POSTER PRESENTATIONS

P1 – 15 YEARS OF COMPREHENSIVE COMMUNITY BASED APPROACH TO ADDRESS ONCOLOGY PATIENTS NEEDS

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EVERYTHING for HER (EfH) was founded in 2008 aiming to provide informational, educational, psychological, and logistical assistance to persons affected by oncological diseases through a permanent project - Centre for Psychological Assistance (Centre). Various complementary projects, health campaigns and programs addressing patients' needs have been implemented since for beneficiaries.

Beneficiaries for whom data is collected through a initial interview by psychologists use programs divided into psychological treatments, follow-up, counselling centres (nutrition, informing about genetic diseases), lectures by medical professionals to improve health literacy, workshops, the accommodation program. The coordinator provides various information daily, often guiding beneficiaries through the health and social system. Before, counselling in person prevailed but pandemic impacted the way services are delivered and they are now more accessible for beneficiaries throughout Croatia (phone, video calls). This asked for more flexibility from everyone but now it is easier for beneficiaries to be involved in programs they could benefit most from.

In 2020, 204 new beneficiaries entered the Centre. The total number of interventions only in individual psychological counselling programs was 1,745. In 2021, 334 new beneficiaries entered the Centre with 2,531 individual psychological consultations. During 2022, 345 new beneficiaries entered the Centre, making a total of more than 2,600 registered beneficiaries during the period 2010-2022. In 2022 more than 3000 individual psychological consultations were carried out and more than 5000 visits in various programs registered.

EfH emphasizes that psychosocial cancer care should be integrated into routine care and distress should be measured so Croatian version of ET-HR instrument was validated on patients' sample in Croatia and made available on Psihoonkologija.hr as an online questionnaire. Patients can make an assessment and self-assessment of distress and find an address book of professional counselling services available in the health system and community.

In 15 years EfH became provider for comprehensive services and a checkpoint for informing and directing to various services in the system and community. It is recognized as an important ally amongst patient community and health workers bridging gap between patients and the health system resulting in better adherence, health literacy, strengthening patients' capacities leading to a positive change in the community.

Keywords: community, psycho-oncology, psychological assistance, psychosocial needs

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P2 – 68GA-PSMA PET/CT IN PATIENTS WITH RECURRENT PROSTATE CANCER RELAPSING AFTER PRIMARY TREATMENT: INITIAL SINGLE INSTITUTION UTILITY ANALYSIS

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Introduction: Up to 50% of patients who initially presented with localized prostate cancer and were treated with curative primary therapy ultimately experience biochemical recurrence. It is crucial to detect recurrence early and accurately enough to initiate timely and precise salvage therapy. PSMA PET/CT is a modern imaging modality that is capable of detecting disease recurrence at low levels of PSA. The aim of this study was to analyze the efficacy of 68 Ga-PSMA PET/CT in detecting the presence of local and/or systemic disease in patients with prostate cancer who experienced biochemical recurrence.

Patients and methods: Electronic health records of patients treated in a single center who were referred for an out-of-institution 68 Ga-PSMA PET/CT were retrospectively reviewed. Performance of PSMA PET/CT was analyzed based on clinical factors (initial PSA, PSA at recurrence, PSA doubling time, Gleason score, initial T-stage, surgical margin status, time for primary treatment to biochemical relapse, other imaging studies) and follow up data. The relationship between the PET/CT findings and clinical factors was assessed by univariate and multivariate logistic regression.

Results: Between July 2019 and March 2023, a total of 30 patients with biochemical recurrence underwent 68-Ga-PSMA PET/CT, with imaging results available for analysis. For their initial primary treatment, 26 patients (86%) had radical prostatectomy, 2 patients (7%) had radiotherapy as their primary treatment modality, and 2 patients (7%) had no primary treatment. The median PSA level at the time of the PSMA scan referral was 0.71 ng/mL (range 0.23-214). A total of 23/30 (77%) patients had positive 68 Ga-PSMA PET/CT scans. Among those, 19 (82%) underwent radical prostatectomy as primary treatment. For all patients with a positive PSMA-PET, the detection rate was 5/7 (71%) for PSA 0.2-0.49, 9/13 (69%) for PSA 0.5–1.0, 4/5 (80%) for PSA 1.0–1.5, and 5/5 (100%) for PSA 1.5 and above. PSMA-PET/CT positivity was

significantly associated with receipt of prostatectomy, PSA level at time of PET scan, PSA doubling time, Gleason score, and margin status. No association was found with the initial PSA and time to recurrence.

Conclusions: In our single center analysis, 68 Ga-PSMA PET/CT successfully detected the recurrence of prostate cancer in the majority of patients. There is more room for improved detection at PSA levels below 0.5, where treatment decisions are being made.

Keywords: 68 Ga-PSMA, biochemical recurrence, PSA levels.

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P3 – A RETROSPECTIVE ANALYSIS OF THE MANAGEMENT AND OUTCOME OF PATIENTS WITH UTERINE CARCINOSARCOMA: A ONE INSTITUTION EXPERIENCE

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Introduction: Uterine carcinosarcoma (UCS) is highly aggressive disease with poor prognosis. It has been classified as a subtype of high-grade endometrial cancer. The standard therapy is surgical removal of the cancer followed by adjuvant therapy, including chemotherapy and radiotherapy. Despite such aggressive treatment, these patients have a high recurrence rate. We aimed to explore management and outcome in these patients.

Methods: We retrospectively analysed the archival data of 45 patients with UCS who underwent surgery and adjuvant therapy at the Department of Gynecologic Oncology in the University Hospital Centre Zagreb, from January 2013 to December 2020.

Results: The median follow-up time for 45 eligible cases was 35 months. The median age of patients at diagnosis was 64 years (range 45-80). ECOG status 0-1 was present in 78% of patients. The most common first symptom of the disease was postmenopausal bleeding. Hysterectomy with bilateral adnexectomy was performed in 98% of patients with additional pelvic lymph node dissection in 87% and omentectomy in 49%. Residual disease after surgery was recorded in 25% of patients and one patient was inoperable. Adjuvant chemotherapy was received by 98% of patients and the most commonly used protocols were paclitaxel/carboplatin and ifosfamide/cisplatin. Forty-nine percent of patients received adjuvant radio-

therapy with brachitherapy in 44% of cases. Recurrence of the disease was recorded in 47% of patients, and 56% of patients died (47% due to disease and 9% due to other causes). In patients without residual disease after surgery the median PFS and median OS weren't reached, and in patients with residual disease, the median PFS was 6 months and the median OS was 13.5 months.

Conclusion: UCS is a rare disease that has a poor prognosis despite aggressive treatment. Surgery remains the cornerstone of management, but there are no strict guidelines for adjuvant treatment. Further studies are needed to evaluate which treatment improves outcomes in these patients.

Keywords: uterine carcinosarcoma, therapy, outcome

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P4 – A SINGLE-CENTER EXPERIENCE WITH TREATMENT OUTCOMES OF METASTATIC MALIGNANT MELANOMA

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The most common forms of skin cancer are basal cell carcinoma, squamous cell carcinoma and melanoma. Melanoma represents less than 5% of all skin cancers and it is the cause of > 70% of the deaths. Incidence of melanoma in Croatia in 2020 year was 382 for men and 324 for women.

We restrospectively analized medical records of patients with metastatic melanoma from 1stJanuary 2017. to 1st January 2022. treated in UHC Osijek . We had 51 patients, from which 34 were male and 17 were women. The median age of the patients were 66 years (interquartile range from 54 to 71 years), ranging from a minimum of 27 to a maximum of 85 years. 39 (77%) patients had cutaneus melanoma, while 5 patients had mucosal melanoma and 7 had unknown primary melanoma . Regarding the inital stage of

disease, 26 (51%) had stage I-II, and 12 (24%) stage IV. The median time from initial diagnosis to metastatic disease was 11 months (interquartile range from one to 26 months). According to the BRAF status, 28 (55%) patients had no mutation. Metastases most often appeared on the lungs, in 26 (51%) cases and in 16 (31%) patients on the brain.

In the first line of treatment, 26 patients (50%) were on BRAF and MEK inhibitors, while 23 (43%) were on immunotherapy . The median duration of the 1st line of treatment was 7 months, ranging from at least half a year to 37 months. After the first line of treatment, 34 (67%) patients died.

17 patients had a second line of treatment, of which 13/17 were on immunotherapy, and 4/17 were on chemotherapy. The median duration of the 2nd line of treatment was 6 months, ranging from one to a maximum of 33 months. After the second line of treatment, 8/17 patients died.

The third line of treatment was given to 5 patients, all were on chemotherapy. After the third line of treatment, 2/5 patients died.

The fourth line of treatment had two patients, both on chemotherapy. In first patient, the treatment lasted for one month, and in the second, 3 months. After the fourth line of treatment, 2/2 of the patients died.

Overall survival (from initial diagnosis to outcome) were a median of 41 months (95% CI 26 – 56 months). Survival were significantly longer in patients with a cutaneus melanoma , and significantly shorter in patients with an unknown primary melanoma (Log rank test, P = 0.03).

By using Spearman's rank correlation coefficient we have evaluated the connection between the length of total survival rate and time prior to the occurrence of metastasis. We realize that there is a significant positive correlation between these two. In other words, the longer the time prior to the occurrence of metastasis, the longer is the survival rate, as well. By using Cox's regression analysis only one predictor has been significant in assuming a negative outcome and that was the number of months prior to the occurrence of metastasis.

Keyword: melanoma, immunotherapy, molecular targeted therapy

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P5 – AMBULATORY CHEMOTHERAPY - SINGLE CENTER EXPERIENCE WITH ELASTOMERIC PUMPS

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Background: Historically all chemotherapy infusions in oncology were delivered only in the hospital setting. A huge change was made when new protocols or types of therapy (peroral for example) were introduced. However, there are still chemotherapy protocols that require hospital admissions because of 24 h or 48 h continuous chemotherapy infusions. During hospital stay patients have restricted mobility, they need to mobilize with the saline stand or interrupt the chemotherapy infusion.

An elastomeric infusion pump is a type of infusion pump that delivers chemotherapy in a controlled manner. An elastomeric pump uses pressure to infuse medication. This pressure is created by having the fluid held in a stretchable balloon reservoir, then pressure from the elastic walls of the balloon drives fluid delivery. We wanted to present our experience of ambulatory chemotherapy delivered by elastomeric pumps.

Case series: in Clinical Hospital Center Rijeka, Department of Radiotherapy and Oncology, in January 2023 we started with the ambulatory chemotherapy delivered by elastomeric pump infusion. During January and February, 10 patients underwent (25 applications) chemotherapy by an elastomeric pump. The mean age of our patients was 65 +/- 2 years (8 men, 2 women). All our patients were in very good condition with performance status ECOG 0 or 1 and they had appropriate vascular access via port-a-catheter. They all had a diagnosis of metastatic colorectal carcinoma and were delivered 5 fluorouracil as a part of FOLFOX and FOLFIRI protocols which carries 48 h continuous infusion. According to our experience, there were no technical failures such as chemotherapy-produced leakage, flow rate anomalies, and injection difficulties.

Conclusion: According to our experience elastomeric pumps are preferred by patients, as they do not require a stay in the hospital. This minimizes disruption to their careers and family life. Ambulatory chemotherapy is associated with significant cost savings by using elastomeric pumps. They are easy to use, improve patient flexibility, and can contribute to improving mental and physical health of our patients. Also, they are portable, comfortable, and discreet to use. No significant adverse events were reported. According to the volume of our Center and the growing incidence of gastrointestinal tumors, we are expecting 60 applications monthly.

Keywords: elastomeric pump, chemotherapy delivery via elastomeric pump, daily hospital

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P6 – ATEZOLIZUMAB IN PATIENTS WITH METASTATIC UROTHELIAL CANCER - RETROSPECTIVE ANALYSIS OF THE TREATMENT EXPERIENCE AT THE DEPARTMENT OF ONCOLOGY AND RADIOTHERAPY, UNIVERSITY HOSPITAL OF SPLIT

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Background: There are about 1400 new cases of bladder cancer (BC) patients diagnosed in Croatia annually, and more than 500 people die from it. This makes BC the fifth most common malignancy in Croatia by incidence rate and the seventh by mortality rate. Urothelial carcinoma (UC) accounts for 90% of BC. Although rare at presentation, metastatic UC (mUC) still has a very poor survival, with 5-year survival rate of only 7.7%.

Platinum-based chemotherapy is the standard first-line (1L) treatment, and in patients without progression on induction chemotherapy, maintenance therapy with checkpoint inhibitor (CPI) avelumab is prescribed. In Croatia, 1L treatment in platinum-ineligible patients with tumor PD-L1 expression higher than 5% is another CPI - atezolizumab.

Immunotherapy with CPIs is the standard second-line (2L) therapy for those who received only chemotherapy in 1L. The IMvigor 210 study has shown that atezolizumab in 2L treatment of mUC has an objective response rate (ORR) of 19%, median overall survival (OS) of 7.9 months, the median progression free survival (PFS) of 2.1 months, and the frequency of grade 3 and 4 adverse events (AEs) of 16%. The IMvigor211 study compared the outcomes of atezolizumab versus chemotherapy in the 2L treatment of mUC. There were no significant differences in median OS and ORR (OS 10.6 months vs. 11.1 months; ORR 23% vs. 21.6%). However, atezolizumab caused fewer AEs.

Study objectives: To determine ORR, disease control rate (DCR), PFS, OS, and the frequency of grade 3 and 4 AEs of atezolizumab in the 2L treatment of metastatic UC in daily clinical practice at the Department of Oncology and Radiotherapy, University Hospital of Split.

Methods and materials: We retrospectively analysed the clinical outcomes of 23 patients with mUC treated with atezolizumab in the 2L and 3 patients who received it as the third-line treatment, from January 2019. until October 2022. All of the patients had previously received platinum-based chemotherapy in 1L. Data was analysed using Microsoft Excel 2019 and MedCalc 20.115.

Results: Twenty-six patients were included in the analysis. The median follow-up was 23.3 months (range 0.3–41). There were 17 men (65%) and the median age was 71 years (range 47–84). Twelve patients (46%) had ECOG status 0, 8 (31%) ECOG status 1 and 2 (8%) ECOG status 2. Median number of atezolizumab cycles was 9 (range 1-33). ORR was 0%, while DCR was 19% (all stable disease). The median PFS was 6.7 months, while the median OS was 16.2 months. Four patients (15%) experienced grade 3 AEs (1 extrapyramidal syndrome, 1 hypothyreosis, 1 skin toxicity and 1 adrenal gland insufficiency). There were no grade 4 AEs.

Conclusion: Our retrospective analysis has shown less than expected RR of atezolizumab in the 2L treatment of metastatic UC, but with median survival rates higher than reported in the IMvigor210 and IMvigor211 studies, while the toxicity profile was similar. The main limitations of our research are its retrospective character and the small number of subjects included.

Keywords: atezolizumab; metastatic urothelial cancer; retrospective analysis

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P7 – BILIARY TRACT CANCERS – SINGLE INSTITUTION RETROSPECTIVE ANALYSIS (2019-2021), CROSS-SECTION OF EPIDEMIOLOGICAL DATA

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Background: Biliary tract cancers (BTC) comprise a rare group of malignancies that involve the gallbladder and biliary tree. Due to their aggresive nature and initially asymptomatic course they are typically diagnosed in the advanced and metastatic phase, when therapeutic options and results are usually modest. They are the sixth most common tumor of the digestive system (3%). The incidence of cholangiocarcinoma is low in high-income countries (from 0·35 - 2 per 100 000 annually); however, in endemic regions of Thailand and China, the incidence is up to 40-times higher and represents a major health problem. Epidemiological studies of these tumors are mostly unreliable due to the numerous divisions and diverse classification systems and must be interpreted with caution. The Croatian Cancer Registry states that in 2020, 120 patients with gallbladder cancer and 148 patients with "other and unspecified" tumors of the bile ducts were registered, and there is no clear distinction between intrahepatic cholangiocellular and hepatocellular carcinomas (a total of 523 patients), therefore it is impossible to obtain accurate data on the inci-

dence of these tumors. The incidence of intrahepatic cholangiocarcinoma is rising globally, while the incidence of other biliary cancers is relatively stable. Five-year survival of patients with BTC in all stages according to studies is from 10 to 40% and merely 2 % for those diagnosed in the metastatic phase of the disease. The real-world prognosis of metastatic BTC is remarkably poorer than described in clinical trials, and in recently published study using real-world data (SEER database, 13,287 patients diagnosed with mBTC from 2010 to 2018) the mOS was 4.5 months, and large proportion (41%) of patients lived less than 3 months.

Methods: A retrospective analysis of patients with newly diagnosed invasive carcinoma of the biliary tract that were presented on our MDT over the course of 2 years (1/19 - 12/21) was conducted. The data were analyzed using descriptive statistics methods, with the use of Microsoft Excel tools.

Results: A total of 56 patients (31 men and 25 women) were identified. The median age was 79 years; 3 patients were younger than 50 years, and the youngest patient was 31 years old at the time of diagnosis. In 55.3% (n=31) patients, the disease was diagnosed in the metastatic stage and in the remaining patients, there was no evidence of distant metastases at diagnosis (distribution by stage: 3 T1N0, 4 T2N0, 5 T3N0, 6 T2N1, 5 T3N1, 2 T3N2). According to anatomical location, the most common were gallbladder carcinomas (n=19), followed by extrahepatic bile ducts (n=16; 6 tm Klatskin), intrahepatic bile ducts (n=9), then 6 tumors of the papilla Vateri and 1 perihilar tumor. In 5 patients with metastatic disease, it was impossible to determine where the tumor originated from exactly. The patients were predominantly in a poor general condition (a total of 12 patients with ECOG status 0, 26 with ECOG status 1, 12 with ECOG status 2, 5 with ECOG status 3, and 1 with unknown ECOG status). 9 patients received adjuvant therapy (6 capecitabine, 2 CG protocol, 1 monogemcitabine). Out of a total of 31 patients in the metastatic phase of the disease, 24 (77.5%) were treated with first-line chemotherapy, and 7 (22.5%) were treated by best supportive care only.

Conclusion: The limitations of this study are its retrospective nature and the small number of patients included. We confirmed that in our institution the tumors of the billiary system are diagnosed in an advanced stage, in people of an older age and in a poor general condition and due to that a large proportion of patients never become candidates for chemotherapeutic treatment, either in adjuvant or in the metastatic setting. BTC represent an area of unmet need globally, and in order to optimize the therapeutic approach and outcomes of BTC, it is necessary to evolve this field by improvement of data management, development of methods for their earlier diagnosis and evolvement of novel therapeutic and supportive care options.

Keywords: biliary tract cancers; epidemiology; data management

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P8 – CCND1 AMPLIFICATION AND CYCLIN D1 EXPRESSION IN NODULAR MELANOMA

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Backround: Malignant melanoma (MM) is one of the tumours that certainly belongs to the group of the most genetically complex malignancies. Bound to cyclin-dependent kinases (CDK4/6), cyclin D1 protein promotes the phosphorylation of retinoblastoma protein (pRb) and thus activates the transition from the G1 to the S phase of the cell cycle. Cyclin D1 has been analyzed in several studies with different types of melanoma, where it showed conflicting prognostic relevance. A correlation was found between CCDN1 gene amplification and patient survival prognosis, while other study linked the amplification of the CCDN1 gene with melanoma ulceration, but with no correlation to survival.

Aim: The aim of our study is to investigate the relationships of cyclin D1 protein expression with the genetic rearrangement of the BRAF gene and the amplification of CCND1 gene.

Methods: A specialist in dermatopathology carefully selected the paraffin blocks with enough tumour tissue, and consequently 52 tissue samples of NM were included into the research. Tissue microarrays (TMA) methods were used in immunohistochemical analyses of NM samples. Cyclin D1 staining patterns were observed as nuclear staining of NM cells. DNA isolations were performed using the NucleoSpin Tissue Kit. Amplification of CCND1 gene was performed by SybrGreen QReal-time PCR. BRAF gene amplification containing the 600th amino acid in the exon 15 was performed using 5 to 10 ng of DNA and the primers.

Results: The immunohistochemical analysis of cyclin D1 protein expression showed that: in 21 (40.4%) samples expression was less than 25%, 19 (36.5%) had an expression of 25 to 50%, and 12 (23.1 %) had an expression greater than 50%. The median expression of cyclin D1 is 35.0%, ranging from 10 to 80%. The QRT- PCR method revealed that the CCND1 gene was amplified in 18 out of 52 (34,6%) nodular melanoma samples. By comparison with other analysed parameters, it was found that the amplification of the CCND1 gene is significantly associated with the expression of cyclin D1 protein in category <50% ($p = 0,001$). In melanoma thicker than 4 mm, 16 (88.8%) samples with CCND1 gene amplification were found ($p = 0.055$). BRAF mutation analysis was successful in 39 samples; 13 samples did not contain sufficient DNA. Fifteen out of 39 NM samples (38,5%) have contained the mutation. Comparison of the BRAF gene status revealed that the mutated type BRAF V600E/K is significantly associated with the expression of cyclin D1 protein ($p = 0.018$)

Conclusion: Increased levels of cyclin D1, resulting from genomic amplification, may contribute to the BRAF inhibitor resistance of BRAF V600E-mutated melanomas. Future studies of this regulatory pathway will certainly determine whether there is a purpose for use of CDK4/6 inhibitors in MM.

Keywords: cyclin d1; CCND1 gene; nodular melanoma

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P9 – CGP-GUIDED THERAPY AS A HIGHLIGHT OF PRECISION ONCOLOGY- RESULTS FROM CROATIAN SINGLE INSTITUTION

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Background: Precision medicine is rapidly evolving field but its application in everyday oncological practice is still debated. While the opponents are calling it *an illusion*, there are several trials that support the off-label use of the drugs with almost doubled overall survival. Nonetheless, classical clinical trials will no longer be able to address all needs of this demanding and challenging field. Consequently, the emphasis is being put on the real-world data and learning from every patient. Here we present our results from first patients treated in accordance to their comprehensive genomic profiling (CGP) since the establishment of National committee for CGP-guided therapy and approval of budget for off-label use of the drugs in 2021.

Methods: The cross-sectional observational study was conducted at the Department of Oncology and Radiotherapy, University Hospital of Split. It included patients whose tumor specimens underwent CGP from 2020 to 2023 and were administered with the treatment in accordance to the results. The analysis was performed through FoundationOneCDx or FoundationOne Liquid and it was carried out in a Clinical Laboratory Improvement Amendments certified, College of American Pathologists accredited laboratory (Foundation Medicine Inc., Cambridge, MA, USA). The data were analyzed with methods of descriptive statistics using Microsoft Excel tools.

Results: There were 12 patients in total, out of which 3 (25%) patients were diagnosed with metastatic uterine cancer, 2 (17%) with metastatic ovarian and breast cancer, and 1 (8%) with metastatic gallbladder, prostate, cholangiocellular, lung and cervical cancer. Median age was 59.5 years (IQR 48.5-69) and majority of patients (75%) had ECOG performance status 0. Median number of previous lines of treatment was 3 (IQR 2-5.5). At the time of analysis, median progression free survival was 3.25 (IQR 2-4.5) month, with 5 (42%) patients still receiving the treatment. Best response to treatments were partial response and stable disease in 4 (33%) and 3 (25%) of patients respectively.

The most common therapy used was checkpoint inhibitors (ICI) and PARP inhibitors in 7 (58%) of patients. While treatments were well-tolerated, one patient had hypothyreosis as a consequence of ICI and one had hyperglycemia as a consequence of alpelisib treatment that required dose reductions.

Conclusion: Despite relatively short time without progression, with certain number of patients that are still receiving the treatment and have good response to it, and the fact that all patients were heavily

pretreated, we believe that the CGP-guided therapy should be introduced to our patients after decision of National Committee when possible. Also, with new findings from every patient, in the future we could be able to optimally position CGP-guided therapy in the treatment strategy.

Keywords: comprehensive genomic profiling; precision oncology; FoundationOneCDx; FoundationOne Liquid

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P10 – CHARACTERISTICS OF PATIENTS TREATED WITH CYCLIN-DEPENDANT KINASE INHIBITORS FOR METASTATIC, HORMONE RECEPTOR POSITIVE, HER2 NEGATIVE BREAST CANCER – A SINGLE CENTRE EXPERIENCE

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The introduction of cyclin-dependent kinase (CDK4/6) inhibitors revolutionised treatment of hormone receptor positive (HR+), HER2 negative (HER2-) breast cancer in a metastatic setting. In phases two and three of the clinical trials, the addition of ribociclib, palbociclib, or abemaciclib to endocrine therapy nearly doubled progression-free survival compared to the endocrine therapy arm. Aside from pharmacokinetic and pharmacodynamic similarities, ribociclib, palbociclib, and abemaciclib all have a low toxicity profile and improve patients' quality of life by extending progression-free survival and delaying the use of chemotherapy in subsequent therapy lines.

In this paper, we will summarize the characteristics of patients treated with CDK4/6 inhibitors and endocrine therapy and their progression free survival rates.

From July 2018 to December 31st 2022, 132 patients were treated with either palbociclib, ribociclib, or abemaciclib at the Clinical Hospital Center Osijek for metastatic HR+, HER2- breast cancer. The median age at the start of treatment was 63, and the majority of patients were postmenopausal (94%). 42% patients were treated with ribociclib, 34% with palbociclib, and 24% with abemaciclib. Their endocrine therapeutic partners were most commonly letrozol (49%) or fulvestrant (49%). Bones were the most common distant metastasis localization (38%) in our patient pool, and only 22% of patients had metastatic disease at diagnosis.

43% of patients have not yet progressed, but the median PFS were similar across all three groups. The abemaciclib group reached 12 months (1 – 40 months), while the palbociclib and ribociclib groups reached 12.9 months (2.9 – 44 months) and 11 months (1 – 43 months), respectively.

57 patients' tumor samples were tested for the PIK3CA mutation, and 19 of them were positive. Apart from one patient who still has a good response to CDK4/6 inhibitors, all of those patients have progressed and are now treated with alpelisib as a second line treatment.

Keywords: metastatic breast cancer, cyclin-dependent kinase (CDK) inhibitors, progression-free survival, abemaciclib, palbociclib, ribociclib

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P11 – CLINICAL OUTCOMES AND TOXIC EFFECTS OF IMMUNE CHECKPOINT INHIBITORS AMONG OLDER PATIENTS WITH CANCER - A SINGLE-CENTRE EXPERIENCE

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Backround: Agents that activate the immune system to target cancer have made major inroads in improving outcomes in patients with metastatic cancer over the last several years. Specifically, immune checkpoint inhibitors (ICIs) have now received regulatory approval in 15 different cancer types and produce long-term responses in a subset of patients. Advancing age remains the single most significant risk factor for most cancers, and adults 65 years or older are most susceptible. The immune system weakens with aging, a phenomenon known as immunosenescence. Precisely for this reason, older adults remain under-represented in cancer clinical trials, including those involving immunotherapies.

Aim: To provide insight into the clinical outcomes and safety of ICIs among older patients (aged ≥70 years) with cancer.

Methods: We have performed a retrospective observational study, reviewing all patients with lung cancer (67.3%), melanoma (25%), kidney and bladder cancer (7.7%) , treated with ICIs in our Institution

over a 2-year period (2019 and 2020), and followed until March 2023. From the medical records, we evaluated the side effects of immunotherapy and the patients comorbidities. The inclusion criteria were: 1) age of 70 years or older at the beginning of immunotherapy treatment and 2) receiving any anti PD-1 or anti PD-L1 therapy in advance disease. We included 52 patients (71.2% male, 28.8% female), mean age 74.7 ± 4.2 years (range 70-91).

Results: Overall survival (OS) of all evaluated patients was 26.8 months (95% CI 18.4-35.3), median was 12 months. When analyzing OS individually in groups of primary tumor site, median survival was best in patients with urogenital cancers 55.5 months (95% CI 30.3-80.4) while in lung cancer group OS was 17.3 months, median 8 months, (95% CI 11.2-23.3) and in melanoma group OS was 25.3 months, median 37.0 months (95% CI 14.7-35.9). There was no statistically significant difference by gender or type of therapy, or the existence of immunologically related adverse effects (irAEs). Interestingly, in subgroup analyses there was no statistically significant differences in OS between patients age 70-79 and patients over age 80 (11.4 vs 17.5; p=0.34).

Conclusion: Our results suggest that immunotherapy is an effective and well tolerated treatment for older patients with solid tumors, even from those over age 80. However, further studies focusing on this specific population are needed because of the increasing incidence of malignant disease with age and overall aging of the population.

Keywords: immunotherapy; older patients; immune checkpoint inhibitors; mmunosenescence

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P12 – COMPARISON OF PD-L EXPRESSION FREQUENCY IN BREAST CARCINOMA USING SP142 AND SP263 ANTIBODIES

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Objective: The immune check point inhibitors have changed the therapy strategies for many advanced or metastatic tumors. There are various commercially available assays and clones for PD-L1 detection as well as multiple expression scoring methods. Although, harmonization studies have been performed to

address this issue and investigate different assay and clones, there is still need to compare different staining and counting methods, especially in breast cancer. Breast cancer is the most frequent cancer type in women worldwide, but it is not robustly immunogenic tumor type. Some new studies have showed, SP263 to be more sensitive assay in formalin fixed paraffin embedded (FFPE) tissue blocks older that 3 years. Therefore, we decided to compare SP142 and SP263 assays for frequency of PD-L1 expression in breast carcinoma FFPE tissue blocks from 2014 and 2015.

Methods: Tissue microarrays were constructed from 128 hormone positive, HER2 negative breast carcinoma FFPE tissue blocks and stained with SP142 and SP263 antibodies. For the evaluation of PD-L1 frequency expression three scoring methods were used estimating positive tumor cells, immune cells and combination of these two (TC-invasive tumor cells; IC-tumor infiltrating-immune cells; TCIC-combination of tumor cells and immune cells) as described earlier. For all three scoring methods the 1% cut-off value was used where <1% was considered negative and ³1% was considered positive.

Results: In the cohort stained with SP142 out of 128 samples, 17 tissue cores were lost or did not have invasive tumor. In the remaining tissue cores stained with SP142 all tumors were negative (TC), 10% samples had positive IC staining and 6% samples had TCIC staining. On the other hand, when SP263 was used, 33 tissue cores were lost or had suboptimal content of tumor tissue. In the remaining tumor tissue cores stained with SP263, there was 6% positive tumors samples (TC), !7% samples had positive IC staining and 12% samples was TCIC positive.

Conclusion: This study indicates that more positive tissue samples from older archival FFPE tissue can be detected when using SP263 antibodies.

Keywords: breast carcinoma, immunohistochemistry, PD-L1, SP142, SP263

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P13 – COMPREHENSIVE GENOMIC PROFILING OF BILIARY TRACT CANCER-RESULTS FROM CROATIAN SINGLE INSTITUTION

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Background: Biliary tract cancers (BTC) are considered as one of the most aggressive tumors with a very poor prognosis. Late presentation of the tumor in many cases leads to advanced and unresectable disease by the time it is diagnosed. Until recently, there have been very few clinical advances in the management of these patients and gemcitabine-based chemotherapy has been the most used systemic therapy.

Recently, it was demonstrated that comprehensive cancer genomic profiling (CGP) has significant benefits and definitive place in detecting potential targets for genotype-matched therapy in patients with BTC. Current conditions for CGP in Croatia are metastatic disease (first line of treatment), ECOG 0 or 1, and life expectancy of more than 6 months. The aim of this analysis was to present results from our instituition regarding CGP in BTCs.

Methods: Retrospective analysis was conducted at the Department of Oncology and Radiotherapy, University Hospital of Split. Patients with advanced biliary tract cancers whose tumor specimens underwent CGP from 2021 to 2023 were included. The analysis was performed through FoundationOneCDx or FoundationOne Liquid and it was carried out in a Clinical Laboratory Improvement Amendments certified, College of American Pathologists accredited laboratory (Foundation Medicine Inc., Cambridge, MA, USA). The data were analyzed with methods of descriptive statistics using Microsoft Excel tools.

Results: CGP was performed on 5 tumor specimens from patients with metastatic BTC. Results were obtained from tumor biopsy on four of them, and one patient underwent liquid biopsy. Three of them had no clinically significant mutations, while two of them had target mutation-BRAFV600E, thus making them eligible for off-label treatment with BRAF and MEK inhibitors. One patient was administered with the treatment in accordance to the results of CGP and so far has been treated with 7 cycles of therapy. Initial presentation of the patient was in December 2021, cholangiocellular carcinoma with multiple lesions in liver. After the progression on gemcitabine based chemoterapy, patient was treated with CAPOX protocol, to bridge the time needed for the approval of the CGP-guided treatment. The treatment with BRAF and MEK inhibitors was started in August 2022, and the last evaluation from December 2022 showed regression most of the liver lesions, also with significant decrease in tumor markers values. The other patient with the same mutation is yet about to start the treatment.

Conclusion: Life expectancy of patients diagnosed with metastatic or locally advanced, unresectable biliary tract cancers rarely exceeds 12 months from the diagnosis. Results from our institution are in line with larger studies that demonstrated that CGP has benefits in decision-making on therapeutic strategies and the prediction of clinical outcomes for patients with advanced BTC. Further efforts are needed to improve implementation of CGP and treatment according to the CGP findings in order to combat this aggressive malignancy and imrpove unacceptable outcomes we are facing today.

Keywords: biliary tract cancer, comprehensive genomic profiling

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P14 – CORRELATION OF RADIOLOGIC AND PATHOLOGIC COMPLETE RESPONSE AFTER NEOADJUVANT TREATMENT OF HER2 POSITIVE BREAST CANCER

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Background: Neoadjuvant systemic therapy represents standard of care for aggressive subtypes of breast cancer – HER2 positive and triple negative. Radiological method of choice for monitoring response to treatment and for planning a surgery is post-treatment breast magnetic resonance imaging (MRI), which determines the rate of response according to RECIST criteria. The primary indicator of outcome of neoadjuvant therapy is pathologic complete response (pCR) which has prognostic and predictive value. This study aimed to compare radiologic and pathologic complete response rates after neoadjuvant treatment of HER2 positive early breast cancer.

Methods: This retrospective study included 83 patients with HER2 positive breast cancer who received neoadjuvant systemic therapy between January 2020 and December 2021 at the University Hospital Centre Zagreb, with prior Ethics Committee approval. Radiological and pathohistological characteristics of the tumor at the time of diagnosis and after neoadjuvant treatment were analyzed for each patient by using the hospital information system (BIS). Furthermore, postneoadjuvant therapy MRI findings were correlated with the postoperative pathohistological findings. Sensitivity, specificity, accuracy, and positive predictive value of radiologic complete response as predictor of pathologic complete response was calculated.

Results: Out of a total of 83 patients, 95% (79/83) completed neoadjuvant treatment. Complete data including post-treatment MRI and postoperative pathology results were available for 89% (74/79) of patients. Radiologic complete response (rCR) was recorded in 44.6% (33/74) patients and radiologic partial response (rPR) in 51.4% (38/74) patients, stable disease in 2, while progressive disease was recorded in 1 patient. 10 patients out of the 33 (30.3%) with a radiologic complete response did not achieve a pathologic complete response. Of the 38 patients with a radiologic partial response, 20 (52.5%) patients achieved pathologic complete response. The sensitivity and specificity of radiologic complete response were 53.4% and 64.9%, respectively, while the positive predictive value was 69.7%. The overall accuracy of breast MRI in predicting pathologic complete response was 57.7%.

Conclusion: Although only a modest number of patients was included in this study, the obtained results indicate that post-neoadjuvant therapy breast MRI is not sufficiently accurate in predicting pathologic complete response.

Keywords: HER2 positive breast cancer; neoadjuvant treatment; radiologic complete response; pathologic complete response

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P15 – DYNAMICS OF NEUTROPHIL-TO-LYMPHOCYTE RATIO AS A BIOMARKER OF CLINICAL RESPONSE TO IMMUNE CHECKPOINT INHIBITOR THERAPY IN A MULTICENTER COHORT OF PATIENTS WITH ADVANCED UROTHELIAL CANCER WITHIN CROATIAN GENITOURINARY CANCER NETWORK

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Introduction: Neutrophil-to-lymphocyte ratio (NLR) is considered biologically associated with immune checkpoint inhibitors (ICI) but has generally been evaluated as a single threshold value. We assessed NLR kinetics and examined its association with treatment outcomes in a multicenter cohort of patients with advanced urothelial cancer (aUC) treated with ICI.

Patients and methods: Data on patients with aUC treated with ICI in three high-volume centers were retrospectively reviewed. Baseline NLR and NLR at every cycle of ICI therapy were calculated and, along with other characteristics, correlated with overall survival (OS) in univariate and multivariate analyses. Longitudinal analysis of NLR dynamics was performed using a mixed-effect regression model.

Results: A total of 85 patients from three centers were included; 38%, 19%, and 4% had 1, 2, and 3 Bellmunt risk factors, respectively. Median and mean NLR at baseline were 2.7 and 4.6; 49% of patients had NLR>median (high NLR). Patients with a more advanced stage at baseline, variant histology, and an increas-

ing number of Bellmunt risk factors were more likely to have high NLR (p=0.01). Median OS was 4.3 months for patients with high NLR and 9.5 months for patients with low NLR (HR 3.1, p=0.02). Furthermore, high NLR was significantly associated with poor OS at all assessed time points during ICI therapy (p<0.05). NLR and previous radical surgery were associated with OS on univariate analysis. On multivariate analysis, NLR as a categorical variable was significantly associated with OS (HR 1.5, p=0.01), meaning that patients with higher NLR lived shorter compared to patients with low NLR. On the next level, patients with NLR increased >50% during ICI therapy compared to baseline and experienced the worst survival (median 3 months). When the slope of the NLR kinetics curves was analyzed based on ICI therapy response using a multinomial regression model, a statistically significant interaction was found for NLR increase in patients experiencing progression of disease (increase by 0.05 (p<0.01) per ICI cycle, and conversely for NLR decrease in patients achieving partial response or stable disease (decrease by 0.09 (p=0.02) per ICI cycle).

Conclusions: NLRs determined at baseline and even more during the course of ICI therapy are prognostic for clinical outcomes. In patients who are not responding to ICI therapy, NLR is likely to increase, while it tends to decrease in patients who derive clinical benefits from ICI therapy. Even the dynamics of NLR change (measured by the slope of the curve) is related to therapy response. Patients with rising NLR early during the course of ICI treatment have a low likelihood of beneficial response to ICI. It remains to be seen how these observations will be applied practically in the clinic.

Keywords: neutrophil-to-lymphocyte ratio kinetics; immune checkpoint inhibitors; urothelial carcinoma.

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P16 – ENDOBRONCHIAL ULTRASOUND IN CANCER DIAGNOSTICS: EXPERIENCE FROM A SINGLE CENTRE

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Introduction: Endobronchial ultrasound (EBUS) is a minimally invasive procedure which revolutionized the diagnostic management of mediastinal lymphadenopathy and has become an irreplacable tool for the diagnosis and staging of lung cancer. University Hospital Dubrava has a 10 year-long experience in EBUS and was the first hospital in Croatia to start performing it.

Aim: We wished to investigate the most common malignancies diagnosed with EBUS in our institution.

Materials and methods: This study in based on our *Registry of patients that underwent endobronchial ultrasound-based procedure in the University Hospital Dubrava*. Methods of descriptive statistics were employed for reporting of the results.

Results: Out of N=925 procedures logged in the Registry (from February 2013 to the beginning of March 2023), N=522 (56.4%) yielded a cytological diagnosis, of which in 75.1% (N=392) a malignant disease was diagnosed. The most commonly diagnosed malignancy was lymph node metastasis of non-small cell lung cancer (NSCLC) in N=228, i.e. in 58.1% cases of malignancy. Among patients with NSCLC, adenocarcinoma was the most prevalent (N=149 cases, 65.3% of NSCLC). Small cell lung cancer was diagnosed in N=43 cases (11% of cases with malignancy). The most commonly diagnosed extrapulmonary malignancy via EBUS was lymph node metastasis originating from breast cancer (N=22, 5.6% of cases with malignancy), followed by malignant disorders of the lymphatic system and renal cell carcinoma (N=14, 3.5% for both categories). Lymph node metastasis originating from head and neck cancers was diagnosed in N=12 cases (3%).

Conclusion: Our experience as the first centre to implement EBUS in Croatia illustrates the potency of EBUS for the diagnosis of cancer. Types of cancer diagnosed by EBUS from our Registry further depict the epidemiological distribution of malignant disorders affecting mediastinal lymph nodes.

Keywords: endobronchial ultrasound; cancer diagnostics

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P17 – IMPACT OF COVID 19 PANDEMIC ON ELECTIVE RECTAL CANCER SURGERY – SINGLE INSTITUTION EXPERIENCE

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Introduction: Surgical treatment of rectal cancer depends on clinical stage, size and location of primary tumor. A sphincter preserving technique such as low anterior resection (LAR) is the preferred method if negative distal margin can be achieved. If an adequate distal margin cannot be obtained, an abdominoperineal resection (APR) is required. A proctosigmoidectomy (Hartmann's procedure) is performed in patients with potentially curable obstructing rectal cancer after neoadjuvant chemoradiotherapy, or as a palliative treatment for locally advanced rectal cancer.

Aim: The aim of this retrospective study was to investigate the impact of COVID 19 pandemic on the number and type of surgeries performed for the treatment of rectal cancer in UHC Zagreb, Department of Surgery.

Material and methods: Collected data were extracted from medical records of the patients who underwent surgery at the Department of Surgery from 1st of January 2016 to 31st of December 2022 with prior Ethics Committee approval. Total of 688 patients were included. Retrospective analysis of number and type of surgery was done consecutively by years for the period of interest.

Results: In 2016 total of 75 patients underwent elective surgery for rectal cancer. LAR was performed in 64% (N=48) of patients, Hartmann's procedure in 20% (N=15), and APR in 16% (N=12). In 2017, 94 surgeries were performed. LAR accounted for 64% (N=60), Hartmann's procedure 17% (N=16), and APR 19% (N=18). In 2018, 115 surgeries were performed. LAR accounted for 69% (N=79), Hartmann's procedure 10% (N=12), and APR 21% (N=24). In 2019, 80 surgeries were performed. LAR accounted for 67% (N=54), Hartmann's procedure 9% (N=80), and APR 24%. In 2020, 78 surgeries were performed. LAR accounted for 59% (N=46), Hartmann's procedure 14% (N=11), and APR 27% (N=21). In 2021, 124 surgeries were performed. LAR accounted for 66% (N=82), Hartmann's procedure 14% (N=17), and APR 20% (N=25). In 2022, 122 surgeries were performed. LAR accounted for 64% (N=78), Hartmann's procedure 15% (N=18), and APR 21% (N=26).

Conclusion: Our results show steady growth in numbers of performed surgeries in the years prior to the pandemic, with exception of the year 2019 when our department underwent organizational changes. In 2020, significant decrease in number of surgeries was observed as a result of restrictive epidemiological measures established to reduce the spread of COVID 19 infection. COVID 19 pandemic measures also resulted in delayed diagnosis and treatment of rectal cancer which is indirectly shown through the increasing share of Hartmann's procedure. In the years following the relaxation of measures, significant increase in number of performed surgeries that exceeded all the pre-pandemic years was recorded. Constant elevated share of Hartmann's procedure was noted as possible consequence of post COVID delay in diagnosis and confirmation of rectal cancer in more advanced stages of disease.

Keywords: rectal cancer; COVID 19; surgical treatment; Hartmann's procedure

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P18 – IMPACT OF IMMUNOHISTOCHEMICAL CHARACTERISTICS OF TUMOR ON RESPONSE TO DUAL ANTI-HER2 BLOCKADE – DATA FROM REAL CLINICAL PRACTICE

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Aim: Multicentric CLEOPATRA trial set new standard in first line treatment of HER2 positive metastatic breast cancer with the use of dual anti-HER2 blockade along with taxane based chemotherapy. Increasing number of clinical trials are searching for adequate biomarkers for predicting response to anti-HER2 therapy, which could contribute to assessment of long term outcomes, as well as earlier implementation of new treatment strategies. The aim of our study was to determine whether HER2 and hormone receptor expression affects dual anti-HER2 treatment response.

Materials and methods: A total of 112 patients were included in our study. All patients started first line treatment with pertuzumab/trastuzumab/docetaxel from January 1st 2015 to August 1st 2020. Duration of treatment was calculated for each patient at the time of analysis. Patients were divided in two subgroups based on presence of estrogen and progesterone receptors (luminal and non-luminal subgroup), along with two subgroups based on immunohistochemical (IHC) expression of HER2 receptor (first subgroup with IHC score 3+, and other with IHC score 2+, where HER2 positivity was confirmed with in situ hybridization).

Mann Whitney (U) test was performed for statistical analysis. In addition, a cross-sectional analysis was done, one year after each patient's treatment started, for the course of treatment observation. There were four groups of patients: patients who stayed in course of first-line treatment, patients who progressed, patients who got lost to follow up and patients who developed cardiac decompensation, and thus further anti-HER2 therapy was not indicated.

Results: Comparing luminal and non-luminal subtype, no statistically significant difference in duration of treatment was found (U = 242; p = 0,349). After completing one year of therapy, 49 patients continued first line treatment; 19 (38%) were non-luminal, and 30 (61%) were luminal subtype.

Out of 48 patients who progressed, 11 (22%) were non-luminal, and 37 (77%) were luminal subtype. Considering difference in immunohistochemical HER2 receptor expression, out of 49 patients who continued first line treatment, 36 (73%) had score 3+ and 13 (26%) had score 2+. In patients who progressed, 9 (18%) had HER2 expression score 2+ and 39 (81%) had score 3+. Mann Whitney (U) test showed no statistically significant difference in duration of treatment between two subgroups (U= 156; p= 0,294). Eight patients were lost to follow up, and 5 patients developed cardiac decompensation.

Conclusion: Results of our research showed that there was no statistically significant difference in duration of treatment between patients with luminal and non-luminal subtype, same as was reported in CLEOPATRA trial. Analyzing correlation between duration of treatment and HER2 receptor expression, there was no statistically significant difference between subgroups with 3+ and 2+ expression. This was not concordant with referent trial results, which have shown shorter progression free survival in subgroup with lower HER2 receptor expression (2+), without impact on overall survival.

Considering day-to-day improvement in treatment and prolonged overall survival of metastatic HER2 positive breast cancer, search for predictive markers, which could anticipate course of treatment, and be used for optimal treatment strategy planning, is continued.

Keywords: HER2 positive breast cancer, dual anti-HER2 blockade, immunohistochemistry

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P19 – INCIDENCE AND CHARACTERISTICS OF OVARIAN YOLK SAC TUMORS TREATED IN THE UNIVERSITY HOSPITAL CENTRE ZAGREB DURING A 10-YEAR PERIOD

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Introduction: The yolk sac tumor of the ovary is a malignant primitive germ cell tumor. It occurs mainly in the second and third decades of life. It accounts for 20% of malignant ovarian germ cell tumors. About 60% of ovarian yolk sac tumors present in a pure form, while 40% present with mixed germ cell tumors. Clinical presentation is characterized by sudden onset of abdominal pain and distention, often with a palpable pelvic mass on the examination. Most patients have a high level of serum alfa-fetoprotein (AFP). On macroscopic examination, the yolk sac tumor is a unilateral large solid mass with focal necrotic, hemorrhagic and cystic tissue. On microscopic examination, multiple patterns are usually present, most commonly a reticular or microcystic pattern. The pathognomonic finding in the yolk sac tumor is the Schiller-Duval body, a tumor cell-lined papilla with a large central vessel. The desired diagnostic criteria is positive immunohistochemical reaction on SALL4, glypican-3 (GPC3) or alfa-fetoprotein (AFP), which is often focal or weak. The 5-year survival rates are > 95% for stages I-II, 70% for stage III and 50% for stage IV. The present-day treatment for yolk sac tumors is surgery and chemotherapy.

Case reports: During 10 years, from January 1st, 2013 to December 31st, 2022, 6 patients with ovarian yolk sac tumors, between the ages of 13 and 20 were treated in the University Hospital Centre (UHC) Zagreb, Clinic of Gynaecology and Obstetrics. All of them have been presented with abdominal pain and elevated levels of alfa-fetoprotein in the serum. The patients were treated with surgical procedures that included unilateral adnexectomy, pelvic lymphadenectomy, omentectomy and partial peritonectomy. All but one were clinically stage I. Three to four cycles of chemotherapy were applied postoperatively. On pathohistological analysis, in two cases, a pure yolk sac tumor was found. In the other four cases, a mixed germ cell tumor, consisting mainly of a high-grade immature teratoma with the finding of microscopic foci of the yolk sac tumor, was found. Immunohistochemically, AFP was focally positive. One patient was treated in another institution, and the remaining five patients, treated in the UHC Zagreb, are under regular control and without relapse of tumor with a follow-up period of 1 month to 7 years.

Conclusion: Ovarian yolk sac tumors are rare tumors in our population. They mostly appear as a component of mixed germ cell tumor in the second decade of life. According to our experience, all of them are tumor-free after the recommended treatment.

Keywords: yolk sac tumor, ovary, alfa-fetoprotein

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P20 – ORGANIZING AND IMPLEMENTING A MULTIDISCIPLINARY APPROACH IN DAILY ONCOLOGY HOSPITAL, CLINICAL CENTER RIJEKA

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Backround: Management of cancer patients is becoming a worldwide challenge, due to rapidly changing evidence, new drugs approval, and scientific guideline updates. The introduction of the multidisciplinary approach has helped clinicians meet the growing needs of cancer patients. Due to the large number and range of healthcare providers who may be involved, there is a potential for poor communication and poor coordination of care. Multidisciplinary cancer care can be delivered using various models of care. These include multidisciplinary clinics staffed by a mix of different health professionals. We consider it essential to provide the opinion of each member of a multidisciplinary team in one place. In this short report, we present our solution for multidisciplinary approach within the daily hospital.

Methods: We have performed a retrospective observational study, reviewing all patients who were included in collaborative outpatient clinics during the last 6 months as part of a multidisciplinary approach.

Results: As of October 2022, our multidisciplinary approach consists of the following clinics: pain management clinic, psychologist clinic, physiatry clinic, dermatology clinic, oncofertility clinic, nutritional clinic, and general oncology consultation. A total of 252 patients were included after being examined by an oncologist in a daily hospital. Most patients were included in the clinic for pain management, 41.3%. Multidimensional tools, including the Brief Pain Inventory and the McGill Pain Questionnaire were used after the examination in the outpatient clinic for pain management. We have shown that 95% of patients achieved improvement.

Coclusion: Our preliminary results confirm the thesis that the approach, in accordance with the needs of oncology patients, must be guided by the idea that "specialists come to patients, not patients to specialists".

Keywords: multidisciplinary team, multidisciplinary approach, pain managemen

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P21 – OUTCOMES OF PATIENTS WITH METASTATIC COLORECTAL CANCER: A SINGLE CENTER EXPERIENCE

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Introduction: Colorectal cancer represents the second most common and the second deadliest form of cancer in Croatia regardless of sex. The introduction of biological therapy as first-line treatment in metastatic colorectal cancer (mCRC) significantly improved outcomes, but resulting in increased costs. Nevertheless, not all patients are eligible for such treatment modality. The principal aim of this study was to present clinical outcomes of patients with mCRC in our general hospital and to compare the outcomes between patients treated with biological therapy (bevacizumab or EGFR inhibitors) and those treated with conventional chemotherapy.

Patients and Methods: In the present retrospective observational study, conducted at the Department of Internal medicine at the General Hospital of Šibenik-Knin county in the period from 2015-2022, we examined the patients' records using locally maintained colorectal cancer clinical registry. PFS was defined as the time from first application of chemotherapy until disease progression was noted.

Results: A total of 105 patients, aged 65.7 ± 10.1 years, with mCRC have been followed for a median period of 34 months. Majority of patients were in good general condition (82.9% of patients had ECOG 0 or 1). The population was mostly comprised of males (61.9%), and most patients had carcinoma in sigmoid colon (41%), followed by rectum (31%), caecum (12%) and transverse colon (16%). The most common site of metastases was liver (64.8%), followed by lungs (50%) and non-regional lymph nodes (32.4%). The first line irinotecan-based chemotherapy was administered to the majority of patients (73.3%), 11,4% of patients received oxaliplatin-based regimen and 10,5% were treated just with fluoropyrimidines. Mutation in the RAS gene was detected in 55.2%. Patients treated with biological agents (58.1% of the studied population) in the first-line had longer PFS in comparison to patients treated with conventional chemotherapy (13.0 (7.5-25.5) months vs. 8.0 (3.9-19.8) months, P=0.016). However, patients treated with biological agents did not reach second (P=0.297) nor third-line therapy (P=0.094) more common than patients treated with conventional chemotherapy. No significant difference with respect to PFS was found between patients treated with EGFR inhibitors and those treated with bevacizumab (20.5 (7.3-30.0) months vs. 12.5 (7.5-20.0) months, P=0.561). Patients with left-sided colon carcinoma had significantly longer PFS in comparison to patients with right-sided colon carcinoma (12.5 (7.0-25.0) months vs. 6 (3.6-12.8) months, P=0.004).

Conclusion: The data from our registry implies that the outcomes in our hospital are consistent with previously reported results. There is clinical benefit of adding biological therapy to standard chemotherapy in metastatic colorectal cancer.

Keywords: metastatic colorectal cancer; biologycal therapy; chemotherapy; bevacizumab; EGFR inhibitors

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P22 – PATHOLOGICAL DOWNSTAGING, DISEASE CONTROL AND SURVIVAL AFTER NEOADJUVANT CHEMOTHERAPY FOR BLADDER CANCER IN CROATIA; A REAL-WORLD STUDY

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Introduction: Neoadjuvant chemotherapy (NAC) before radical cystectomy is associated with pathological downstaging and improved overall survival in patients with muscle-invasive bladder cancer (MIBC). Despite being standard of care, patients are rarely considered for NAC. The aim of this study was to evaluate the extent of NAC administration within national oncology network, identify patterns of care, effect of NAC on pathological downstaging, disease-control, and overall survival (OS) in unselected real-life bladder cancer patients referred for NAC in everyday clinical practice.

Patients and methods: Patients with bladder cancer who received NAC in two high-volume centers were identified and their electronic charts retrospectively reviewed. Follow-up data were available until March 1, 2023. Clinical factors, pathological downstage and complete pathological response rates were

analyzed. Progression-free (PFS) and OS were estimated using Log-rank test. Association of clinical variables with survival was assessed using Cox regression model.

Results: Between October 2014 and October 2022, a total of 96 patients were treated with NAC. Sixty-seven (70%) were male, median age 68 years. Distribution of UICC stages were as follows: stage II: 56 (58%), stage IIIA: 15 (16%), and stage IIIB 25 (26%) patients, respectively. All patients underwent computerized tomography as initial staging method. Used protocols were gemcitabine/cisplatin in 58 (60%), dose-dense MVAC in 33 (34%), gemcitabine/carboplatin in 3 (3%) and cisplatin/etoposide in 2 (2%) patients, respectively. Median number of administered chemotherapy cycles was 3 (range 1-4). Owing to severe toxicity, NAC was stopped prematurely in 40 (42%) patients. Cystectomy was performed in 80 (83%) patients. Reasons for not pursing cystectomy was disease progression in 9, and patient refusal in 7 patients, respectively. Among 7 patients who refused cystectomy, five patients underwent bladder sparing radiotherapy and 2 received no further therapy. Pathological downstaging was found in 47 (59%), major pathological response in 24 (30%), and pathological complete response was found in 22 (28%) patients, respectively. When only patients with initial stage II were analyzed, rates of major pathological response and pathological complete response were similar: 29% and 27%, respectively. After median follow-up of 51 months (range 5-91 months), 24 (30%) patients experienced disease progression and 21 (26%) patients died as a result of progressive bladder cancer. Three-year disease-free survival rates for the whole cohort and for patients undergoing radical cystectomy were 64.2% (95% confidence interval [CI]: 55–76.7) and 61.3 (95% CI: 42.8–77.1), respectively. Presence of pathologic complete response on final bladder pathology was associated with longer PFS and OS, respectively (HR 0.7, 95% confidence interval [CI]: 0.4–0.8, p=0.001, and HR 0.8, 95% confidence interval [CI]: 0.6–0.9, p<0.001), while other variables were not.

Conclusions: In this real-world experience, bladder cancer patients who were treated with NAC have more advanced disease, more serious side-effects and less frequent cystectomy rates compared to clinical trials. However, proportion of patients achieving major pathologic response and long-term disease control in this heterogenous cohort is significant and in line with published studies. More patients should be exposed to NAC through close multidisciplinary care and improved patient counseling.

Keywords: bladder cancer, neoadjuvant chemotherapy, overall survival, pathological downstaging, pathological complete response, real-life studies

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P23 – PATIENT OUTCOMES WITH LOCALLY ADVANCED RECTAL CANCER TREATED WITH TOTAL NEOADJUVANT THERAPY ACCORDING TO THE RAPIDO TRIAL

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Introduction: Colorectal cancer is the most common malignancy in Croatia, with approximately one-third of cases being diagnosed in a locally advanced stage. Neoadjuvant chemoradiotherapy is the standard of care for patients with newly diagnosed locally advanced rectal cancer. One of the options for neoadjuvant treatment is total neoadjuvant therapy (TNT) according to the protocol from the RAPIDO study.

Aims: An analysis of secondary outcomes according to the RAPIDO study was conducted in patients treated at the University Hospital for Tumors May 2021 until the end of 2022. The outcomes studied included therapy toxicity, treatment discontinuation due to adverse effects, and the rate of complete pathological response.

Results: Complete clinical regression of the tumor, after neoadjuvant treatment, was described according to MRI in 36% of the studied patients, while a complete pathological response was verified on the postoperative pathology report in 10% of the patients. In 6% of the patients who had complete clinical regression after neoadjuvant treatment close follow up was continued instead of surgical intervention.

Chemotherapy was discontinued due to adverse events in 16% of patients, with 6% of patients experiencing cardiac toxicity, 3% of patients experiencing neurological toxicity, 3% of patients experiencing an allergic reaction to 5-fluorouracil, and 3% of patients experiencing grade 3 neutropenia with concurrent oral mucositis.

The most commonly reported adverse event was sensory polyneuropathy, that was present in 40% of patients. Diarrhea was reported in 36% of patients, with 26% of patients experiencing grade 1 diarrhea and 10% of patients reporting grade 2 diarrhea. Neither diarrhea nor sensory neuropathy were the cause of treatment discontinuation in any patient.

Myelotoxicity was recorded in 30% of patients at least once during treatment, with 26% of patients having neutropenia (13% of patients with grade 2 neutropenia and 13% of patients with grade 3 neutropenia). Thrombocytopenia was verified in 10% of patients, and 6% of patients had anemia due to chemotherapy. No patient developed febrile neutropenia.

Conclusion: After comparing our data with the data from the RAPIDO study, we conclude that the rate of complete pathological response after treatment with total neoadjuvant therapy was lower in our patients. Treatment discontinuation due to adverse events was recorded in almost the same percentage of patients as in the RAPIDO study. Neurological toxicity was reported in fewer cases.

Keywords: locally advanced rectal cancer; total neoadjuvant therapy; RAPIDO trial

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P24 – POSTRADIATION PNEUMONITIS

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Introduction: Activation the program for early detection of lung cancer, the number of patients, in the early stage with lung cancer has increased. By detecting cancer earlier, there are greater possibilities for treatment, but the number of patients who have completed the radiation process is also increasing.

Aim: Comparison of lung irradiation methods. Palliative radiation in patients with advanced disease and 2 types of radical radiation (hypofractionated and conventional radiation) in patients with local disease.

Methods: Retrospectively collected data, from December 2019 to the end of December 2022, on the number of lung cancer patients irradiated with the VMAT (Volumetric modulated arc therapy) technique and monitored with the chest CT (computed tomography) imaging method will be presented in tables and descriptively.

Results: In a period of 3 years, 398 patients diagnosed with lung cancer were irradiated at the Department of Oncology. Of that number, 212 patients were treated as primary radiotherapy for lung cancer. 172 patients were irradiated radically, and 50 palliative. The occurrence of postradiation pneumonitis in monitored patients, in a period of 6 months, was 14.29%.

Conclusion: Postradiation pneumonitis is a serious side effect that occurs after lung cancer radiation; occurs one month to 6 months after the therapy. According to available data, the incidence of pneumonitis ranges from 5 to 15%. Although the data for Department of Oncology are within the given interval, there are differences depending on the type of fractionation. While with hypofractionation, the incidence of postradiation pneumonitis is 11.94%, the percentage of patients who didn't develop disease progression is 58.21%. On the other side, the percentage of patients irradiated with conventional fractionation in which pneumonitis developed is 16.95%, but there is also a higher percentage of patients in which disease progression didn't occur within 6 months, 67.80%.

Keywords: radiotherapy, VMAT, lung cancer, radiation pneumonitis.

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P25 – PROTEOMIC PROFILING AND CORRELATION WITH CLINICOPATHOLOGICAL CHARACTERISTICS OF PATIENTS WITH SMALL CELL LUNG CANCER – A PILOT STUDY

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Introduction: Lung cancer is the leading cause of death from cancer in Bosnia and Herzegovina and worldwide. Small-cell lung cancer (SCLC) accounts for 15% of all lung cancers, and due to aggressiveness and rapid growth in most cases, it is detected in the advanced metastatic stage of the disease. We investigate proteome dynamics in newly diagnosed advanced and/or metastatic SCLC patients to explore biomarkers/pathways that can predict response to chemotherapy and immunotherapy and to collect the clinicopathologic characteristics of the patient and correlate them with the obtained proteomic data (biomarkers).

Materials Methods: We used functional enrichment analysis and label-free quantitative mass spectrometry on formalin-fixed paraffin-embedded tissue. We investigated four samples of patients diagnosed with SCLC and treated at the Department of Oncology, University Hospital Mostar and compared them with four normal lung tissues.

Results: We included three male and one female patient with a median age of 59 years. All patients were smokers. In two patients, the disease stage was locally advanced (IIIA and IIIB), and the remaining two patients had distant metastases. The patients were treated with conventional chemotherapy (cisplatin

with etoposide). Three patients died with a median progression-free survival of five months and median overall survival of seven months. One patient is alive and in regular clinical follow-up for four years and six months. Based on 825 proteins that are detected in at least 70% of the samples in each group, the number of proteins that are identified in each of the control tissues was lower (around 1000) than the number detected in each of the SCLC tissues (around 1600-2000). The volcano plot shows 295 significant differentially expressed proteins ($p<0.01$). The most significantly upregulated proteins in the SCLC samples included poly [ADP-ribose] polymerase (PARP), thymopoietin (TMPO), DNA replication licensing factor MCM2, Alcohol Dehydrogenase 1B (Class I), Beta Polypeptide (ADH1B), Amine oxidase, copper containing 3 (AOC3 or vascular adhesion protein 1) and pulmonary-surfactant associated protein A2 (SFTPA2).

Conclusion: Our preliminary data indicate that several novel proteomic biomarkers may be identified in SCLC samples using quantitative mass spectrometry. Further studies are necessary to confirm the preliminary results and validate the role of identified biomarkers in SCLC.

Keywords: lung cancer, small cell lung cancer, proteomics, biomarkers

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P26 – REAL WORLD SURVIVAL OUTCOMES IN ADVANCED GASTRIC AND ESOPHAGOGASTRIC ADENOCARCINOMA – A RETROSPECTIVE ANALYSIS FROM UNIVERSITY HOSPITAL CENTRES ZAGREB AND SPLIT

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Background: Gastric cancer (GC) represents a significant global health burden with being the fifth most common cancer and the fourth leading cause of death worldwide. The problem, among others, lies in the fact that around 40% of patients are initially diagnosed with incurable stage IV disease. Although progress in the treatment of advanced and esophagogastric (EGC) adenocarcinoma is slow, in the last few years there have been reports of improved overall survival (OS) with the increase in the number of chemotherapy lines. The aim of this study was to evaluate the impact of the number of chemotherapy lines on OS in this group of patients in two Croatian high-volume tertiary centres.

Patients and Methods: A retrospective analysis of 225 patients treated with one or more lines of chemotherapy during the period from January 2018 to December 2021 in the Clinical Hospital Center Zagreb and Split was performed. Patients treated only with supportive and symptomatic treatment were not included in this analysis. Data were collected by review of the electronic patient medical records.

Results: There were 76% of patients with GC and 24% with EGC. HER2 status was positive in 28 (12%) patients. Median OS for the whole cohort was 11 months. Median survival increased from 8.7 months for those who received only one line (N = 118, 52%), 12 months for those who received two lines (N = 69, 31%) to 19 months for those who received 3 lines (N = 31, 14%) and 27 months for those who received four lines (N =7, 3.1%) of chemotherapy.

Conclusion: This study confirmed that increasing the number of treatment lines in patients with advanced GC and EGC significantly increases survival. These results are consistent with previously published real world data from other countries.

Keywords: gastric cancer; esophagogastric cancer, chemotherapy line; overall survival; real world data

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P27 – SENTINEL LYMPH NODE LOCALIZATION IN PATIENTS WITH BREAST CANCER.

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Aim: The aim of this study was to demonstrate the advantages of ultrasound-guided peri-tumoral injection of Tc-99m labeled nanocolloid in breast cancer sentinel lymph node localization.

Methods: So far we were able to involve 116 female patients with 120 breast cancer in this study. Four patient had bilateral breast cancer. All patients had preoperative lymphoscintigraphy followed with sentinel lymph node biopsy using ^{99m}Tc–nanocolloid at the same day. In all patients an ultrasound-guided

(Affiniti 70g, Philips, US) peri-tumoral injection has been done with 37 MBq of ^{99m}Tc–nanocolloid in up to 2 ml volume was administered. Preoperative lymphoscintigraphy was performed on double head gamma camera platform (Symbia, Siemens, US). The sentinel lymph nodes were marked on the skin using an external radioactive marker. A hand held gamma probe (neo2000, Neoprobe, Ireland) was used for intraoperative detection of sentinel lymph nodes.

Results: Sentinel lymph nodes were successfully detected in all patients on scintigraphy one hour after injection of ^{99m}Tc–nanocolloid. In all patients sentinel lymph nodes were situated in axillary basins. In four patient, additionally to axillary, an internal mammary sentinel lymph node was observed. A hand held gamma probe was able to find all axillary sentinel lymph nodes. According to age distribution: 8 patients were 30-40 year old, 22 patients were 40-50 year old, 32 patients were 50-60 year old, 28 patients were 60-70 year old, 20 patients were 70-80 year old and 6 patients were 80-90 year old.

Conclusion: Ultrasound-guided peri-tumoral injection of tc-99m labeled albumin nanocolloid in breast cancer sentinel lymph node localization seems to be a reasonable and neceseary diagnostic approach to the management of patients with breast cancer.

Keywords: sentinel, breast cancer, ultrasound-guided peri-tumoral injection, Tc-99m labeled nanocolloid.

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P28 – SERUM CONCENTRATIONS OF SIRTUIN 1 IN PATIENTS WITH HEPATOCELLULAR CARCINOMA

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Introduction: Sirtuin 1 belongs to the family of NAD (nicotinamide adenine dinucleotide)-dependent histone deacetylases that catalyze deacetylation of histone lysines and some non-histone proteins. Deacetylation of non-histone proteins includes: p53, NFκB (nuclear factor kappa-light-chain-enhancer of activated B cells) and PPAR (peroxisome proliferator-activated receptor). Sirtuin 1 participates in the control of various processes in the cell such as: DNA repair, cell cycle, cell response to stress, cell metabolism, starvation, telomerase activity and apoptosis. It has a controversial role in the origin and development of cancer and can play the role of tumor suppressor gene and oncogene. Research has shown increased expression of Sirtuin 1 in breast, prostate, ovarian and liver cancer.

Aim: The aim of this study was to determine the concentration of Sirtuin 1 in the serum of patients with hepatocellular carcinoma and compare it with the values of healthy subjects. We compared the obtained results with the gender and age of patients.

Materials and methods: We included 33 patients with hepatocellular carcinoma and 30 healthy subjects in the study. We analyzed serum samples of patients and healthy controls. Sirtuin 1 concentrations in serum were determined by the ELISA method. The cut-off value for Sirtuin 1 in serum was 25.9 pmol/mL, determined by the ROC curve (AUC 0.841; $p<0.001$).

Results: Patients with hepatocellular carcinoma had significantly higher concentrations of Sirtuin 1 (11.2-96.3; Median 36.3) in serum compared to healthy controls (10.1-26.9; Median 17.1), ($p<0.00013$). Sixty four percent (21/33) of patients with hepatocellular carcinoma had values higher than the cut-off value for Sirtuin 1, while 13% (4/30) of healthy subjects had higher values than cut-off value. We also analyzed the association of Sirtuin 1 in the patient's serum with the patient's age and obtained a negative statistically significant difference ($p=0.0008$). We did not find a statistically significant association between the concentration of Sirtuin 1 and the gender of patients.

Conclusion: Our results suggest the possible value of Sirtuin 1 concentration in the serum of patients with hepatocellular carcinoma as a possible biomarker of this malignant tumor.

Keywords: sirtuin 1; hepatocellular carcinoma; biomarker

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P29 – STEREOTACTIC BODY RADIATION THERAPY IN PATIENTS WITH ADVANCED UROTHELIAL CANCER TREATED WITH IMMUNOTHERAPY: EARLY EXPERIENCE WITHIN CROATIAN ONCOLOGY REFERRAL NETWORK

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Introduction: Despite recent adoption of immunotherapy in the treatment landscape, metastatic urothelial cancer (mUC) remains aggressive disease with limited therapeutic options, low responses on systemic therapy, and poor survival. Stereotactic body radiation therapy (SBRT) is increasingly used metastasis-directed modality, characterized by precise delivery of ablative doses of radiotherapy and potential synergistic effect with immune check-point inhibitors (ICI). Data are scarce of real-life utilization of SBRT in patients with mUC. The aim of this study was to investigate patterns of SBRT use for patients with mUC treated with ICI, to assess its impact on patient management and analyze early efficacy data.

Patients and methods: Data on patients with mUC referred for SBRT within Croatian oncology referral network were retrieved. Study was approved by local ethics committee. All included patients were treated with ICI in two large centers with available follow-up data. SBRT treatments were performed in standalone cancer center which operates within public healthcare network. Endpoints analyzed were prevalence of SBRT use, local control of treated metastases, progression-free (PFS), and overall survival (OS).

Results: From total pool of 80 patients with mUC treated with ICI, 9 patients (11%) received SBRT for 13 oligoprogressive lesions. The primary tumor was located in bladder in 8 patients (88%). Treated metas-

tasis were located in lymph nodes (31%), lungs (15%), suprarenal gland (15%), bones (15%), and cystectomy bed (7%). All patients were receiving ICI during the course of SBRT (first-line and second-line therapy in 2 and 7 patients, respectively). Median number of treated lesions per patient was 1 (range 1-3). The median GTV volume was 11.3 ccm (range 1-168 ccm), the median BED10 value was 62 Gy (range 25-88 Gy). The median follow-up was 17 months (range 6-33 months). Four patients died, 2 are ongoing on ICI therapy. 1- and 2-year local control rates were 100%, and 85%, respectively. SBRT allowed for continuation of ICI in 7 patients (78%). Although small and disbalanced sample allowed no formal subgroup comparison, both PFS and OS were numerically longer in patients treated with SBRT compared to patients that received ICI alone (PFS 17 months vs 11 months, p=0.09; OS 33 months vs 18 months, p=0.1).

Conclusions: In real life, SBRT is rarely used in mUC patients treated with ICI in Croatia, however, when used it may provide excellent local control and durable PFS and OS benefits. Limitations include retrospective nature of study, providers bias, highly selected and heterogenous patient cohort and the lack of toxicity data. Prospective studies are needed to address role of SBRT in mUC patients treated with ICI. Simultaneously, barriers to adopting SBRT in this patient population need to be identified and acted upon.

Keywords: stereotactic body radiation therapy; SBRT; advanced urothelial cancer; immunotherapy; Croatian oncology referral network

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P30 – THE DIAGNOSTIC ACCURACY OF PIVKA-II AND AFP IN DIFFERENTIATING HCC AND NON-MALIGNANT HIGH-RISK GROUPS IN PATIENTS WITH NAFLD RELATED CHRONIC LIVER DISEASE

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Background: Nonalcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease (CLD) and the growing cause of liver cirrhosis and hepatocellular carcinoma (HCC). In 2020 HCC was the sixth most diagnosed cancer and the third leading cause of cancer death worldwide. The aim of our investigation was to investigate the diagnostic accuracy of Protein induced by vitamin K absence-II (PIVKA-II), and alpha-fetoprotein (AFP) in differentiating HCC and non-malignant high-risk (NMHR) groups in patients with NAFLD related CLD as well as to determine their cut-off values.

Materials and Methods: A total of 92 patients, including 16 with HCC and 76 with NMHR (21 with liver cirrhosis and 55 with non-cirrhotic high-risk patients) were prospectively enrolled. Non-cirrhotic high-risk patients were defined by demographic, laboratory and transient elastographic parameter characteristic. In all patients serum levels of AFP and PIVKA-II were analyzed. We investigated the areas under the receiver operating characteristic (AUROC) curves of two biomarkers PIVKA-II, AFP, as well as their combination.

Results: According to our results the levels of both biomarkers were found to be statistically significantly higher in the HCC in comparison to the NMHR group of patients ($p < 0.0001$). Analyzing the optimal cut-off values of both biomarkers for the differentiation of HCC from NMHR, the best cutoff values for PIVKA-II and AFP were 120.6 mAU/mL (90% sensitivity; 86.1% specificity) and 72.5 ng/mL (78% sensitivity; 88.5% specificity), respectively. Serum biomarker PIVKA-II was superior in comparison to the AFP in detecting HCC in NAFLD patients; the AUROC of PIVKA-II (0.902, $p < 0.0001$) vs. AFP (0.820, $p < 0.0001$). However, AUROC curve value was the highest for the combination of PIVKA–II and AFP (0.911, $p < 0.0001$).

Conclusions: Our results show that both biomarkers were significantly higher in NAFLD patients with HCC compared to NMHR NAFLD patients. However, in NAFLD patients PIVKA-II is preferable serum biomarker for HCC detection. Thus, PIVKA-II might have an added value in surveillance of HCC in NAFLD patients. In NAFLD patients the optimal diagnostic approach for HCC detection in everyday clinical practice is combination of PIVKA-II and AFP due to different tumor biology in NAFLD patients.

Keywords: nonalcoholic fatty liver disease; Protein induced by vitamin K absence-II; alpha-fetoprotein

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P31 – THE EXPERIENCE OF ONE CLINICAL HOSPITAL CENTER WITH TOTAL NEOADJUVANT THERAPY AND PATHOLOGIC COMPLETE RESPONSE (PCR) RATES IN RECTAL CANCER

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Introduction: One of the leading cancer-related deaths that occur worldwide is rectal adenocarcinoma. The anatomic distinctions between the rectum and the colon have a substantial impact on the management of rectal cancer. The best treatment for rectal cancer patients is determined through imaging. Magnetic resonance imaging (MRI) enables precise staging of both early and late rectal cancer, as well as reliable response assessment. Concurrent chemoradiotherapy (CRT), surgery, and adjuvant chemotherapy are the standard treatments for locally advanced rectal cancer. Total neoadjuvant therapy (TNT) is an alternate technique that combines CRT with neoadjuvant chemotherapy before surgery with the goal of giving continuous systemic therapy to remove micrometastases. Induction chemotherapy combined with concurrent neoadjuvant chemoradiation for locally advanced rectal cancer may improve pathologic downstaging and influence micrometastatic disease, raise pathologic complete response (pCR) rates, and eventually result in a better prognosis. TNT treatment resulted in a statistically significant increase in pCR rate, as well as improvements in disease-free survival (DFS) and overall survival (OS) when compared to normal chemoradiotherapy, according to a meta-analysis. Furthermore, the TNT treatment was found to be effective in lowering the chance of distant metastases.

Methods: Patients with locally advanced rectal cancer who were diagnosed in 2022 provided the data, which was collected retrospectively. They underwent TNT.

Results: This research included 35 participants, 60% were men and 40% were women. With a maximum age of 76 years and minimum patient age of 50, the average patient age is 64.06 ± 6.4 years. The distance from the anocutaneous border ranged from a minimum of 3 cm to a maximum of 15 cm, with an average distance of 7.74 cm ± 3.23. A relative frequency of 57.1% of patients received long-course radiotherapy (20 patients), compared to 42.9% of patients who received short-course radiotherapy (15 patients). The rectal staging was done using MRI in 52% of patients and computed tomography (CT) in 48% of individuals. We determined that 8 patients, or 22.9% of participants, had pCR, while the remaining respondents had an incomplete response.

Conclusion: Regarding the data and global studies, we note that TNT was associated with a higher chance of achieving a pCR. Our clinical center's research produced good results that are consistent with global statistics and support the idea that this kind of treatment is an excellent choice for these types of patients.

Keywords: rectal neoplasms, neoadjuvant therapy, chemoradiotherapy

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P32 – THE IMPACT OF THE SARS-COV-2 PANDEMIC ON THE EPIDEMIOLOGICAL PICTURE AND CHARACTERISTICS OF COLORECTAL CANCER - A RETROSPECTIVE ANALYSIS OF THE DEPARTMENT OF ONCOLOGY AND RADIOTHERAPY, UH of SPLIT, FOR THE YEAR 2020 IN COMPARISON TO PRE PANDEMIC 2017

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Introduction: Colorectal cancer is the third most common cause of cancer in the world, after lung and breast cancer, while in Croatia is the most common malignant disease. Among the EU members, Croatia ranks ninth in terms of the incidence of colon cancer and a high second place by mortality. Since 2007, Croatia has had a National Colon Cancer Early Detection Program, but the response rate is still very low - 36% (25-52% depending on county and year).[2] Despite the prevention program, approximately 13% of patients in Croatia is initially diagnosed with metastatic disease.[1] According to the results of the CONCORD 3 study[3], Croatia is at the bottom of the five-year survival (48%) compared to some other western countries (up to 71%) in the world.

Methods: A retrospective analysis was conducted at the Clinic of Oncology and Radiotherapy, CHC Split. Patients with newly diagnosed colorectal adenocarcinoma enrolled in the clinic from January 1, 2020 to December 31, 2020 were processed. The data were analyzed using descriptive statistics methods, with the use of Microsoft Excel tools.

Results: A retrospective analysis of the medical history identified 269 patients (compared to 387 in 2017) presented at the multidisciplinary team (MDT) of CHC Split who were diagnosed with colorectal adenocarcinoma in 2020. All patients were presented to the MDT before starting the treatment. The median age of patients was 66 years, and the youngest patient was 22 years old. Patients from other counties who did not undergo the entire treatment/monitoring in our institution were excluded from the analysis. 52 patients (19.3%) were diagnosed in the metastatic stage of the disease, in stage 0 4 patients (1.5%), in stage I 32 (12%), in stage II 91 (34%), and in stage III 88 (33%). In 2 patients, the stage couldn't be precisely determined. There is a significant decrease in the number (81 in 2017 and 52 in 2020) but no percentage wise (20.9% in 2017 and 19.3% in 2020) of patients diagnosed with *de novo* metastatic colorectal cancer compared to the previous analysis from 2017, when 81 of them were detected. Patients diagnosed with metastatic

disease were mostly in good general condition: ECOG 0 status 21 patients (40.3%), ECOG 1 24 patients (46.2%), ECOG 2 7 patients (13.5%), while no patient was ECOG status 3 or 4. 32 (57.7%) patients had a left-sided tumor, while 20 (42.3%) patients had a right-sided tumor.

Conclusion: The results of our retrospective analysis showed a significant decrease in the number of patients compared to previous years. The effect of the smaller number of newly diagnosed patients will be analyzed and the real consequences will be seen, however, the appearance of patients in the later stages of the disease is to be expected.

Keywords: colorectal cancer, SARS-CoV-2, epidemiologic picture, characteristics

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P33 – THE MAGNITUDE OF COVID-19 EFFECT ON MELANOMA DIAGNOSIS, HISTOPATHOLOGIC FEATURES AND STAGE OF THE DISEASE IN UNIVERSITY HOSPITAL OF SPLIT

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Introduction: Due to the COVID-19 pandemic, some planned medical activities have been postponed, for both national directives and out of concern of the patients who were afraid to go to hospitals. Skin cancers, especially melanomas, diagnosed during lockdown also differed from pre-lockdown tumors in several notable ways, such as number of newly diagnosed patients and histopathologic features. The primary tumor thickness (mm), ulceration (%), anatomic localization, and regional lymph node involvements are important elements for determining the melanoma staging and prognosis.

Aim: The aim of this report was to investigate the difference in number of newly diagnosed melanoma patients, histopathological features and melanoma TNM-staging between comparable pre-pandemic (March 2019 until March 2020) and pandemic periods (March 2020 until March 2021).

Methods: We collected the data from hospital clinical and pathohistological databases on the total number of newly diagnosed patients with melanoma in University Hospital of Split. Comparative analyses were performed in a pre-pandemic and a pandemic cohort.

Results: Comparing the first year of the pandemic (N=57) with the same period one year before (N=69), 17,4% decrease of melanoma cases was observed. Cohort analysis showed no differences in the distribution of age and sex. The median age of the melanoma patients in a pre-pandemic cohort was 66 years (29-86), and in pandemic cohort 68 years (31-88). The male gender predominated among melanoma patients. In a pre-pandemic cohort, 63,8% of melanoma patients were man, and in pandemic cohort 68,4%. Cohort analysis showed differences in the primary localization of skin melanoma. In pre-pandemic cohort, primary localization of melanoma were head and neck in 17 patients (25%), trunk in 26 patients (38%), upper extremities in 13 patients (19,1%), lower extremities in 10 patients (14.7%) and unknown primary site in 2 patients (2,9%). In pandemic cohort, primary localization of melanoma were head and neck in 10 patients (17,5%), trunk in 32 patients (56,1%), upper extremities in 8 patients (14%), lower extremities in 5 patients (8,8%) and unknown primary site in 2 patients (3,5%). Cohort analysis showed no differences in the pathohistological subtypes. The most common pathohistological subtypes in both cohorts were superficial spreading subtype (21,7% vs 25,8%), unclassified (21,7% vs 17,5%) and nodular subtype (14,5% vs 17,5%). In pandemic cohort we diagnosed patients with increased tumor thickness and positive lymph nodes. In pre-pandemic cohorts we had more patients with thickness less than 1 mm (40,6% vs 31,6%). We found more patients with tumor thickness between 1 to 2 mm (17,5% vs 4,3%) and more than 4 mm (25% vs 20%) in pandemic. Accordingly, in pandemic cohort we found more patients with positive lymph nodes then in pre-pandemic (22,9% vs 5,9%), and more patients with initially metastatic disease (22,8% vs 15,9%). We did not observed any differences in presence of ulceration among the studied cohorts (26% vs 28%).

Conclusion: In the analysis conducted in University Hospital of Split, we observed a marked decrease of newly diagnosed melanoma patients in the first year of the pandemic compared to the same period before the pandemic. We observed increased tumor thickness, more patients with lymph nodes involvements and initially metastatic disease in post-lockdown period. These findings may be the result of delays in diagnosis due to the disruptions in routine dermatologic and oncologic care during Covid-19 pandemic. The further analyses are needed to fully understand the impact of the Covid-19 pandemic on melanoma outcomes.

Keywords: melanoma, diagnosis, TNM-staging, histopathologic subtype, Covid-19 pandemic

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P34 – TRANSITION TROUGHOUT THE TREATMENT LINES AND THE OUTCOMES OF METASTATIC BILIARY TRACT CANCERS AT THE DEPARTMENT OF ONCOLOGY AND RADIOTHERAPY, UNIVERSITY HOSPITAL OF SPLIT DURING 2019-2021 - A RETROSPECTIVE ANALYSIS.

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Introduction: Tumors of the biliary tract (BTC - biliary tract cancer) are a group of tumors that are diagnosed, in most of the cases, in the advanced and metastatic phase of the disease, when therapeutic options and results are modest. Patients in an advanced stage of the disease have a poor prognosis and overall survival often does not exceed 12 months. Knowledge about the effectiveness of second and subsequent lines of treatment is limited. Unfortunately, due to the worsening of the patient's general condition, after the failure of the first line of treatment, symptomatic supportive therapy often remains the only option.

Methods: A retrospective analysis was conducted at the Department for Oncology and Radiotherapy KBC Split from January 1, 2019, to December 31, 2021. Patients with newly diagnosed metastatic cancer of the biliary tract were included. The data were analyzed using descriptive statistics methods, with the use of Microsoft Excel tools.

Results: By retrospectively analyzing the medical history of patients diagnosed with invasive carcinoma of the biliary tract in our center from 2019 - 2021, 31 patients were identified in the metastatic phase of the disease. The median age at the time of diagnosis was 70 years (95% confidence interval (CI 66.2-73.8). The median OS was 10.20 months (95 confidence interval (CI) 7.71-14.09). The most frequently prescribed treatment protocol in the first line was CG (cisplatin/gemcitabine), n=19 (61%). In patients with a slightly worse general condition, monotherapy with gemcitabine was prescribed, n=5 (16%). The Multidisciplinary tumor board decided to prescribe symptomatic supportive therapy for 7 (23%) patients. The median number of cycles in the 1st line was 6 (95% CI 4.37-6.31). At the first evaluation of the treatment effect, 1 patient (3%) achieved a partial response, stable disease was established in 6 (19%), disease progression occurred in 11 (35%), and 3 (9%) patients died. About a one third of the patients received second-line treatment (n=10, 32%). The CAPOX/FOLFOX protocol was most often prescribed (n=6, in 50% of SD), and in those with a slightly weaker general condition, monocapecitabine (n=4, in 0% of SD).

Conclusion: The results of our retrospective analysis showed a significant decrease in the number of patients in later lines of treatment and overall survival of 10.2 months, which is in accordance with previously published studies. With establishment of new targeted therapy options as a treatment options precision oncology principles should be established and diagnostic and treatment should be available to majority of patients undergoing chemotherapy. Obviously, there is a need for further research regarding management strategies for patients with biliary tract cancers.

Keywords: biliary tract cancer, chemotherapy, treatment outcome

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P35 – TREATMENT OF PATIENTS WITH HEPATOCELLULAR CARCINOMA - EXPERIENCE OF THE DEPARTMENT OF ONCOLOGY AND RADIOTHERAPY, UNIVERSITY HOSPITAL OF SPLIT

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Background: Liver cancer is the sixth most common cancer worldwide and the third most common cause of cancer mortality in 2020. There were more than 900,000 new cases of liver cancer in 2020. The number of new cases of liver cancer is predicted to increase by 55% between 2020 and 2040.

Hepatocellular carcinoma (HCC) contributed to 80% of the world total liver cancer burden. In the latest years, progresses in the management of HCC, including incorporation of new drugs in the treatment of advanced HCC, have certainly improved patients' survival rate.

In this work we present the real world results of treatment of patients with hepatocellular cancer at the Department of Oncology, University Hospital of Split.

Methods: The analysis included all patients with hepatocellular carcinoma who were treated at the Department of Oncology, University Hospital of Split, in the period from January 1st, 2019 to December 31st, 2022. A retrospective analysis of data collected from the patients' medical histories was performed. Data collection and processing was performed using Excel 2007, Microsoft corp. and ORIGIN 2016, OriginLab Corporation.

Results: In the observed period a total of 84 patients were treated, 76 men and 8 women. The median age was 68.

Stage of disease (TNM) at diagnosis was as follows: 5 patients (6%) had stage II, 28 patients (33%) had stage III, while 51 patients (61%) had stage IV. A total of 67 patients (80%) were histologically diagnosed. At diagnoses 31 patients (37%) had AFP value ≥ 400.

Median overall survival (OS) of patients with stage II was 34.5 months, with stage III 12.4 months, with stage IV 4.9 months. OS medians according to Child Pugh score were: A 9.6 months, B 3.8 months, C 2.9 months.

Breakdown of patients in the first-line treatment: only symptomatic supportive therapy - 28 patients (33%), sorafenib - 18 patients (21%), TAE/TACE - 13 patients (15%), surgery - 10 patients (12%), atezoli-

zumab + bevacizumab - 8 patients (10%), durvalumab + tremelimumab - 3 patients (4%), transplantation - 4 patients (5%).

Median OS of patients whose treatment initiated with surgery was 26.4 months, while of those whose treatment started with TAE/TACE was 20.1 months. Patients who received sorafenib in first-line treatment had median PFS of 3 months and median OS of 8.5 months. Median OS of patients who received only symptomatic supportive therapy was 4.1 months.

A total of 39 patients (46%) received one line of systemic treatment, while 7 patients (8%) received two lines of systemic treatment. For patients who received atezolizumab + bevacizumab (9 in total) and for patients who received durvalumab + tremelimumab (4 in total) the OS medians are still not reached.

At present, 67 patients (80%) have died. Median overall survival of all patients was 7.7 months.

Conclusion: The results of the treatment of patients with hepatocellular carcinoma in our department are quite poor. One of the possible reasons lies in the fact that a great majority of the patients were diagnosed in an advanced stage of the disease. To evaluate a possible positive impact of the implementation of new systemic treatment modalities a longer follow-up is needed. These results emphasize the need for raising awareness about this disease and for improvements in health care system in order to obtain better primary prevention and disease diagnose at earlier stages.

The weaknesses of this analysis are its retrospective nature and small number of patients.

Keywords: hepatocellular carcinoma; systemic treatment

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