tumor mutational burden (TMB) was 4 mut/Mb (IQR 3-6), while 9 (10%) patients had TMB \geq 10 mut/Mb. According to the results, CGP guided therapy approved in patients tumor type was opted for 46 (52%) patients.

Extrapolating the data from Croatian cancer registry, high mortality rate from colorectal cancer mostly due to dissemination, and considering the criteria for CGP testing, we can say that in observed two years only 5% of potentially eligible patients was tested.

Conclusion: Our results have shown that majority of patients with metastatic colorectal cancer had some kind of mutation which could be target for precise therapy from which they could potentially have

benefit. Unfortunately, smaller sample of tested patients speaks in favor of beginnings of CGP testing, time for testing and administrative challenges and further steps forward are needed to fully implement precision oncology in metastatic colorectal cancer.

Keywords: comprehensive genomic profiling, metastatic colorectal cancer, Croatia

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P20 - IMPACT OF COVID-19 ON MELANOMA DIAGNOSIS IN UNIVERSITY HOSPITAL SPLIT

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Introduction: Melanoma, the leading cause of death from skin tumors, has a strong propensity for rapid local growth and distant spread unless diagnosed and removed promptly. Covid-19 has dramatically changed diagnosis and treatment procedure in hospital all over the world. On March 2020, the Croatian government implemented lockdown measures with a reorganized health care system to optimally manage the COVID-19 outbreak. Diagnosing melanoma in reprogrammed health systems became markedly more challenging.

Aim: The aim of this report was to investigate in there was an any significant difference in the number of newly diagnosed melanoma, histopathological features and melanoma staging between comparable periods in 2019 and in 2022.

Methods: Data from hospital clinical databases on the total number of newly diagnosed patients with melanoma in University hospital Split were analyzed. Comparative analyses were performed in a pre-

pandemic (March 2019 until March 2020), in a pandemic cohort (March 2020 until March 2021) and in a post-pandemic (March 2021 until March 2022).

Results: Comparing the first year of the pandemic (N=57) with the same period before (N=69), 17,4% decrease of melanoma cases was observed. But, comparing a year of the pandemic with a year after pandemic (N=84), we observed 32,2% increase in number of newly diagnosed melanoma patients. Cohort analysis showed no differences in the distribution of sex and age. The median age of the melanoma patients was similar in comparable periods. In a pre-pandemic cohort median age was 66 years (29-86), in a pandemic cohort 68 years (31-88) and in a post-pandemic 67 years (29-88). The male gender predominated among melanoma patients. Cohort analysis showed no differences in the pathohistological subtypes and primary localization of skin melanoma. We observed statistically significant difference in number of melanoma patients with positive regional lymph nodes in pre-pandemic in comparison with pandemic (5,9% vs 22,9%) and post-pandemic (5,9% vs 23,7%) ($p < 0.05$).

Conclusion: Data from University hospital Split shown a marked decrease in the number of newly discovered melanomas during the pandemic compared to the same period before and after the pandemic. We observed statistically significant increase in newly diagnosed patients with stage III melanoma in pandemic and post-pandemic as consequence of lockdown measures due to COVID-19.

Keywords: melanoma, diagnosis, Covid-19, pandemia

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P21 - IMPACT OF SPECIFIC TYPE OF PIK3CA MUTATION ON DISEASE RECURRENCE IN PATIENTS WITH HR+, HER2- TUMORS TREATED WITH ADJUVANT HORMONAL THERAPY - RESULTS FROM CROATIA.

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Background: Primary and secondary endocrine resistance are the reason why in almost a quarter of patients with early hormone receptor positive (HR+), human epidermal growth factor 2 negative (HER2-) breast tumor, the disease returns despite hormone therapy as the backbone of adjuvant treatment(1,2). Currently, there are numerous studies of potential biomarkers that would predict the response to adjuvant treatment and thus lead to its personalization and improvement of outcomes. Recently, the prognostic value of the phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit alpha (PIK3CA) mutation has been increasingly emphasized, but previous research has not provided a uniform answer(3,4). Hence, we have investigated the association and impact of specific PIK3CA mutations in relation to the time of the disease recurrence.

Methods: This was observational and retrospective study, conducted at five Croatian institutions from July 2020 to December 2021. It included initially early and locally advanced operable HR+/HER2- breast cancer patients who were diagnosed with disease recurrence during adjuvant hormonal treatment or within the first six years of follow up.

Results: There was total of 186 patients, out of which 40.9% were tested positive for PIK3CA mutation, and 59.1% were negative. Two cohorts were well balanced regarding the age, primary and adjuvant treatment, toxicity profile and rate of withdrawal. The two most prevalent PIK3CA mutations were H1047 and E545 found in 19.4% and 15.1% of patients. Among all mutations, statistical significance was only found in patients with H1047 mutations which was related to longer disease free survival (HR 0.47; p=0.002) in comparison to patients without PIK3CA mutation. Also, H1047 mutations were associated with higher odds for late recurrence (p=0.028), but after imputation of missing covariate data analysis, false discovery rate was >10%.

Conclusion: Our study emphasizes the importance of specific PIK3CA mutations and their potential prognostic value in predicting disease recurrence among women with HR+/HER2- early or locally advanced operable breast cancer.

Keywords: breast cancer, PIK3CA mutation, disease recurrence, Croatia

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P22 - INFLUENCE OF HORMONAL THERAPY ON NUTRITION AND METABOLIC PARAMETER AS WELL AS THE DEVELOPMENT OF LIVER STEATOSIS AND INFLAMMATION IN BREAST CANCER PATIENCE

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Introduction: Hormone therapy is one of the key treatments for hormone-sensitive breast cancer. It may involve blocking the production of estrogen or blocking the action of estrogen on tumor cells to stop the growth of the tumor or prevent the disease from coming back after primary therapy (eg, surgery or chemotherapy). Until now, it has been known that weight gain can be one of the side effects of hormonal therapy for breast cancer, and bioelectrical impedance (BIA) analysis is an excellent method of monitoring body composition in these patients. The reason for weight gain can be a change in the hormonal status of the body that occurs as a result of therapy, i.e. slower metabolism, increased appetite and increased fluid retention. The aim of the study was to investigate the influence of hormonal therapy on nutrition and metabolic parameters as well as the development of liver steatosis and inflammation.

Methods: In this prospective study we included 86 female patients, average age 63, who were introduced to hormonal therapy with complete hormonal blockade of estrogen production. The examined group of patients were analyzed at the beginning and three months after the start of hormonal treatment with BIA, fibroscan and laboratory parameters. BIA is used to analyze body composition, including body fat percentage, muscle mass, bone mass, total body water, sarcopenic index, and phase angle. Fibroscan is an ultrasound method that measures steatosis, liver inflammation and fibrosis, elastographic parameter of steatosis is controlled attenuation parameter (CAP) while elastographic parameter of inflammation and fibrosis is liver stiffness parameter (LSM). Insulin resistance was defined by HOMA-IR score.

Results: After the follow-up period there was no statistically significant difference in phase angle (5.30 vs. 5.32, $p=NS$), body fat percentage (30.4 vs. 31, $p=NS$), muscle mass (65.7 vs. 65.3, $p=NS$). Although there was no statistically significant difference regarding HOMA-IR at the beginning of the study and after the follow-up period of three months we noticed the tendency of higher HOMA-IR score values (3.98 vs. 4.19, $p=NS$). According to our results, there was a statistically significant increase in CAP value during the follow-up period (251.9 vs. 270.8, $p=0.04$). Although there was no statistically significant difference regarding LSM values at the beginning of the study and after the follow-up period we observed the tendency of higher LSM values (4.87 vs. 5.2, $p=NS$).

Conclusion: According to the results of our study there is significant influence on the development of non-alcoholic fatty liver disease as a consequence of hormonal therapy in breast cancer patients.

Keywords: breast cancer, hormonal therapy, bioelectrical impedance, fibroscan, NAFLD

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P23 - MY SURVIVORSHIP PLAN - WHAT WORKS FOR ME?

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Survivorship focuses on physical, psychological, social, and economic issues affecting people after the primary treatment for cancer. Post-treatment cancer survivors range from people having no disease after finishing treatment, people who continue to receive treatment to reduce the risk of cancer recurrence and people with well controlled disease and few symptoms, who receive treatment to manage cancer as a chronic disease.

Survivorship care plan contains a summary with recommendations for follow-up care, based on the type of cancer and the suggested treatment. Treatment outcomes are one of the vital components of the survivorship plan that involve ongoing assessment of the initial cancer treatment effectiveness, monitoring for signs of cancer recurrence and managing long-term side effects and late effects. The plan may include schedules for physical exams and medical tests (laboratory, imaging) to check if the cancer has come back or spread to other parts of the body.

Quality of life is another crucial aspect of survivorship. Survivorship plan needs to address potential physical and psychological challenges that can deteriorate it. It involves managing and mitigating treatment-related side effects, promoting healthy lifestyle choices, and addressing any chronic health conditions due to cancer or its treatment. It should include activities which support not only health quality of life but also emotional and social well-being, crucial for the person to have the capacity to implement survivorship plan.

Survivorship plan also includes information that can help with the emotional, social, legal, and financial needs the patient may have. It may include referrals to specialists and recommendations for a healthier lifestyle, such as diet change, exercise and regulating smoking. The primary goal is to enhance the quality of life and ensure ongoing support for the unique and unmet needs.

Emotional well-being is a key consideration in survivorship planning. When distress levels are high, mental health support should be included. Psychosocial support helps individuals cope with the emotional burden of cancer, addressing issues like anxiety and depression symptoms and supporting them to build a better capacity to follow the survivorship plan. Sometimes professional support from psychologists, or psychiatrists may be recommended. These professionals can provide tailored interventions to address specific psychological needs.

Socialization and community engagement also have important role in a survivorship plan. Maintaining a social support system is essential for emotional well-being and can positively impact the overall quality of life. The plan may involve connecting patients with support groups, counselling services or community organizations that specialize in cancer survivors.

Eight women show in their separate poster presentations what is important to each of them individually for their quality of life and how civil society organizations and programs are included in their survivorship plan.

Keywords: survivorship, survivorship plan, quality of life, distress, psychosocial support

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P24 - NEOADJUVANT OR INDUCTION CHEMOTHERAPY (N/IC) FOR BLADDER CANCER: UPDATED REAL WORLD EXPERIENCE ON 157 PATIENTS – RESULTS FROM CROATIAN URO-ONCOLOGY NETWORK

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Introduction: Despite the level I evidence and known overall survival (OS) benefit with cisplatin-based neoadjuvant chemotherapy for localized muscle-invasive bladder cancer; such neoadjuvant chemotherapy remains underutilized, with variability based on the geographical region. We describe the patterns of use of neoadjuvant or induction chemotherapy (N/IC) and oncologic outcomes in patients (pts) treated within Croatian uro-oncology public network.

Patients and methods: Available records of all consecutive pts treated with N/IC were retrospectively reviewed. The primary endpoints included pathologic complete response (pCR, i.e. ypT0N0), major patho-

logic response (ypT \leq 1N0) disease-free and overall survival (DFS, OS). DFS and OS were estimated using Log-rank test and calculated from N/IC start. Association of clinical variables (age, sex, clinical and pathologic stage, ECOG PS, histology subtype) with survival was assessed using Cox regression model.

Results: Between March 2018 and December 2023, 157 pts received N/IC in 5 oncology centers. Distribution of clinical stage were as follow: II: 72 (45%), IIIA: 46 (29%), IIIB: 39 (24%); distribution of clinical T stage: cT2 56%, cT3 35%, T4 9%, distribution of cN stage (based on CT): cN0 63%, cN1 10%, cN2 11%, and cN3 12%, median age was 66 (43-82), 76% male, 18% ECOG PS 1, 19% had histology subtype. Protocols used were cisplatin/gemcitabine 70%, dose dense MVAC 24%, carboplatin/gemcitabine 3%, cisplatin/etoposide 2%. Median duration of N/IC was 2 months (0-5 mo), median number of cycles was 4 (1-6); 40 % of pts had grade \geq 3 N/IC-related toxicity [neutropenia (G3 18%, G4 10%, G5 0.03%), anemia (G3 6%, G4 0.6%), thrombocytopenia G3 11%, mucositis G3 4%]; 126 pts (82%) underwent cystectomy. The median time from start of N/IC to cystectomy was 4 months (2-9 mo), and from end of N/IC to cystectomy 2 months (0-8 mo). Reasons for not pursuing cystectomy were cancer progression (8 pts), patient refusal (11 pts), decision for bladder preservation (5 pts) and N/IC-related toxicity with ECOG PS deterioration (7 pts). pCR and major pathologic response were achieved in 32% and 61% of pts who underwent cystectomy. After median follow-up of 37 months (95%CI 28-101 mo, measured from N/IC start), 45% of pts had recurrence (distant only 22%; locoregional only 9%, 14% both). Median DFS and OS were 28 mo (95%CI 15-43 mo), and 41 mo (95%CI 26-73 mo), respectively. Patients who achieved pCR had median OS 91 mo (95%CI 73-91 mo) vs 26 mo (95%CI 19-39 mo) for those attained no pCR ($p=0.0002$). In MVA, the only factor associated with longer DFS and OS was pCR [HR 0.3 (95%CI 0.1-0.4) $p<0.0001$; HR 0.2 (95%CI 0.1-0.5) $p=0.0008$, respectively]; 9 pts (6%) received adjuvant radiotherapy post cystectomy.

Conclusions: pCR rate was in line with prior data and was associated with longer survival. However, N/IC has significant toxicity and there is no biomarker of patient benefit. Limitations include retrospective nature, heterogeneity, no central scan/path review, patient selection, and residual confounding. Expert multidisciplinary care and detailed patient counseling are needed to increase the use of N/IC.

Keywords: bladder cancer, neoadjuvant, induction chemotherapy, Croatian uro-oncology network

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P25 - OLAPARIB FIRST-LINE MAINTENANCE THERAPY FOR PATIENTS WITH NEWLY DIAGNOSED, ADVANCED HIGH-GRADE SEROUS OVARIAN CANCER AND A BRCA MUTATION: AN ONE INSTITUTION EXPERIENCE

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Introduction: Olaparib, a poly(ADP-ribose) polymerase inhibitor, is indicated as monotherapy for the maintenance treatment of adult patients with newly diagnosed BRCA-mutated (germline or somatic) high grade serous or endometrioid epithelial ovarian, fallopian tube, or primary peritoneal cancer who have an objective response to platinum-based chemotherapy. Patients can continue therapy until radiological disease progression, unacceptable toxicity or for up to two years if there is no radiological evidence of disease. Our aim was to present real-world experience with olaparib monotherapy in our institution.

Methods: We retrospectively analysed the archival data of 29 patients with newly diagnosed advanced high grade serous ovarian, primary peritoneal or fallopian tube cancer treated with olaparib maintenance therapy at the Department of Gynecologic Oncology in the University Hospital Centre Zagreb, from July 2021 to February 2024. All patients had confirmation of germline or somatic BRCA 1/2 mutation.

Results: The median follow-up time for 29 eligible cases was 16 months. The median age of patients at diagnosis was 56 years (range 40-78). ECOG status 0-1 was present in 89% of patients. Primary cytoreduction was performed in 58%, interval debulking surgery in 38% of patients and one patient was inoperable. Residual disease after surgery was recorded in 45% of patients. The most commonly used chemotherapy protocol was paclitaxel/carboplatin. A complete radiological response to chemotherapy was achieved in 76% of patient. For now, the median olaparib treatment duration is 11 months (range 1-24 months). The median progression free survival has not yet been reached. 55% of patients continue to receive olaparib therapy and in 45% of patients the therapy was discontinued (in nine patients due to progression of the disease, in one patient because of toxicity and three patients discontinued therapy after two years and are still in complete remission). The most common side effects associated with the olaparib therapy were: fatigue, anemia and nausea.

Conclusion: In Croatia, from April 2021 we have opportunity to treat patients with newly diagnosed BRCA-mutated high grade serous or endometrioid epithelial ovarian, fallopian tube, or primary peritoneal cancer with olaparib as the maintenance therapy. Our experience in treating patients with olaparib showed good results with acceptable toxicity.

Keywords: olaparib, ovarian cancer. maintenance therapy, outcome

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P26 - PATHOLOGICAL CHARACTERISTICS OF LUMINAL B SUBTYPE OF BREAST CANCER BEFORE AND AFTER NEOADJUVANT THERAPY - SINGLE CENTER EXPERIENCES FROM UNIVERSITY HOSPITAL OF SPLIT

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Introduction: Luminal breast cancer still lacks indicators to classify patients who will benefit from neoadjuvant therapy (NAT). HER2 low is a potential novel subtype of breast cancer that express HER2 protein on cell membrane on some level, but not enough to be classified as HER2-positive. It accounts for around of 50-55% of all breast cancer. Majority of HER2-low breast cancers are grades 1 or 2, early-stage, hormonal receptor positive and are less likely to achieve pCR to NAT.

Aim: The aim of this report was to investigate the pathological characteristics of luminal B breast cancers: status of ER, PR, HER2 and Ki 67, at the time of diagnosis and after NAT for patients treated in Department of Oncology and Radiotherapy of University hospital of Split.

Methods: Data from the pathohistological reports and medical history of 41 patients with luminal B subtype of breast cancer treated with NAT in the period from January 1, 2018 to June 1, 2021, were retrospectively collected and processed.

Results: Forty female patients and 1 male patient were included in the study. We analyzed breast cancer specimens for each patient before and after NAT. Breast cancer was diagnosed by needle biopsy in 40 patients (95%). Multicentric tumors were diagnosed in 24% of patients and 17% were lobular histology. ER were positive in $\geq 80\%$ of tumor cells in 90% of patients, and progesterone receptors were positive in $\leq 20\%$ of tumor cells in 27% of patients. HER2-low level (HER2 1+ and HER2 2+) was observed in 61% of patients with luminal B subtype. Ki 67 was high expressed. In 93% of patients it was above 20%.

Majority of patients (80%) received neoadjuvant chemotherapy (ACdd-T protocol). Other patients received neoadjuvant endocrine therapy, mostly combination SERD and AI.

After surgery, effect of NAT was evaluated through Residual Cancer Burden (RCB). Only three patients (7%) had RCB 0 (pCR), 4 patients (10%) had RCB 1, 20 patients (49%) RCB 2 and 14 patients (34%) RCB 3. Patients with pCR were treated with neoadjuvant chemotherapy.

Conclusion: The incidence of luminal B HER2-low subtype of breast cancer in our study population is 61%. Three patients (7%) with pCR had luminal B HER2-low subtype of breast cancer.

Keywords: Luminal B breast cancer, pathologic complete response, neoadjuvant therapy

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P27 - POSITION OF COMPREHENSIVE GENOMIC PROFILING (CGP) IN THE MANAGEMENT OF METASTATIC GASTRIC CANCER. REAL WORLD DATA AMONG CROATIAN PATIENTS IN THE FIRST TWO YEARS OF TESTING.

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Background: Gastric cancer ranks in top 10 cancers by incidence in Croatia and with one of the highest mortality to incidence ratio of 0.82, represents major oncological burden(1). This is why it is crucial to enhance current treatment strategies in order to improve the outcomes. Eventhough gastric cancer is very heterogeneous disease, knowledge about its genomic landscape is expanding and studies with comprehensive genomic profiling (CGP) are becoming more common(2). Here we present our experience and CGP results with the aim to set its position in everyday clinical work.

Methods: The retrospective observational study was conducted in Croatia among patients who were diagnosed metastatic gastric cancer from January 1, 2020 to December 31, 2021, and on whose tumors CGP analysis was performed in line with the existing criteria(3). The analysis was done through FoundationOneCDx for vast majority of patients(4). The data were analyzed with methods of descriptive statistics using Microsoft Excel tools.

Results: There was 12 patients in total. Median age of patients was 61 (IQR 48-71). The ECOG (Eastern Cooperative status) performance status 0 had 5 (42%) patients, ECOG 1 had 2 (16%) patients and for 5 (42%) patients data were missing. CGP analysis revealed at least one clinically relevant genomic alteration in 8 (67%) patients, with median number of mutations of 1.5 (IQR 1-2.5). Only ERBB2 gene mutation was present in two (16%) patients. Genomic alterations without clinical significance were present in 11 (92%) patients with the median of 4 (IQR 2-5). The two most common were TP53 and CDKN2A/B mutations in 6 (50%) and 4 (33%) patients. Microsatellite status was stable in 8 (67%) patients and one (8%) patient had highly instable status, while for 3 (25%) patients it was not determined. Median tumor mutational burden (TMB) was 3 (IQR 2-5.5), with only one (8%) patient having TMB≥10. Some kind of targeted therapy was opted in 5 (42%) patients.

Conclusion: Our results, despite on a rather small sample, have shown that almost half of the patients have mutation that could be potential target for precise treatment. However, true position of CGP and precision oncology in gastric cancer will be determined only by continuing collecting the data on impact of the CGP-guided therapy on the outcomes in real-world setting.

Keywords: comprehensive genomic profiling, metastasis gastric cancer

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P28 - RADIUM-223 IN PATIENTS WITH METASTATIC CASTRATION-RESISTANT PROSTATE CANCER - RETROSPECTIVE ANALYSIS OF THE TREATMENT EXPERIENCE AT THE UNIVERSITY HOSPITAL SPLIT

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Background: Based on ALSYMPCA trial radium-223 (Ra-223) was approved for the treatment of patients with metastatic castration-resistant prostate cancer (mCRPC). Ra-223, an alpha emitter, selectively targets bone metastases with alpha particles. Ra-223 is the standard treatment of patient with mCRPC and bone metastases who progressed to previous docetaxel and androgen receptor signaling inhibitors (ARSI).

Study objectives: To determine PSA response rate, PSA time to progression, overall survival (OS), and the frequency of adverse events (AEs) of Ra-223 in the treatment of patients with mCRPC and bone metastases in daily clinical practice at the University Hospital Split.

Methods and materials: We retrospectively analysed the clinical outcomes of 12 patients with mCRPC treated with Ra-223 after progression on previous docetaxel and ARSI from October 2017 until March 2024. Data was analysed using Microsoft Excel 2019 and MedCalc 20.115.

Results: Twelve patients (n=12) were included in the analysis. The median follow-up was 4.2 months (range 0.1-15). The median age was 71.5 years (range 56–84). One patient (8%) had ECOG PS 0, 7 patients

(58%) had ECOG PS 1 and 4 patients (33%) had ECOG PS 2. The median PSA and alkaline phosphatase values at the start of the treatment with Ra-223 were 81 ng/ml (range 1.2-762) and 228 IU (range 65-832), respectively. The median number of lines of treatment for mCRPC prior to Ra-223 was 3 (range 2-5). The median number of administered cycles of Ra-223 was 4 (range 1-6). The median duration of treatment with Ra-223 was 3 months (range 1-4.5). A 25-50% reduction in PSA blood levels was achieved in 2 patients (16%). Median time to increase in PSA level was 2 months (range 0.7-6) while the median OS was 4.2 months. Two patients (16 %) experienced grade 3 AEs (thrombocytopenia, anemia) and 4 patients (33%) experienced grade 2 AEs (nausea, vomiting, weight loss, leucopenia, thrombocytopenia, anemia). There were no grade 4 AEs.

Conclusion: Our retrospective analysis showed poorer-than-expected efficacy results compared to treatment outcomes with Ra-223 in the ALSYMPCA trial, while treatment safety was similar. Limitations are the retrospective nature and the small number of included subjects. A better multidisciplinary approach and patient selection are needed to achieve a greater benefit of Ra-223 in daily clinical practice.

Keywords: Radium-223, prostate cancer, retrospective analysis

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P29 - REAL-WORLD OUTCOMES OF CHEMOTHERAPY IN FIRST-LINE TREATMENT FOR EXTENSIVE SMALL CELL LUNG CANCER: A SINGLE CENTER EXPERIENCE FROM BOSNIA AND HERZEGOVINA

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Introduction: Small cell lung cancer (SCLC) is an aggressive subtype of lung tumor that accounts for 15% of all lung tumors. The first line of treatment for extensive stage (ES) SCLC consists of a combination of platinum and etoposide chemotherapy, along with the immune checkpoint inhibitor (ICI) atezolizumab (anti-PD-L1) or durvalumab (anti-PD-L1). While standard chemotherapy alone yields a median overall survival (OS) of around 10 months for SCLC patients, the addition of immunotherapy to chemotherapy can extend OS to 12 months^{1, 2}. In our abstract, we will present the results of the first-line chemotherapy administered to patients with ES-SCLC at our institution.

Methods: We conducted a comprehensive search through the medical records and hospital information system to identify patients diagnosed with ES-SCLC and treated with first-line chemotherapy comprising platinum and etoposide. This retrospective analysis encompassed the period from 2011 to 2021 at the Department of Oncology, University Clinical Hospital Mostar, Bosnia and Herzegovina. We analyzed the median OS of the patients treated with first-line chemotherapy for ES-SCLC.

Results: Our analysis included 60 patients with ES-SCLC. The median age of the patients was 64 years. The study population was predominantly male, accounting for 78% (47 patients). Fifty-two patients (87%) were active or ex-smokers. Only one patient (2%) was a non-smoker, while the smoking status of seven patients (11%) was unknown. The majority of patients had good performance status, with 17 (28%) patients having an Eastern Cooperative Oncology Group (ECOG) performance status of 0, and 32 (54%) patients having an ECOG status of 1. Additionally, 9 (15%) patients had an ECOG status of 2, while 2 (3%) patients had an ECOG status of 3. The first line of chemotherapy based on cisplatin and etoposide was prescribed for 48 (80%), carboplatin and etoposide for seven patients (12%), and five patients (8%) started chemotherapy with cisplatin and etoposide then switched to carboplatin and etoposide. The median OS of patients treated with first-line chemotherapy for ES-SCLC was only six months.

Conclusion: First-line platinum and etoposide chemotherapy resulted in a median OS of six months, which is lower compared with the outcomes observed with chemotherapy in the control arms of two registration studies for immunotherapy in ES-SCLC. These findings highlight the need for further improvement and investment in therapy for this underserved patient group.

Keywords: Small cell lung cancer, extensive stage, chemotherapy, survival

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P30 - RESULTS OF TREATMENT WITH PD-1 INHIBITOR PEMBROLIZUMAB IN PATIENTS WITH METASTATIC MELANOMA AT UHC SESTRE MILOSRDNICE ZAGREB

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Introduction: The annual incidence of malignant melanoma is still rising steadily; in Europe it varies between 3 to 5 people per 100.000 in Mediterranean countries and 12 to 35 people per 100.000 in Nordic countries. Melanoma is the most dangerous type of skin cancer. Melanoma incidence peaks at 65 years, though any age can be affected. According to Croatian National Cancer Registry there were 753 new melanoma cases reported in 2020., with 104 deaths reported. Treatment of metastatic disease may include surgery, immunotherapy, targeted therapy and radiotherapy. Programmed cell death 1 (PD-1) blockade is now a standard of care for all advanced and metastatic melanoma patients in the first-line setting. There are two available mono immunotherapies and one combination immunotherapy at this moment in Croatia for patients with metastatic melanoma regardless of BRAF status (pembrolizumab, nivolumab and nivolumab-ipilimumab). Based on recent data from clinical trials, the immune checkpoint inhibitor pembrolizumab prolongs survival in patients with advanced or metastatic melanoma.

Aim, patients and methods: The aim of this analysis was to determine the overall survival and time to progression in patients treated with pembrolizumab in first line therapy.

In this analysis we included patients with stage metastatic and unresectable melanoma treated with pembrolizumab between January 2017 and January 2024. The patients were classified according to gender, CNS metastases and age at the time of diagnosis of metastatic disease, ECOG status, number of organs involved, LDH level. Patient and treatment characteristics were retrospectively collected from hospital data base. Survival rate was calculated with the Kaplan-Meier method.

Results: We analyzed 136 treatment-naive melanoma patients treated with pembrolizumab. Median age was 60,3 years. Out of a total of 136 patients, 29% of patients had elevated LDH, 17% of patients had CNS metastases and 41% of patients had 3 or more metastatic sites. 9% of patients had CR and 66 patients are still alive. Most of the patients, 90% (122 patients) were ECOG status 0. Out of the total number of patients, 80 patients had a BRAF mutation. Median PFS for first line treatment was 13 months (95% CI 8-38 months), and OS was 36 months (95% CI 32-75 months).

Conclusion: Our results were similar compared to those in studies with PD-1 inhibitor pembrolizumab. This type of retrospective analysis gives us an insight into real-life patient care and represents an important contribution for oncological community and, most importantly, enables a better care for our patients.

Keywords: metastatic melanoma, pembrolizumab, retrospective analysis

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P31 - ROLE OF COMPREHENSIVE GENOMIC PROFILING (CGP) IN THE PERSONALIZED GYNECOLOGICAL CANCER CARE. REAL WORLD DATA ON A NATIONAL LEVEL.

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Background: Gynecological cancers affect significant number of women in Croatia and are comprised of several entities such as uterine, ovarian, cervical, vaginal and vulvar cancer(1). Despite recent breakthroughs with immunotherapy in uterine and cervical cancer, for majority gynecological cancers conservative therapy remains the gold standard(2-5). The most promising way to further improve the outcomes in the field of gynecological cancers is implementation of precision oncology(6,7). Here we present our results of CGP testing in the everyday management of locally advanced or metastatic gynecological cancers.

Methods: This was observational retrospective study, conducted in seven Croatian institutions from January 1, 2020 to December 31, 2021. Patients included were diagnosed with locally advanced or metastatic gynecological cancer and on their tumors CGP was performed. The data was analyzed using Microsoft Excel descriptive statistics tools.

Results: There was 152 patients in total, out of which ovarian cancer was diagnosed in 87 (57%) patients, uterine in 52 (34%), cervical in 11 (7%) and vaginal in 2 (1%) patients. Median age at the time of diagnosis was 58 years (IQR 52-67). Majority of patients (74%) had ECOG (Eastern Cooperative status) performance status 0 and for vast majority (97%) CGP was performed through FoundationOne CDx testing. CGP found clinically relevant genomic alteration in 132 (87%) patients with median number of mutations of 2 (IQR 1-4). The most prevalent mutations were TP53, PIK3CA, BRCA and KRAS in 51 (37%), 31 (23%), 29 (22%) and 24 (18%) patients. Genomic alterations with unknown significance were found in 123 (81%) patients with median number of mutations of also 2 (IQR 1-4). There was very heterogeneous spectrum of these mutations but the most common were TP53, BCL2 and NOTCH in 41 (33%), 16 (13%) and (12%) patients. Tumor mutational burden (TMB) was determined for 142 (93%) patients and median TMB was 3 Mut/Mb (IQR 1-6), while 20 (14%) patients had TMB \geq 10. Microsatellite status was determined as stable in 130 (85%) patients, highly instable in 13 (9%) and for 9 (6%) patients it was not determined. Loss of heterozygosity (LOH) was determined for ovarian cancer and median LOH was 14.6 (IQR 6.8-21.7), with 35 (41%) patients having LOH \geq 16. CGP-guided therapy was opted for 84 (55%) patients in total, while for 68 (45%) patients on-label therapy was opted and the most common were PARP inhibitors and immune checkpoint inhibitors.

Conclusion: Our results have shown that looking at the gynecological cancers in overall, CGP has firmly set its position in the diagnostic and therapeutic management of these entities. To fully capture its impact, we must continue to collect data and monitor outcomes of the CGP-guided therapy.

Keywords: comprehensive genomic profiling, metastatic gynecological cancer, national level

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P32 - SAFETY AND EFFICACY OF IMMUNE CHECKPOINT INHIBITORS IN PATIENTS WITH RENAL CANCER ON HEMODIALYSIS; A SINGLE CENTRE EXPERIENCE

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Introduction: Immune checkpoint inhibitors (ICI) are immunomodulatory antibodies that enhance the immune system in fight with cancer. They are widely used for treating different types of cancer such as renal cell carcinoma. Some of the patients with renal cancer have end stage renal disease and have to regularly receive hemodialysis. ICI can cause multisystem immune-related adverse events (irAEs) that may lead to serious complications in treatment and patients death. Mild irAEs require drug dose adjustment. Data regarding the safety and efficacy of ICIs in the patients with renal cancer receiving maintenance haemodialysis are limited because these patients were excluded from all pivotal clinical trials of ICIs. To address this question, we aimed to evaluate efficacy and safety of ICI in patients with renal cell carcinoma and who are on haemodialysis program.

Methods: We retrospectively analysed patients with renal cell carcinoma that were on haemodialysis and received ICI therapy in Clinical Hospital Osijek in the period from December 2021st till January 2024th. All patients were on haemodialysis because of end-stage renal disease and had received combination therapy of four cycles of nivolumab and ipilimumab and then monotherapy of nivolumab. Patients were periodically examined before every cycle, also laboratory and radiological parameters were followed for disease evaluation and treatment response according to iRECIST criteria.

Results: A total of four patients (2 female and 2 male) were included in the study. Median age of the patients was 59 years. All patients underwent nephrectomy and had metastatic disease. Median treatment duration with ICI was 13 months. Progression free survival (PFS) was 19 months (95% CI 18,040 to 21,960). The standard ICI dosing regimens for nivolumab were administered without dose reductions, while ipilimumab dose was reduced for 50%. None of four patients experienced irAEs or discontinuation of ICI therapy was needed. One patient died 19 months after the beginning of the ICI treatment. Till its death the patient had stable disease and did not have any side effects from ICI therapy. One patient had disease progression after 21 months of therapy. The progression of disease included progression in size and number of metastases in liver and pancreas. This patient ended ICI therapy and started therapy with axitinib and denosumab. The remaining two patients are still on ICI treatment and have stable disease according to iRECIST criteria without recorded irAEs.

Conclusion: In our study patients with end stage renal diseases on haemodialysis and ICI treatment did not experience irAEs and majority of them had stable disease according to iRECIST criteria. According to our findings ICI treatment is safe and can effectively control tumour in patients with renal cell cancer that are on haemodialysis. Haemodialysis does not affect the pharmacokinetic of nivolumab. Additional larger studies are needed to more precisely define safety and efficacy of ICI in patients receiving haemodialysis.

Keywords: renal cancer, immune checkpoint inhibitors, hemodialysis,

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P33 - SPECTRUM OF BRAF MUTATIONS IN SKIN MELANOMAS IN THE DALMATIAN REGION OF CROATIA

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Introduction: Mutation of the BRAF oncogene is one of the most common mutation detected in human neoplasia, occurring in 40-60% of all cutaneous melanoma. BRAF is a serine/threonine protein kinase which is an essential part of mitogen-activated protein kinase (MAPK) pathway, whose inhibition by BRAF inhibitors and combined BRAF/MEK inhibitors in BRAF mutated melanoma has become a standard therapeutic approach. The effect of inhibitory therapy may be conditioned by the type of BRAF mutation.

Aim: The aim of this report is to determine the spectrum and frequency of different BRAF mutations in a group of skin melanomas in the Dalmatian region of Croatia, detected by the PCR based Roche BRAF/NRAS mutation test.

Methods: The analysis included 179 patients with stage 3 and stage 4 cutaneous melanoma with known BRAF/NRAS mutational status. The paraffin blocks were forwarded from four Dalmatian hospitals (Split 139 cases, Zadar 17 cases, Šibenik 13 cases, Dubrovnik 10 cases). BRAF/NRAS mutation analysis was performed at the Institute of Pathology, University Hospital Center Split, Croatia, in the period from the second half of 2017 to the end of 2022. For mutation analysis the target DNA was amplified and detected on the Cobas z 480 analyzer using the amplification and detection reagents provided in the Roche BRAF/NRAS mutation test (LSR) kit.

Results: BRAF mutation was observed in 87 patients (48.6%), NRAS mutation in 27 patients (15.1%), while 65 patients (36.3%) were without BRAF/NRAS mutation. In the group of BRAF mutated melanomas,

61 cases (70.1%) were with V600E/E2/D mutation, 20 cases (23%) with V600K mutation, 3 cases (3.4%) with exon 11 mutation, 2 cases (2.3%) with V600R mutation, and 1 case (1.2%) with K601E mutation. The vast majority of BRAF mutations (93.1%) belonged to the group of V600 E/E2/D and V600K mutations (class I V600E/K mutation) with high response rate to inhibitory therapy. We detected only 6 cases (6.9%) with expected lower response rate to MAPK pathway inhibition: 2 cases with V600R mutation (class I non-V600E/K mutation), 1 case with K601E mutation (class II mutation) and 3 cases with exon 11 mutation (class II and III mutations).

Conclusion: The majority of skin melanomas (93.1%) detected in the Dalmatian region of Croatia contained the types of BRAF mutation with expected high response rate to inhibitory therapy (class I V600E/K mutation). However, in some patients (6.9%) BRAF mutations with expected lower response rate to inhibitory therapy were detected (class I non-V600E/K mutation, class II and III mutations).

Keywords: cutaneous melanoma, BRAF V600E, mutation, MAPK pathway inhibition

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P34 - SPECTRUM OF TRUE AND FALSE POSITIVE RADIOLOGICAL IMAGING FINDINGS IN LUNG SCREENING PROGRAMME AT UHC OSIJEK

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Introduction: Lung cancer is one of the top three cancers most often misdiagnosed, due to shortages of specialists and heavy workload on the healthcare system being the leading cause.

The International Early Lung and Cardiac Action Program (I-ELCAP) is an ongoing screening program that began accruing participants in 1994. It initially had two participating institutions, NYU and Cornell and now includes over 80 sites worldwide. The Principal Investigator for this program is Claudia Henschke PhD, MD, who is currently at Mount Sinai, which is the coordinating centre for the program.

I-ELCAP's mission is to achieve early diagnosis, treatment, and ultimate cure of lung cancer through the rapid dissemination and advancement of research among a diversified, collaborative network.

Numerous publications document the findings of the I-ELCAP members' work of which the most significant conclusion is that curability of stage 1 lung cancer is 80-90% and that annual CT screening allows at least 80% of lung cancers to be diagnosed at stage 1.

In Croatia I-ELCAP program started in octobar 2020. Lung screening consists of several steps- first patients undergo imaging in hospitals included in the screening program, then the artificial intelligence program processes the images and marks suspicious nodules and then the radiologist examines the images and writes the final report. Implementing Artificial intelligence (AI) software for detecting lung nodules has proved to be very useful in decreasing reading time for radiologists and for making the implementation of large-scale lung cancer screening projects feasible, financially and operationally.

The aim of this research was to evaluate patients who underwent lung screening program in UHC Osijek and had a positive screening results- suspected lung cancer marked as C1 category and were referred to pulmologist.

Methods: This study included total number of 1927 patients who underwent lung screening program in UHC Osijek from 1.October 2020. until 1.December 2023. The data were obtained from medical documentation.

Results: Positive lung screening marked as C1 category had 66 patients. Among them, cancer was pathohistological proven in 13 patients through further diagnostic procedure.

In 35 patients, the finding marked as C1 category have showed regressive dynamic on the next CT scan.

Also, 55 patients refused further treatment due to other comorbidities, mostly malignant.

Discussion: For lung screening, it is critically important to accurately distinguish benign and malignant nodules, and hilar entities. The main reason for high number of patients with C1 category in whom subsequent diagnostics procedure ruled out a cancer are inflammatory changes or lung metastases.

Conclusion: The inclusion of patients in lung cancer screening should be reserved for patients who fall into the risk group for the development of primary lung cancer without currently known other primary malignant disease and acute inflammatory changes.

Keywords: lung cancer, lung cancer screening, artificial intelligence

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P35 - SYSTEMIC IMMUNE-INFLAMMATION INDEX (SII) AS A PREDICTIVE VALUE FOR COMPLETE PATHOLOGICAL RESPONSE AFTER NEOADJUVANT THERAPY IN BREAST CANCER

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Introduction: Breast cancer is one of the most common cancers in the female population. The main treatment method for localised breast cancer in most cases is surgery and neoadjuvant therapy. There is no reliable potential biomarker that could predict response to neoadjuvant therapy or risk of recurrence or mortality. Tumour tissue is a heterogeneous population of cells in which immune cells have an important role in cancer surveillance and elimination. Neutrophils, platelets and lymphocytes influence the growth of cancer cells and their metastatic potential. Several immunity-based indicators, such as neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR) and systemic immune-inflammation index (SII) can reflect the homeostasis of immune system and have been used to predict survival outcomes in several cancer types. In several malignancies prognostic value of those immunity-based indicators has been demonstrated, indicating that elevated values determine worse prognosis. The prognostic value of systemic immune-inflammation index (SII) in breast cancer patients is still unclear. To address this question, we aimed to evaluate the prognostic value of SII and its impact on pathologic complete response after neoadjuvant therapy in locally advanced breast cancer patients.

Methods: We retrospectively analysed patients' data that received neoadjuvant treatment in Clinical Hospital Osijek in the period from January 2021st till December 2022nd. Collected data included patients' age, laboratory values of blood cells count (neutrophils, platelets and lymphocytes), molecular characteristics of breast cancer and pathological report after surgical treatment. Based on laboratory findings, values of SII were calculated at the start of neoadjuvant therapy. The cutoff value of SII was determined based on ROC curve analysis. The aim was to compare the complete pathological response (pCR) depending on the values of SII before the start of neoadjuvant treatment.

Results: Among 73 patients that underwent neoadjuvant therapy, 21 (28,7%) patients achieved a pCR. Median age of the patients was 55 years. All patients with pCR had Ki-67 above 20% and 53.3% of the patients had HER2/neu positive breast cancer. The cutoff value for SII was 578.4. SII values ranged from 188,38 to 1531,8. The median SII values were different for pCR and non-pCR arm (492,5 vs. 580,9). In the patients' group with low SII (<578.4) 30,5% of patients had pCR, while in the group with high SII (>578.4) 27% had pCR.

Conclusion: Previous research showed that SII is a good prognostic marker for predicting long-term outcomes for breast cancer patients undergoing surgery. Our research shows that patients with lower SII (<578.4) before the start of neoadjuvant treatment have better pCR in comparison with patients with higher

SII (>578.4). Additional larger studies are needed to confirm correlation between SII and pCR to neoadjuvant therapy in breast cancer.

Keywords: breast cancer, neoadjuvant therapy, complete pathological response, systemic immune-inflammation index

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P36 - THE RELIABILITY OF PREOPERATIVE ULTRASOUND EVALUATION OF AXILLARY LYMPH NODES IN PATIENTS WITH BREAST CANCER

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Introduction: The status of axillary lymph nodes is one of the most important prognostic factors in breast cancer. The most accessible and cost-effective non-invasive method for checking and detecting lymph nodes in the axilla is ultrasound examination.

Aim: The aim of this study is to assess the accuracy of preoperative determination of axillary lymph node status in patients with confirmed breast cancer using ultrasound examination.

Methods: Retrospectively collected data, from 2021, on the number of patients who were primarily operated with a diagnosis of breast cancer without positive axillary lymph nodes.

Results: A total of 98 samples were examined under the diagnosis of breast cancer that was primarily operated. Out of this number, suspicious lymph nodes were not found on ultrasound in 81 patients, suspi-

cious lymph nodes were found in 13 patients, and we have no data for 4 patients. Among these 13 patients, fine needle puncture of the suspicious lymph node was not performed only in 3 cases. After the surgical procedure, out of the 13 suspicious lymph nodes, 9 patients did not have positive lymph nodes, while 4 patients had positive axillary lymph nodes.

Conclusion: Various causes can underlie axillary lymphadenopathy, with breast cancer being the most common. Ultrasound examination of the lymph node should characterize multiple morphological features, such as size, shape, hilum, cortex thickness, margins, echogenicity, and vascularity. From the obtained data, it is evident that in 82.65% of patients, the ultrasound findings were normal. In all of these patients, no positive lymph nodes were found after the surgical procedure. The overall results show that in 96% of patients, suspicion of positive axillary lymph nodes was eliminated by ultrasound examination, while only 4% of patients had a positive finding after surgery. Although the mentioned data are satisfactory, in case of any suspicion node, additional invasive evaluation should be pursued.

Keywords: ultrasound, breast, lymph node, reliability

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P37 - TREATMENT INDUCED CHANGES OF KI67 LEVEL IN NEOADJUVANT HORMONAL THERAPY WITH FULVESTRANT AND AROMATASE INHIBITORS IN PATIENTS WITH LOCALLY ADVANCED ER+, HER2- EARLY BREAST CANCER

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Introduction: Neoadjuvant endocrine therapy (NET) was for a long time confined to frail, older patients, who were not candidates for upfront surgery, to improve outcomes and to increase rates of breast conserving surgery (BCS). (1,2) Aim of neoadjuvant approach at its beginnings was to increase rates of breast conserving surgery (BCS), but today it gives us opportunity to monitor responses during treatment and provides informations about biomarkers and predictive factors. One of those is Ki67, useful clinical marker for breast cancer subtype classification, prognosis, and prediction of therapeutic response. (4) The aim of our study was to evaluate treatment-induced changes in Ki67, that may later be used as a predictor for outcomes as well as to modify initial treatment strategy.

Methods: We did retrospective analysis of collective data from January 2019 until November 2023 for 20 patients who had been treated with neoadjuvant endocrine therapy with fulvestrant and aromatase inhibitors for a period of at least 6 months, and who had surgery afterwards. Patients have signed informed consent and medical data was analysed.

Results: Our analysis included 20 patients treated with neoadjuvant endocrine therapy, with median age of 65. Median duration of therapy was 9.5 months, with average of 11 cycles of therapy. Average Ki67 values in preoperative specimen of all patients were 15.2%, and postoperative 8.4%. Analysis of pathologic results showed that 14 patients (70%) had lower level of Ki67 value in surgery specimen analysis. In 3 patients (15%) there was no change in Ki67 levels, and in 3 patients (15%) postoperative Ki67 values were higher than values in initial pathological report. Response to neoadjuvant endocrine therapy was defined by Residual Cancer Burden score (RCB). Out of 14 patients who had lower levels of Ki67 values in surgical specimen, 14% had RCB score I, 72% of patients had RCB score II, and 14% had RCB score III.

Conclusion: According to meta analysis, high Ki-67 after NET is associated with worse survival outcomes, emphasising the prognostic value of this biomarker in women with ER-positive/HER2-negative early breast cancer.(5) Our data analysis showed that combination of fulvestrant and aromatase inhibitors as NET resulted in significant decrease of Ki67 levels in 70% of patients. Results from large clinical trials evaluating efficacy of neoadjuvant endocrine therapy showed decrease in Ki67 values in range of 75-85%. (6,7) Comparing our results with mentioned data, aromatase inhibitors and fulvestrant combination is potent and effective treatment option to be further investigated in neoadjuvant setting.

Keywords: Neoadjuvant endocrine therapy, Ki67 level, RCB score, pathologic response

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P38 - TREATMENT OF PRIMARY SALIVARY GLAND MALIGNANCIES – 12-YEAR SINGLE INSTITUTION EXPERIENCE

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Introduction: Salivary gland malignancies are a heterogeneous group of entities with different prognosis that account for less than 5% of all head and neck tumours. Surgery is the mainstay of treatment followed by adjuvant radiotherapy (RT) or even chemoradiotherapy in patients with a high risk of disease recurrence although the level of evidence for combining chemotherapy with RT is low.

Patients and methods: Retrospective analysis of 75 patients treated at the Division for radiotherapy, Department of Oncology, University Hospital Centre Zagreb from January 2011 until November 2023 was performed. Data were collected by review of the electronic patient medical records. The overall survival (OS) and relapse-free survival (RFS) were estimated using the Kaplan–Meier method. The Cox proportional hazards regression model was used for multivariate analysis. Statistical analysis was performed using the SPSS software package 21.0. All reported p values were two sided and $p \leq 0.05$ was considered statistically significant.

Results: Median follow-up time was 3.4 years. The median age was 63 years (range 21 – 90). Fifty two percent of patients were males. Parotid gland was the most frequent site of the disease (61 patients, 81.3%) followed by submandibular gland (7 patients, 9.3%). The most frequent histological subtypes were adenoid cystic carcinoma (16 patients, 21.3%), mucoepidermoid carcinoma (15 patients, 20.0%), squamous cell carcinoma (13 patients, 17.3%) and adenocarcinoma (7 patients, 9.3%). Local disease was found in 39 (52%), locoregional in 33 (44%) and metastatic disease in 3 (4.0%) patients. Sixty seven patients (89.3%) were treated with adjuvant RT, while only 8 (10.7%) patients received concomitant chemotherapy. Majority of patients (84%) were treated with three-dimensional conformal radiotherapy. Relapse of the disease was found in 26 patients (34.7%). Among them 9 patients had distant metastasis only, 7 locoregional relapse and 10 both locoregional relapse and distant metastasis. Most relapses were found in the heterogeneous group entitled ‘other’ containing different, mostly high-grade subtypes of low frequencies (34.6%) followed by adenoid cystic carcinoma (23.1%) and mucoepidermoid carcinoma (19.2%).

Five and 10-year OS rates were 48% and 35% respectively. In multivariate analysis age (≤ 60 or > 60 years), surgery and relapse had significant impact on OS. Five-year RFS was 12.0%.

Conclusion: Five-year OS was lower in our cohort than in the North European countries and North America but similar to the reports for Eastern European countries.

Keywords: salivary gland, radiotherapy, retrospective analysis

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P39 - TREATMENT OF SARCOPENIA IN ELDERLY CANCER PATIENTS BY SPECIFIC FARMACONUTRIENT - PROSPECTIVE, RANDOMIZED STUDY

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Introduction: The term sarcopenia is defined by progressive skeletal muscle degeneration and also associated with functional decline. Sarcopenia has primary and secondary aetiology, arising as a result of the ageing process or through chronic cytokine-mediated inflammation (associated with health conditions including cancer), respectively. Early identification and treatment of sarcopenia is imperative in improving patient survival. Thus, the aim of this prospective study was to investigate the influence of enteral nutrition specific for sarcopenia on the muscle mass and sarcopenic indeks in elderly patients with breast and prostate cancer.

Methods: This prospective study that was conducted in The Department of Radiotherapy and Oncology of the CHC of Rijeka included 100 (58% women) patients older than 70 with a localized breast or prostate cancer. The follow-up period was six months. We analyzed the influence of enteral formulation specific for sarcopenia on muscle mass by the help of bioelectrical impedance (BIA). Compliance of patients in the context of drinking enteral preparation was evaluated every 3 months by MMSA score. Patients were divided in two groups based on the MMSA score; compliance (n=61) vs. non-compliance (n=39).

Results: The mean age of our patients was 76±1 years. According to our results there was a statistically significant difference between groups in terms of average muscle mass after three and six months of follow-up (65±3 vs. 72±4, p=0.02). Also, during the three and six-months of follow-up we observed a rise in average skeletal muscle mass in the group of patients that had MMSA score of 0 or 1 in comparison to those who had MMSA score of 2 or more (33,4±2 vs. 38±3, p=0,04). The phase angle values have also risen in the group of patients who had better compliance for enteral formulation drinking in the same period, but the result was not statistically significant.

Conclusion: According to the results of our study, the compliance in enteral formulation drinking is associated with improvement in muscle mass in older cancer patients.

Thus, by the enteral formulation that are specific for sarcopenia we can prevent and treat sarcopenia in this patients as well we to improve treatment outcomes.

Keywords: sarcopenia, phase angle, BIA

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P40 - TREATMENT OUTCOMES AND TOXICITY IN LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER PATIENTS UNDERGOING RADICAL RADIOTHERAPY: A SINGLE-CENTRE RETROSPECTIVE ANALYSIS

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Introduction: Lung cancer represents the most frequently diagnosed cancer and the leading cause of cancer-related mortality worldwide, predominantly attributed to non-small cell lung cancer (NSCLC). Radiotherapy (RT) plays a pivotal role in the curative management of locally advanced stages and can be delivered either concurrently with chemotherapy or sequentially after prior chemotherapy.

This study aimed to compare overall survival (OS), disease-free survival (DFS), and treatment toxicity in patients undergoing radical radiotherapy for inoperable stage III non-small cell lung cancer.

Materials and methods: A retrospective review was conducted on patients receiving definitive radiotherapy (RT) between January 2016 and December 2021. The study included 152 patients with NSCLC, aged between 47 and 83 years, with a median age at diagnosis of 64 years. Male patients constituted 73% (111) of the cohort, while females accounted for 27% (41). Among them, 70 patients (46%) received concurrent chemoradiotherapy, while 82 patients (54%) were treated sequentially. Of the sequentially treated patients, 64 (77%) patients received standard fractionation, while 19 (23%) patients were treated with hypofractionated regimens. Radiation doses were prescribed to the planning target volume and administered in daily fractions ranging from 2 to 2.75 Gy (median 2 Gy) using three-dimensional conformal radiation therapy.

Results: The median follow-up period was 19 months (95% CI 17- 22). The 2- and 5- year OS rates were 41% and 18%, respectively. Stratified analysis revealed 2- and 5- year OS rates 47 % and 30% in the concomitantly irradiated group compared to 35% and 9% in the sequentially irradiated group (p= 0,014).

Furthermore, significant differences were observed in 2- and 5-year OS rates between sequentially treated patients receiving standard fractionation (31% and 7%) and hypofractionation (56% and 17%) (p=0.049).

The 2- and 5-year DFS rates were 21% and 12% in all radically treated patients. Additionally, 2- and 5-year DFS analysis indicated superior outcomes in the concurrent treatment group compared to the sequential treatment group, 29 % and 21% vs 13% and 3%, respectively (p= 0,035).

Relapse occurred in 106 (81%) patients, with thoracic relapses being the most common in 64 (49%) patients. Notably, intrathoracic relapses were more prevalent in sequentially irradiated patients 41 (31%) than in concomitantly irradiated patients 23 (18%), respectively ($p=0.004$).

Acute side effects were observed in 49 (32%) of patients, with a higher incidence in the concurrent treatment group 27 (18%) patients compared to the sequential group 22 (14%) patients, although not statistically significant.

Conclusion: We have found that in patients undergoing radical radiotherapy for inoperable stage III NSCLC, concurrent chemoradiotherapy is superior to sequential radiotherapy treatment in terms of OS and DFS. It would be interesting to see how chemotherapy protocols and the addition of immunotherapy affect the effectiveness and toxicity of radical treatment of locally advanced NSCLC.

MeSH/ Keywords: Non-Small Cell Lung Cancer; Radiotherapy, Radiochemotherapy, Sequential treatment, Toxicity, Survival

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P41 - TREATMENT OUTCOMES OF ALK POSITIVE METASTATIC NON-SMALL CELL LUNG CANCER – A SMALL CENTER EXPERIENCE

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Introduction: Translocations of the ALK gene are found in 3-7% of lung cancers and they lead to the promotion of tumor growth. Clinical trials have confirmed the advantage of the second generation ALK inhibitors (alectinib in the ALEX and J-ALEX trials and brigatinib in the ALTA-1L trial) and the third generation inhibitor, lorlatinib (CROWN trial), over crizotinib, the first generation inhibitor. We analyzed data on treatment with second and third generation inhibitors in our institution.

Methods: In this retrospective study, data on the treatment of all patients with metastatic ALK - positive NSCLC who were treated with ALK inhibitors at Clinical Hospital Centre Osijek were analyzed, regardless of the line of treatment. Basic patient demographic data and data on previous oncological treatment were collected and the main research objectives were overall survival (OS) for the total sample and OS and progression free survival (PFS) for alectinib.

Results: A total of 30 patients received ALK inhibitors at Clinical Hospital Centre Osijek from January 22, 2019 until the end of 2023. Of the total number of patients, 20 (67%) were female, 10 (33%) were male and the median age at diagnosis was 61 years. 26 (87%) patients were diagnosed with malignancy in the metastatic stage. When metastatic disease was confirmed, the largest number of patients (40%) had pulmonary metastases. At the end of data collection, 7 (23%) patients were still alive.

Kaplan-Meier analysis of the survival of all the observed patients determined that the median OS was 17 (95% CI, 8-26) months. The median OS for 21 patients treated with alectinib in the first line of treatment was 17 (95% CI, 6-49) months and the median PFS was 6 (95% CI, 2-26) months. 4 patients were treated with brigatinib of which 2 patients received it in the first line of treatment and 2 received it in the second line of treatment. 5 patients were treated with lorlatinib of which 4 patients received it in the second line of treatment and 1 received it in the first line of treatment.

Conclusion: In clinical trials, alectinib and brigatinib achieved similar OS with a slightly higher PFS of alectinib. However, according to certain studies, lorlatinib and alectinib have shown the greatest effectiveness of treatment. The cause of the discrepancies between our results and the results of clinical trials is our small sample of patients. Also, very few patients received lorlatinib and brigatinib and they received them in different lines of treatment. Therefore, it was not possible to objectively assess OS and PFS for these patients. Considering that even in our sample some patients received over 50 cycles of alectinib, it is important to further monitor the results of the treatment in order to objectively assess the effectiveness of the drug.

Keywords: ALK inhibitors, lung cancer, OS, PFS

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P42 - TREATMENT OF ADJUVANT MELANOMA IN KBC OSIJEK - EXPERIENCE OF ONE CENTER

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Introduction: Adjuvant treatment of melanoma refers to the treatment administered after surgical intervention aimed at destroying remaining cancer cells that may not have been removed during the surgery, thus reducing the likelihood of disease recurrence. In Croatia, we have the option of using adjuvant immunotherapy and BRAF and MEK Inhibitors.

Methods: This is a retrospective prospective study conducted on patients treated with adjuvant therapy for malignant melanoma at the Clinical Hospital Osijek. The study included eleven patients from 01/2023 to 01/2024. Patients were primarily biopsied, followed by scar re-excision with SLNB. In three out of eleven patients, subsequent dissection of the lymphatic drainage area was performed. Eight patients had BRAF V600E mutation. According to the guideline, the patients were of stage III. Based on the BRAF V600E mutation, patients were treated with BRAF and MEK Inhibitors; if the mutation was not found, they were treated with immunotherapy. Eight patients were on BRAF and MEK Inhibitors, while three were on pembrolizumab.

Result: The study examined the tolerability of side effects of adjuvant therapy for malignant melanoma. Six out of eleven patients developed some form of side effects. Four had pyrexia induced by BRAF and MEK Inhibitors, while two patients on adjuvant pembrolizumab developed immune thyroiditis requiring replacement therapy. Among them, one patient progressed with a DFS of 4 months, the remaining patients are undergoing adjuvant treatment.

Discussion: Adjuvant therapy plays a crucial role in preventing disease recurrence and metastasis. It is important to individualize treatment to prevent unwanted side effects.

Keywords: Melanoma, Immunotherapy, adjuvant, targeted therapy

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P43 - THE USE OF TUMOR FREE DISTANCE AS PROGNOSTIC FACTOR FOR FIVE-YEAR SURVIVAL IN ENDOMETRIAL CANCER

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Background: Myometrial invasion (MI) with tumor has been shown as a significant prognostic indicator and expressed as a percentage (50%) is used in the FIGO (International Federation of Gynecology and Obstetrics) classification and is calculated by determining the depth of the myometrial invasion (DOI) and the total thickness of myometrium. Due to the variability in DOI estimation, there is attempt to find a prognostic factor that would have the lower variability. The outer tumor free myometrial part is defined by the distance from the point of the deepest invasion to the serosal surface (tumor free distance TFD). TFD is independent of the thickness of myometrium and has low variability. The aim of this study is to determine the TFD cut off value as an indicator of survival.

Methods: The present study retrospectively analyzed 223 cases of endometrial carcinoma with complete surgical staging, carried out from 2011. to 2014. All clinicopathological findings were extracted from medical records. In Department of pathology and cytology of KBC Zagreb is measured distance of deepest invasion to the serosa of uterus. A receiver operating characteristic (ROC analysis) was performed comparing TFD and five-year survival.

Results: As a diagnostic indicator of five-year survival, the thickness of the preserved outer part of the myometrium (TFD) is significant, expressed in millimeters (cut off ≤ 11 mm, AUC = 0.637, sensitivity = 96 %, specificity = 26 %) P 0.03, or as a proportion (cut off $\leq 71.4\%$, AUC = 0.641, sensitivity = 83%, specificity = 46%) P 0.02.

Conclusion: We can conclude that TFD at predicting survival show significant importance.

Keywords: TFD, endometrial cancer, myometrial invasion

P44 - RADIATION-INDUCED CYSTITIS TREATED WITH HYPERBARIC OXYGEN THERAPY IN UNIVERSITY HOSPITAL SPLIT

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Introduction: Radiation cystitis (RC) is an adverse effect of cancer treatment with radiotherapy (RT) in the pelvic region. Hyperbaric oxygen therapy (HBOT) reduces symptoms from RC, but the evidence is predominantly based on non-randomised and retrospective studies. RC has a reported incidence of 6.5% following radiation therapy for pelvic malignancy. Onset of RC has range from 6 months to 20 years following RT. If conservative treatment of RC fails (bladder irrigation with clot-evacuation, i.v. hydration, blood transfusion, intravesical instillation of astringents, transurethral fulguration of bleeding vessels using electrocautery or laser, arterial embolization, or urinary diversion with or without cystectomy are options), thus HBOT represents a low-risk alternative. Consensus regarding the systematic management of RC has not yet been established.

Methods: We analysed medical documentation of 14 patients treated with HBOT due to RC in three year period (2020-2023). The main cause of RT is adjuvant or salvage RT due to prostate cancer. Time from RT to onset of RC has range from 6 months to 9 year.

Results: Median age of patients was 73 year, average number HBOT per patient, surgical interventions, blood transfusions and hospitalisations is 23.9, 1.5, 2.5 and 1.8 respectively.

Nine of 14 patient has reported resolution of blood in urine and improvement quality of life due to resolving of lower urinary tract symptoms and reduced number of hospitalisations, blood transfusions and need for surgical interventions. No adverse events were recorded on study population due to HBOT.

Conclusion: HBOT is an effective treatment for RC associated with high success rates and few adverse effects. HBOT is non-invasive and treats both: bleeding and lower urinary tract symptoms associated with RC. Widespread use of HBOT is limited with high upfront cost, limited availability, and intensive time requirement for treatment.

Our results give a little wind in sails to this story. In the future we expect more prospective trials and better recommendations how to treat this condition.

Key words: Radiation cystitis, Hyperbaric oxygen therapy, HBOT, Radiotherapy

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