POSTER PRESENTATIONS

P1 – REVIEW OF SECOND PRIMARY TUMORS IN PATIENTS WITH HEAD AND NECK CANCER IN UNIVERSITY HOSPITAL CENTER OSIJEK FROM 2017 TO 2021

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Introduction: Patients with head and neck squamous cell carcinoma (HNSCC) are at increased risk for the development of a second primary malignancy (SPM), which is defined as a second malignancy that presents either simultaneously or after the diagnosis of an index tumor. A synchronous SPM is diagnosed simultaneously or within six months of the index tumor, while a metachronous SPM is diagnosed greater than six months after the index tumor. SPMs need to be distinguished from local recurrences or metastasis of the primary tumor. SPM represents the second leading cause of death in patients with HNSCC. One-quarter to one-third of deaths in these patients are attributable to SPM, highlighting the importance of SPM in the successful management of HNSCC.

Case report: The risk of second primary malignancy (SPM) in patients who have had a head and neck squamous cell carcinoma (HNSCC) is significantly increased compared with the age-matched general population. This increased risk is largely restricted to cancers of the aerodigestive tract and remains relatively constant over time after the initial diagnosis.The concept of field cancerization has been used to explain the occurrence of second primary malignancies (SPMs).The classic view of the term "field cancerization" hypothesized that large areas of head and neck mucosa are affected by carcinogen exposure, resulting in a wide field of premalignant disease that gives rise to multiple independent primary tumors. In University Hospital Center Osijek database of oncologic patients,from 2017 to 2021 we had 412 patients with HNSCC,from which 11 had second primary malignancy located in lung.8 from 11 patient had locally advanced disease and other 3 had metastatic disease of lung.

Conclusion: Regular follow-up after treatment of an initial head and neck cancer is mandatory to identify recurrent disease and a potential SPM and to look for evidence of recurrent disease from the index cancer. As an example, in our review of 11 patients with SPM, nearly all were asymptomatic and the SPM was detected on routine examination and investigations.Although the risk of locoregional recurrence from the original tumor decreases over time, continued surveillance is needed because the increased risk of a second primary tumor can be very extended.

Keywords: head and neck squamous cell carcinoma (HNSCC); Second primary malignancy (SPM); Surveillance

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P2 – ASSESSMENT OF CUTANEOUS TOXCITIY IN CANCER PATIENTS TREATED WITH CDK 4/6 INHIBITORS AND ENDOCRINE THERAPY ACCORDING TO PATIENT-RELATED OUTCOMES AT THE UNIVERSITY HOSPITAL FOR TUMORS

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Cyclin-dependent kinases 4/6 inhibitors (CDKi), abemaciclib, ribociclib, and palbociclib, along with endocrine therapy are standard of care in patients with hormone receptor-positive and human epidermal growth factor receptor 2-negative advanced breast cancer. This specific therapy improves treatment outcomes for this defined population adjacent to a manageable toxicity profile. As stated in the summary of product characteristics (SmPC) for particularly drug, ribociclib, or palbociclib, skin and subcutaneous tissue disorders are reported as very common. Recently, there is emerging information from real-world data and cutaneous adverse effects due to this specific treatment.

The objective of this analysis was to evaluate the occurrence of skin toxicity rash reported as an adverse event by the patient in patient-reported outcomes (PROs) and the European Organization for Research and Treatment of Cancer Quality of life Questionnaire - BR23 (EORTC-QLQ- BR23).

We conducted reports of patients with advanced hormone receptor-positive, human epidermal growth factor receptor 2-negative breast cancer who received a CDKi ribociclib or palbociclib, in combination with endocrine therapy, at any line of treatment, treated at Division of Medical Oncology, University hospital for tumors, Zagreb. Observed patients had to complete at least one therapy cycle and fill in the previously mentioned questionnaires. Data from 187 patients treated from 08/2018 to 12/2020 at the Division of Medical Oncology with palbociclib or ribociclib and endocrine therapy were eligible for a detailed analysis. Around 65% of the treated and observed population had reported rash or skin problem as an adverse event. Due to skin toxicity, one patient discontinued treatment.

In conclusion, this analysis of real-life clinical practice has asserted that cutaneous toxicity is prevalent in this observed population also announced the requirement for enhanced compassion of symptoms experienced by patients on this specific treatment.

Keywords: CDKi, cutaneous toxicity, rash

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P3 – ASSOCIATION BETWEEN PRETREATMENT NEUTROPHIL-TO-LYMPHOCYTE RATIO AND OUTCOME OF PATIENTS WITH METASTATIC RENAL CELL CARCINOMA TREATED WITH NIVOLUMAB – A SINGLE INSTITUTION ANALYSIS

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Introduction: Biomarkers to personalize treatment of metastatic renal cell carcinoma (mRCC) remain elusive and a high unmet need. Presence of systemic inflammation, measured by neutrophil-to-lymphocyte ratio (NLR), portends poor prognosis in many malignancies. It has been previously shown that NLR is prognostic for clinical outcome in mRCC patients treated with tyrosine-kinase inhibitors. Data on the respective prognostic role of NLR in patients with mRCC receiving immune check-point inhibitors are conflicting. The aim of this study was to assess association between pretreatment NLR and clinical outcome in patients receiving nivolumab as second line therapy for mRCC.

Patients and methods: We retrospectively reviewed patient records using locally maintained kidney cancer clinical registry. Forty-two patients who received second line nivolumab following progression on tyrosine kinase inhibitor therapy between 2018 and 2021 were identified. NLR was determined from complete blood count as part of baseline blood work before initiation of nivolumab therapy. Therapy response assessment was done using iRECIST. Optimal discriminatory NLR cutoff point associated with clinical outcomes was determined by log rank test. Univariate analysis of progression-free survival (PFS) and overall survival (OS) was performed using Cox proportional regression model and Kaplan-Meier method.

Results: Baseline NLR was available for 34 patients (81% of all patients who received nivolumab therapy). Median age was 63 years. According to IMDC criteria, 6 patients (18%) were at favorable-risk, 18 (53%) were intermediate-risk and 10 (29%) had poor-risk features. One-year PFS and OS were 42% and 60%, respectively. Median baseline NLR was 2.4, with a range of 0.7-11.8. Optimal NLR cutoff point that discriminates patient outcomes was identified as 4.4. The median PFS was 3 months for patients with high NLR (≥4.4) and 12 months for patients with low NLR (<4.4), with associated HR of 3.1 (95% CI 1.2-8.5, p=0.02). Correspondingly, the median OS was 4 months for patients with high NLR (≥4.4) and was not reached for patients with low NLR (<4.4), with associated HR of 8.9 (95% CI 2.0-39.0, p=0.004).

Conclusions: Pre-treatment NLR has strong prognostic value in patients with mRCC receiving second line nivolumab. Patients with baseline NLR equal or higher than 4.4 are more likely to fail nivolumab therapy. In addition to IMDC risk group, NLR should also be regularly calculated and noted for every patient with aRCC. Finally, prospective validation of NLR as predictive marker of immunotherapy outcome is warranted.

Keywords: kidney cancer, renal cell carcinoma, immune check-point inhibitors, biomarkers, neutrophil-to-lymphocyte ratio

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P4 – ASSOCIATIONS OF TILS COMPONENTS CD8, CD4, PD-L1, CTLA4 AND FOXP3 IN TRIPLE NEGATIVE BREAST CARCINOMA WITH THE CLINICOPATHOLOGICAL PROGNOSTIC FACTORS

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Background: Triple-negative breast cancer (TNBC) has the worst prognosis and the highest immunogenic potential of all breast cancer subtypes. The tumour microenvironment (TME) of TNBC consists mostly of tumour-infiltrating lymphocytes (TILs), tumour-associated macrophages and dendritic cells. TILs are involved in host immunity against tumour cells through the activation of tumour-specific CD8+ cytotoxic T cells. However, there are opposing data about the prognostic value of TILs in TNBC. Programmed cell death receptor ligand 1 (PD-L1) from immune or tumour cells binding programmed cell death receptor 1 (PD-1) disable the effector role of CD8 T cells. Therefore, antibodies that block the target in the PD-1 signalling pathway elicit a stronger immune response. Cytotoxic T lymphocyte-associated protein 4 (CTLA-4) mediates immunosuppression and it is expressed in tumours on infiltrating Tregs, activated CD4+ T cells, exhausted T cells and tumour cells. In tumours with high TILs, PD-L1 and CTLA-4 blockades are more effective.

Methods: We have performed a comprehensive IHC analysis of all major TIL components (CD8, CD4, FOXP3 Tregs) as well as inhibitory molecules PD-L1 and CTLA4) in a superficial (invasive tumour front, ITF) and deep tumour layer of TNBC, and compared it with established clinicopathological and prognostic parameters. Clinical data and surgical tissue samples from 68 TNBC patients who underwent initial surgery were included in the analysis and 36 control samples from benign breast tissue biopsies.

Results: Several statistically significant associations between the TILs status of TNBC patients and the established prognostic factors were observed. In the ITF, the proportion of TILs and CD8+T cells were increasing toward second pathological T status (pT2), and decreasing thereafter toward higher pT status (P=0.017, P=0.021, Chi-square test). Similar trends for both variables were observed in association with anatomic (P=0.057, P=0.050, Chi-square test) and prognostic (P=0.059, P=0.048, Chi-square test) stages of the disease. Furthermore, the increase of CD8+T cells at ITF was statistically correlated with the increased expression of PDL-1, CTLA-4, FOXP3 and CD4+T cells (N=65, rho 0.31, P=0.011; N=65, rho 0.40, P<0.001; N=61, rho 0.32, P=0.012; N=66, rho 0.40, P<0.001).

Conclusion: The TILs dynamic in relation to the stage of the disease, observed in the ITF, suggests that commencing checkpoint inhibitors immunotherapy in the earlier stages of the disease may be more effective, as compared to current clinical practice.

Keywords: triple-negative breast cancer, tumour infiltrating lymphocytes, immunohistochemistry

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P5 – BREATHING EXERCISE IMPACT ON QUALITY OF LIFE WITH LUNG CANCER PATIENTS

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Introduction: Lung cancer patients have difficulties in breathing, witch, among other, leads to appearance of fatigue and reduced functioning within daily life activities, directly impacting on overall quality of life. By induction of specific breathing exercise in those patients we can decrease these types of difficulties as well to prevent reduction of patient general condition status. Indirectly, with improvement of patient's subjective health experience there is a potential improvement of self-assessed quality of life.

Goal: Examining breathing exercises effects on objective changes in oxygen supply process Examining breathing exercise effects on self-assessed health.

Method: Participants were divided within 2 groups. Each group contained 12 up to 14 participants during ongoing radiotherapy treatment. First group performed exercise two times a day during 20 minutes under supervision of physiotherapist. Second group performed exercises at home with similar schedule. Measure instruments were quality of life questionnaire, self-assessed health and fatigue, exhalation length, holding of breath, breathing range, stairs-climbing fatigue test.

Results: Correlation between variables of the examined groups show that there is no significant statistical difference in achieved results, but there is a significant statistical indicator of increase experimental group self-assessed health. Perceived signs of illness such as chest pain, or shoulder pain have meaningful impact on self-assessed health and quality of life within experimental group, as well as coughing. Furthermore, holding of breath is significant for participants in control group, thus the stairs climbing is significant for both groups of participants, slightly higher within control group.

Conclusion:: Breathing exercises have a positive impact on daily life activities with lung cancer patients, through increasement of oxygen entry. Self-assessed health is one of many types how to evaluate positive exercise impact on everyday life, but in correlation with quality of life it can be interpreted as meaningful for those who suffer from lung cancer.

Keywords: lung cancer, breathing, exercise

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P6 – CERVICAL CANCER IN PREGNANCY - A CASE REPORT

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Introduction: Cervical cancer is the most common gynecological cancer in women of reproductive age.

It most often occurs as a final result of human papilloma virus (HPV) infection with high risk oncogenic types (predominantly 16 and 18). Although rare in pregnancy, in recent years, there has been an increase in the incidence of this malignancy in pregnancy due to the increased number of old age pregnancy. The treatment of cervical cancer during pregnancy is related to many factors, such as tumor size, histological type, lymph node involvement, gestational age ant the patient's desire to preserve the pregnancy.

Patient report: In November 2020 a 32-year-old pregnant woman came to the Department of Gynecological Oncology, University Hospital Centre Zagreb, for a second opinion due to diagnosed cervical cancer in the 16th week of pregnancy.

In an external institution, to which she was referred by a general gynecologist dut to bleeding in pregnancy and suspected pap smear findings, colposcopy and biopsy were performed and a diagnosis of cervical adenocarcinoma was made. According to the radiological findings termination of pregnancy and radical surgery were suggested as treatment option in that institution.

By the desire of the pregnant patient and her husband to maintain the pregnancy, an additional diagnostic processing was done in our Department of Gynecological Oncology.

Gynecological examination findings were: exophyte 2-3 cm on the anterior lip of the cervix, smaller exophyte up to 1 cm on the posterior cervical lip and ulcerated endocervix. Vaginal fornicis end mucosa were free of tumor. Rectal examination findings: right parameter free, left parameter with suspicious initial infiltration but examination was difficult due to a pregnant uterus.

MRI of the pelvis: cervical neoplasia CC lenght 2 cm in the distal part of the cervix. The whole cervix is of altered structure and signal intensity suspected of neoplasia. No sure signs of parametrial infiltration. Rectum, bladder and vagina are without signs of infiltration. There are no enlarged lymph nodes.

The disease is according to FIGO classified as IB2 stage, and due to the guidelines from the literature, neoadjuvant chemotherapy with Paclitaxel and Carboplatin protocol (4 cycles) is indicated and after that termination of pregnancy by Caesarean section with radical surgery.

The patient was aware of all the consequences and successes of the treatment and agreed to the proposal. Chemotherapy was started at the 21st week of pregnancy according to amenorrhea. Ultrasound pregnancy was 3-4 days older. The patient received 4 cycles of neoadjuvant chemotherapy Paclitaxel (175 mg/m2) and Carboplatin (AUC 5) at standard intervals of 21 days. She conducted the therapy properly, without major side effects and without delays. During chemotherapy, ultrasound monitoring of fetal development was performed every 3 weeks. All control findings showed orderly dynamics of pregnancy development. Before the 3rd cycle of chemotherapy, a control MR of the pelvis was performed, which showed regression of the primary neoplastic process of the cervix with a significant reduction in the cellularity of the process. Gynecological examination also showed a significant regression of the primary tumor. The fourth cycle of the chemotherapy was administered in the 30th week of pregnancy according to amenorrhea, ultrasound 31st week.

At the end of the 33rd week of pregnancy, she was admitted to the Clinic for the planned procedure. At 34th week, surgery was performed: Lap.med. inf.; Saectio caesarea; Hysterectomia radicalis sec. Rutledge III; Lymphadenectomia pelvis; Drainage abd.

Cesarean section gave birth to a live female newborn 2280 g/48 cm, A.S. 8/9.

The pathohistological findings were: post chemotherapy status; carcinoma adenosquamosum cervicis uteri (0/14 lymp.nodes; size of tumor 2.5x1.7 cm; LVSI negative; negative surgical edges). Pathohistoligical description: histologically tumor is partly composed of solid clusters of atypical squamous cells and partly of atypical glandular formations lined with atypical epithelial cells. On a smaller part of the surface a multilayered squamous epithelium of disturbed cell distribution and maturation can be seen with mitotic activity in more than 2/3 of the thickness of the visible layer. Immunohistochemically in the altered squamous epithelium as well as in the cells of both components of the tumor, the reaction is diffusely positive for p16, in the squamous part of the tumor for p63, while SMA in both components of the tumor is negative. ER is positive in 30% tumor cells and PR is negative. Isthmus and dparameters are without signs of malignancy, the endometrium is decidually altered. Focal decidualization without signs of malignancy in the adnexa. WHO Tumor Classification, 2020: Adenosquamous cervical cancer (HPV-related).

After the operation no additional treatment was indicated but regular oncology controls.

The patient is properly monitored. Now, exactly one year after the completition the treatment, all control findings are clear, without signs of disease recurrence.

The child is also great, developing according to age.

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P7 – CLINICAL CHARACTERISTICS OF BRCA MUTATED PATIENTS WITH HIGH GRADE SEROUS OVARIAN CANCER – SINGLE CENTER EXPERIENCES FROM UNIVERSITY HOSPITAL OF SPLIT

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Introduction: The prevalence of germline and somatic mutation in the BRCA1 and BRCA2 genes varies among different subtypes of ovarian cancer, which is a very heterogeneous disease. It is highest in high grade serous subtype which was reported up to 20-25%. Since the presence of this mutation is related to the development of the malignant disease (breast cancer, prostate cancer, pancreatic cancer, melanoma), it is interesting to investigate their occurrence and family burden of malignant disease.

Methods: Data from the medical history of 56 patients with BRCA mutated ovarian cancer treated and followed at the Department of Oncology and Radiotherapy in Split, in the period from June 1, 2016 to December 31, 2021, were retrospectively analyzed.

Results: The median age of patients with BRCA mutated serous ovarian cancer was 54 years (range 38-76). The primary site of the disease is most often the ovary, in 41 patients (76%). The disease was mostly diagnosed in FIGO stage III (44 patients, 78,6%) and stage IV (5 patients, 12,5%). The menopausal status of BRCA mutated patients at the time of diagnosis was next: 7 patients had premenopausal (12,5%), 8 patients had perimenopausal (14,3%) and 41 patients had postmenopausal status (73,2%). The vast majority of patients, 46 of them (82%), had a positive family history of malignancies. Breast cancer was present in relatives of 30 BRCA mutated patients, ovarian cancer in relatives of 9 patients, prostate cancer in relatives of 4 patients and pancreatic cancer in a relative of 1 patient. Fifteen patients with ovarian cancer developed synchronous/metachronic breast cancer and one patient developed pancreatic cancer. Breast cancer in most patients (12 patients, 80%) was diagnosed and treated before diagnosis of ovarian cancer. A patient with pancreatic cancer was diagnosed 6 years after ovarian cancer. The condition for BRCA testing for ovarian recurrence was platinum sensitivity, so it was confirmed in all subjects with relapse. From June 2021, PARP inhibitors are also indicated in first-line setting, so BRCA testing becomes reflex, immediately after diagnosis of disease. During the study period, 30 patients has been treated or is still being treated with olaparib in maintenance therapy after responding to platinum-based chemotherapy administered to platinum-sensitive relapse, and 6 patients receive olaparib in 1st line of treatment, also after responding to the 1st line TC protocol.

Conclusion: The family burden of malignant disease in the studied group of BRCA mutated ovarian/fallopian tube cancers is high and amounts to 82%. The incidence of hereditary breast and ovarian cancer in our study group was recorded in 15 patients (27%).

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P8 – CLINICAL CHARACTERISTICS OF PATIENTS WITH HEREDITARY BREAST AND OVARIAN CANCER – SINGLE CENTER EXPERIENCES FROM UNIVERSITY HOSPITAL OF SPLIT

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Background: Hereditary breast and ovarian cancer syndrome (HBOC) is a well-described hereditary cancer predisposition syndrome caused by mutations in BRCA1 and BRCA2 genes. The lifetime risk for women with BRCA1 mutations is estimated to be about 72% for breast cancer and 44% for ovarian cancer. The corresponding estimates for BRCA2 are 69% and 17%, respectively. However, synchronous or metachronous breast cancer and ovarian cancer diagnoses have been documented also in the absence of a germline BRCA mutation, suggesting other common etiological factors such as hormonal and reproductive aspects and mutation of other genes involved in tumor suppression.

Methods: Data from the medical history of 15 patients with high grade serous ovarian cancer and breast cancer at the Department of Oncology and Radiotherapy in Split, in the period from June 1, 2016 to December 31, 2021, were retrospectively analyzed.

Results: The median age of patients with BRCA mutated high grade serous ovarian cancer at the time of diagnosis was 56 years (range 41-67). The disease was mostly diagnosed in FIGO stage III (14 patients, 93%). At the time of ovarian cancer diagnosis 2 patients had premenopausal (13%), 3 patients had perimenopausal (20%) and 10 patients had postmenopausal status (67%). The vast majority of patients, 13 of them (87%), had a positive family history for malignancies. Breast cancer was present in relatives of 9 patients, ovarian cancer in relatives of 2 patients and prostate cancer in relatives of 2 patients. During the study period, 5 patients have been treated or are still being treated with olaparib in maintenance therapy after responding to platinum-based chemotherapy administered to platinum-sensitive relapse, and 2 patients receive olaparib in 1st line of treatment, also after responding to the 1st line TC protocol.

The median age of patients with BRCA mutated breast cancer in the time of diagnosis was 53 years (range 33-67). Breast cancer was diagnosed and treated before diagnosis of ovarian cancer in 12 patients

(80%). Four patients developed bilateral breast cancer. All patients were diagnosed with local or locoregional disease: 5 patients had stage IA (T1 N0 M0), 5 patients stage IIA (T2 N0 M0), 3 patients stage IIB (T2 N1 M0) and 2 patients stage IIIA (T1 N2 M0 and T2 N2 M0). At the time of breast cancer diagnosis, 7 patients had premenopausal (47%) and 8 patients had postmenopausal status (53%). Fourteen patients received adjuvant chemotherapy (mostly FEC and ACTdd protocol), 9 patients received adjuvant local/locoregional radiotherapy and 9 patients adjuvant hormonal therapy.

At the end of the analysis, 7 patients were alive without disease, 4 patients were alive with the disease, 3 patients died due to ovarian cancer and one was lost in follow-up. So, median overall survival for our study population has not been reached.

Conclusion: Experience from study confirm that the clinical characteristics of our patients with hereditary breast and ovarian cancer are specific to this syndrome. Our data may be useful to plan and carry out surveillance programs, preventive measures, timely diagnostics and personalized treatment.

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P9 – CLINICAL OUTCOMES OF PATIENTS WITH METASTATIC NON-SMALL CELL LUNG CANCER TREATED WITH PEMBROLIZUMAB MONOTHERAPY OR IN COMBINATION WITH CHEMOTHERAPY – UPDATED ANALYSIS OF A SINGLE CENTER EXPERIENCE

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Introduction: Pembrolizumab monotherapy is nowadays considered as the standard treatment for patients with metastatic non-small cell lung cancer (NSCLC) who have high expression of programmed-death ligand 1 (PD-L1>50%), whilst for patients with PD-L1 expression of 1-49% standard of care is pembrolizumab in combination with chemotherapy. The aim of this study was to assess clinical outcomes of both patient populations treated in a single center.

Patients and methods: Records of patients with NSCLC who had positive (1-100%) PD-L1 expression treated at our Institution from January 2018 to January 2022 were retrospectively reviewed. Progression-free survival (PFS) and overall survival (OS) were calculated using Kaplan Meier method.

Results: In total, 89 patients were treated with pembrolizumab: 38% of patients were female, and 62% were male; 57 patients had PD-L1 expression greater than 50% and they were treated with pembrolizumab monotherapy. Thirty-two patients with PD-L1 expression of 1-49% were treated with pembrolizumab in combination with platinum- based chemotherapy. Median follow up for the cohort with PD-L1 expression > 50% was 6 months (range 0-35 months). Number of progression events for this cohort was 17 (30%). The 2-year disease control rate was 51%. The median PFS for this cohort was not reached. For the cohort with PD-L1 expression 1-49%, median PFS was 12 months (95%CI 6-19 months), with 6 patients experienced progression (19%).

Conclusion: The results of treatment with pembrolizumab in monotherapy or in combination with platinum-based chemotherapy for patients with NSCLC at our Institution are mostly in keeping with real-world data reported in the literature. Given relatively short follow-up, we are yet unable to make conclusions on differential outcomes of these two patient populations.

Keywords: pembrolizumab, advanced NSCLC, chemotherapy, immunotherapy

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P10 – COLLABORATION OF DALMATIAN HOSPITALS: IMPACT OF COVID-19 ON THE REPORTED INCIDENCE OF BREAST CANCER IN THE FIRST WAVE OF THE PANDEMIC IN DALMATIA

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Introduction: Breast cancer is the most diagnosed carcinoma in the world[1]. The incidence of breast cancer is on the rise. In breast cancer, early detection and initiation of treatment showed significant benefits in survival[2]. At the time of the pandemic and lockdown breast cancer patients had limited access to

the diagnosis and treatment. Several observational studies reported a temporary shutdown of the early detection program, and in countries where there was no shutdown of the program, there were almost twice as many patients who did not respond to the calls for the preventive examinations [3],[4]. Official data for the Republic of Croatia for the period 2020-2022. are expected from 2024 to 2026. (data based on the current practice of publishing a newsletter). The collaborative study aims to show the effect of pandemic and epidemiological measures on the number of newly registered patients with invasive breast cancer in three Dalmatian general hospitals and the Clinical Hospital Center Split.

Methods: A retrospective observational study was conducted at the Clinic for Oncology and Radiotherapy, Clinical Hospital Center Split, Department of Oncology General hospital (GH) Dubrovnik, Department of Oncology GH Šibenik, and Department of Oncology and nuclear medicine GH Zadar. The analysis includes medical histories of newly reported patients with breast cancer in the period from 1 January 2018 to 31 December 2020

Results: The analysis covered three years. A total of 2297 medical histories were reviewed. The number of patients with newly diagnosed breast cancer was 754 (2018), 818 (2019) and 707 (2020). The most significant decrease in the number of patients was observed in the Clinical Hospital Center Split, while the number of patients with breast cancer maintained the trend in the areas gravitating to general/county hospitals. The largest decline in the number of patients was recorded in the "lockdown" months, without the "rebound" phenomenon in later months.

Conglusion: The number of newly diagnosed patients with breast cancer was declining in 2020. in relation to 2019. This decrease is 14% of the absolute number, which is in significant contrast to the expected increase in the incidence of breast cancer in Croatia and the world. The COVID 19 pandemic and consequent lockdown limited patients 'access to health care at the Clinical Hospital Center. Epidemiological measures, as well as the reluctance of patients described in other studies to go for examinations, reduced the number of newly diagnosed patients with breast cancer. The number of patients did not change significantly in the area of general hospitals in Dalmatia.

The strength of the research is in the coverage of the geographical region, general hospitals in Dalmatia, and the Clinical Hospital Center Split, and it represents a unique collaboration of oncological institutions and a collection of oncological and epidemiological data on breast cancer incidence, while national-level data are still expected. More precise data on the stages of the disease, the condition of patients at diagnosis are currently being collected and will be published in later publications.

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P11 – COMBINATION OF THE GEMCITABINE AND PACLITAXEL IN THE SECOND LINE TREATMENT SETTING AFTER PROGRESSION TO FOLFIRINOX - A SINGLE INSTITUTION ANALYSIS AT THE DEPARTMENT OF ONCOLOGY AND RADIOTHERAPY, UNIVERSITY HOSPITAL OF SPLIT

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Background: Pancreatic cancer accounts almost for as many deaths as newly diagnosed cases with significant proportion of patients diagnosed with metastatic disease where survival rates are devastating (1). Golden standard first line treatments in such cases are two chemotherapy regimens, one with oxaliplatin, 5-fluorouracile and irinotecan (FOLFIRINOX) and one with combination of gemcitabine and nab-paclitaxel (2,3). Even though, they were never head to head compared, these two regimens are, according to the reviews and real world data, equally effective in the first line setting (4). Furthermore, their sequencing in the first and second line setting have yielded the same results regarding the order and recent findings have proved efficacy of the second line treatment, particularly combination of gemcitabine and nab-paclitaxel (5,6). Considering, nab-paclitaxel is not approved for the second line treatment of metastatic pancreatic cancer in Croatia, here we present our results of combination therapy with gemcitabine and paclitaxel after progression to FOLFIRINOX.

Methods: The cross-sectional retrospective study was conducted at the Department of Oncology and Radiotherapy, University Hospital of Split. It included patients who were newly diagnosed with metastatic pancreatic adenocarcinoma from January 1, 2018 to December 31, 2021, who had disease progression to the first line treatment with FOLFIRINOX regimen and who were treated with combination of gemcitabine and paclitaxel. The data were analyzed with methods of descriptive statistics using Microsoft Excel tools.

Results: There were 97 patients in total, out of which 66 (68%) have started with the first line treatment and 6 (6%) patients have refused chemotherapy. At the time of diagnosis treated patients had median age of 67 years (IQR 59-73), median number of metastatic sites was 1 (IQR 1-2) and majority (85%) had ECOG performance status 0 or 1. Median overall survival (OS) for the treated patients was 5,44 months (IQR 3,22-10,22). Median progression free survival (mPFS) for the first line treatment was 2,28 months (IQR 1,05-4,37). In the first line setting, FOLFIRINOX was administered to 27 (41%) patients, out of which 13 (48%) were treated with the second line treatment. There were 24 patients (36%) in total that have started the second line treatment, with mPFS of 2,32 months (IQR 1,26-3,86). Furthermore, 8 (33%) patients out of them were treated with gemcitabine and paclitaxel after progression to FOLFIRINOX, while 16 (67%) patients were treated with other chemotherapy, mostly monochemotherapy, according to the physician's choice and general health of patients. Also, 4 (17%) patients are still receiving the second line treatment, out of which two patients are treated with gemcitabine and paclitaxel. Median PFS of the group treated with paclitaxel and gemcitabine was 2,48 months (IQR 2,17-4,37), while the mPFS for other group was 1,48 months (IQR 0,80-3,50). There was no significant difference regarding the toxicity profiles.

Conclusion: Even though, nab-paclitaxel is not approved as second line treatment in Croatia, our group of patients treated with gemcitabine and paclitaxel after progression to FOLFIRINOX has shown

numerically longer PFS and comparable toxicity profile in comparison to monochemotherapy. In conclusion, our results support potential use of combination of gemcitabine and paclitaxel, especially in the developing countries where nab-paclitaxel is not widely available for the second line treatment of metastatic pancreatic cancer.

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P12 – COMPARISON OF ER AND PR RECEPTOR AND HER2 ANALYSIS BETWEEN CELL BLOCKS AND PATHOLOGY SAMPLES

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Introduction: Breast cancer is still the most common malignancy diagnosed in women in Croatia. With the introduction of screening programs, we diagnose more cases in the earliest stages of the disease. These small lesions are sometimes more accessible by fine-needle aspiration (FNA) than by core biopsy.

Aim: was to determine the reliability of the immunohistochemical status of estrogen and progesterone (ER and PR) and HER2 receptors on cell blocks samples compared to histological sections.

Materials and methods: We analyzed samples of 60 consecutive patients treated at the University Hospital for Tumors, Sestre milosrdnice UHC for breast cancer in 2020. Patients underwent fine-needle aspiration, core biopsy, and surgical procedure. Immunohistochemical expression of ER, PR, and HER2 in samples of FNA was compared to the expression of receptors in histological samples of the same tumors. In the assessment of receptor status, the limit value of positive status for ER is> 1% of nuclear positivity; for PR> 20% positive nuclear positivity, HER2 positivity was complete, strong membrane positivity in> 10% of cells, while partially positive samples were considered HER2-negative.

Results: By comparing cell blocks and histological specimens, we calculated that the diagnostic reliability of cell blocks was 94.7%, positive predictive value 84.6%, diagnostic sensitivity 95.7%, and specificity 95.7%.

Conclusion: In centers with experienced cytologists where FNA cell block technology is available, a diagnostic alternative to core biopsy for tumors smaller than a centimeter may be valid.

P13 – COMPARISON OF PERCUTANEOUS CT-GUIDED MICROWAVE ABLATION AND PARTIAL NEPHRECTOMY IN THE TREATMENT OF T1A RENAL CARCINOMA

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Introduction: An increase in the incidence of early- stage renal cell carcinoma (RCC) lead to the development of percutanoues ablative therapies in patients with comorbidities that contraindicate surgical treatment. Microwave ablation (MWA) has not been introduced into treatment guidelines and is still considered to be experimental. Despite existing literature confirming the efficacy and safety of MWA, there is still a lack of studies that directly compare partial nephrectomy (PN) and percutaneous MWA.

Aim: The aims of this study were to compare local recurrence rates, overall survival, metastasis-free survival and cancer specific survival after percutaneous high-energy CT-guided MWA and PN in the treatment of T1a stage RCC and to compare complication rates and the effect on renal function.

Patients and methods: The retrospective study involved 80 patients with T1a stage of RCC from January 1 st 2015 to June 30 th 2018. Patients who were treated surgically were chosen, according to their tumour size and complexity, to match the patients treated with MWA. All patients were under radiological and clinical follow-up for a period of at least 12 months. The results did not show statistically significant difference between MWA and PN in overall survival, recurrence-free survival, disease-free survival, metastasis-free survival or disease-free survival. Decrease in the glomerular filtration rate was significantly lower after MWA, and a significantly higher complication rate was found after PN compared to MWA.

Results: The hypothesis that MWA has better oncological outcomes compared to PN for T1a RCC has not been proven in our study, however the results suggest equal value of both treatment approaches. It can be concluded that, when compared to the partial nephrectomy as the golden standard, MWA can be used as an equally successful therapeutic tool in small RCCs in patients with severe comorbidities, but also in other patients due to its nephron sparing qualities.

Keywords: renal cell carcinoma, microwave ablation, partial nephrectomy

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P14 – COMPARISON OF RADIOTHERAPY TECHNIQUES – EXPERIENCES OF A CLINICAL HOSPITAL CENTER

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Introduction: Using new techniques of radiation (new for Croatia) in radiotherapy, in regards to previous experiences, we want to present results collected at Clinical hospital centre Osijek.

Aim: Comparison of 2 radiotherapy techniques, three-dimensional conformal radiation therapy (3D CRT) with Volumetric modulated arc therapy (VMAT).

Methods: Retrospectively collected data over a period of 3 years for each technique will be presented in tables and graphs to see if there is a growth trend. The radiotherapy techniques themselves will be compared by showing on dose-volume histograms (DVH).

Results: In a period of 3 years, 2 544 patients were irradiated with 3D CRT technique, while 3 226 patients were irradiated with VMAT technique. Of all the patients, we took only three regions of interest, namely the radiation regions of the stomach, prostate, and lungs. By making a plan for both techniques on the same patient, we provided the same conditions for comparing techniques. A comparison of radiation doses for clinical target volume (CTV), planning target volume (PTV) and organs at risk (OARs) was performed on DVH.

Conclusion: VMAT radiotherapy technique provides better coverage of clinical target volume, planning target volume and saving organs at risk. It is also significantly more sensitive to changes in the volume of organs at risk.

P15 – COMPARISON OF THREE CALCULATION ALGORITHMS FOR POST-OPERATIVE RADIOTHERAPY OF BREAST CANCER

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Introduction: In Croatia, breast cancer makes 11.1% of all cancers and it is the most common diagnosed cancer in females (25%). It is reported that 63% of breast cancer patients require radiotherapy as part of their primary treatment. The quality of radiation therapy depends on the ability to optimize the ratio of tumour control probability and normal tissue complication probability. This ratio is directly related to the absorbed dose distribution and the accuracy of its calculation and delivery. Dose calculation accuracy varies significantly in the presence of tissue inhomogeneities. Motivation for this work was to investigate the influence of three different calculation algorithms on dose distribution in breast cancer irradiation.

Methods and Materials: Retrospective analysis of dose distributions calculated using three different calculation algorithms for fifteen patients requiring post-operative left breast radiotherapy was carried out. Treatment method was whole breast irradiation with total prescribed dose of 5000cGy in 25 fractions. Planning technique was forward IMRT using field-in-field technique. Dose distributions were created in Elekta Monaco treatment planning system (TPS) using Collapsed Cone Convolution (CCC) calculation algorithm following international guidelines. Absorbed dose distributions were calculated so that 100% of prescribed dose covers ≥80% of PTV. Pre-treatment dosimetric verification was performed for each patient.

Dose distributions for fifteen patients were retrospectively recalculated using Monte Carlo (MC) (Elekta, Monaco) and Anisotropic Analytical Algorithm (AAA) (Varian, Eclipse) calculation algorithm and compared to CCC. For all three algorithms, 6MV beam of the same linear accelerator was used. Gantry angles, field number and field shapes were kept constant. Dose distributions were recalculated to achieve the same planning target volume (PTV) coverage with 100% isovolumes in original CCC plan. Parameters related to PTV and OARs were analyzed.

Results and Discussion: The average number of therapy fields was 7.73 per patient. The average coverage of PTV with $D_{100\%}$ was 85.23%. To achieve the same PTV coverage, it was observed that D_{max} increases when using MC (109,64%, p=0.000000) and AAA (107.69%, p=0.000876) as compared to CCC (106.84%). Looking at $D_{95\%}$, lower coverage of 97.49% was obtained using AAA which was shown to be statistically significant different with p=0.035551. Considering absorbed dose to ipsilateral lung, dose increases when AAA is applied, however it is not statistically significant. This difference could be attributed to the fact that MC and CCC algorithms are based on dose-to-medium (D_m) calculation formalism as opposed to dose-to-water (D_w) used by AAA algorithm. No statistically significant difference was found when comparing doses to the heart. Difference between average numbers of monitor units (MUs) was also found to be statistically insignificant.

Conclusion: Retrospective analysis of absorbed dose distributions for 15 patients using three calculation algorithms showed statistically significant difference only in D_{max} and $D_{95\%}$. Differences for other parameters were small and therefore any of these algorithms can be used as an algorithm of choice for

post-operative radiotherapy of breast cancer. However, for AAA, lower PTV dose coverage and higher D_{max} is observed which should be taken into consideration.

Key words: calculation algorithms, absorbed dose distributions, breast cancer radiotherapy

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P16 – COMPREHENSIVE GENOMIC PROFILING (CGP) IN THE UPFRONT DIAGNOSTIC WORKUP OF LOCALLY ADVANCED OR METASTATIC OVARIAN CANCER- A SINGLE INSTITUTION ANALYSIS

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Background: Ovarian cancer ranks seventh both in incidence and mortality among women in Croatia (1). However, due to its obscure clinical presentation, lack of screening methods and consequently high mortality to incidence ratio, ovarian cancer represents a significant burden on the oncological and health care system in Croatia. As precision medicine is evolving, a paradigm shift is happening in the approach to ovarian cancer management with molecular classification and targeted therapy becoming the mainstay of the treatment of locally advanced and metastatic disease (2). Herein we present the results of the comprehensive genomic profiling (CGP) comparing the number of patients opted with targeted therapy with PARP inhibitors after CGP, to the number of patients opted with same treatment after just detecting BRCA 1 and BRCA 2 status. The aim was to set position for the CGP of ovarian cancer in everyday clinical practice.

Methods: The cross-sectional retrospective study was conducted at the Department of Oncology and Radiotherapy, University Hospital of Split. It included patients who were either newly diagnosed with locally advanced or metastatic ovarian cancer from January 1, 2020 to December 1, 2021, and on whose tumors CGP analysis was performed. The analysis was done through FoundationOneCDx for all patients and it was carried out in a Clinical Laboratory Improvement Amendments certified, College of American Pathologists accredited laboratory (Foundation Medicine Inc., Cambridge, MA, USA) (3). The data were analyzed with methods of descriptive statistics using Microsoft Excel tools.

Results: There were 33 patients in total with 5 (15%) of them initially diagnosed with metastatic disease. Median age of patients was 59 (IQR 51.5-65). The vast majority of patients had ECOG (Eastern Coop-

erative status) performance status 0 (94%) and had high grade serous cancer (82%). Also, majority of patients (76%) has received chemotherapy in the neoadjuvant, adjuvant or metastatic setting. Median number of previous lines of chemotherapy for metastatic disease was 0 (IQR 0-1). CGP analysis showed that all patients had at least one genomic alteration (GA), which are separated into clinically relevant (CRGA) with approved targeted therapy in patients' tumor type (on-label) or approved in other tumor type (off-label), or with existing clinical trials available, and into alterations without clinical significance (GAwCS), defined as those without reportable therapeutic or clinical trials options. CRGA had 30 (91%) patients and the most common was TP53 mutation in 25 (76%) patients. GAwCS had 26 (79%) patients with the PRKCI (encodes protein kinase C iota (PKCi)) and TERC (the human telomerase RNA gene) mutations as the most common, in 5 (15%) and 6 (18%) patients respectively. Microsatellite status was determined as stable in all patients and median tumor mutational burden (TMB) was 3 (IQR 1-4), with no patients having TMB≥10.

Median loss of heterozygosity (LOH) was 15.7 (IQR 8.85-21.9), with 15 (45%) patients having LOH ≥16. LOH was not determined for 2 (0.06%) patients. We have found BRCA positive status in 12 (36%) patients and 11 out of those 12 had LOH ≥16 (92%).

Some kind of targeted therapy was opted in 23 (70%) patients. On-label therapy with PARP inhibitors was reported in 17 (52%) patients. Furthermore, targeted therapy without approval but also driven by patients GA was reported in 23 (70%) patients. The CGP-driven therapy was administered to 9 (27%) patients.

Conclusion: Although, CGP is now only a recommendation for patients with ovarian cancer, our results have shown that all patients had at least one GA (4). Furthermore, significantly higher number of women is opted with targeted therapy with PARP inhibitors after CGP (52%), instead of just after determining BRCA status from our group of patients (36%). Thus, we believe that the CGP should be integrated in the diagnostic workup of the locally advanced and metastatic ovarian cancer as a backbone diagnostic tool and could potentially be next step toward more precise approach to individual with significant impact on the outcomes.

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P17 – COVID 19 IMPACT ON REPORTED INCIDENCE OF COLORECTAL CANCER DURING THE FIRST WAVE OF PANDEMIC IN DALMATIA

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Introduction: Since the start of COVID-19 pandemic almost six million people succumbed to the illness, with more that 430 million people infected [1].[2]. To mitigate the spread of the virus, various public health measures were deployed, affecting all spheres of the society, including healthcare in every level, without sparing cancer patients worldwide. The „lockdown" period initiated during the first wave of pandemic limited the access to diagnostics and treatment of colorectal cancer, exposing the vulnerable population of colorectal cancer patients to additional risk[3]. Previous publications report the decrease in number of patients diagnosed with colorectal cancer, in diagnostic procedures, and treatment initiation. Given the fact the incidence of colorectal cancer is in constant rise, these factors hurt not only patients but healthcare system in general [4]. It is estimated that the decrease in diagnostic will be in the range absolute of 5,4-26% [5].

Official records for the period of 2020-2022. published by Croatian Cancer registry are expected between 2024-2026. The goal of this collaboration was to define the effect of epidemiologic measures deployed to contain the virus spread on the number of newly registered colorectal patients in three general hospitals in Dalmatia and the university hospital center in Split.

Methods: This retrospective observational study was conducted at the Department of oncology and nuclear medicine at the General hospital in Zadar, Department of internal medicine at General hospital Šibenik and Department of oncology at General hospital Dubrovnik as well as the Department of oncology and radiotherapy at the University hospital in Split. Analysis included patient history files of patients being registered at the Departments between January 1st, 2018. to December 31st, 2020.

Results:Analysis included a three-years period and consisted of evaluating 1864 patients. The numbers of patients diagnosed with colorectal cancer was 648 (2018), 605 (2019) and 611 (2020).

The most significant drop in 2020 compared to the average of the two preceeding years was observed in the area gravitating the University hospital center (-7,7%), and the General hospital Šibenik (-3%). On the area of Dubrovnik-Neretva County and Zadar County an increase of number of patients was observed (+18% and + 33%, respectively).

Conclusion: Number of newly reported colorectal cancer patients was in slight decline in 2020, compared to the average in the pre-pandemic years. The decline in Dalmatia was -2,5% in absolute, which contrasts with projected incidence of colorectal in Croatia and the world. It is also discordant to the previously published papers.

This unique and thus far the biggest collaboration of oncology institutions in Dalmatia offered a comprised data on incidence of colorectal cancer in real time, while the nationwide (Croatian Cancer registry) data are expected within 2.4 years (based on previous publishing practice).

True impact of the public health measures on patients characteristics, tumor characteristics and disease stage at diagnosis will be reported in the upcoming period.

Keywords: colorectal cancer, incidence, COVID pandemic, Dalmatia, Croatia

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P18 – COVID-19 PANDEMIC IMPACT ON RADIOTHERAPY IN PATIENTS WITH HEAD AND NECK CANCER

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Introduction: The COVID-19 pandemic has a significant impact on the primary, secondary and tertiary levels of the health system. In a low-middle income countries such as Bosnia and Herzegovina, ensuring optimal oncology care was challenging even before the COVID-19 pandemic. Since the beginning of the COVID-19 pandemic, there was a warning of the possible impact of worsening mortality and/or morbidity due to delayed diagnosis and suboptimal treatment.1 The COVID 19 pandemic has impact on reducing the number of patients treated with radiotherapy.2 The aim of our study was to analyze the impact of the COVID-19 pandemic on radiotherapy in a patient with head and neck cancer who were treated with radiotherapy in a tertiary health care facility.

Methods: We analyzed data from the institutional databases for radiotherapy of the Oncology Department at University Clinical Hospital Mostar, Bosnia and Herzegovina. We performed data extraction for patients with head and neck cancer who were treated with primary or adjuvant radiotherapy with or without chemotherapy from January 2018 to December 2021.

Results: A total of 114 patients were treated with radiotherapy for head and neck cancer in the pre-COVID-19 period (2018-2019) and COVID-19 period (2020-2021). There were more patients treated with radiotherapy in the preCOVID19 period, 64 (56%) compared to the COVID19 period, 50 (44%). In the COVID 19 period, the number of patients treated with radiotherapy was reduced by 22% compared to the preCOVID19 period.

Conclusion: A decline innumber of patients treated with radiotherapy in the COVID 19 period was detected. Health system optimization and education of the general population about the negative indirect impact of COVID 19 on the health system, diagnosis and treatment of cancer is needed.

Keywords: COVID-19 Pandemics, Radiation Therapy, Head and Neck Cancer

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P19 – DEVELOPMENT AND IMPLEMENTATION OF 2D RADIOCHROMIC FILM DOSIMETRY METHODOLOGY FOR VERIFICATION OF ADVANCED RADIATION THERAPY TECHNIQUE DELIVERY AS A PART OF IAEA CRO 6019 PROJECT

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Introduction:The most common dosimetry systems for verification of advanced radiation therapy technique delivery are 2D arrays of ionisation chambers/diodes. Their main drawback is relatively low resolution, especially when measuring highly modulated absorbed dose distributions containing numerous irregular fields. In contrast, radiochromic film has superior spatial resolution while retaining absorbed dose measurement accuracy. In order to exploit this advantage, an in-house radiochromic film dosimetry methodology was developed and implemented.

Materials and methods: The dosimetry system used consists of radiochromic films (GafChromic EBT 3), flatbed scanner (Epson Expression 10000XL) and film analysis software (radiochromic.com). The methodology was developed following the protocol by Mendez et al.

Films from the same batch were used, minimising sensitivity fluctuations. Scans were acquired in reflection mode with fixed image acquisition parameters and resolution. Films were scanned prior and post irradiation correcting for scanner lateral response and film inhomogeneity.

To achieve darkening saturation, irradiated films were scanned after a fixed 3-day interval.

Film dose calibration curves were created for 0-5Gy in 0.5Gy steps.

Absorbed dose distributions were measured using films positioned at the isocentric plane of IBA MultiCube phantom and irradiated by the Siemens Oncor Expression 6MV photon beam.

They were analysed in comparison to absorbed dose distributions calculated using the Elekta Monaco Monte Carlo based treatment planning system together with those acquired with IBA Matrixx 2D ionisation chamber array in equivalent geometry.

The methodology accuracy was tested analysing absorbed dose calibration curves, noise, geometric accuracy, absorbed dose linearity. Additionally, Gamma index passing rates were assessed using 3%/3mm, 3%/2mm (reference) and 2%/2mm dose difference/distance to agreement criteria.

Absorbed dose distributions of increasing complexity were analysed, from rectangular fields to single and multiple dose level head and neck (h&n) IMRT plans.

Results: In-house methodology results show that the mean absorbed dose error of radiochromic film measurements is under 2% and geometric accuracy under 1mm, making it suitable for advanced radiation therapy technique verification.

Over 95% of points passed the 3%/3mm and 3%/2mm Gamma index criteria for all analysed absorbed dose distributions using either film or the 2D array.

As expected, due to its higher resolution, when applying the stricter 2%/2mm criterium, film pass rates become lower than the ones obtained using the 2D array, falling with increasing plan complexity with largest discrepancies found at field edges and high dose gradients of multiple dose level h&n IMRT plans

Conclusion: The developed radiochromic film methodology is shown to be equivalent to 2D array methodology at reference level.

With stricter criteria applied, better spatial resolution of film allows for identification of errors arising from imprecise multileaf collimator motion and positioning, leaf edge and penumbra modelling, particularly in high dose gradient areas. Such errors mean that in clinical cases, while the calculated h&n IMRT dose distribution may seem optimal, the one patient actually receiving may have large errors affecting tumour control probability and/or organ at risk sparing.

These errors are not detectable using 2D array equipment, justifying the use of radiochromic film for advanced technique delivery verification.

Keywords: dosimetry, film, h&n, IMRT

P20 – DURVALUMAB IN THE TREATMENT OF STAGE III NSCLC – SINGLE CENTER EXPERIENCE

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Background: In the phase 3, placebo-controlled PACIFIC trial of patients with unresectable, stage III non-small cell lung cancer (NSCLC) without disease progression after concurrent chemoradiotherapy, consolidative durvalumab was associated with significant improvements in the overall survival (OS) and progression-free survival (PFS). Based on these results, durvalumab become the new standard of care for patients with locally advanced NSCLC who didn't progress on concomitant chemoradiotherapy. In this work we present the real world results of consolidation immunotherapy with durvalumab in patients with PD-L1 expression positive stage III NSCLC in the Department of Oncology, University Hospital of Split.

Methods: This retrospective analysis included 26 patients with PD-L1 expression positive stage III NSCLC who were treated with concomitant chemoradiotherapy and there were no signs of disease progression on control lung CT, and who received at least one cycle of durvalumab in the period from 2018-2021. First cycle of durvalumab had to be applied within 42 days from the last radiotherapy fraction. Durvalumab dose was 10 mg/kg every two weeks. Maximal treatment duration was one year.

Results: Out of 26 included patients there were 19 men and 7 women. Median patient's age was 67,5 years. Squamous cell carcinoma was present in 17 patients (65%) and 9 patients (35%) had adenocarcinoma. PD-L1 tumor-membrane expression was as follows: 1-49% in 18 patients (70%), 50% or more in 8 patients (30%). The median number of administered cycles of durvalumab was 14 (range 1-25). The median PFS was 11 months. The median OS was not reached (at the time of analysis 16 patients (61,5%) were alive). The objective response rate on durvalumab was 34,6%. Stable disease was the best response to therapy in 12 patients (46%), disease progression was observed in 4 patients (15%), while 1 patient (3%) had not yet undergone control diagnostic procedure. Sites of disease progression on durvalumab were: intrathoracic in 4 patients and extrathoracal in 4 patients - brain and bones in 3 patients and kidney in one patient.

The immune-related adverse events were observed in 13 patients (50%): hypothyroidism and hyperthyroidism grade 1-2 in 8 patients (30%), pneumonitis grade 1-2 in 2 patients, rash grade 1 in one patient and creatine kinase elevation grade 2 in one patient. In one patient there were hepatitis grade 2 and that was the reason for treatment discontinuation.

Conclusion: Treatment with durvalumab in patients with unresectable stage III NSCLC without disease progression after concurrent chemoradiotherapy in our institution was effective and well tolerated. To draw firm conclusions and to compare it with results from registrational study longer follow up and larger sample size are needed.

Key words: durvalumab, immunotherapy, non-small cell lung cancer, stage III

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P21 – EFFICACY AND SAFETY OF OLAPARIB IN THE TREATMENT OF BRCA MUTATED OVARIAN CANCER – SINGLE CENTER EXPERIENCE FROM UNIVERSITY HOSPITAL OF SPLIT

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Introduction: Maintenance therapy with the PARP inhibitor olaparib in platinum sensitivity and confirmed BRCA mutations prolongs progression free survival and affects the long-term outcomes of patients with recurrent ovarian, fallopian tube and peritoneal cancers. In Croatia, olaparib was approved in 2015 in maintenance therapy for ovarian relapse, and in 2021 in first-line treatment. Data from everyday

clinical practice are unusually valuable because of a true understanding of the efficacy and a better understanding of adverse drug events.

Methods: Data from the medical history of 28 patients with platinum-sensitive, BRCA mutated recurrence of ovarian cancer treated with olaparib at the Department of Oncology and Radiotherapy in Split, in the period from June 1, 2016 to April 1, 2021, were retrospectively collected and processed. Median follow-up was 27 months. Thirteen subjects were treated with capsules at a daily dose of 800 mg, 12 subjects with tablets at a daily dose of 600 mg, and 3 subjects underwent conversion from capsules to tablets upon arrival of the new drug formulation.

Results: The median age of the patients at the time of diagnosis was 55 years (36-78). The primary site of the disease was mostly ovarian cancer (71%) of serous papillary pathohistological subtype (96%) of grade 3 (100%). The disease was most commonly diagnosed in FIGO stage III (75%). All patients were BRCA mutated, with a predominance of BRCA 1 mutation (75%) defined mainly from peripheral blood (93%). Breast cancer was concomitantly diagnosed and treated in five patients (18%). More than half of the patients had a positive family history of breast cancer (57%). The median platinum-free interval was 13 months. Most patients were treated after the first relapse (64%) with a three-weekly TC protocol (68%). All responded to chemotherapy, so the complete response was achieved in one third of the respondents, and the partial response in the rest. A complete response to olaparib was achieved in three patients (11%). Clinical control of the disease was defined in 43% of patients. The median progression free survival was 24 months. Discontinuation of olaparib treatment was reported due to disease progression in 16 subjects. The median overall survival is not reached. Side effects of olaparib, mostly of low grade, have been reported in 75% of patients. The most common non-haematological toxicity were fatigue and nausea (71-75%), and the most common haematological toxicity was anemia (25%). None of the subjects discontinued olaparib therapy due to severe toxicity.

Conclusion: The selection of patients for targeted therapy is a postulate for effective treatment and guarantees a shift in long-term treatment outcomes. The characteristics of the subjects in our report matched the inclusive criteria of a randomized clinical trial SOLO2. Olaparib maintenance therapy shows excellent efficacy and acceptable tolerability when administered to patients in daily clinical practice. Given the different median follow-up of patients, we can confirm that the results of treatment in our institution are comparable to the reports of randomized clinical studies.

Keywords: ovarian cancer, olaparib, PFS, OS, tolerability

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P22 – EFFICACY OF RAMUCIRUMAB IN COMBINATION WITH PACLITAXEL IN THE SECOND LINE TREATMENT OF METASTATIC GASTRIC CANCER – RETROSPECTIVE ANALYSIS FROM THREE CROATIAN ONCOLOGY CENTERS

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Background: Gastric cancer (GC) is a global public health problem. In Croatia, about 900 new cases of GC are diagnosed annually, and about 700 people die from this disease. Most patients are diagnosed at an advanced stage of the disease and there is an unmet need for improving of outcomes of GC patients. Patients with metastatic GC have an expected median survival (OS) of up to one year with 5-year relative survival rate of 5%. Triplet first-line (1L) chemotherapy regimens (ECF, EOX, DCF) are superior to doublet regimens (FP, FOLFOX) in terms of response rate (RR), but with greater toxicity. Trastuzumab given with cisplatin-based first-line chemotherapy is the only drug that has contributed to prolonging median survival for more than a year. Paclitaxel, docetaxel, and irinotecan in the second line (2L) of treatment have comparable efficacy with a median PFS between 2-3 months and an OS of 6-7 months. Ramucirumab is an IgG1 monoclonal antibody that binds to the extracellular domain of the VEGF receptor-2, blocking the binding of VEGF ligand and stopping its activation. Phase 3 registration trial RAINBOW, showed that ramucirumab in combination with paclitaxel (RP) in the 2L of treatment, improved PFS (4.4 vs 2.8 months, HR: 0.635) and OS (9.6 vs 7.4 months, HR 0.80) compared to paclitaxel plus placebo. Objective response rate (ORR) was 27% with 52% of patients with stable disease. Based on this trial ramucirumab in combination with paclitaxel has become standard 2L therapy for advanced GC.

Objectives: ORR, PFS and OS of RP as 2L treatment of advanced GC in daily clinical practice in three leading Croatian oncology centers.

Methods And Materials: We retrospectively analyzed the clinical outcome of 51 patients with metastatic GC treated from June 2018 to February 2022, with RP in the 2L of treatment, in three Croatian oncology centers (UH Split, UH "Sestre milosrdnice" and UH Zagreb). The data was analyzed with methods of descriptive statistics by using Microsoft Excel tools.

Results: Fifty one patients (n=51) were included in the analysis. The median follow-up was 9 months (range 0.2-20 months). The median age was 62 years (range 31-77). Men made up 68% (n=34) and women 32% (n=17) of the patients included in analysis. HER2 positive GC was detected in 20% of patients (n=10), HER2 negative tumor in 70% (n=36), and 10% of patients (n=5) had unknown HER2 status. Ninety percent of HER2-positive patients received trastuzumab in 1L treatment (n=9). Fifty nine percent of patients had ECOG status 0 (n=30) and 41% ECOG status 1 (N=21). Forty five percent of patients had resected primary tumor (n= 23). Peritoneal carcinomatosis with ascites was present in 37% of patients (n=19) and liver involvement in 39% of patients (n=20). In the 1L of therapy, cis/5Fu received 67% of patients (n=34), 25% of patients (n=13) received FOLFOX, while triplet chemotherapy (ECF, FLOT, ECX) received 8% of patients (n=4). The 3L of therapy was received by 8% of patients (n=4). Objective RR was 12% (CR 1%, PR 11%).

Stable disease was achieved in 29% of patients. The median PFS and OS were 3.7 months and 9.2 months, respectively. Total median OS from the start of 1L treatment was 17.3 months.

Conclusions: Our retrospective analysis showed promising efficacy of RP in the 2L treatment of metastatic GC in everyday clinical practice with median PFS and OS comparable to those achieved in the RAINBOW trial.

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P23 – FOLFIRINOX VS. GEMCITABINE + NAB-PACLITAXEL IN THE FIRST LINE TREATMENT SETTING OF METASTATIC PANCREATIC CANCER – A SINGLE INSTITUTION ANALYSIS OF THE OUTCOMES

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Background: Pancreatic cancer is the fourth leading cause of the cancer-related death among both sexes. Unfortunately, more than 50% of patients presents with metastatic disease where survival rates are discouraging (1). Currently two chemotherapy regimens, one with oxaliplatin, 5-fluorouracile and irinotecan (FOLFIRINOX) and one with combination of gemcitabine and nab-paclitaxel, are approved as equally effective first line treatment in the metastatic setting (2,3,4). However, this is based upon systematic reviews and real world data because up until now there wasn`t head to head comparison of the two protocols in

randomized controlled trial (4). Here we present our results of the first line treatment for metastatic pancreatic cancer.

Methods: The cross-sectional retrospective study was conducted at the Department of Oncology and Radiotherapy, University Hospital of Split. It included patients who were newly diagnosed with metastatic pancreatic adenocarcinoma from January 1, 2018 to December 31, 2021. The data were analyzed with methods of descriptive statistics using Microsoft Excel tools.

Results: There were 97 patients in total, out of which 66 (68%) have started with the treatment, 6 (6%) patients have refused chemotherapy and 25 (26%) patients were initially treated with best supportive care. Median age at the time of diagnosis was 68 years (IQR 61-74) and median number of metastatic sites was 2 (IQR 1-2). Majority of patients had ECOG performance status between 1-3. Median overall survival (OS) for the treated patients was 5,44 months (IQR 3,22-10,22) and mOS for untreated patients was 1,84 months (IQR 0,92-4,21). Median progression free survival for the first line treatment was 2,28 months (IQR 1,05-4,37). FOLFIRINOX was administered to 27 (41%) patients with mPFS of 2,56 months (IQR 1,59-5,22). Combination of gemcitabine and nab-paclitaxel was administered to 19 (29%) patients with mPFS of 1,22 months (IQR 0,53-3,61). The rest of the patients (20; 30%) were treated mostly with monochemotherapy in the first line setting and mPFS was 1,08 months (IQR 0,64-1,95). Patients treated with FOLFIRINOX had median number of metastatic sites 1 (IQR 1-2) and all of them had ECOG performance status 0 or 1. They have received average of 6,37 cycles and half of the patients had partial regression or stable disease as best response to therapy, while other 50% had disease progression. Meanwhile, patients treated with gemcitabine and nab-paclitaxel had median number of metastatic sites 2 (IQR 1-2) and majority had ECOG performance status 1 or 2. They have received average of 4,58 cycles and only 5 (26%) had partial response or stable disease as best response, while 8 (42%) patients had disease progression and for 6 (32%) patients the overall response could not be determined. Toxicity profile was rather similar between both regimens. Second line of treatment was administered to 13 (48%) patients receiving FOLFIRINOX and to 5 (26%) patients receiving combination of gemcitabine and nab-paclitaxel, respectively.

Conclusion: Despite numerically different values of the mPFS for different first line chemotherapy regimens, due to the significant difference among included patients, it is difficult to put the final verdict regarding their efficacy in the first line everyday set-up. Our group of patients treated with gemcitabine and nab-paclitaxel, and particularly those treated with monochemotherapy, were in a rather worse situation at the beginning, more metastatic sites and worse ECOG performance status. In conclusion, because we are selecting treatment for our patients based on their general performance status, patients that do receive FOLFIRINOX protocol are obviously those younger age with less comorbidities, better ECOG performance status and consequently better outcomes.

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P24 – HOW OFTEN ONCOLOGISTS RECORD THE PATIENTS' COVID-19 INFECTION IN THEIR FINDINGS

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Introduction: COVID-19 pandemic significantly affects cancer care and the work of oncologists. Also, in cancer patients experiencing COVID-19 infection, oncological care, and therapeutic sequence may be disrupted by the infection itself. In our Inpatient Oncology Department at University Clinical Hospital Mostar, during the pandemic, all patients that are hospitalized in the regular procedure should possess a negative RT-PCR COVID-19 test. Until this pandemic, the epidemiological history for most infectious diseases was not part of the standard information collected for cancer patients by their oncologists. There is also a known fact of under-reporting by physicians.Talking about toxicities, under-reporting of severe toxicities ranged from 13 to 50% even in prospectively randomized trials. During the pandemic, our Hospital Information System (BIS) was adjusted, so if the patient has been RT-PCR COVID-19 tested in our institution, oncologists can see the last test results through the BIS and the Electronic Medical History (EPB), also for all previous test results too. But we were interested in how much oncologists changed their practice, and whether they record information about patients' COVID-19 infection in their findings.

Methods: We retrospectively reviewed data from the Hospital Information System (BIS) of the Oncology Department at University Clinical Hospital Mostar. We extracted data on patients who tested positive for COVID-19 in our hospital before visiting the Inpatient Oncology Department, for patients hospitalized in the period from 1st December 2021 to 20 February 2022.

Determining the date of the positive RT-PCR COVID-19 test, we reviewed oncological findings after infection in Electronic Medical History (EPB) to detect whether the prevalence of the COVID-19 infection was recorded in the oncological findings of these patients.

Results: Within the period from 1st December 2021 until 20 February 2022, we detected 41 patients with previous RT-PCR COVID-19 positive test results, tested at University Clinical Hospital Mostar. We found records of the COVID-19 infection in oncological findings for 25 of detected 41 patients (60.9%). All other patients, 16 of them (39%), did not have records of previous COVID-19 infection or positive results in oncological findings.

Conclusion: Even thoughCOVID-19 infection can affect the morbidity and mortality of cancer patients and the therapeutic sequence, and although oncologists in their findings do report this infection, it is still under-reported in high percent.

Keywords: oncologist, findings, report, covid-19

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P25 – HOW TO SEQUENCE CHEMOTHERAPY AFTER PROGRESSION TO OLAPARIB MAINTENANCE THERAPY IN PATIENTS WITH BRCA MUTATED OVARIAN RECURRENCE? – SINGLE CENTER EXPERIENCE FROM UNIVERSITY HOSPITAL OF SPLIT

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Introduction: A large number of patients progress after maintenance therapy with olaparib in platinum-sensitive, BRCA mutated recurrence of ovarian, fallopian tube, and peritoneal cancers. We still do not know how to sequence chemotherapy after progression to olaparib. The first results, which seek to recommend the type and manner of sequencing of chemotherapy after olaparib, suggest that reinforcement of platinum-based chemotherapy has poorer outcomes than non-platinum chemotherapy. Experiences from everyday clinical practice are unusually valuable because they help to develop guidelines aimed at improving the long-term outcomes of this group of patients.

Methods: Data from the medical history of 28 patients with platinum-sensitive, BRCA mutated recurrence of ovarian cancer treated with olaparib at the Department of Oncology and Radiotherapy in Split, in the period from June 1, 2016 to April 1, 2021, were retrospectively collected and processed. Median follow-up was 27 months (1.5-52). Thirteen subjects were treated with capsules at a daily dose of 800 mg, 12 subjects with tablets at a daily dose of 600 mg, and 3 subjects underwent conversion from capsules to tablets upon arrival of the new drug formulation.

Results: Discontinuation of olaparib treatment was reported solely due to disease progression in 16 subjects. One patient did not report to an oncologist after disease progression. The median period from olaparib initiation to chemotherapy initiation for first relapse (TFST, time to first subsequent treatment) was 31 months (3-39). The three-weekly TC protocol was most often prescribed (73.3%). All patients progressed to TC chemotherapy, in a median time of 4 months (2-11). The median period from olaparib initiation to chemotherapy initiation for the second relapse (TSST, time to second subsequent treatment) was 38 months (6-44). The most common monochemotherapy for the second relapse was etoposide (53%).

Conclusion: The long-term treatment outcomes of patients defined through TFST and TSST in the registration studies (Study 19 and SOLO2) and our report are comparable. In our study group of patients who progressed to olaparib and were subsequently treated, most of them (13 patients, 87%) were treated with platinum chemotherapy since olaparib provided a long platinum-free interval. Unfortunately, all subjects progressed relatively rapidly, confirming the low efficacy of platinum chemotherapy. Guidelines for optimal treatment require longer follow-up of groups with a larger number of patients.

Keywords: ovarian cancer, olaparib, TFST, TSST

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P26 – IMMUNE CHECKPOINT INHIBITORS IN THE TREATMENT OF METASTATIC UROTHELIAL CANCER: A SINGLE-CENTER RETROSPECTIVE STUDY

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Introduction: Scarce data exists on the safety and efficacy of immune checkpoint inhibitors (ICIs) in metastatic urothelial cancer (mUC) in routine clinical practice. The aim of this study was to assess clinical outcomes of ICI therapy among unselected patient population with mUC treated at a high-volume center.

Patients and methods: Retrospective patient record review of 46 previously treated or untreated mUC patients that received ICI therapy between 2018-2021 was performed. Response assessment was done combining iRECIST and clinical criteria. Univariate analysis of progression-free survival (PFS) and overall survival (OS) was performed using Cox proportional regression model and Kaplan-Meier method.

Results: Median age of treated patients was 67 years (range 52-83 years), 70% were males. Other patient and tumor characteristics included: 72% with bladder as primary site, 26% had variant histology, 67% underwent radical surgery (cystectomy or nephroureterectomy), primary chemoradiotherapy was used in 4% of patients, 28% had liver metastases, 57% of patients had more than one site of metastatic disease and 22% received palliative radiotherapy for cancer-associated pain or for local control. To further

characterize our high-risk patient population, 20% received neoadjuvant chemotherapy, 13% underwent adjuvant chemotherapy and 13% received adjuvant radiotherapy for unfavorable pathohistological features on cystectomy specimen. ICIs were given in 24% patients as first-line therapy, while 76% received ICIs in the second line or beyond (only two patients). In total, 40 patients were treated with atezolizumab and 6 received nivolumab. After median follow up of 11 months (95% CI 7-31 months), 72% of patients died. Median OS was 5 months (95% CI 3-6 months), median PFS was 4 months (95% CI 2-5 months), disease control rate (DCR) was 32% and overall response rate (ORR) was 11%. Presence of liver metastasis was associated with poor PFS and OS (HR 3.2, 95% CI 1.5-6.9, p=0.003) while variant histology and previous radical surgery were associated with longer PFS and OS (HR 0.2, 95% CI 0.1-0.7, p=0.005, and HR 0.4, 95% CI 0.2-0.9, p=0.003), respectively. Both PFS and OS were numerically longer for first line ICI therapy in comparison to second line ICI (9 months and not reached vs 3 and 4 months, respectively). However, this was not statistically significant.

Conclusions: While ICI therapy offers a certain level of disease control for one third of mUC patients, regardless of therapy line, overall clinical outcomes remain poor, and marginally inferior when compared to published randomized trials. Only a small fraction of patients benefits from ICI therapy in the long term. Prognostic role of radical surgery and liver metastasis was confirmed in our sample.

Keywords: immunotherapy, immune checkpoint inhibitors, urothelial carcinoma, bladder cancer, atezolizumab, nivolumab, chemotherapy

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P27 – IMPACT OF THE COVID-19 PANDEMIC ON BREAST CANCER PRESENTATION AT UHC SESTRE MILOSRDNICE

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Introduction: The COVID-19 pandemic has dramatically impacted all aspects of healthcare services. Resources and medical staff were diverted to caring for COVID-19 patients causing delays and interruptions in screening programs, diagnostic procedures and changes in cancer management.

Aim: The aim of our study was to evaluate the impact of the COVID-19 pandemic on the number of initial oncologist consultations for breast cancer at our Department and compare the proportion of patients presenting with early-stage breast cancer and metastatic disease on initial presentation in the pre-pandemic year 2019 and the years following.

Patients and methods: We retrospectively analyzed patients who had their first oncologist consultation at our institution from January 2019 to December 2021. The total number of new patient visits was 241; 91 in the year 2019, 75 in 2020 and 75 in 2021. We divided the patients into three categories according to the treatment decision of the multidisciplinary tumor board: neoadjuvant, adjuvant and primary treatment for stage IV breast cancer. We also evaluated axillary involvement in the early-stage group.

Results: During the pandemic years 2020 and 2021, we had 17.5% fewer initial oncologist consultations compared to the pre-pandemic 2019. In 2019, 81% of patients were given adjuvant therapy, 10% neoadjuvant and 9% were patients given treatment for de novo metastatic disease. In the early-stage group, 35% were node-positive. In 2020, the decision to initiate adjuvant treatment was made in 67% of patients, 16% were given neoadjuvant therapy and 16% of patients were diagnosed and treated for advanced stage disease (7 % more than the previous year). One patient had a histologically benign tumor. In the early-stage group, 32% of the patients had axillary involvement. In 2021, 67% of patients were given adjuvant treatment, 17% neoadjuvant and 16% were treated for initially metastatic disease (also 7 % more than in the pre-pandemic year). In the early-stage group, 43% had node-positive breast cancer.

Conclusions: When comparing the pre-pandemic year 2019 and 2020 and 2021, we noticed a reduction in the number of initial oncologist consultations, a slight increase in the amount of patients presenting with advanced stage disease and more patients with axillary involvement in the early-stage group. The full effect of the pandemic on delayed diagnostics, missed examinations and changes in cancer management is yet to be seen but is of great interest due to the potential longer-term implications for patient prognosis and mortality.

Key words: breast cancer, COVID-19 pandemic, cancer care

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P28 – INPATIENT ONCOLOGY CARE – IMPACT OF COVID-19 PANDEMIC, SINGLE-CENTER EXPERIENCE

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Introduction: Last two pandemic years significantly changed our lives in many ways and also oncology care. Medical centers adapted to the situation and reorganized the service, including service on oncology departments. Inpatient Oncology Department, University Clinical Hospital Mostar, had a reduced number of hospital beds for oncology patients, patients had to own a negative RT-PCR COVID-19 test before admission, visits to patients were prohibited and patients were restricted from moving outside the department. We were interested in how these measures impacted our inpatient care in terms of the number of visits.

Methods: We retrospectively analysed data from the Hospital Information System (BIS) for the University Clinical Hospital Mostar, Inpatient Oncology Department. We looked for the number of inpatient visits at our department within the "pre-pandemic period", between 9 March 2018 to 31 January 2020, compared with the "pandemic period", between 9 March 2020 to 31 January 2022. Furthermore, we made additional analyses by subunits: radiotherapy subunit and chemotherapy subunit. We calculated the percentage difference between the "pre-pandemic period" and the "pandemic period".

Results: Within the "pre-pandemic period", the total number of inpatient visits was 1818, of which 1601 were at the chemotherapy subunit, and 217 were at the radiotherapy subunit. In the "pandemic period" we had the total number of inpatient visits 1591, 1443 at the chemotherapy subunit, and 148 at the radiotherapy subunit.

In the "pandemic period" we had 87.5% of the total number of inpatient visits from the "pre-pandemic period", 90.1% of the chemotherapy inpatient visits, and 68.2% of the radiotherapy visits. This was a 12.5% decrease in the total number of inpatient visits in the "pandemic period" as compared with the "pre-pandemic period". The decrease in the number of chemotherapy visits was 9.9% and 31.8% for radiotherapy visits in the "pandemic period" compared with the "pre-pandemic period".

Conclusion: Measures that were taken to control the COVID-19 pandemic had a noticeable impact on inpatient oncology care in terms of patient visits, especially in terms of radiotherapy admissions. The extent to which these measures affect patient outcomes will be shown in the future and should be the subject of research.

Keywords: inpatient, oncology, pandemic

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P29 – IS FRONTOLATERAL LARYNGECTOMY STILL USEFUL PROCEDURE IN THE TREATMENT OF LARYNGEAL MALIGNANCY IN THE MODERN ERA?

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Background: Over the last few decades there have been some groundbreaking changes in the treatment of the head and neck tumors, particularly laryngeal tumors. However, there is still room for improvement because mortality rate is still relatively high. According to NCCN guidelines (version 3.2021), the treatment modalities of early stage glottic malignancy are radiotherapy, laryngeal laser resection or partial laryngectomy. Our experiences with patients who underwent frontolateral laryngectomy are presented.

Methods: Patients with an early stage glottic malignancy treated with frontolateral laryngectomy at a tertiary care center were included in this retrospective study. Patient's demographics, tumor stage, histopathological examination and oncological outcome were evaluated.

Results: 45 patients were treated with aforementioned surgery due to T1 (60%) or T2 (40%) laryngeal squamous cell cancer without nodal involvement. 3 female (6,7%) and 42 male (93,3%) patients were included in the study. Mean age was 62,7 ± 8,1 years. Only 2 patients experienced local and one regional recurrence. Both patients who developed local recurrences had anterior commissure involvement. 5-year disease specific survival was 100%. 5-year overall survival was 93,3%. During the follow-up (mean 92 months) ten patients died. Secondary primary tumors or other causes unrelated to primary cancer were the causes of death. Complications, granuloma and synechia, were noticed in 7 and 1 patients, respectively.

Conclusion: Laryngeal cancer has a very good prognosis when its caught at early stage. When results were compared to the results of studies where the treatment modality was RT, laser surgery or transoral robotic surgery, a similar success rate was observed. Certainly, new modalities have some advantages, but in certain cases of patients, frontolateral laryngectomy is a viable option.

Keywords: laryngeal carcinoma, partial laryngectomy, survival, recurrence

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P30 – LONG-LASTING COMPLETE RESPONSE ON THIRD-LINE IMMUNOTHERAPY IN PATIENT WITH MALIGNANT PLEURAL MESOTHELIOMA – CASE REPORT

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Introduction: Malignant pleural mesothelioma (MPM) is an aggressive inflamatory cancer associated with exposure to asbestos. The median survival time ranges from 8 to 14 months, and the 5-year survival rate is less than 10%, indicating a poor prognosis. Standard treatment of MPM for a long time has been polychemotherapy with pemetrexed and cisplatin for fit patients. Currrently, first-line combination of anti PD-1 inhibitor nivolumab and anti-CTLA4 inhibitor ipilimumab has been recognised as the best treatment option (especially in non-epitheloid type) due to improved outcomes in comparison with standard chemotherapy combination. Unfortunately, this immunotherapy combination is still not reimbursed in Republic of Croatia, as well as an alternative chemoimmunotherapy option- combination of platinum compound with pemetrexed and anti VEGF monoclonal antibody bevacizumab. Second, and subsequent, lines of treatment usually consist of sequential use of monochemotherapy options. Recent dana point out on possible effectiveness of checkpoint inhibitors in this indication.

Case presentation: We report a case of a male patient diagnosed at the age of 67 with advanced MPM (diffuse epithelioid type). Patient was operated in May 2016 by the decision of thoracic surgeon. Right thoracotomy was performed with extrapleural right pulmectomy and mediastinal lymphadenectomy, and stage III disease was diagnosed (T3N2M0). Postoperative fluorodeoxyglucose position-emission tomography revealed the residual disease in right thoracic wall and paraesophageal lymph node. Patient was treated with first-line chemotherapy (cisplatin and pemetrexed, standard protocol) for 2 cycles. Best response to therapy was progressive disease, and, because the patient was still in good condition without toxity from previous chemotherapy, seeking for alternative treatment options, we made a shared decision to incorporate bevacizumab (at his own expense) with second-line gemcitabine. From October 2016. to December 2017. the patient received 15 cycles of chemoimmunotherapy with the best radiological response being partial response. After the disease progression in January 2018., we have chosen pembrolizumab as a third-line therapy, after thorough discussion on treatment options and expected benefits of it with the patient, at his own expense. From February 2018. to September 2018., patient received a total of 12 cycles

of pembrolizumab given every three weeks with complete response to therapy. Given the complete response, significant toxicity of the treatment (grade 3 pneumonitis) and in the light of the fact that patient had right pneumenectomy, the multidisciplinary team decided to stop further treatment with pembrolizumab and carefully monitor the patient. Six-years from the diagnosis, patient is still alive and in complete remission.

Conclusion: This report described a case of the patient diagnosed with advanced MPM, who although chemorefractory to the first –line chemotherapy option, experienced great benefit of second line chemotherapy in combination with angiogenic agent, and especially immunotherapy with pembrolizumab in third line of treatment with long-term complete remission. Future research should focus on identification of molecular, genetic and clinical biomarkers that could help us lead the treatment selection on individual basis for every patient in this rare disease.

Keywords: malignant pleural mesothelioma, bevacizumab, immunotherapy, pembrolizumab, chemotherapy

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P31 – MASTECTOMY SHOULD NOT BE OFFERED TO THE EARLY-STAGE BREAST CANCER PATIENTS

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Background: European Society of Breast Cancer Specialists (EUSOMA) set up the minimum requirements for specialized Breast Centre (BC) as well as the set of 15 mandatory quality indicators (Q.I.) benchmarks for certification purposes. Surgical management of breast cancer patients in quality-assured specialized BC should provide not only optimal oncological outcomes but also the highest level of quality of life for breast cancer survivors. The quality of surgical treatment for early-stage breast cancer patients is evaluated with seven Q.I. The Q.I.5 is defined as a breast conservation rate for the invasive disease with a primary tumour less than 3 cm (T<3 cm) and the benchmark for certification purposes is set up at a minimum of 70%.

Methods: In BC of Clinical Hospital Centre (CHC) Rijeka data were collected retrospectively for 2019 and prospectively thereafter in a clinical register, encrypted according to the EUSOMA instructions and uploaded into the collective EUSOMA database. Following database validation, all Q.I. were calculated for BC of CHC Rijeka. Data of the Breast working Group Registry, Croatian society of pathology (2017-2020) was used for the determination of the annual Q.I. 5 values at the national level.

Results: Q.I. 5 calculated for BC of CHC Rijeka was high above the EUSOMA benchmark of 70% in all 3 consecutive years (96%, 92% and 97%). However, at the national level, all values were significantly below the minimum of EUSOMA requirements (58%, 59%, 66% and 63%).

Conclusion: Uniform comprehensive institutional and national databases are essential for quality control and identification of non-compliance with the guidelines. The recognition of a deviation in clinical practice is the first step toward its improvement. Mastectomy does not improve oncological outcomes for early-stage breast cancer patients. Several population-based studies suggest even inferior survival for mastectomy patients when compared to breast conservation. In addition, the morbidity and surgery-related complications are significantly higher in mastectomy patients when compared to the breast conservation group and the quality-of-life scores are lower, irrespective of post-mastectomy breast reconstruc-

tion as well as the type of reconstruction. Moreover, the overall costs of the procedure are an additional unnecessary burden for the whole healthcare system. Considering all this, the EUSOMA Q.I. 5 benchmark of at least 70% of breast conservation, for invasive tumours<3 cm, is more than justified and should not be difficult to reach in near future. Additional clinical data are required to determine the background of sub-optimal breast cancer surgical management identified in Croatia. Mastectomy, with or without breast reconstruction, should no longer be offered as an option to the early-stage breast cancer patient without solid oncological indication.

Keywords: breast cancer, surgery, quality indicator

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P32 – MELANOMA PATIENTS WITH BRAIN METASTASIS – A SINGLE-CENTER EXPERIENCE

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Introduction: Melanoma is a highly malignant form of skin cancer with a propensity to metastasize to multiple organs aggressively. The brain is one of the most common sites of melanoma metastases. About 20–28% of patients have brain metastases (BM) at diagnosis and about 49–75% of patients have BM on autopsy. Various studies identified risk factors for the development of melanoma BM, which include male sex, age >60 years, mucosal melanoma or skin melanomas of the trunk, head, neck or scalp, deep or ulcerated primary lesions; acral, lentiginous, or nodular histology; involvement>3 regional nodes at diagnosis or relapse and visceral metastasis. Over the past decade, the frequency of BM is on the rise due to the increased survival of patients diagnosed with melanoma. Previously, thesepatients had limited treatment options, including chemotherapy, whole-brain radiation therapy (WBRT), stereotactic radiosurgery (SRS), and surgical resection.Since 2011, checkpoint inhibitors and BRAF/MEK targeted therapy have revolutionizedthe treatment of melanoma, resulting in dramatically improved survival.

Changes in the current management of melanoma BM comprise the use of immunotherapy – preferably combined anti-CTLA-4/PD-1-immunotherapy, ipilimumab and nivolumab with or without SRS.

Aim: The aim of our analysis was to determine progression-free survival (PFS) and overall survival (OS) of our patients with metastatic melanoma with brain metastasis.

Patients and methods: We retrospectively analyzed patients with melanoma BM treated at our institution from May 2016 to August 2021. In total, 37 patients. We stratified them by sex, age, and BRAF mutation. Not all patients had BM at the diagnosis of stage IV disease.

Results: Median PFS for patients in first-line therapy was five months (95%CI: 3-47 months), and median OS was seven months (95%CI: 5-12 months). 62% of patients were men and 38% were women. The median age of the diagnosis of brain metastases was 55 years for men, and 59 years for women. BRAF mutation was detected in 75% of the patients. The majority of BRAF-positive patients received targeted therapy in the first line, and only two patients (7%) with BRAF-positive tumors received immune checkpoint inhibitors monotherapy as first-line. 16% of patients had BM at diagnosis of metastatic disease; the rest had central nervous system dissemination after or during initial therapy.

Conclusions: Treatment of patients with BM is still an unmet need. The majority of patients had BRAF mutated melanomas, which was expected due to their more aggressive biologic behavior. The lack of combined anti-CTLA/PD-1 therapeutic option in our patient population has a clear negative impact on PFS and OS in this patient cohort.

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P33 – MULTIPARAMETIC MAGNETIC RESONANCE IMAGING FOR BLADDER CARCINOMA

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Bladder cancer is among ten most common malignancies worldwide, with strong male predominance and significantly high recurrence rate.

Currently imaging methods, like ultrasound and computed tomography have a role in diagnosing and determining the stage of disease spread. On contrary multiparametric magnetic resonance imaging of bladder, with its high contrast and spatial resolution, enables the differentiation of the bladder wall layers and surrounding structures and has a role in the locoregional assessment of the disease stage.

In newly diagnosed bladder carcinoma, existence of detrusor muscle invasion is crucial for estimation of disease stage and accordingly the decision on therapeutic approach. Having a multiparametric approach to magnetic resonance imaging, with combination of morphological sequences such as T2-weighted image, and functional sequences like diffusion (DWI) and dynamic contrast enhanced (DCE) imaging, magnetic resonance provides the possibility of grading and assessing the risk of detrusor muscle invasion. Also, functional sequences, especially DWI, allow to distinguish tumour recurrence and benign changes in patients after resection.

In order to standardize the performance and interpretation of bladder examination with magnetic resonance imaging, in 2018. a multidisciplinary team of experts developed VI-RADS categorization.

The goal is to maximize the potential of magnetic resonance imaging as an imaging modality capable of non-invasive assessment of the locoregional disease stage and to improve communication between specialists within a multidisciplinary team in selecting the best therapeutic options for patients.

Here we present the experience of our multidisciplinary team.

P34 – NEOADJUVANT CHEMOTHERAPY IN PATIENTS WITH BREAST CANCER, ATM MUTATION CARRIERS

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The genetic background of breast cancer (BC) is associated with several highly penetrating and moderately penetrating mutations in genes. Mutations in the BRCA1, BRCA2, TP53, and ATM genes are the most studied tumor suppressor gene mutations that affect the therapeutic approach to BC. Ataxia telangiectasia mutated (ATM) is a protein kinase enzyme with a key role in DNA double-strand repair. While AT syndrome is a rare occurrence (1 in 40,000-100,000 people), heterozygosity of the ATM gene occurs in approximately 1% of the population and has been associated with increased cancer susceptibility. ATM mutations involved in BC can be divided into three main categories: truncating mutations associated with no protein production, mutations leading to the expression of a mutant protein lacking kinase activity and missense mutations associated with reduced kinase activity. Neoadjuvant chemotherapy (NAC) had been developed as a treatment of locally advanced or inoperable breast cancer. Today, NAC includes patients with early-stage, operable breast cancer because it is revealed that the achievement of a pathologic complete response (pCR) is associated with excellent long-term outcomes, especially in patients with aggressive phenotype breast cancer.

In this series of cases, 3 patients with breast cancer, carriers of ATM mutations, are presented. Patient 1 was diagnosed with invasive breast cancer (grade II, luminal B, her-2 negative) in 2019. Gene sequencing revealed a heterozygous variant in the ATM gene classified as pathogenic (NM_000051.3 c.4642_4645 del GATA), which causes a shift in the reading frame. She was treated with neoadjuvant therapy ddAC-wT (dose-dense anthracycline & cyclophosphamide (ddAC) followed by weekly paclitaxel (wT)) and after treatment RCB (residual cancer burden number) was 1,575, RCB (residual cancer burden class) II. Patient 2 was diagnosed with invasive breast cancer (G2, ER90%, PR 90%, HER 2 1+, Ki 67 27%, luminal B). Gene

sequencing revealed an ATM pathogenic mutation NM_000051.3 c7789-3 that causes T and G substitution. She was treated with AC-wT adjuvant therapy and after treatment with RCB was 1,625, RCB II. Patient 3 was diagnosed with invasive breast cancer (ER100%, PR 10%, Ki 67 50%, luminal B similar). Gene sequencing revealed an ATM pathogenic mutation NM_000051.3 c1564_1565delGA that causes a shift in the reading frame. She was treated with ddAC-wT adjuvant therapy and after treatment RCB was 1,288, RCB I.

After application of neoadjuvant chemotherapy, all three patients experienced regression of the tumor after which they underwent surgery. RCB in all 3 patients corresponds to minimal to moderate tumor residue. For patient 1 estimated five-year survival rate is 66%, for patient 2 is 76% while for patient 3 is 80%. While, the ATM mutation causes increased cell resistance to adjuvant radiotherapy, the impact of the ATM outcome of neoadjuvant therapy is still insufficiently investigated.

Keywords: ATM mutation, breast cancer, neoadjuvant chemotherapy

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P35 – OUTCOME OF PATIENTS WITH ADVANCED LARYNGEAL CARCINOMA - A MULTICENTRIC RETROSPECTIVE STUDY

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Background: The purpose of this study was to assess the oncological and long-term functional outcomes of patients who underwent total laryngectomy (TL) or primary radiotherapy (RT) for advanced laryngeal carcinoma.

Methods: Of the 190 patients, 146 had TL without flap reconstruction and 44 had primary RT. Overall (OS) and disease-free survival (DFS), and functional outcome according to the Vienna classification system were evaluated and analyzed.

Results: According to the Vienna classification system, all laryngectomy patients were classified as IA patients. Post-surgical complications occurred in 33 (22.6 %) of the cases, with 18 (12.3 %) experiencing pharyngocutaneous fistulae and 11 (5.8 %) experiencing stenosis.

Voice rehabilitation was achieved in 132 (90.4 %) of 146 patients using voice prosthesis insertion (n=113, 77.4 %), esophageal speech (n=14, 9.6 %), and electrolarynx (n=5, 3.4 %). Patients who were primarily treated with RT (class IR) had less satisfactory outcomes. In particular, 56.8 % (n=25), 20.5 % (n=9), and 22.7 %(n=10) of patients achieved total, partial, or no oral food intake, respectively. Voice rehabilitation was not required in any of the RT patients. Altogether, oral nutrition was established in 93.7% (n=178) of 190 cases (84.7%, n=161 completely, and 8.9%, n=17 partially) with a poorer outcome in patients treated with RT (P<.001). At the end of follow-up, DFS and OS were significantly better for patients who were treated with primary surgery when compared to the RT group (P<.001; P=.002, retrospectively).

Conclusion: When compared to primary RT, surgical treatment of advanced laryngeal tumors without pharyngeal involvement has a significantly better oncological and functional outcome, and adequate voice rehabilitation can be achieved in the vast majority of cases.

Keywords: laryngeal cancer, larynx, radiotherapy, outcomes, head and neck.

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P36 – PALLIATIVE RADIOTHERAPY (PR) FOR BONE METASTASES – PATTERNS OF CARE AND OUTCOMES ANALYSIS FROM A LARGE TERTIARY CENTER

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Introduction: Bone metastases are a common site of disseminated disease in cancer patients and are often associated with a high symptom burden, complex medical management, and considerable resource utilization. Despite providing effective and safe symptom palliation, radiation therapy remains globally underused, partly due to ongoing controversies surrounding optimal fractionation and techniques for palliative radiotherapy. The aim of this study was to assess the utilization rate, treatment patterns of PR in the modern systemic treatment era and identify factors associated with outcomes.

Patients and methods: Electronic patient records from January 2017 to December 2021 were retrospectively reviewed. The Kaplan-Meier method and Cox proportional hazard model were used to calculate survival and identify factors associated with overall survival, calculated from the start date of the first course of PR to the date of death or date of the last follow-up. The logistic regression analysis was used to identify potential predictors of PR fractionation.

Results: Two hundred twenty-seven patients with bone metastases who received conventional PR were identified. After excluding patients with at least one radiotherapy course for bone metastases prior to 2017 (2 patients), and patients lost to follow-up (25 patients), a total of 200 patients remained in the study. A total of 351 radiation treatments were delivered (10% of the whole radiotherapy workload) for cancer-associated pain, with or without pathologic fracture (16%), and/or spinal cord compression syndrome-SCCS (13%). Median follow-up for living patients was 31 months (range 25-55 months), while 144 patients died (70%). Three-year overall survival was 15%. Factors significantly associated with poor overall survival were increased ECOG performance status (HR 1.9, 95%CI 1.6-2.2, p<0.0001), presence of soft tissue component (HR 1.6, 95%CI 1.1-2.3, p=0.02), SCCS (HR 1.6, 95%CI 1.1-2.4, p=0.03), no systemic treatment (HR 2.9, 95%CI 1.7-4.8, p=0.001) and presence of visceral metastasis (HR 1.7, 95%CI 1.2-2.4, p=0.003). Factors significantly associated with improved overall survival were reirradiation (HR 0.6, 95%CI 0.4-0.9, p=0.04) and stable disease (HR 0.2, 95%CI 0.1-0.3, p<0.0001). Single-fraction (SF) radiation was employed in 58% of palliative courses and its use fell during the study period (p=0.01). Reirradiation accounted for 5% of total treatments and was more prevalent in patients who received SF (p=0.02). When all PR courses were analyzed, factors significantly associated with SF PR on univariate logistic regression analysis were poor ECOG performance status (OR 3.6) and primary cancer type (breast cancer OR 3.0, melanoma OR 3.1). Factors associated with multi-fraction PR were bone metastasis surgery (OR 6.6), soft tissue component (OR 6.8), SCCS (OR 3.8), and systemic treatment with immunotherapy (OR 2.4). In the multivariate model, only bone metastasis surgery (OR 3.3) and soft tissue component (2.9) remained significant and patients with those factors were more likely to receive multi-fraction PR.

Conclusions: Our study identified important prognostic and predictive factors for palliative radiotherapy which can help in complex clinical decision making. In the absence of survival benefit, multiple factors need to be considered in determining PR fractionation.

Keywords: bone metastases; conventional palliative radiotherapy; prognostic factors; overall survival; single fraction radiotherapy; multiple fraction radiotherapy

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P37 – PATIENTS WITH LEPTOMENINGEAL METASTASES, THEIR TREATMENT AND OUTCOME

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In some individuals with late-stage solid or hematological malignancies, leptomeningeal metastasis (LM) is a catastrophic central nervous system (CNS) consequence. Cancer cells penetrate the subarachnoid space and multiply in the cerebrospinal fluid (CSF) compartment inside the leptomeninges. This complication is linked to a wide range of symptoms as well as a bad prognosis. If left untreated, the interval from diagnosis to mortality is typically 4 to 6 weeks. Overall survival is about 2 to 4 months with treatment. However, we will show a couple of patients who have survived significantly longer.

Our first patient, a 26-year-old woman, was diagnosed with stomach cancer in November 2014 and underwent surgery straightaway. Tumor on the ovaries was noticed during frequent gynecological ultrasound surveillance and biopsy confirmed Krukenberg tumor. This finding was followed by the administration of systemic chemotherapy. The patient's general condition deteriorated in May 2017, and a lumbar puncture revealed LM. Two doses of methotrexate (MTX) along with RT of the CNS were administered. The general condition has improved, and cytological tests no longer showed cancer cells. Five further cycles of systemic chemotherapy were administered, but the patient's condition deteriorated, and she died in the February of 2018. The other two patients were both diagnosed with breast cancer. The patient, 52 years old, was diagnosed with cancer in the October of 2018 and was treated neoadjuvant before being operated on and receiving RT. The patient was in a poor general condition in November 2019, with headaches and visual impairment. MTX was administrated twice intrathecally along with RT of the CNS. The patient was in stable overall condition during the oncologist's assessment on October 26, 2020. However, the patient's relatives reported in November that the patient's condition had unexpectedly worsened and

that he had died. In June 2018, the third patient was diagnosed with metastatic breast cancer with bone metastases. Systemic polychemotherapy was used, followed by tamoxifen and an LHRH agonist treatment. The patient's condition worsens in December 2018, and she becomes sleepy, agitated, and uncontactable. MTX is given intrathecally two times, as well as CNS irradiation. The patient's condition improves, and she begins further systemic and endocrine therapy, which she continues until July 2021 when her condition worsens and she died.

There are currently no standardized therapeutic alternatives for the treatment of LM. Intrathecal chemotherapy (IT) with or without fractionated radiation has relatively limited effectiveness, and most patients' prognoses are still poor. Although patients with LM have a dismal prognosis, IT treatment and RT can reduce neurological symptoms, improve quality of life, and hence improve survival in some individuals. Those with no bulky LM, no hydrocephalus, and no parenchymal brain metastases are the best candidates for IT therapy. Whenever possible, radiation therapy (RT) should be used to treat symptomatic areas of LMD. As a result, new, more forceful multimodality therapy techniques are urgently required. Immune checkpoint inhibitors, especially molecular-focused treatment, have shown promise in a small number of patients. In addition, stereotactic radiosurgery may play a significant role.

P38 – PATHOLOGICAL CHARACTERISTICS AND SPECTRUM OF BRCA MUTATIONS IN PATIENTS WITH HEREDITARY BREAST AND OVARIAN CANCER – SINGLE CENTER EXPERIENCES FROM UNIVERSITY HOSPITAL OF SPLIT

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Background: Hereditary breast and ovarian cancer (HBOC) syndrome is most commonly characterized by deleterious germline mutations in BRCA1 and BRCA2. HBOC patients are prone to the development of malignant neoplasms in multiple organs including the breast, ovary and fallopian tube.

Breast cancers diagnosed in BRCA1-mutation carriers are frequently of a high grade and display medullary morphology and a triple-negative and/or a basal-like immunophenotype. In contrast, breast cancers in BRCA2-mutation carriers are similar to sporadic luminal-type tumors that are positive for hormone receptors and lack expression of human epidermal growth factor receptor 2.

Cancers arising in the fallopian tube and ovary are almost exclusively of a high grade serous histotype with frequent Solid, pseudo-Endometrioid, and Transitional cell carcinoma-like morphology ("SET features").

Methods: Data from the medical history of 15 patients with high grade serous ovarian cancer and breast cancer treated and followed at the Department of Oncology and Radiotherapy in Split in the period from June 1, 2016 to December 31, 2021 were retrospectively analyzed. BRCA testing was performed mostly from a blood sample.

Results: All subjects were treated for BRCA mutated high grade serous ovarian/fallopian tube cancer. Breast cancer was diagnosed and treated in 12 patients before the diagnosis of ovarian cancer.

BRCA1 mutation was found in 12 patients (80%) and BRCA2 mutation in 3 patients (20%).

The most common BRCA1 mutations were c.5266dupC – in 6 patients (50%), and c.1252G>T and c.843_846delCTCA – in 2 patients (17%). The remaining individual BRCA1 mutations were c.5503C-T and c.1508del. The identified BRCA2 mutations were c.5073dupA, c.9371A>T and c.6641dupC.

Of the 12 patients with an established BRCA1 mutations, 4 patients developed bilateral metachronic breast cancer. The most common BRCA1 mutation, c.5266dupC, p.Gln1756fs, frameshift, was detected in 3 patients. The breast cancer immunophenotype found in these patients was as follows: 2 patients had triple negative and luminal B, 1 patient triple negative and luminal B HER2 positive, while 1 patients developed bilateral triple negative immunophenotype. In the remaining 8 patients, 6 patients developed a triple negative, and other luminal A and luminal B HER2 negative breast cancer.

All 3 patients with the BRCA2 mutation developed the luminal B HER2 negative breast cancer immunophenotype.

Breast and ovarian cancer were diagnosed synchronously in 2 patients. In one patient, BRCA1 mutation (c.843_846delCTCA) was found with a variant of uncertain significance of BRCA2 gene, and breast cancer immunophenotype was triple negative. In another patient with luminal B HER2 negative immunophenotype, a BRCA2 mutation (c.6641dupC) was detected.

Conclusion: The most common BRCA mutation in our study population is mutation of BRCA1 gene (c.5266dupC, p.Gln1756Pfs, frameshift). Immunophenotype of breast and ovarian cancer in BRCA mutated patients are consistent with current medical knowledge.

Keywords: BRCA mutations, hereditary breast and ovarian cancer

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P39 – PROSTATE CANCER IN THE FIRST WAVE OF PANDEMIC: HAS COVID-19 CHANGED THE PERSPECTIVE OF PROSTATE CANCER

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Introduction: Prostate cancer is the most common cancer in men[1]. The incidence of prostate cancer in Croatia is in steady increase[2]. One of the possible reasons in the early screening via PSA screening, but also, global aging of the population. Pandemic has greatly affected all levels of healthcare, including, unfortunately, cancer patients. The „lockdown" period during the first wave of pandemic limited patients' access to diagnostics and subsequently, timely treatment [3]. Several observational studies reported temporary suspensions of early detection programs, and, in the countries where such suspensions did not occur, a lesser number of patients underwent screening programs [4],[5]. The number of patients increased afterwards, to the pre-pandemic level[6].

Based on the current publishing practice, Croatian Cancer registry bulletin for Croatia in the period 2022-2022 are expected in 2024 at soonest. The goal of this collaboration was to test the impact of epidemiologic measures on the number of newly registered prostate cancer patients within three dalmatian general hospitals and the University hospital center in Split.

Methods: Retrospective observational study was conducted at the Department of internal medicine at the General hospital of Šibenik- Knin County, Department of oncology at the General hospital Zadar, Department of oncology at the General hospital Dubrovnik, and the Department of oncology and radiotherapy at the University hospital in Split. Analysis involved newly diagnosed prostate cancer patients' medical charts in the period of January 1st, 2018, till December 31st, 2020.

Results: Analysis encompassed a three-year period, and 1644 patients' medicals files were examined. The number of newly diagnosed prostate cancer patients in 2018 was 634, 524 in 2019 and 486 in 2020. Most patients were from the area surrounding University hospital Split (865), followed by the Zadar County (506). General hospitals in Šibenik and Dubrovnik had fewer patients (136 and 137, respectively).

The most significant decrease in number of newly diagnosed patients in 2020 compared to the average of the two pre-pandemic years was in the area belonging to General hospital Dubrovnik (-36%), followed by General hospital Zadar (-31%), University Hospital of Split (-7%), while the number of newly diagnosed patients in General hospital Šibenik-Knin County was increased (+7%).

Conclusion: The number of newly diagnosed prostate cancer patients in Dalmatia decreased during the first wave of pandemics compared to the average of the previous years. The decrease was 23% in absolute, contradicting the increase of incidence expected both in Croatia and worldwide. Public health measures, and previously reported patients' unwillingness to participate in the screening programs during the pandemics decreased the number of newly diagnosed prostate cancer patients.

True consequences of these measures, described through patients' and tumors' characteristics, disease stage at diagnosis and the treatment initiation are to be analyzed.

Keywords: prostate cancer, COVID-19, Dalmatia, incidence

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P40 – RE-PLANNING IN GAMMA KNIFE RADIOSURGICAL CENTRE

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Introduction: Gamma-Knife, stereotactic radiosurgery method, is non-surgical ablative treatment of intracranial pathologies using small Co-60 photon beams. For Leksell Gamma-Knife unit Icon (Elekta AB, Stockholm, Sweden), radiosurgery uses 192 convergent narrow Co-60 photon beams, collimated with the 16, 8 and 4 mm collimator. There is only one Leksell Gamma-Knife Icon unit installed in Croatia located in Gamma-Knife Centre Zagreb, University Hospital Center Zagreb. Leksell Gamma Knife Icon comes with integrated cone-beam CT (CBCT), used for the patient position verification and correction immediately before the treatment. CBCT is considered the most accurate modality for stereotactic definition of coordinate space.

Co-registration is the process of spatially matching common spatial information of MR and CBCT images. In Gamma Knife Center Zagreb, co-registration is part of the procedure for each patient treatment, and if significant deviations in the stereotactic space are found, treatment re-planning is performed.

Purpose: The aim of this study was to explore the frequency of treatment re-planning in daily work and to investigate in which cases the treatment plans were re-planned. Also, we wanted to establish a relation between dose coverage decrease and tumour volume, or tumour location in stereotactic space, with a final goal to evaluate the clinical importance of treatment re-planning in certain cases.

Methods: We conducted retrospective study using the dosimetric data from the Gamma Plan treatment planning software (Elekta AB, Stockholm, Sweden) in the Department of stereotactic, functional neurosurgery and radioneurosurgery of University Hospital Centre Zagreb. Dosimetric data for 50 patients diagnosed with solitary brain metastasis and for 50 patients diagnosed with vestibular schwannoma treated with Gamma-Knife radiosurgery were analyzed. Input data such as the dose coverage, anatomical displacement, tumour volume, and tumour histology were correlated with re-planning frequency, and statistical significance was obtained using a t-test. The difference was accepted as significant with a p-value less than 0.05.

Results: The median target dose in patients with solitary metastasis was 22 Gy (range 18-25 Gy), and in the group of patients with vestibular schwannoma 12 Gy (range 12 Gy), respectively. Out of 100 patients, a total of 26% of the plans were re-planned, of which 28% were plans for metastasis, and 24% were plans for vestibular schwannoma. In the group of 26 re-planned tumours, the mean tumour volume was 1.83 ± 2.39 cm^3 (Std. Error Mean = 0.47), and in the group of 74 tumours that were not re-planned, the mean tumour volume was 3.60 ± 3.08 cm^3. The chance of re-planning was statistically significantly higher for smaller tumours (P = 0.009; CI = 95). The chance of re-planning did not depend on the distance of the tumour from the centre of the stereotactic space (P = 0.865; CI = 95), or the tumour histology (P = 0.6; CI = 95).

Conclusion: Target volume position correction and re-planning using CBCT are feasible and recommendable in everyday work. Its' use is most valuable in the treatment planning for smaller tumours, thus allowing accurate delivery of the dose to the tumour and improving the quality of the treatment.

Keywords: Gamma-Knife, isodose coverage, re-planning, stereotactic space, CBCT

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P41 – SETTING UP THE FIRST QUALITY-ASSURED SPECIALIZED BREAST CENTRE IN CROATIA

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Background: In 2019, the highest European age-standardized breast cancer mortality rate of 145/100 000 was reported for Croatia, although the breast cancer incidence rate was lower as compared to many other European countries. The European Partnership for Action Against Cancer (EPAAC) has identified and reported that quality of care, national guidelines, quality control and professional training are factors associated with the differences in mortality rates between countries. Multidisciplinary care provided in quality-assured specialized Brest Centre (BC) is nowadays considered optimal management of breast cancer patients and is therefore strongly supported by the European Society of Breast Cancer Specialists (EUSOMA).

Methods: EUSOMA set up the minimum requirements for a specialized BC and defined a set of 17 quality indicators (Q.I.) benchmarks for quality control in the certification process of a specialized BC. Following EUSOMA validation of our clinical database, all 17 Q.I. were calculated for BC of Clinical Hospital Centre (CHC) Rijeka. In addition, a comprehensive on-site audit was performed for all services included in breast cancer care in CHC Rijeka.

Results: Noncompliance with EUSOMA recommendations were reported and categorized as major, minor, recommendations and observations. The suggestions for the improvements were discussed between the audit committee members and BC representatives. In a proposed deadline of four months, we have successfully corrected all major non-conformities and following re-evaluation we have acquired a title of EUSOMA quality-assured specialized Breast Centre.

Conclusion: We have voluntarily initiated and performed quality control of our BC. The high-quality audit pointed out specific major and minor flaws of all evaluated services. However, specific corrective measures, with the goal of service improvements, were suggested and performed as well. The achieved certificate is a confirmation of the high quality of care for a breast cancer patient. With respect to the latest reports of breast cancer mortality rates in Croatia, quality control of all centres involved in breast cancer care should be considered at the national level.

Keywords: Breast Centre, quality control, certificate, EUSOMA

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P42 – SINGLE INSTITUTION EXPERIENCE WITH NIVOLUMAB AS SECOND LINE THERAPY IN ADVANCED RENAL CELL CARCINOMA: EXPLORATORY ANALYSIS OF PROGNOSTIC FACTORS

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Introduction: Immune checkpoint inhibitors (ICIs) opened a new era in the treatment of advanced renal cell carcinoma (RCC). Nivolumab is the standard ICI second line therapy following progression on first line tyrosine-kinase inhibitors (TKIs) in patients with advanced RCC. The aim of this study was to assess the efficacy and toxicity of nivolumab in our unselected population of real-world patients with advanced RCC and to investigate prognostic value of established prognostic factors.

Patients and methods: Retrospective analysis of our institution's database of patients with advanced RCC was performed. All clinically relevant data on patients who received second line nivolumab were

retrieved. Progression-free survival (PFS) and overall survival (OS) were estimated by the Kaplan-Meier log-rank method. Cox regression analysis was used to assess association of prognostic factors and PFS and OS.

Results: Between January 2018 and December 2021, a total of 42 patients received nivolumab as second line therapy. First line was sunitinib, pazopanib, and temsirolimus in 25, 15, and 2 patients, respectively. Forty patients (95%) had clear cell histology; 34 patients (81%) had previous nephrectomy. Three patients (8%) had sarcomatoid features. Median age was 64 years. The baseline IMDC risk status was known for 39 patients (93%). Six (15%) patients were categorized as favorable, 22 (56%) as intermediate and 11 (28%) as poor-risk. Data on baseline NLR and TSH were available for 34 (81%), and 24 (57%) patients, respectively. Median follow-up for living patients was 26 months (95%CI 15-44 months). PFS and OS were 6 months (95% CI 3-30 months), and 21 months (95%CI 12-30 months), respectively. Factors significantly associated with PFS were ECOG performance status (HR 2.2, 95%CI 1.0-4.6, p=0.04) and history of stereotactic body radiotherapy (SBRT) treatment (HR 0.4, 95%CI 0.2-1.0, p=0.03). A factor significantly associated with OS was history of stereotactic body radiotherapy (SBRT) treatment (HR 0.1, 95%CI 0.01-0.8, p=0.03), meaning that patients treated with SBRT lived longer. Objective response rate (ORR) and disease control rate (DCR) associated with nivolumab therapy were 26% and 50%, respectively. The most common grade 3 or higher side-effect leading to treatment discontinuation was skin toxicity (2 patients, 4%) and pneumonitis (1 patient, 2%).

Conclusions: In our experience, nivolumab therapy was shown to be associated with significant disease control rate, prolonged PFS and OS, similar to the landmark CheckMate-025 trial, with no additional safety concerns. Association of SBRT with prolonged PFS and OS in patients receiving nivolumab is intriguing and may be related to selection bias in our limited patient sample. This warrants prospective validation which has been recently initiated within the Croatian oncology network.

Keywords: kidney cancer, renal cell carcinoma, nivolumab, immune checkpoint inhibitors, stereotactic body radiotherapy

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P43 – SPECTRUM OF BRCA1 AND BRCA2 MUTATIONS IN PATIENTS WITH HIGH GRADE SEROUS OVARIAN CANCER IN DALMATIA – SINGLE CENTER EXPERIENCE FROM UNIVERSITY HOSPITAL OF SPLIT

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Background: Mutations in BRCA1 and BRCA2 are well-established risk factor for breast and ovarian cancer. The spectrum of BRCA1/2 mutations in high grade serous ovarian cancer patients have not yet been fully described in Croatia. These observations may be important to optimize the genetic testing, primary and secondary prevention strategies and individualize treatment for our ovarian cancer patients.

Methods: Data from the medical history of 56 patients with BRCA mutated ovarian cancer treated and followed at the Department of Oncology and Radiotherapy in Split in the period from June 1, 2016 to December 31, 2021 were retrospectively analyzed. Initially, BRCA testing was performed from a blood sample, and later from a tumor sample. Patients were tested mostly in University Hospital of Split.

Results: We were analyzed 56 patients with newly diagnosed and/or recurrent BRCA mutated high grade serous ovarian cancer, unselected for age or family history. The median age of diagnosis was 54 years (range 38-76).

We detected 37 patients with BRCA1 mutations (66%) and 19 patients with BRCA2 mutations (34%). The median age of diagnosis for BRCA1m patients was 52 years (range 38-76), and for BRCA2m patients 56 years (range 45-69).

Among those with BRCA1 mutations the most frequently detected mutations were c.5266dupC in 18 patients (49%), c.1252G>T in 8 patients (22%) and c.4113delG and c.843-846delCTCA in 2 patients (5%). Other BRCA1 mutations detected in 1 patient were c.3342delA, c.5409>A, c.181T>G, c.3343del, c.4356delA, c.5503C>T and c.1508del.

Among BRCA2 mutations the most frequently detected mutations were c.6641dupC in 6 patients (32%), c.9371A>T in 3 patients (16%) and c.5073dupA and c.8331+1G>T in 2 patients (10,5%). Other BRCA2 mutations detected in 1 patient were c.6486_6489del, c.4593delA, 3663delT, c.4563_4564delAT, c.6037A>T and c.9286G>T.

Conclusions: The most common BRCA1 mutation in our study (c.5266dupC, p.Gln1756fs, frameshift) is the most common mutation among other Slavic countries such as Russia, Belarus, Poland, Czech Republic, Slovenia as well as in northern Greece, and the second common BRCA1 mutation in the Ashkenazi Jewish population. No new or specific mutations for our population has been detected.

Keywords: BRCA1/2 mutations, high grade serous ovarian cancer, Dalmatia

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P44 – SPECTRUM OF RADIOLOGICAL IMAGING FINDINGS OF IMMUNE-CHECKPOINT BLOCKADE FOR LUNG CANCER AT UNIVERSITY HOSPITAL CENTRE OSIJEK

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Cancer immunotherapy based on immune-checkpoint blockade has resulted in yet another paradigm shift in advanced cancer treatment.ICIs block tumor-induced immune inhibitionand thereby activate cellular immune response against tumors.

Programmed death-1 (PD-1) and programmed death-ligand 1 (PD-L1) inhibitors are two major groups of agents used in the treatment of advanced NSCLC.

Prior to ICIs introduction, the mainstay of treatment for patients with advanced NSCLC who had no targetable mutations was cytotoxic chemotherapy, but without meaningful improvement in outcomes.

We are going to present different cases of stage IIIA/IIIB/IV NSCLC, with an emphasis on radiological imaging and analysis in correlation with the effect of immune-checkpoint therapy. Baseline diagnostic imaging for all the patients included a chest X-ray and/or a chest CT, bronchoscopy,and/or a CT-guided transthoracic needle biopsy with immunohistochemistry analysis. The first follow-up and therapy follow-up chest CT scans were obtained at three-month intervals, with assessed based on iRecist criteria.

Chest CT scanning protocol was performed using a 128-row CT scanner.The slice thickness was 0.7-1 mm.The arterial or venous phase chest CT, and venous phase imaging in the abdomen and pelvis (if necessary) was acquired after the injection of iodinated contrast medium.

Case 1. We present a case of a 67-year-old man with stage IIIA NSCLC. Immunohistochemistry was negative.The patient was treated with platinum-based chemotherapy and received radiotherapy of 60 Gy. After 2 months, evaluation CT showed bone metastases in thoracic column, and the patient started treatment with atezolizumab **as second-line** treatment without PD-L1 expression.After the first 9 cycles, the patient had an excellent response, and after 27 cycles, he has stable disease according to iRecist.

Case 2. We present a case of a 63-year-old man with stage IIIB NSCLC.Immunohistochemistry analysis showed PD-L1 expression 5%. After concomitant chemoradiotherapy and 6 cycles of durvalumab monotherapy, CT scans showed the regression of tumor and lymphadenopathy.After 8 cycles of immunotherapy,the patient has stable disease according to iRecist.

Case 3. We present a case of a 50-year-old man with NSCLC stage IV. PD-L1 expression was 1- 49%. After 27 cycles of continued pembrolizumab with chemotherapy as first-line treatment for enlarged lung adenocarcinoma,the patient has stable disease.

Case 4. We present a case of a 68-year-old man with stage IV NSCLC, PD-L1 expression 45%.Platina-based chemotherapy was introduced as first-line treatment.After the progression of the disease, atezolizumab was introduced as second-line therapy,with pseudoprogression at evaluation chest CT after 3 cycles of therapy,followed by regression after 6 cycles of immunotherapy.

Case 5. We present a case of a 70-year-old man with stage IV NSCLC,PCC,PD-L1 expression 40%. Platina-based chemotherapy was introduced as first-line treatment.After the progression of the disease, atezolizumab was introduced as second-line therapy,with hyperprogression after the evaluation CT and whole spine MRI after 3 cycles of therapy.

Keywords: hyperprogression,NSCLC, PD-L1 pseudoprogression.

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P45 – SPECTRUM OF RADIOLOGICAL IMAGING FINDINGS OF SPECIFIC TARGET THERAPY FOR LUNG CANCER AT UNIVERSITY HOSPITAL CENTRE OSIJEK

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Discovery of oncogenic driver mutations and precise targeted therapy directed at these mutations have resulted in progress for treatment approaches in patients with advanced lung cancer.

Epidermal growth factor receptor (EGFR) mutations and anaplastic lymphoma kinase (ALK) rearrangements are two well-known oncogenic mutations in NSCLC, particularly in adenocarcinomas, and are representative examples of successful clinical application of precision lung cancer therapy, just like the ROS1 mutation, which is less pronounced.

Some of specific target therapies had a superior efficacy in the central nervous system (CNS), reducing the risk of CNS progression.

The abstract is intended to demonstrate how the key members of multidisciplinary teams care for patients with NSCLC.

We are going to present different cases of stage IV NSCLC, with an emphasis on radiological imaging and analysis in correlation with the effect of therapy. Baseline diagnostic imaging included a chest X-ray and/or a chest CT, bronchoscopy and/or CT-guided transthoracic needle biopsy with immunohistochemistry analysis. The first follow-up and therapy follow-up chest CT scans were obtained at three-month intervals with the RECIST criteria.

CT scanning protocol was performed using a 128-row CT scanner. The slice thickness was 0.7-1 mm.The arterial or venous phase chest CT, and venous phase imaging in the abdomen and pelvis (if necessary) was acquired after the injection of iodinated contrast medium.

Case 1. We present a case of a 36-year-old man with stage IV NSCLC, with metastases in pleura, lungs, lymph nodes, liver, skin, bones and thyroid gland. Pathohistological analysis confirmed adenocarcinoma, and immunohistochemistry analysis showed ALK positivity. Alectinib was introduced, and after 34 cycles of therapy, 32 months after his diagnosis, the patient is in complete remission.

Case 2. We present a case of a 65- year-old man with incidental finding of the right lower lung tumor stage IV. Pathohistological analysis confirmed NSCLC, and immunohistochemistry analysis showed EGFR positivity. After 22 cycles of afatinib and radiation therapy for bone metastases, the patient has stable disease according to Recist.

Case 3. We present a case of a 59-year-old woman with stage IV. Immunohistochemistry analysis showed ROS 1 positivity.Krizotinib was introduced, and after 8 cycles of therapy, she had Recist stable

disease.Due to progression of the disease, platinum-based chemotherapy was introduced as second-line treatment, which is still ongoing.

Keywords: ALK, EGFR, chest CT, NSCLC, RECIST

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P46 – SUBTYPING OF TRIPLE-NEGATIVE BREAST CANCER

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Introduction: Recent researches show a high heterogeneity of triple-negative breast cancers (TNBC). According to molecular profiling, there are 6 subtypes of TNBC, which have different responses to therapy. According to the expression of different markers, TNBC can be subtyped as basal-like 1 associated with cell and DNA damage (BRCA mutations), basal-like 2 with activated growth factor pathways, mesenchymal type (epithelial-mesenchymal transition pathway), mesenchymal stem-like (low expression of claudin and E-cadherin), immunomodulatory type (cell immune process), and luminal androgen receptor (LAR, hormone receptor pathways)[1,2]. Subtyping of TNBC would better select patients for different therapeutic approaches. That would ensure proper treatment in the early stages of cancer, which increases the effectiveness of treatment and better control of the disease.

Results: TNBCs do not express estrogen, progesterone, or epidermal growth factor 2 receptors, and according to our data, they account for about 10% of total breast cancers. Since the end of 2017, immunohistochemical staining has been routinely used in the Laboratory of Oncological Pathology KBCSM to determine the status of androgen receptor (AR) and basal cytokeratins CK5/6 and CK14 (CK5/14) in TNBCs, and more recently the status of epidermal growth factor receptor (EGFR). We also determine the expression status of PD-L1 in tumor-infiltrating immune cells (TIL). Our paper presents retrospectively collected data on the status of AR, basal cytokeratins 5/14, EGFR, and PD-L1 in TNBC determined over four years. AR status was assessed in 305 TNBC cases, and 34.4% was positive (LAR). The basal-like subtype of TNBC is mainly classified based on the expression of basal cytokeratins CK5 / 14, and we found that more than half of the TNBC (52.3%) was of a basal-like subtype. Only a quarter of the basal-like TNBC (25.2%) have pronounced AR compared to 43.4% of AR-positive in the non-basal group ($\chi 2=10.36$; $P=0.001$). EGFR expression was determined in 61 cases, and 42.6% was positive. PD-L1 status in TILs was determined in 128 cases, and 54.7% was positive. Although PD-L1 expression was found more frequently in

basal-like TNBCs (51.3%) than non-basal (34.1%), there was no statistically significant difference depending on basal-like status (χ2 test, P=0.173), expression of AR (χ^2 test, P=0.852) or CK5/14 (χ^2 test, P=0.571).

Conclusion: Based on the expression of AR, CK5/14, EGFR, and PDL1, we cannot fully classify TNBC. More than half of non-basal TNBC are AR-negative (quadruple-negative), and further research is needed in this direction. However, determining the underlying subgroup (basal-like or luminal) and the expression of markers that may have therapeutic significance (EGFR, PD-L1) stratify patients suitable for tailored therapeutic options.

Keywords: triple-negative breast cancer, subtypes, androgen receptor, CK5/14, EGFR, PD-L1

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P47 – THE POTENTIAL OF COMBINATION THERAPY WITH FULVESTRANT AND LETROZOLE IN NEOADJUVANT HORMONAL THERAPY OF BREAST CANCER

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Introduction: Neoadjuvant endocrine therapy (NET) - compared to neoadjuvant chemotherapy (NCT) in breast cancer has been inadequately investigated and utilized. [1] Three categories of NET in everyday clinical practice are available: selective ER (estrogen receptor) modulators (primarily tamoxifen), selective ER degraders (fulvestrant), and aromatase inhibitors (letrozole, anastrozole, and exemestane). Trials comparing efficacy of different hormonal agents showed similar results for all three aromatase inhibitors.[2] Guidelines for best choice of treatment agent used in neoadjuvant setting are still limited and optimal duration of treatment is still unknown. For example, in study of Allevi from 2013, investigators showed that pCR (complete response) rates improved from 4 (2%) to 8 (8%) and 12 months (17%)[3]. Aim of our analysis was to provide single institution experience of efficacy of hormonal therapy in neoadjuvant setting, as well as early evaluation of potential of fulvestrant and aromatase inhibitor combination as a treatment of choice in these patients.

Methods: We did retrospective analysis of collective data from January 2017 until February 2022 for 35 female patients who had been treated with neoadjuvant hormonal therapy. Patients have signed informed consent and medical data was analysed.

Results: Our analysis included 35 patients who recieved neoadjuvant endocrine therapy, with median age of 74. 15 patients (42.9%) had luminal A and 20 patients (57.1%) had luminal B immunophenotype breast cancer. Average size od tumor was 3.7cm. Majority of patients (54.3%) had T4 tumor, and were

diagnosed with stage IIIB. 20% of patients were diagnosed with stage IIA and 20% with stage IIB. 5.7% of patients had stage IIIC disease. 15 patients (42.9%) recieved combination therapy with fulvestrant and aromatase inhibitor with median time of follow-up of 7,6 months and 20 patients (57.1%) recieved aromatase inhibitor as a monotherapy with mFU time of 23,9 months. 22 (62.9%) patients had partial response on radiologic exam, 6 patients (17.1%) had stable disease and 1(6.8%) had complete response. 6 patients (17.1%) started treatment recently, so radiologic evaluation was still not done. At the data analysis, February 22nd 2022, 12 patients finished preplaned neoadjuvant treatment and had surgery treatment. Average duration of hormonal therapy in these patients was 8.5 months. Pathologic analysis of response to treatment showed that 1 patient (2.9%) had residual cancer burden (RCB) score 1,9. 25.7% of patients had RCB score 2 and 2 patients (5.7%) had RCB score 3. 4 (11%) patients had died during follow up period and 4 (11%) patients refused surgical treatment. One patient developed metastatic disease during neoadjuvant treatment. At the time of data analysis, 15 (42%) of patients are still recieving hormonal therapy. Efficacy analysis, based on radiologic evaluation showed that out of 20 patients who recived aromatase inhibitors, 20% had stable disease, 60% partial response, 5% complete response. Patients who recieved combination therapy with fulvestrant and aromatase inhibitors had partial response in 66% of cases, stable disease in 6%, and no complete responses.

Conclusion: Our analysis showed that NET could be safe and efficient treatment option for population of selected patients with well differentiated, luminal A and lower risk luminal B tumors, with one of the main benefits in reducing the number of patients exposed chemotherapy-related toxicities, but still providing significant clinical benefit and efficacy similar to more toxic therapeutic options for such pateints. Results of efficacy of aromatase inhibitors and combination of fulvestrant and aromatase inhibitos are comparable, but taking in account the fact that we just recently implemented this combination as our choice of tretament, and taking in account optimal duration of hormonal therapy in neoadjuvant setting, longer follow up period is needed before making valuable comparisment.

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P48 – THE TREATMENT RESULTS OF MRCC PATIENTS 6 YEARS AFTER FIRST APPLICATION OF NIVOLUMAB AS SECOND LINE THERAPY

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Introduction: Nivolumab is a PD-1 checkpoint inhibitor that restores the pre-existing antitumor immune response by selectively blocking the interaction between PD-1 receptors on T-cells and PD-1 ligands, PD-L1 and PD-L2, on tumor cells and antigen presenting cells. Nivolumab prolongs survival in patients with metastatic kidney cancer with a good safety profile as demonstrated in the CheckMate 025 clinical trial.

Material And Methods: This retrospective data involved prospectively monitored patients (named patient programm) treated with second-line nivolumab for mRCC at the University Hospital Centre Zagreb from 2016 to 2018 and the treatment continued to be funded by the Croatian Health Insurance. Patients with metastatic kidney cancer (mRCC) received tyrosine kinase inhibitors (TKI), (29/30), one patient received mTOR inhibitor as first line therapy, and subsequently they initially received nivolumab 3 mg kg NPP every 2 weeks. Later we applied a monthly dose 480 mg. Nivolumab treatment was continued in patients who did not have disease progression or grade 3 and 4 toxicity. Patients were monitored every three momths with CT of the chest, abdomen and pelvis and laboratory tests (hemathology, biochemistry, T4, TSH). We also respected patients´ preference in regard to cycle dynamic by stopping nivolumab therapy or introducing SBRT during nivolumab therapy.

Results: We treated a total of 30 patients (22 men and 8 women) with mRCC, who initially received TKI or mTOR therapy with median age 60.2 ± 9.79 years at diagnosis of kidney cancer. Most patients belonged to intermediate-risk groups. Majority of patients (23/30) were treated with sunitinib as the first line treatment after nephrectomy. Six patients had CR (20%) but two of them died in 2021, one of COVID-19 and one of haed and neck cancer. Currently, 6 (20%) are alive, ECOG=0, 4 (13.3%) have CR without therapy, expressed in months-23, 33, 35 and 53 (treatment-free survival). Median OS first line with TKI therapy was 34 months while median OS second line with nivolumab was 17 months. Patients with sarcomatoid component in pathohistology report have longer survival. Patients with bone metastases have shorter survival to patients with other metastases.

Conclusion: Nivolumab demonstrated clinical efficacy in the CheckMate 025 clinical trial and in clinical practice as second line treatment after patients had previously received TKI. Our results show that six years after first cycle of nivolumab as second line therapy 6 out of 30 patient (20%) are alive, ECOG=0. Further research should show which sequence therapy would be the best for each patient. Research about potential immunotherapy biomarkers which would indicate who responds to the therapy and who does not is ongoing.

Key words: metastatic kidney cancer, second line, nivolumab, complete response, treatment-free survival

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P49 – THE UNMET NEEDS OF CANCER PATIENTS - A STEP FORWARD

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Psycho-oncology is a discipline that deals with studying, understanding, and treating psychological, emotional, social, spiritual, and functional aspects of living with cancer aiming to reduce distress and improve the quality of life for patients and their families. Distress or general mental distress is an unpleasant experience of psychological (cognitive, behavioural, emotional), social, spiritual, and physical nature that can impair or interfere with the ability to cope effectively with cancer, its physical symptoms, and treatment. Distress extends on a continuum from common feelings of vulnerability, sadness, and fear, to difficulties that can disable, such as anxiety, panic, social isolation, existential, and spiritual crisis. General mental distress is a normal reaction to diagnosis, relapse, and treatment failure. Increased distress should be recognized, monitored, and addressed immediately at all stages of the disease during various medical procedures. Psychological support for cancer patients should be integrated into the care system. To this end, it is necessary to identify the most vulnerable patients early and organize professional counselling services available to patients and family members. It is also necessary to educate patients about distress and mental health and encourage them to check their mental state and seek professional help.

IPOS International Standard of Quality Cancer Care (2010, rev. 2014) emphasizes that psychosocial cancer care should be recognised as a universal human right, quality cancer care must integrate the psychosocial domain into routine care and distress should be measured as the 6th vital sign after temperature, blood pressure, pulse, respiratory rate, and pain.

One of the instruments suitable for measuring distress is the visual analogue scale Emotion Thermometers (ET) developed by Alex Mitchell. Research and studies support the usefulness of ET as a valid tool for measuring distress, including anxiety, depression, and screening patients with high distress. The Croatian version of the Emotion Thermometers (ET-HR) instrument was validated on patients' sample in Croatia and made available on Psihoonkologija.hr as an online questionnaire for patient assessment and self-assessment accompanied with a map showing locations of free professional counselling services for oncology patients who need psychological assistance in Croatia.

It is estimated that at least 30% of cancer patients experience elevated levels of distress and need professional help at some stage of treatment or recovery. Reducing distress is good for the patient, his adherence, quality of life and mental health, for the family and caregivers, and for the medical staff, because it helps to improve the efficiency of procedures. On Psihoonkologija.hr website, patients can make an assess-

ment and self-assessment of distress and find an address book of professional counselling services in the health system and community.

Keywords: psycho-oncology, distress, psychological help, Emotion Thermometers

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P50 – THE UP-DATED INSIGHT INTO IMMUNOTHERAPY WITH CHECKPOINT INHIBITORS IN PATIENTS WITH METASTATIC COLORECTAL CANCER - OUR DAILY PRACTICE

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Background: Immune checkpoint inhibitors (CPI) have significantly improved outcomes in patients with various types of solid tumors. Efficacy and safety of those drugs have been investigated in many clinical trials including those with patients having metastatic colorectal cancer (mCRC). Based on results from KEYNOTE-164, 177 and CheckMate-142 trial, pembrolizumab and nivolumab have been approved for treatment of patients with microsatellite instability-high (MSI-H) mCRC. KEYNOTE-164 investigated the efficacy of pembrolizmab in 124 of those patients. There were two cohorts of patients based on whether they received two or more (cohort A) or one or more prior lines of standard therapy (cohort B). ORR was 33% for both cohorts. Median PFS and OS were 2.3 and 31.4 months for cohort A and 4.1 months and not reached for cohort B. KEYNOTE-177 investigated the efficacy of first line pembrolizmab compared with

standard therapy in 307 patients. Median PFS and ORR were 16.5 month and 43.8% with pembrolizumab versus 8.2 months and 33.1% with standard therapy. In CheckMate-142 multicohort, phase II trial nivolumab with or without ipilimumab was studied. One cohort included 74 patients treated with nivolumab. ORR was 31.1%. PFS and OS were 50% and 73% at 1 year. Other cohort included 45 patients treated with first line nivolumab and ipilimumab. ORR and disease control rate were 69% and 84%. PFS and OS were 74% and 79% at 1 year.

Based on the results of those clinical trials, small number of MSI-H patients with mCRC have been treated with CPI in every day clinical practice. Here we present our up-dated every day clinical practice experience with CPI in the treatment of MSI-H mCRC.

Methods: After approval of local authorities, retrospective analysis of patient charts was done. Results: In our database we found 7 patients with MSI-H mCRC treated with pembrolizumab (N=5) and nivolumab (N=2). Five patients received immunotherapy as second, and one as first and one as third line of treatment. Average number of cycles was 17 (5-34). For two patients treatment is still ongoing (for 18 and 7.5 months). Partial response was observed in 5 patients and stable disease in 2 of them. Among the patients who progressed, duration of treatment ranged from 2.5 to 24 months. Three patients died. Grade III adverse events included hypothyroidism in 1 and arthritis in 3 patients.

Conclusion: Due to small sample size, and relatively short follow up, firm conclusion about efficacy and safety cannot be drown. Further investigation with longer follow up and larger sample size is required. For now, we may notice that toxicity and efficacy are comparable with results of previously mentioned clinical trials. We consider this short report valuable, due the fact that is our first experience with CPI in mCRC in our daily practice.

Keywords: metastatic colorectal cancer, immune checkpoint inhibitors

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P51 – TRANSITION TROUGHOUT THE TREATMENT LINES AND THE OUTCOMES OF METASTATIC PANCREATIC CANCER AT THE DEPARTMENT OF ONCOLOGY AND RADIOTHERAPY, UNIVERSITY HOSPITAL OF SPLIT DURING 2018-2021 - A RETROSPECTIVE ANALYSIS.

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Background: Pancreatic cancer is the seventh leading cause of cancer-related deaths, contributing to 466 003 deaths in 2020(1). This disease is often not presented with visible and distinctive symptoms early on, and more than 50% of patients are diagnosed with metastatic disease(2). Thus, systemic treatment becomes essential in the management of these patients. Treatment options for first-line chemotherapy regimen are: i)a combination of either 5-fluorouracil (5-FU), leucovorin (LV), irinotecan, and oxaliplatin (FOLFIRINOX); or ii) gemcitabine and nab-paclitaxel (GEM/nab-P) combination, with monochemotherapy reserved for a patients not able to receive polichemotherapy protocols (3)(4). Regarding the second-line treatments options, evidence from the conducted trials show modest improvement in terms of overall survival(5). Therefore, a treating oncologist should choose a treatment regimen based on patient's performance status, medical comorbidities and the toxicity of the recommended regimens. The aim of this abstract is to present our results regarding the treatment patterns used at our Department.

Materials And Methods: A retrospective chart analysis of 97 patients with newly diagnosed metastatic pancreatic adenocarcinoma (mPC) who were referred to the Department of Oncology and Radiotherapy, University Hospital Split during 4-year period, from 2018 to 2021. First line treatment regimens being used at that time included 1) FOLFIRINOX regimen; 2) combination of cisplatin and gemcitabine; 3) combination gemcitabine and nab-paclitaxel; and for elderly patients or those with poorer performance status: 4) monogemcitabine; 5) weekly paclitaxel. The data was analyzed with methods of descriptive statistics by using Microsoft Excel tools.

Results: There were 97 patients in total. Approximately one third, i.e., 31 (32%) patients were initially treated with the best supportive care, minding that 6 (6%) patients refused the treatment. 66 patients (68%) have started with the treatment. Median age at the time of diagnosis was 68 years (IQR 61-74) and median number of metastatic sites was 2 (IQR 1-2). Majority of patients had ECOG performance status between 1-3.

Median overall survival (OS) for the treated patients was 5,44 months (IQR 3,22-10,22) and mOS for untreated patients was 1,84 months (IQR 0,92-4,21).

Regarding the first line treatment, median progression free survival was 2,28 months (IQR 1,05-4,37).

Second line of treatment was administered to 23 patients, where 10 of them were given combination of gemcitabine and paclitaxel. The other regimens used were weekly paclitaxel, FOLFOX, CAPOX and FOLFIRI. Overall, the median PFS for the second line treatment was 2.48 months (IQR 1.38-3.86).

Third line treatment was reached by 7 patients, with mPFS being 1.61 (IQR 0.82-2.86) months. Regimens used were weekly paclitaxel, capecitabin and monogemcitabine.

Finally, only two people started the fourth line treatment. One used monogemcitabine for one cycle, and the other one used combination of trastuzumab and pertuzumab for 2 months.

Conclusion: Unfortunately, 37% of patients diagnosed with advanced pancreatic cancer have not received systemic therapy. Transition throughout the lines where as follows: first line of systemic therapy was started by 66 (68%) patients; second line by 23 (24%) patients; third line was reached by 7 (7%) patients; and finally, fourth line was administered to 2 (2%) patients. The results of our analysis show a decrease in the number of patients with mPC in later lines of treatment, which is in line with published results(5)(6)(7).

Keywords: pancreatic neoplasms, efficacy outcomes, chemotherapy

P52 – TREATMENT OF PATIENTS WITH ESOPHAGEAL CARCINOMA - EXPERIENCE OF THE DEPARTMENT OF ONCOLOGY, UNIVERSITY HOSPITAL OF SPLIT

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Background: Cancer of the esophagus is a devastating disease with very bad prognosis. For example, in the USA the 5-year overall survival is just 20%. After a long period without significant improvement in treatment results, the introduction of immunotherapy in the last few years, changed the situation for the better. Unfortunatelly, immunotherapy is still not available in Croatia for esophageal carcinoma patients.

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

Methods:The analysis included all patients with esophageal carcinoma who were treated at the Department of Oncology, University Hospital of Split, in the period from January 1st, 2018 until December 31st, 2020. A retrospective analysis of data collected from the patients' medical histories was performed. For data collection and processing we used Excel 2007, Microsoft corp. and ORIGIN 2016, OriginLab Corporation.

Results: In the observed period a total of 39 patients were treated, of whom 29 were men and 10 women. The median age was 72 years.

3 patients (8%) had ECOG status 0, 20 patients had ECOG status 1 (51%), 11 patients (28%) had ECOG status 2, while 5 patients (13%) had ECOG status 3. Adenocarcinoma was present in 25 patients (64%), 12 patients (31%) had squamous cell carcinoma and 2 patients (5%) had undifferentiated carcinoma. Stage of disease at diagnosis was as follows: 1 patient (3%) had stage I, 4 patients (10%) had stage II, 15 patients (38%) had stage III, while 19 patients (49%) had stage IV.

Median OS of patients with stage II and III was 15 months. The treatment for 8 patients (42%) of this group started with concurrent chemoradiotherapy with the response rate of 50%, median PFS of 8,9 months, median OS of 23,5 months. Of 8 of them 3 are still alive (median follow up of 33,5 months). Unfortunately, for as many as 6 patients with stage II or III the treatment started with the surgery (in other hospitals), their median OS was 20,4 months. Only one of them is still alive (follow up of 48 months).

Median OS of patients with stage IV was 5,4 months. 12 patients (63%) received 1st line chemotherapy, with response rate of 25%, median PFS 3,5 months. 2 patients (10%) received 2nd line chemotherapy and 1 patient (5%) received 3rd line chemotherapy. All patients diagnosed with stage IV died.

23% of overall population (9 patients – 7 with stage IV and 2 with stage III) received only symptomatic supportive therapy, their median OS was 4,5 months.

Conclusion: The results of the treatment of patients with esophageal carcinoma in our department are poor, worse than in the developed western countries. Possible reasons for this are higher percentage of patients with stage IV at diagnosis and lack of obligatory multidisciplinary team presentation before starting the treatment in some hospitals in Croatia, which lead to inappropriate way of treatment.

These results emphasize the need to install obligatory MDTs in all hospitals that treat carcinoma patients and to approve immunotherapy for the treatment of esophageal cancer patients in Croatia.

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

Key words: esophageal carcinoma, treatment procedures, overall survival

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P53 – TREATMENT PATTERNS AND SURVIVAL OUTCOMES OF PATIENTS WITH METASTATIC GASTRIC CANCER AT THE DEPARTMENT OF ONCOLOGY AND RADIOTHERAPY, UNIVERSITY HOSPITAL OF SPLIT FROM 2018 TO 2020 - A RETROSPECTIVE ANALYSIS.

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Backround: Gastric cancer (GC) is the fifth most common cancer and the fourth leading cause of death worldwide. Although there are substantial decreases in incidence in the Western countries, the wide geographic variations based on differences of risk factors still make GC a considerable global health burden with an unfavorable mortality to incidence ratio and poor treatment outcomes. One of the reasons for

such outcomes is the fact that 40% of patients are initially presented in an advanced stage where 5-year overall survival does not extend 5%. Over time, the overall survival (OS) of patients with metastatic gastric cancer (mGC) has increased from 3 to 6 months with monochemotherapy regimens to 10-14 months with platinum-based doublet or triplet combinations or its combinations with trastuzumab in HER2 positive patients. However, with the evolution of molecular profiling and biomarkers such as programmed death ligand -1 (PD-L1), microsatellite instability (MSI) and tumor mutational burden (TMB), immune checkpoint inhibitors alone or in combination with chemotherapy regimens are now pushing the boundaries and prolonging the survival even further. Despite the recent advances in GC treatment, the proportion of patients transitioning through multiple lines of treatment remains very small due to its aggressive biology and unpredictable behaviour. Improvement in rather poor outcomes could be achieved by moving more patients throughout the lines of therapy. The goal of this study was to investigate the percentage of patients receiving different lines of therapy in the management of gastric cancer.

Materials And Methods: We retrospectively evaluated health charts of 99 patients with mGC who were presented at our Multidisciplinary gastrointestinal tumor board at the Department of Oncology and Radiotherapy, University Hospital of Split from 2018 to 2020. The data was analyzed with methods of descriptive statistics by using Microsoft Excel tools.

Results: A total of 99 patients (n=99) with mGC were presented at our Multidisciplinary gastrointestinal tumor board from 2018 to 2020. The median age at diagnosis was 69 (range 31-90). The majority of patients were Eastern Cooperative Oncology Group (ECOG) performance status 0 and 1, reported in 33% (n=32) and 35% (n=35) patients, respectively. The median progression free survival (mPFS) of the entire population was 4.0 months and the median overall survival (mOS) was 7.8 months. Best supportive care was provided in 28.3% patients (n=28) with their mOS being 2 months. 71.7% of patients (n=71) entered first line treatment with mPFS and mOS being 6.1 and 9.7 months, respectively. Second line treatment started 51% of patients (n=36) whereas 17% of patients (n=12) were treated in the third line. The most common first line treatment regimen were cisplatin and fluoropyridine combinations, reported in 58% of patients (n=41). Paclitaxel with or without ramucirumab was the most common second line regimen, reported in 70% of patients (n=25) whereas in the third line 100% of patients (n=12) were treated with irinotecan. In 2022, 6.1% of patients (n=6) are still receiving treatment or being in follow-up.

Conclusion: Compared to previously published relevant clinical studies, the results of our retrospective analysis show similar treatment outcomes as well as the proportion of patients in the later treatment lines. However, a substantial number of patients do not even start systemic treatment as they are provided initially with best supportive care due to their poor performance status, late diagnosis and consequently high disease burden. Therefore, finding the ideal balance between earlier diagnosis, optimal staging, multiple lines of efficient treatment as well as future research is essential for the improvement of mGC outcomes and quality of cancer care in general.

Keywords: metastatic gastric cancer, treatment outcomes, chemotherapy

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