POSTER PRESENTATIONS

P1 - ALND CAN BE OMITTED IN AT LEAST 72% OF BREAST CANCER PATIENTS FOLLOWING NEOADJUVANT SYSTEMIC TREATMENT

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Background: In the upfront surgery setting, SLNB is universally accepted standard of care for early-stage breast cancer (BC) patients diagnosed with uninvolved axilla (cN0). Even in the case of macrometastasis detected in up to 2 sentinel lymph nodes (SLN), ALND can be safely omitted, due to Z0011 trial results. Although the risk of additional positive non-SLN was 27%, it did not translate in any clinical significance in 10 years of follow up. For the higher risk patients with positive SLN(s), axillary irradiation was proven to be equally effective as ALND for both disease control and overall survival in the upfront surgery setting. However, following neoadjuvant systemic treatment (NST), ALND is still considered as a mandatory procedure in case of any metastatic disease detected in the SLN, irrespective of its size and pretreatment nodal status. Moreover, in many institutions, SLNB is still not accepted as a standard of care in this setting, although it is declared as a valid option in all relevant guidelines since 2017.

Patients and methods: With the approval of the institutional ethic committee, all patients surgically treated following NST in Clinical Hospital Centre Rijeka, in period from 2017 till 2020, were included in the present analysis. All relevant data were collected retrospectively from Integrated Hospital Informatic System and analysed with Statistica 13.5 software.

Results: Overall 222 BC patients were included; 48.2% diagnosed as cN0 and 51.8% as cN1-2. Following NST, SLNB was performed in 147 patients (66.4%) and metastasis in SLN were detected in 49 patients (33%), therefore ALND was performed in addition to SLNB. Additional positive lymph nodes in ALND specimens were detected in 17 patients (34.7% of SLN+ cases), but exclusively in cases with macrometastasis detected in the SLN. However, overall risk of significant nodal involvement (>2 additional positive LN) in SLN+ patients was 18.4%, and it was three times higher in patients diagnosed with cN+ disease. In addition to initial cN status and size of metastasis detected in SLN, involvement of more than 2 vs. up to 2 SLN was correlated to statistically significant higher risk of metastasis in more than 2 additional non-SLN (p=0.0162).

Conclusions: With the acceptance of SLNB procedure as a standard of care in the neoadjuvant setting, unnecessary ALND was omitted in 43.3% of sentinel node negative patients According to present analysis, ALND following NST is also overtreatment in 65.3% of ypSN(+), including all patients with micrometastatic disease detected in the SLN, as well as 30% of all ALND performed without SLNB, based exclusively on false positive post-treatment MRI findings. Could we already start to accept Z0011 and AMAROS strategy for selected patients following NST? Several ongoing trials are searching for this answer. However, while waiting for these results, we should at least consider to omit ALND for all ycN0 patients with micrometastatic disease detected in sentinel LN especially for those cases diagnosed as cN0,

for whom the risk of clinically significant additional nodal involvement is only 2.8%. New clinical and pathological biomarkers, that could help us to select additional low-risk ypSN(+) patients are urgently needed.

Keywords: breast cancer, neoadjuvant systemic treatment, sentinel lymph node biopsy

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

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Selective cyclin-dependent kinases 4/6 (CDK 4/6) inhibitors, in addition to endocrine therapy, are standard of care for metastatic hormone receptor (HR) positive HER-2 negative breast cancer for the last few years. These agents have acceptable and easily manageable adverse events. Alopecia is one of the frequent adverse events that remarkably affect patients' quality of life, but is equally neglected. There is only one systematic review and meta-analysis that discuss this issue.

This study aims to discuss and evaluate the alopecia in patients with hormone-positive, HER-2 negative metastatic disease with the patient-related outcome (PRO) and by the European Organization for Research and Treatment of Cancer Quality of life Questionnaire - BR23 (EORTC-QLQ- BR23).

We obtained data from 158 patients with HR-positive HER-2 negative breast cancer who were treated at the Division of Medical Oncology with ribociclib or palbociclib and endocrine therapy, in the period from 08/2018 to 12/2020 and had alopecia as an adverse event. Patients had to complete at least one four-week cycle of therapy and necessitate fill in the questionnaires. For further analysis 149 of them were eligible, all female patients. During therapy with ribociclib, around 55% of patients had reported alopecia as an adverse event, whilst during therapy with palbociclib around 45% of patients.

This is somewhat more than data on alopecia mentioned in the PALOMA 3 QoL assessment, yet in line with the data in the mentioned systematic review, and serves as warning and reminder of this for patients difficult symptom, because of its possible severe distress potential. It is not a life-threatening adverse event, but it directly contributes to worsening of patients' quality of life.

Keywords: HR+ breast cancer, CDK 4/6 inhibitors, alopecia

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P3 - BODY IMAGE SCALE: PSYCHOMETRIC VALIDATION ON A SAMPLE OF CROATIAN BREAST CANCER PATIENTS

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Objectives/purpose: Breast cancer treatment often results in disfigurement which can vastly alter one's body image and negatively impact quality of life. In this context, the Body Image Scale (BIS) was developed as a standardized self-report questionnaire to assess affective, behavioral, and cognitive body image changes in patients with cancer. Even though it is the most frequently used instrument for assessing body image, so far it has not been validated in Croatia. Therefore, this study aimed to examine its factor structure, reliability, and discriminant validity on a sample of Croatian breast cancer patients.

Methods: Participants were 325 women (age range 31-83 years, mean age of 59 years, sd=10.95) recruited between 2009 and 2013 from two large tertiary institutions in a cross-sectional study at four points of adjuvant treatment (two weeks after primary surgery, during adjuvant chemotherapy, adjuvant radiotherapy, and at a 6-month follow-up). Basic socio-demographic and medical data were also collected (age, body mass index, surgery type).

Results: A confirmatory factor analyses was conducted in the Mplus 8.3 software in order to examine the one factor structure of the scale. The CFA showed a good fit, confirming the original unidimensional structure of the BIS (χ2(df) = 96.67 (35), RMSEA =.07, CFI =.95, SRMR =.04). The internal consistency for the scale was high (α =.92). Next, it was negatively correlated with age (r = -.24, p <.01), and not correlated with body mass index (r = -.03, p >.05). Differences in BIS scores were also found between women who underwent a conserving and radical surgery, with latter having higher scores (F=3,56, p<.01). In addition, there were some differences in BIS scores based on phase of treatment. At the point of adjuvant chemotherapy, the women showed a worse body image then those at adjuvant radiotherapy, and 6-months follow up (F=5,62, p<.01).

Conclusion and clinical implications: The obtained results provide support for the original unidimensional structure, reliability, and discriminant validity of the Body Image Scale on a sample of Croatian breast cancer patients. It was found to be negatively correlated with age, while there was no correlation with body mass index. Moreover, it was found to be sensitive to type of surgery and phase of treatment – radical surgery and adjuvant chemotherapy were associated with worst body image. These results demonstrate this instrument has overall good psychometric validity and can be useful in adjuvant care of women with breast cancer.

Keywords: body image, breast cancer, mastectomy, validation

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P4 - BREAST CANCER IMMUNOPHENOTYPE AS PREDICTOR OF RESPONSE TO NEAODJUVANT THERAPY – SINGLE INSTITUTION EXPERIENCE FROM UNIVERSITY HOSPITAL OF SPLIT FROM 2017 – 2020

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Introduction: Historically, neoadjuvant therapy (NAT) has been administered for large inoperable, ulcerated and/or inflammatory breast cancer. Recently, as a consequence of better knowledge about cancer biology, NAT is becoming a standard of care even for certain proportion of operable (ie. T2) tumors. The aim of NAT is to reduce tumor size and facilitate breast conservative surgery, along with monitoring treatment response *in vivo* and eradicating possible micrometastasis. Neoadjuvant treatment is tailored according to surrogate tumor immunophenotype and cancer staging. Mainly, patients with luminal A subtype receive endocrine therapy, TNBC and Luminal B neoadjuvant chemotherapy, and tumors with HER 2 expression chemotherapy with anti HER2 therapy. After surgery, residual cancer burden (RCB), should be analysed. A RCB is treatment response evaluation taking into account size of the primary tumor, cellularity of residual tumor, and the involvement of lymph nodes. MD Anderson calculator counts RCB index and assigns a pathologic response as: PCR (pathological complete response), RCB-I (minimal burden), RCB-II (moderate burden), or RCB-III (extensive burden). A large meta-analysis showed that RCB after neoadjuvant chemotherapy is an accurate long-term predictor of recurrence and survival defining the PCR as a strong survival predictor across all breast cancer subtypes.

Methods: Retrospective analysis of medical data was done for 169 consecutive breast cancer patients who recieved NAT from January 2017 – December 2020 at a Department for oncology and radiotherapy, University Hospital of Split. We analysed patohistologic results and evaluated the response to neoadjuvant therapy according to results of MD Anderson calculator.

Results: From January 1st 2017 to December 31st 2020, 169 breast cancer patients have recieved NAT. Treatment response evaluation was done in 134/169 (79%) of patients. The other did not finished NAT or obtain an operation yet. Overall population showed rate of PCR 33% (45/134). The PCR was 52% (19/36) in HER2 enriched and luminal B HER2 positive immunophenotype; 37% (11/29) in TNBC, 5% (4/25) in luminal A and 25% (11/44) in luminal B HER2 negative.

Conclusion: Our results showed different PCR rate across different breast cancer subtypes similar from those from clinical trials. The highest benefit in HER 2 positive and TNBC was shown. Further follow up of those patients should be done in order to investigate value po PCR in long time outcomes from real world data. The limitation of this data is relatively small number of patients, and short follow up period.

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P5 - CANCER TREATMENT DURING THE COVID19 PANDEMIC AT THE CLINIC FOR RADIOTHERAPY AND ONCOLOGY, CLINICAL HOSPITAL CENTER RIJEKA

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Introduction: Consequences of COVID19 disease have mostly affected the health care system worldwide, including Croatia. A particularly vulnerable group of oncology patients found themselves in a sensitive and dangerous situation. At the Clinic for Radiotherapy and Oncology of the Clinical Hospital Center Rijeka, we were guided by ESMO guidelines as well as the guidelines of the Croatian Oncology Society, which soon issued instructions for the organization of the oncology service and oncology treatment. Numerous papers and large studies cite different delays in oncology treatment as well as the inability to tumor diagnose in a timely manner. In this research, we will present some of our results and challenges in oncology treatment at our Clinic.

Methods: Retrospectively, 55 patients with a diagnosis of malignant disease who had a positive PCR test for SARS-CoV-2 virus were detected from the database of the Clinical Hospital Center Rijeka. In time between March 2020 and February 2021, the same patients were oncologically treated or were in oncological follow-up. The date of a positive PCR test was taken as the first day of COVID19.

Results: The median age of the patients was 64 years. The study group consisted of 35 women and 20 men. Most patients had stage IV disease (n=32). At the time of COVID19, 21 patients were receiving chemotherapy, 8 were on hormone therapy, 1 patient was ongoing radiochemotherapy and 1 ongoing radiotherapy, 4 were being treated with immunotherapy, 8 were ongoing biotherapy. Also, 13 patients were not in active treatment but in oncological follow-up. It is interesting to note that patients in chemotherapy treatment became positive on average 11 days after the application of the planned cycle. The primary cancer site of COVID19 patients followed current epidemiological trends, with the largest number of patients with breast cancer (n=19) and colon cancer (n=14). 16 patients state that their possible source of SARS-CoV-2 virus infection is a health facility. If we analyze the severity of COVID19 disease, 43 patients had a mild or asymptomatic form of the disease, 6 patients had a developed moderate clinical picture and at some point needed oxygenation. In the analyzed group, we detected 4 patients who had a severe form of the disease, 3 of them died of COVID19 disease. 18 patients were hospitalized in one of the COVID depart-

ments of our Institution with an average hospitalization time of 8 days. We specifically analyzed the delay in oncology treatment. In 31 patients there was a delay of an average of 22 days. When we analyze the type of oncology therapy, the next cycle of chemotherapy was delayed by an average of 22 days, biological therapy by 28 days while the delay in immunotherapy was 20 days.

Conclusion: Cancer therapies are of proven benefit, but in light of the serious consequences of potential concurrent SARS-CoV-2 infection, risk-to-benefit considerations are becoming increasingly important. A multidisciplinary approach as well as a personalized treatment plan seems more important than ever for successful oncology treatment during the COVID19 pandemic.

Keywords: COVID-19; cancer treatment, SARS-CoV-2

P6 - CLINICAL OUTCOMES OF PATIENTS WITH METASTATIC NON- SMALL CELL LUNG CANCER TREATED WITH PEMBROLIZUMAB ALONE OR IN COMBINATION WITH CHEMOTHERAPY - A SINGLE CENTER EXPERIENCE

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Introduction: Immunotherapy with pembrolizumab alone is nowadays the standard treatment for patients with metastatic non- small cell lung cancer (NSCLC) with expression of programmed- death ligand 1 (PD-L1) on tumor cells greater than 50%, while patients with PD-L1 expression of 1-49% are treated with chemotherapy plus pembrolizumab. There is a relationship between the extent of PD-L1 expression on tumor cells or, in some trials, on tumor infiltrating immune cells (ICs) and the probability of clinical benefit from numerous anti-PD-1 or PD-L1 agents, in first- and second-line monotherapy.

Patients and methods: We retrospectively analyzed the correlation of PD-L1 expression and clinical outcomes of patients with NSCLC with positive (1-100%) PD-L1 expression treated at our Institution from January 2018 to January 2021. In total, 51 patients were treated with pembrolizumab: 39% of patients were women, and 61% were men. There were 37 patients with PD-L1 expression greater than 50% (ranging from 51% to 100%) and they were treated with pembrolizumab monotherapy. Fourteen patients with PD-L1 expression of 1-49% were treated with pembrolizumab plus platinum- based chemotherapy.

Results: Median follow up for the cohort with PD-L1 expression > 50% was 10 months. Number of events (progression) for this cohort was 14, and median duration of response was 17 months (range 3 to 28 months). For the cohort with PD-L1 expression 1-49%, median progression- free survival (PFS) was not reached. Number of events (progression) for this cohort was 2. Duration of response to treatment was ranging between 3 and 28 months, but median duration of response could not be calculated. We also used the presence of PD-L1 greater than 80% as a stratifying factor for disease progression risk. Our results have shown that the presence of PD-L1 greater than 80% is related to 49% reduction of risk for disease progression, but without statistical significance due to the small patient sample (HR 0.51 (95%CI 0.17-1.56), p=0.24).

Conclusion: The results of treatment with pembrolizumab alone or in combination with platinum-based chemotherapy at our Institution are mostly in accordance to real- world data reported in the literature. Whether higher PD-L1 levels within the expression range of 50%-100% predict for even greater benefit to pembrolizumab is currently unknown. These results show that those patients with very high PD-L1 expression levels might be better suited for treatment with pembrolizumab monotherapy, but additional research is needed.

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P7 - COMPREHENSIVE GENOMIC PROFILING (CGP) AS A CORNERSTONE FOR PRECISION MEDICINE IN METASTATIC UTERINE CANCER - A SINGLE INSTITUTION EXPERIENCE FOR 2020

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Background: According to the TCGA (The Cancer Genome Atlas), uterine cancer is one of the most suitable tumors for precision oncology, divided into 4 subgroups based on the genomic profiling with opted possible targeted therapy for the each subgroup. Nevertheless, the main treatment strategy for the metastatic disease still remains chemotherapy or hormonal therapy with less than 12 months of the median overall survival (mOS).

Matching the right drug with the right tumor and patient, based on the comprehensive genomic profiling (CGP) is the foundation of precision oncology. Croatia is one of the first countries in the World that have started country wide personalized medicine project based on the CGP in 2019.

Considering the fact that uterine cancer harbours high level of potentially actionable genomic alterations and has unacceptable low mOS time for metastatic disease, it is ideal candidate to test the concept of precision oncology. In this abstract we present the first-year data for the CGP analyzed patients with metastatic uterine cancer in a single institution in Croatia.

Methods: The observational retrospective study was conducted at the Department of Oncology and Radiotherapy, University Hospital of Split. It included patients who were either newly diagnosed with metastatic uterine cancer or whose disease has progressed in 2020. and on whose tumors CGP was performed via FoundationOneCDx or FoundationOneHeme (one patient with sarcoma). The data were analyzed with methods of descriptive statistics using Microsoft Excel tools.

Results: There were eighteen patients in total, 10 (55.6%) of them were newly diagnosed and 8 (44.4%) have progressed during 2020. Median age of patients was 64 years (range from 53-71 years). CGP reports

showed that every specimen analyzed had at least one genomic alteration (GA). We have divided GA 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 alterations without clinical significance (GAwCS), defined as those without reportable therapeutic or clinical trials options. CRGA had 16 (88.9%) patients with an average of 3.6 alterations and the most common were those of phosphatide-inositol-3 kinase pathway (PIK3) in 14 (77.8%) patients of which 57% were PIK3CA mutation. GAwCS had 16 (88.9%) patients with an average of 3.4 alterations and the most common was TP53 mutation, reported in 10 (55.6%) patients.

Microsatellite status was determined as stable (MSS) in 13 (72.2%) patients and as high instability (MSI-high) in 4 (22.2%) patients. High TMB (≥16) was reported in 5 (27.8%) patients and the average of TMB was 9.8 of Muts/Mb. PD-L1 status was determined for 16 (88.9%) patients; three had low positive (two had 5% and one had 15%) and one had moderately positive PD-L1 (45%) score.

Some kind of targeted therapy was opted in 15 (83.3%) patients, while for 3 (16.7%) patients there was no reportable therapeutic option. On-label therapy was reported in one patient (5.6%), while off-label therapy was opted for 14 (77.8%) patients. Furthermore, targeted therapy without approval but also driven by patients GA was reported in 14 (77.8%) patients. Most common targeted therapies opted were mTOR inhibitors and immune check-point inhibitors.

Conclusion: Our results have shown high mutation load of uterine cancer with at least one genomic alteration found in every patient tested and with majority of patients having CRGA, which is in accordance to the previous observations. However, being the first year of the testing we cannot draw conclusions about its impact on the course of the treatment and the outcomes. Despite the above, majority of positive results have shown utility of CGP analyses of the metastatic uterine cancer in everyday clinical practice, aiming to create optimal treatment strategy for every patient individually, making a precision oncology potentially new standard of care.

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P8 - CONCURRENT CHEMORADIOTHERAPY IN PATIENTS WITH ANAL SQUAMOUS CELL CARCINOMAS - A SINGLE CENTER EXPERIENCE

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Introduction: Anal cancer is an uncommon cancer accounting for 1-2% of all digestive tract tumors. The incidence of invasive anal carcinoma is increasing due to the rising prevalence of infection with high-risk Human Papilloma Virus (HPV). The treatment paradigm for anal cancer has shifted from abdominoperineal resection (APR) with permanent colostomy to concurrent chemoradiation (CRT) with sphincter preservation. The complete response (CR) rate for CRT is high (80%), with local recurrence rate of 10-30% and 5-year survival rate of more than 80%.

Patients and methods: We retrospectively analyzed 17 patients treated with concurrent CRT in our institution between January 2013 and December 2020. All patients were presented at the multidisciplinary tumor board prior to treatment. Radiotherapy was delivered to pelvis and inguinal lymph nodes (tumor dose of 5040-5400 cGy in 28-30 fractions) concurrent with mitomycin-C/5-FU or mitomycin-C/capecitabine. Treatment response was assessed with MRI.

Results: The median age of 17 patients (7 males, 10 females) at presentation was 56 years (range: 45-73 years). All patients had histologically proven squamous cell carcinoma. Fifteen patients had tumor in the anal canal and 2 patients at the anal margin. It was not possible to perform the HPV analysis because the initial biopsy for the majority of patients was carried out in other institutions. Eight weeks after completion of CRT, 12 (70%) patients had MRI- confirmed CR of the primary tumor. During the median follow-up of 49 months (range 7-89 months), 4 (33%) patients with CR had disease recurrence; median time to recurrence was 13 months. They all underwent APR as salvage treatment. Of these, 3 patients are still alive with no evidence of disease, and one patient died as a consequence of comorbidity complications. The remaining 8 patients with CR are without evidence of disease and alive at the time of this analysis. Mean 3-year relapse- free survival (RFS) was 41,7 months (95% CI 30-53 months), and 3- year RFS rate was 66%. Five (30%) patients who had a partial tumor regression were followed up to 6 months after completion of CRT. Four patients with disease present after 6 months who underwent a salvage APR are still alive. One patient died due to development of metastatic disease (patient refused any proposed treatment).

The mean 3-year overall survival (OS) in our patient cohort was 75,2 months (95% CI 61-89 months), and 3-year OS rate was 80%. Median OS and RFS were not reached due to short period of follow up.

Conclusion: In our cohort of patients, concurrent CRT has proven to be effective in achieving tumor response. The CR rate was concordant with literature data.

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P9 - CUTANEOUS MELANOMA NEOADJUVANT MODERN SYSTEMIC THERAPY: A COMMENT

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Significant therapeutic improvement in progression-free survival (PFS) and overall survival (OS) of patients having cutaneous metastatic melanoma in comparison with the previous cytotoxic drug therapy has been noticed since 2011, when two new drug classes, so-called immune checkpoint inhibitors (ICI) and kinase-targeted therapies, were introduced. ICI is a form of immunotherapy where immunomodulatory humanized monoclonal antibodies (mabs) against inhibitory checkpoint cell membrane proteins (*inhibitory receptor molecules*) on CD8+ T cells or their ligands on antigen-presenting cells (APC) or tumor cells block inhibitory signals and thus enable nonspecific T cell activation and clonal proliferation. In this way nonspecifically activated T cells recognize and eliminate autologous tumor cells in oncological patients. The curiosity of this approach is that these monoclonal antibodies are not directed against tumor cells but against molecules on (immune) cells which physiologically regulate T cell activity. This form of immunotherapy in metastatic melanoma patients first started with anti-CTLA-4 mab ipilumumab and soon afterward anti-PD-1 mabs nivolumab and pembrolizumab were approved. In the same period, small molecular weight molecules called *smart* drugs which target and block the activity of intracellular mutated BRAFV600 and MEK molecules which have tyrosine kinase activity and are physiologically involved in the transmission of cell proliferation and survival signals were also approved. Approximately 40% of cutaneous melanomas have a V600 BRAF mutation, which leads to constitutive activation of the mitogen-activated protein kinase (MAPK) cascade signaling pathway. Approved representatives of this BRAF/MEK inhibitors for patients having metastatic cutaneous melanoma are dabrafenib and trametinib, vemurafenib and cobimetinib, and encorafenib and binimetinib.

With the introduction of these new drugs, some 30 to 50% of treated patients, depending on the drugs and drug combinations used, have been probably cured, which was not the case before and hence this is a significant clinical improvement. Moreover, based on the results of clinical studies, ipilimumab, nivolumab, pembrolizumab and the dabrafenib and trametinib combination were approved in the adjuvant setting for stage III disease operated melanoma patients since the obtained long-term recurrence-free survival (RFS) rates ranged from 40 to 60% depending again on the drug or drug combination used and the follow-up times. The question which arises from PFS, OS and RFS data is why only a percentage of treated patients respond satisfactorily (in the range of 30 to 50% of patients) while in the case of the remaining ones there is no effect? Patients who are unresponsive to these treatments include patients who unfortunately do not respond to the treatment from the very beginning (primary resistance) and others who stop responding

after an initial response (acquired resistance). It seems that in the case of both ICI and intracellular kinase-targeted therapies given in the present way a therapeutic plateau is obtained, which is why some new therapeutic approaches, mechanisms, drugs, and drug combinations should be explored. Also, both types of therapies are quite often accompanied by non-negligible side-effects in patients and this should also be taken into account when planning or choosing any form of these therapies, especially in the adjuvant setting.

In order to improve their clinical effectiveness, these drugs are also tested in the neoadjuvant setting, although at present it is hard to prove that this approach will generate therapeutically better results compared with the same therapy in the adjuvant setting. Also, in view of its possible serious side-effects, adjuvant therapy raises similar concers when compared with treatment in the metastatic setting?

There is still no approved neoadjuvant regimen for melanoma. On the *https://www.clinicaltrials.gov* website, the combination of keywords *melanoma stage III* and *neoadjuvant* lists 48 clinical studies, which is promising. The NCCN cutaneous melanoma guidelines (PDF version 2.2021, page 24/225) state the following indication, quote: *in patients with resectable nodal disease at very high risk of recurrence after complete resection, or if resectability of nodal disease is uncertain, recommend multidisciplinary tumor board review to consider neoadjuvant systemic therapy, preferably in the context of a clinical trial* (1).

One preclinical study suggests that treatment with neoadjuvant immune checkpoint blockade is associated with enhanced survival and antigen-specific T cell responses over adjuvant treatment.

A similar observation about the induction of more tumor-resident T cell clones was reported in a clinical study where 10 patients had stage III disease and received neoadjuvant ipilimumab plus nivolumab in comparison with 10 patients who received this ICI combination adjuvantly. This observation might indicate that neoadjuvant ICI can result in a more efficient anti-tumor immune response. In both groups of patients the applied regimens induced high toxicity rates, which is not to be ignored!

A recent publication of the International Neoadjuvant Melanoma Consortium (INMC) analyzes the association among the pathological response (PR), RFS, and OS in stage III disease melanoma patients with neoadjuvant therapy. This study includes pooled data from six clinical trials with 192 patients receiving anti-PD-1-based immunotherapy (four studies) or BRAF plus MEK targeted therapy (two studies). The obtained results indicate that pathological complete response (PCR) correlated with improved RFS and OS. In patients with a PCR, near PCR, or partial pathological response with immunotherapy, very few relapses were seen (2-year RFS 96%; OS 100%), whereas, even with PCR from targeted therapy, the 2-year RFS was only 79%, and OS was only 91%. The authors' conclusion was that the pathological response should be an early surrogate endpoint for clinical trials and a new benchmark for developments and approval in melanoma.

In conclusion, modern neoadjuvant therapy in melanoma appears effective and has a rationale indication for the subgroup of patients having stage III disease with bulky but resectable disease, which is seen as preferable in the context of a clinical trial. Further investigation is required in order to preserve efficacy while reducing toxicity. Moreover, the fact that biopsies are routinely available provides an opportunity to better understand therapeutic responses and to carry out reverse translation whereby these data are used to select therapies in clinical settings or in trials which are more likely to improve patient outcomes. Optimal regimens have not yet been defined. Other therapeutic approaches should also be investigated because, as has already been mentioned, a relatively big proportion of melanoma patients have primary or develop subsequent secondary resistance to ICI or to tyrosine-kinase targeted therapies.

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P10 - EFFICACY AND SAFETY OF BEVACIZUMAB THERAPY IN PATIENTS WITH CERVICAL CANCER: AN ONE INSTITUTION EXPERIENCE

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Introduction: Cervical cancer (CC) is one of the most successfully treatable forms of cancer, as long as it is detected early and managed effectively. Cancers diagnosed in late stages can also be controlled with appropriate treatment. According to GOG-240 trial, adding bevacizumab to chemotherapy had improved the survival of these patients. We aimed to evaluate efficacy and safety of bevacizumab therapy that is the standard of care in our institution.

Methods: We have retrospectively analyzed the archive data of 38 patients with metastatic, recurrent or persistent CC who started treatment with bevacizumab at the Department of Gynecologic Oncology in the University Hospital Centre Zagreb in the period from January 2017 to August 2020.

Results: Of the 38 patients, 14 (37%) had recurrent, 13 (34%) metastatic and 11 (29%) persistent disease. Median age of the patients at the time of diagnosis was 48 years (range 24-76). ECOG status 0-1 had 92% of patients. Prior platinum exposure had thirty-two patients (85%) and thirty patients (79%) had prior radiotherapy exposure. The median number of cycles of bevacizumab was 9 (range 1-59). Objective response rate was achieved in 63% of patients. Median progression free survival was 8 months, and median overall survival from the time of including bevacizumab in the therapy was 13 months. Median OS from the date of metastatic, persistent or recurrent disease was 17 months. 26% of the patients continue to receive bevacizumab therapy and in 76% of the patients the therapy was discontinued (in twenty patients due to progression of the disease, in six patient because of toxicity and two patients decided to discontinue the further therapy). Possible bevacizumab-related serious adverse events included hypertension (10%), fistula (8%) and renal failure (3%).

Conclusions: Our experience in treating patients with bevacizumab showed good results with acceptable toxicity.

Keywords: cervical cancer, bevacizumab, side effects.

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P11 - EFFICACY AND TOLERABILITY OF TRIFLURIDINE/TIPIRACIL IN PATIENTS WITH REFRACTORY METASTATIC COLORECTAL CANCER AT THE GENERAL HOSPITAL OF ŠIBENIK-KNIN COUNTRY

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Introduction: The backbone of the treatment of patients with metastatic colorectal cancer (mCRC) is irinotecan- and oxaliplatin-based therapy in combination with fluoropyrimidines. In randomized clinical trials, trifluridine/tipiracil (TT) demonstrated a beneficial effect on progression-free survival (PFS) and overall survival (OS) in patients with mCRC refractory to standard chemotherapy. The aim of this unicentric study was to evaluate efficacy and safety of TT in patients with refractory mCRC.

Patients and methods: Treatment outcomes of patients with refractory mCRC at the General Hospital of Šibenik-Knin County from March 2018 to March 2021 were retrospectively analyzed. PFS was defined as the time from first TT application until disease progression, while OS was measured as the time from first TT application until death or the last follow-up visit. The results were presented by descriptive statistical methods and the survivals between the groups were compared with the Kaplan-Meier method and the log-rank test.

Results: A total of 20 patients with mCRC were treated with TT; the median age was 67 years (range 53–83), and the majority were male (70%). The patients were in good general condition (performance status 0-2). Ten patients (50%) had left-sided cancer, six patients had rectal cancer (30%) and four patiens had primary cancer located in the right colon (20%). The most common site of metastasis was the liver (75%), and in three patients it was the only site. Mutation in the RAS gene was detected in 85% of patients; three patients were RAS "wild" type. The majority of patients (80%) received TT in the third line of treatment. The first line irinotecan-based chemotherapy was administered to the majority of patients (80%) and four patients received oxaliplatin-based therapy. Thirteen patients (65%) received biological therapy. The median number of TT cycles received was 3 (range 1–13), and more than one-third of patients (35%) achieved a therapeutic response; two partial response, and five patients stable disease. The median OS was 6.25 months (1-18); five patients (25%) died during follow-up. The median PFS was 2.75 months (range 0.5–13) and all patients progressed during follow-up. Male sex (HR 4.45; $p = 0.026$), better performance status ($p = 0.021$), neutropenia grade ≥2 (HR 5.64; $p = 0.013$) and positive therapeutic response to TT (HR 12.76; $p < 0.001$) were associated with better PFS. There were no significant correlations of PFS with age, previous treatment duration and RAS status ($p > 0.050$ for all analyses). The most common (80%) side effect of TT was neutropenia; grade 3 in 30% and grade 4 in 5% of patients, while febrile neutropenia was present in two patients (10%). There were no deaths associated with neutropenia.

Conclusion: Our study confirmed the efficacy of TT in patients with refractory mCRC with manageable toxicities. The treatment outcomes were comparable to those from clinical studies.

Keywords: refractory metastatic colorectal cancer, trifluridine/tipiracil

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P12 - ENHANCING QUALITY AND SAFETY OF ADVANCED RADIATION THERAPY TREATMENTS IN CROATIA UNDER THE IAEA PROJECT CRO6019 - AN OVERVIEW

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Introduction: The International Atomic Energy Agency (IAEA), under the Technical Cooperation with member states, supports projects related to medical use of ionizing radiation. During three former IAEA TC cycles medical physics group committed to radiation oncology at the University Hospital (UH) Rijeka developed a comprehensive quality assurance programme in radiation oncology.

Under the first project quality assurance/quality control (QA/QC) programmes between two hospitals (Rijeka and Osijek) were upgraded and harmonized, while the main objective of the second one was the extension of established good local QA/QC practices at the national level as well as putting the relevant requirements into the legislation. Under the third project preconditions for the clinical use of advanced radiotherapy techniques were specified and developed for implementation.

Materials and methods: Under the ongoing IAEA project *Verifying intensity modulated radiotherapy (IMRT) treatment dose delivery - method development, standardization and implementation throughout organization of a national audit* (CRO/6019, 2020-2021), Medical Physics Department of the UH Rijeka are developing a robust methodology to quantify, evaluate and optimize IMRT dose delivery at the national level.

In the first phase of the project, the QA/QC procedures required to evaluate, and optimize IMRT dose delivery were thought out, developed, prepared, and verified. The methodology was verified using a set of IMRT optimized dose distributions for the most common patient anatomies.

Results: After the analysis of IMRT dose delivery quality based on the two-dimensional array detector IBA Matrixx, software IBA OmniPro I'mRT, IBA MultiCube and CIRS 002LFC semi-anthropomorphic phantom, comprehensive QA/QC programme for the clinical use of advanced radiotherapy techniques was developed, improved and functional at University Hospital Rijeka. QA/QC protocols for verification of IMRT dose delivery were upgraded in accordance with developed methodology and QA manuals were upgraded accordingly. The methodology for verifying IMRT treatment dose delivery was upgraded and improved according to new equipment: Plan Verification System OCTAVIUS 4D which contains OCTAVIUS detector 1500 and motorized cylindrical phantom OCTAVIUS 4D. To reconstruct 3D absorbed dose distributions from measured data and to evaluate the dosimetric agreement between measured and calculated dose, we used a VeriSoft Patient Plan Verification software.

Discussion: In the second phase of the project, the methodology that has been developed in UH Rijeka will be generalized with the purpose of verifying IMRT dose delivery at Croatian radiation oncology departments where advanced treatment modalities are in clinical practice. After the analysis of the baseline situation, required steps will be taken to propose measures for adjustment of dose delivery protocols for IMRT planning and delivery at the national level.

Conclusion: The required conditions to attain the best possible quality of IMRT dose delivery with available equipment and technology will be fulfilled and a Croatian standard of good practice concerning advanced radiation therapy techniques will be established. Overall objective of this project is to enhance quality and safety of advanced radiation therapy treatments in Croatia.

Keywords: IAEA, Technical Cooperation Project, QA/QC procedures, IMRT dose delivery verification

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P13 - EXPERIENCE WITH TRIFLURIDINE TIPIRACIL IN TREATMENT OF METASTATIC COLORECTAL CANCER - DO REAL WORLD DATA FOLLOW THE RESULTS OF CLINICAL TRIALS?

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Introduction: Trifluridine tipiracil (FTD/TPI) is nowadays a standard third- line treatment for patients (pts) with metastatic colorectal cancer (mCRC). According to RECOURSE trial, FTD/TPI was superior to placebo in terms of overall survival (OS) and progression- free survival (PFS) (7.1 vs 5.3 months, and 2.0 vs 1.7 months, respectively). Exploratory post-hoc analysis of RECOURSE trial defined favorable prognostic subgroups with low tumor burden (<3 metastatic sites) and less aggressive disease (≥18 months from diagnosis of metastatic disease to start of FTD/TPI), while pts with no liver metastases were likely to have the best prognosis. The aim of this study was to compare our own real-world data with those from clinical trials.

Patients and methods: The effects of prognostic factors on outcomes of 33 pts treated with FTD/TPI from May 2018 to October 2020 at the University Hospital Sestre Milosrdnice, Department of Oncology and Nuclear Medicine were analyzed.

Results: Of 33 pts, 21 were men and 12 were women; median age was 64.0 years. At the start of third-line treatment majority of pts had Eastern Cooperative Group performance status (ECOG PS) 0-1. Out of 33 pts for whom FTD/TPI was prescribed, in 29 of them the therapy was started by the study cut-off date and these pts were included in final statistical analysis. Median PFS in the third line treatment was 2.3 months, with FTD/TPI still in progress in 5 pts. Fourth line treatment was started in 7 patients. Five patients treated with FTD/TPI experienced grade 3 or 4 toxicity (neutropenia in all cases), while the others had low-grade or no side effects. Regarding the prognostic subgroups, the criterion ≥18 months from the diagnosis of metastatic disease to the start of FTD/TPI therapy was met by 16 pts, while 20 pts had <3 metastatic sites. A total of 12 pts met the criteria of a good prognostic subgroup. There was no difference in PFS between the good and poor prognostic subgroup (PFS 2.3 months in both subgroups). Median PFS in pts with liver metastases (20 pts) was 2.3 months, compared to 2.1 months in pts without liver metastases.

Conclusion: Overall, there was no statistically significant difference between prognostic subgroups, but the strength of the test was low due to the small sample. Total PFS was consistent with the previous clinical trials, while OS was not reached.

Keywords: metastatic colorectal cancer, trifluridine tipiracil, real world data, prognostic subgroups.

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P14 - GIANT LIPOMA WITH INTRAPELVIC AND EXTRAPELVIC EXTENSION PRESENTING AS A SCIATIC HERNIA

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Introduction: Lipomas are the most common type of soft tissue tumor, they are benign mesenchymal tumors. They are usually found in the subcutaneous tissue and in most cases remain asymptomatic. Lipomas are rarely deeper located and can become symptomatic if they compress surrounding neurovascular structures. Sciatic hernia can occur through a greater or lesser sciatic foramina, they are a rare type of pelvic floor hernia. The major conduit of neurovascular structures from the pelvis to the lower limb is the greater sciatic foramen. The sacrospinous ligament separates the greater sciatic foramen from the smaller lesser sciatic foramen. Structures that enter or exit through the greater sciatic foramen are divided depending on the position towards the piriformis muscle into suprapiriform or infrapiriform. Sciatic hernia symptoms will depend upon the organs inside of the hernia sac. Sciatic hernia can lead to back pain, sciatica, pelvic pain, bowel obstruction or ureteral obstruction. A sciatic hernia can develop at any age.

Case report: We report an unusual case of a 50-year-old white Caucasian with a large intrapelvic mass found as an accidental finding on an computed tomography (CT) examination of the abdomen. The patient was referred for a colonoscopy due to gastrointestinal problems. During the colonoscopy, polyps were found and a polypectomy was performed. The pathohistological finding corresponds to an adenomatous polyp with pseudoinvasion. Therefore, the patient underwent an CT examination of the abdomen and pelvis and then an magnetic resonance imaging (MRI) of the pelvis was ordered. MRI demonstrated a large mass with extra and intra pelvic extension. MRI scan showed a well-defined mass 8cm x 4cm x 4.5cm in diameter homogeneously isointense with fat that traversed the greater sciatic foramen through the suprapiriform area. Also MRI showed the compression of the mass on the sciatic nerve. anamnesis revealed that the patient occasionally had pain in his left leg. The patient was referred for surgery to remove the pelvic mass, surgery confirmed the diagnosis of lipoma.

Conclusion: Sciatic hernia are mostly incidental finding but can cause a sciatica. The radiological method of choice for diagnosis is MRI.

Keywords: lipoma, sciatic hernia, pelvic floor, magnetic resonance imaging

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P15 - HOSPITAL ANXIETY AND DEPRESSION SCALE: PSYCHOMETRIC VALIDATION ON A SAMPLE OF CROATIAN BREAST CANCER PATIENTS

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Objectives/purpose: Research repeatedly shows that breast cancer can have detrimental effects on mental health as well. To increase the awareness of clinicians treating breast cancer on the psychological burden of this disease and provide adequate care, it is important to implement screening for mental health disturbances in adjuvant treatment. Quick and validated standardized tools are therefore necessary in

clinical practice. Among those, the Hospital and Anxiety and Depression Scale (HADS) is a standardized self-report questionnaire aimed at measuring psychological distress, namely anxiety and depression, in non-psychiatric patients. Although HADS is a frequently used and quick screening tool, so far it has not been validated in Croatia. Therefore, this study aimed to examine its psychometric properties, including factor structure, reliability, and discriminant validity on a sample of Croatian breast cancer patients.

Methods: In this study, 325 women (age range 31-83 years, mean age of 59 years, sd=10.95) were recruited between 2009 and 2013 from two large tertiary institutions in a cross-sectional study at four points of adjuvant treatment (two weeks after primary surgery, during adjuvant chemotherapy, adjuvant radiotherapy, and at a 6-month follow-up). Apart from pen-paper questionnaires (HADS, Body Image Scale), basic socio-demographic and relevant medical data were also collected (treatment point, comorbidity, surgery type).

Results: Confirmatory factor analyses was conducted in the Mplus 8.3 software where we compared several alternative models of HADS. The two-factor model, which consist of Anxiety (HADS-A) and Depression (HADS-D) subscales, showed a good fit ($\chi 2(df) = 118.63$ (76), RMSEA =.04, CFI =.96, SRMR =.04). However, some of items on the HADS-A subscale had low loadings. The internal consistency reliability coefficients were acceptable for both HADS-A (α =.75), and HADS-D (α =.74). There were no differences in HADS-A and HADS-D scores in various points of adjuvant treatment, nor between those who had different types of surgery (mastectomy and breast conservation surgery). However, women without comorbidity experienced lower depression. Anxiety and Depression subscales were moderately correlated (r =.62, p <.01). Women with higher body image concerns experienced higher anxiety and higher depression (r =.37, p <.01, r =.34, p <.01).

Conclusion and clinical implications: The obtained results provide support for the original two-dimensional structure, reliability, and discriminant validity of the Hospital Anxiety and Depression Scale on a sample of Croatian breast cancer patients. No differences were found concerning points of adjuvant treatment or surgery type, but higher depression was found in women with other comorbidities, while both anxiety and depression were higher in women with higher body image concerns. These results demonstrate this instrument has overall good psychometric validity and can be useful in adjuvant care of women with breast cancer.

Keywords: anxiety, breast cancer, depression, validation

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P16 - IMMUNOHISTOCHEMICAL PATERNS IMP3, KI-67, P53 AND CYCLIN D1 IN LARYNGEAL CARCINOGENESIS

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There are only a few studies so far on IMP3 role as a potential diagnostic biomarker in the laryngeal carcinogenesis. Therefore, it makes sense to analyze IMP3 together with other biomarkers of carcinogenesis. The aim of this study was to investigate the immunohistochemical expression patterns of IMP3, Ki-67, p53 and cyclin D1 in laryngeal carcinogenesis. The study included 153 patients divided into three groups: 68 operated for primary invasive laryngeal squamous cell carcinoma (LSCC); 41 with precancerous lesions of atypical and abnormal hyperplasia and 44 with hyperplastic laryngeal nodule without atypia. Tissue microarray technique was used for immunohistochemical analysis. As for the IMP3 staining pattern, a cytoplasmic staining of low intensity in a few cells of superficial layers was found in both control and precancerosis groups.

On the other hand, in tumor cells of LSCC there was a high percentage of cytoplasmic staining against IMP3 of high intensity. Additionally, IMP3 staining showed significant intertumoral and intratumoral heterogeneity in different cases of LSCC. In well-differentiated LSCC with present keratinization we noticed that negative areas of the tumor alternate with areas of cytoplasmic staining of low intensity. In tumor cells of moderately differentiated LSCC there was a pattern of combined focal cytoplasmic staining of strong intensity with cytoplasmic staining of low intensity, while a diffuse cytoplasmic staining of moderate to strong intensity was found in tumor cells of poorly differentiated LSCC. Ki67 staining showed a low percentage of nuclear staining of medium to high intensity against Ki-67 in parabasal and a few suprabasal layers of samples from both control and precancerosis groups. High percentage of nuclear staining of high intensity was found in samples from the LSCC group. p53 staining showed different patterns in all three groups. In control group, there was a low percentage of nuclear staining of moderate to strong intensity in parabasal and few suprabasal layers, while in precancerosis group it was medium percentage of nuclear staining of moderate to strong intensity in basal, parabasal and few suprabasal layers. In the LSCC group there was a high percentage of nuclear staining of moderate to strong intensity in tumor cells. Cyclin D1 showed a high percentage of nuclear staining of moderate to strong intensity in parabasal and few suprabasal layers of samples from the control group and in tumor cells of LSCC.

However, in the precancerosis group there was a medium percentage of nuclear staining of moderate to strong intensity in a few basal, parabasal and several suprabasal layers. Immunohistochemical expressions of Ki-67 and pronouncedly IMP3 generally follow the same pattern where control and precancerosis are similar and LSCC significantly differs, as opposed to p53 and cyclin D1. In that sense, IMP3 expression increase and difference in LSCC, as opposed to control and precancerosis, is especially pronounced, which

points toward its possibly important diagnostic, therapeutic and prognostic value.Further studies on the exact molecular mechanisms behind these differences are, of course, needed.

Key words: cyclin D1; immunohistochemical expression pattern; IMP3; Ki-67; laryngeal carcinogenesis; p53

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P17 - IMPACT OF COVID-19 PANDEMIC ON NUMBER OF OUTPATIENT ONCOLOGY VISITS: A SINGLE CENTER EXPERIENCE

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Introduction: The COVID-19 pandemic has a significant detrimental impact on cancer care worldwide, resulting in a reduced number of newly diagnosed cancer patients, advanced stage and delay of therapy. We investigated the impact of the COVID-19 pandemic on the number of outpatient visits at our Department. The first COVID-19 patient in Federation of Bosnia and Herzegovina was detected on 9 March 2020.

Methods: We retrospectively analysed data of the number of outpatient visits between 9 March 2020 to 8 March 2021 (*COVID year*) in comparison to the same period of time before COVID pandemic, from 9 March 2019 to 8 March 2020 (*pre-COVID year*), at Department of Oncology, University Clinical Hospital Mostar. We searched the Hospital information system (BIS) by outpatient visits through our Department subunits: Daily oncology hospital for systemic therapy visits, Radiotherapy clinic for examinations during radiation treatment and Oncology clinic for regular oncology follow-up visits. We calculated the percentage difference between one *pre-COVID year* and one *COVID year.*

Results: In *COVID year*, 11333 patients visited Daily oncology hospital, 1515 patients visited Radiotherapy clinic and 7337 patients visited Oncology clinic. During the same period of time, in *pre-COVID year*, Daily oncology hospital visited 12440 patients, Radiotherapy clinic 1781 patients and 8758 patients visited Oncology clinic. The percentage difference between one *pre-COVID year* and *COVID year* was 8.9% decrease in Daily oncology hospital visits, 14.9% decrease in Radiotherapy clinic visits and 16.2% decrease in Oncology clinic visits in COVID year. Total number of outpatient visits at Department of oncology in *pre-COVID year* was 22979 and in *COVID year* 20 185, decrease was 12.2%.

Conclusion: During the COVID-19 pandemic decreased number of outpatients was detected compared to the same period of time in previous year.

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P18 - IMPACT OF TYPE OF PRIMARY SURGERY ON QUALITY OF LIFE, ANXIETY, DEPRESSION AND BODY IMAGE IN BREAST CANCER PATIENTS RECEIVING ADJUVANT TREATMENT: A CROSS-SECTIONAL STUDY

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Introduction: Breast cancer is the leading cause of cancer-related death in women and a major public health issue in developed countries. Primary surgery is the key treatment modality for localized breast cancer and there has been a shift towards breast conservation over the last two decades. Robust evidence suggests the longstanding impact of type of primary surgery on health-related quality of life (QoL) and integral well-being of patients with breast cancer going through adjuvant oncologic treatment. The aim of this study was to compare QoL, anxiety (A), depression (D) and body image (BI) of breast cancer patients during different phases of adjuvant treatment with respect to type of primary breast surgery received.

Patients and methods: A total of 425 breast cancer patients were recruited in a cross-sectional study at key points of their adjuvant treatment trajectory: two weeks after primary surgery, during adjuvant chemotherapy, adjuvant radiotherapy, and at a 6-month follow-up. They completed pen-paper questionnaires, including the EORTC core questionnaire QLQ-C30 and breast cancer-specific module QLQ-BR23, Hospital Anxiety Depression Scale (HADS) and Body Image Scale. Differences in clinical and treatment factors and differences in mean scores across QoL domains, A, D, and BIS for all cohort and for each phase of adjuvant treatment were analyzed using chi square test, ANOVA or student t-test. Association of type of surgery with global QoL as the main QoL domain was explored using linear regression.

Results: Two-hundred eighty-nine (69%) and 133 (31%) patients were treated with primary breast-conserving surgery (BCS) and mastectomy (M). With respect to baseline clinical and sociodemographic factors, significant differences between women with BCS and M were observed in tumor stage ($p<0.0001$),

tumor grade (p=0.002), phase of adjuvant treatment (p<0.0001), and in comorbidity level (p=0.02). Patients with more advanced stage, higher tumor grade, patients receiving adjuvant chemotherapy, and patients with less comorbidity were more likely to undergo M as opposed to BCS. Furthermore, patients who had mastectomy had lower body image (higher scores on Body Image scale and body image at functional QLQ-BR23 scale) (both p=0.0001), while there were no significant differences in A, D, and other QoL scales. Analysis was repeated for each phase of adjuvant treatment (surgery, adjuvant chemotherapy, adjuvant radiotherapy, and 6-month follow-up post treatment). Again, apart from body image domains, no other scales were significantly different between patients who had BSC or M, respectively.

Conclusions: These results show that type of primary surgery has no impact on QoL, anxiety, depression and is limited to the self-image of breast cancer patients. Therefore, mastectomy may not be perceived as a priory negative factor for QoL. However, we found it contributed to a worse body image in breast cancer patients. Limitations include a cross-sectional study design where heterogeneity between patient groups might have affected study results.

Keywords: anxiety, body image, breast cancer, depression, mastectomy, quality of life

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P19 - IMPROVEMENTS IN SURGICAL APPROACH TO NEWLY DIAGNOSED BREAST CANCER PATIENTS BY IMPLEMENTING MULTIDISCIPLINARITY – SINGLE CENTER EXPERIENCE FROM UNIVERSITY HOSPITAL OF SPLIT

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Introduction: All relevant clinical guidelines recommend patohistological confirmation (either needle biopsy eventually surgical biopsy in some circumstances such as very small lesions, diffuse breast cancer…) and treatment goal and strategy from the MDT prior to any treatment modality given. Following this well established approach, we are enabling adequate cancer care for all newly diagnosed breast cancer patients. Multidisciplinary approach is recommended for the diagnosis and treatment of cancer, in order to optimize quality of life and survival. Leaving these patients on behalf of only one discipline may cause

skipping some of the important steps in diagnostics and treatment, causing them to be underserved, despite the fact that all the modern and new treatment options being available, but unfortunately, not implemented. In order to objectively analyze the status or quality of multidiscipliray work in our hospital a retrospective analyses of patterns of care was done.

Methods: Retrospective analysis of available medical data was done for the patients who had breast cancer diagnosis from 2017 – 2020, and who were presented on breast cancer MDT on Department of Oncology and Radiotherapy, University Hospital of Split. The data was analyzed with methods of descriptive statistics using Microsoft Excel tools.

Results: From 2017 – 2020, 1650 patients were presented on our multidisciplinary team for breast cancer. According to our results, in 2017 and 2018 only 24% of patients were presented on MDT before planned operation procedure, and 76% were presented after they already had an operation. Significant improvement in approach was seen in 2020, when 48% of newly diagnosed breast cancer patients had an MDT treatment plan before proceeding any treatment including surgery, in contrary with results from 2019, which had shown that 89/385 (23%) had an operation before presentation on MDT.

In 2017 breast cancer was diagnosed and patients committed to surgery by cytology confirmation only in 52% breast cancer patients while 45% of patients did have patohistological (PH) confirmation of disease. Unfortunately, 3% of patients went to surgery without any confirmation of malignant disease.

Similar results were observed in 2018: 53% was diagnosed cytologically, 45% with PH, and 2% of patients had an operation without cytology or biopsy performed. In 2019 no change was observed, 58% of patients went to surgery with cytology only, and 41% of patients had core/surgical biopsy. 1% of patients were operated without having cytology or biopsy before surgery.

Improvements in diagnostics and guidelines pnetration were seen in 2020, 32% of patients had a surgery after cytological diagnosis of breast cancer, 67.3% had core/surgical biopsy before surgery, and there were no patients who had an operation without confirmed breast cancer.

Conclusion: We have find a signes of multidiscipliry team disfunction in our hospital. Namely, number of breast cancer patients presented at the MDT before commencing to any treatment was unacceptably low. Moreover, the number of patients undergoing surgery procedures without appropriate PhD diagnoses as well as MDT presentation was unacceptably high. Results from 2020 as well recent results from 2021 defines a good direction and better function of MDT in our hospital.

Our analysis have addressed our clinical problem in breast cancer diagnose and initial treatment due to avoiding initial presentation on MDT prior to any treatment including surgery. Making an effort to raise awareness of other specialties especially surgeons, radiologist and family doctors who see patient prior to oncologist to send patients to MDT helped us to improve our results in practice. Longer follow up and larger number of patients is required to estimate weather this improvement would lead to improvement long time outcome measures.

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P20 - INFLUENCE OF BODY COMPOSITION ON QUALITY OF LIFE (QOL) OF BREAST CANCER PATIENTS TREATED WITH ADJUVANT CHEMOTHERAPY

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Body composition has been studied relatively recently as part of oncology trials in different types of tumors. There are numerous studies that clearly define the impact of chemotherapy and its side effects on quality of life of breast cancer patients, however there have been few studies that have analysed the impact of body composition on chemotherapy tolerance as well as on the quality of life of premenopausal patients in the course of cytotoxic treatment.

The study was performed on a consecutive sample of patients treated with neoadjuvant or adjuvant chemotherapy for early-stage breast cancer at the daily hospital of the Department of Medical Oncology of University hospital for Tumors in Zagreb between December 2018. and April 2019. All patients were premenopausal and received four cycles of doxorubicin + cyclophosphamide chemotherapy in standard dose, every three weeks, before or after the surgery. During the each visit patients filled standardized quality of life questionnaires (EORTC QLQ-C30 and QLQ-B23) and patient's body composition was estimated using Tanita BC-420MA analyzer. The data were presented as averages with standard deviations for numeric data, or numbers and percentages for categorical data. The testing was performed with Pearson's correlation coefficient. All analyses were performed in R, with significance set at $P<0.05$.

The study included 68 patients with median age of 52,6 years (range 29-55 years). Analysis of the results of body composition measurements in correlation with QoL showed the impact of body composition on certain QoL subdomains during treatment. At the beginning of the study, at the first measurement, patients with higher body mass and increased visceral fat index have shown worse physical performance than other patients. During the entire study, sexual functioning in patients with higher visceral fat index was significantly reduced. In a later course of the study, it was shown that body composition significantly influenced the occurrence of fatigue during treatment, that is, that patients with a higher percentage of body fat and visceral fat index were significantly more tired than patients who had a higher percentage of muscle mass.

In conclusion, our research showed significant correlation between some components of body composition and QoL subdomains in premenopausal patients with early breast cancer treated with chemo-

therapy. This kind of information can be used in planning interventions for specific subgroup of patients which can bring an improvement in the patient's well-being during chemotherapy, improve patient's adherence to therapy and thus indirectly influence prognosis of the disease.

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P21 - LOCAL DISEASE CONTROL IN PATIENTS WITH LOCALLY ADVANCED CERVICAL CANCER TREATED IN ONCOLOGY AND NUCLEAR MEDICINE CLINIC, UHC SESTRE MILOSRDNICE

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Primary treatment of choice for patients with locally advanced cervical cancer, stages IB3 to IVA, is concurrent chemoradiotherapy (external beam radiotherapy with concurrent platinum-containing chemotherapy) and brachytherapy.

In Oncology and nuclear medicine clinic of UHC Sestre milosrdnice, patients with locally advanced cervical cancer are beeing treated with 3D-conformal external beam radiotherapy (EBRT, TD=45-50.4 Gy/25-28 fractions) concurrent with weekly cisplatin chemotherapy (40 mg/m^2) and image-guided high-dose rate brachytherapy (HDR-BT) with 192-Iridium (TD=28 Gy/4 fractions). We do 3D brachytherapy treatment planning (volumetric delineation of targets and OARs) on CT slices, and as a help to guide brachytherapy we use MRI prior and at the end or after concurrent chemoradiotherapy. The goal is to achieve equivalent dose at 2 Gy (EQD2) to the high-risk CTV (HR-CTV) D90 of 80-85 Gy and for larger disease or poor response to EBRT D90 of 87 Gy or more.

In time period from January 1st 2019 until December 31st 2020, 407 applications of HDR-BT have been conducted in our Clinic, of which 120 applications were conducted in 30 patients with locally advanced

cervical cancer. The results of our analysis are based on the data for 29 of these patients because one patient was lost to follow-up. Median age of our patients was 57 years, range 22-78 years. Our patients were stage IIB-IVA disease. Complete radiological response, which was evaluated by MRI +/- PET/CT (in 2 patients), was achieved in 72% (21/29) of patients. Twenty seven procent (8/30) of patients underwent surgery because of residual disease on imaging. Complete pathological response was achieved in 75% (6/8) of operated patients. Total proportion of radiological or pathological complete response was 93% (27/29). Median D90 for HR-CTV of 86.9 Gy +/-2.6 Gy (standard deviation) was achieved, range 80.9-92.5 Gy.

The combined use of imaging and development of advanced radiotherapeutic (EBRT and BT) techniques leads to better treatment of cervical cancer.

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P22 - MULTIDISCIPILINARY BREAST CANCER MANAGEMENT IN CLINICAL HOSPITAL CENTRE RIJEKA; COMPLIANCE WITH EUSOMA BENCHMARK QUALITY INDICATORS

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Background: Taking into account significant fluctuations in the treatment outcomes for breast cancer patients among European countries and with the intention to minimize those differences, in 2013 European Society of Breast Cancer Specialists (EUSOMA) has produced the guidelines on the requirements of the Specialised Breast Centre (BC). These, recently updated, guidelines are defining the minimum requirements needed for set up a BC and requirements for each breast service in such institution, identified as the optimal approach in breast cancer management. In the position paper, EUSOMA appointed a set of benchmark quality indicators (QIs) to establish an agreed minimum quality of care and to allow standardization in monitoring the compliance with the proposed guidelines. Herein, we present the evaluation of quality of care for breast cancer patients in Clinical Hospital Centre (CHC) Rijeka, according to current official EUSOMA QIs.

Patients and methods: All patients with breast surgery performed in 2019 in CHC Rijeka were included in present analysis. According to EUSOMA model version 3.1., pseudonymised dataset was cre-

ated upon 66 (48 mandatory) clinical data per patient, collected retrospectively from Integrated Hospital Informatic System (IBIS). Following encryption all data were electronically transferred into collective EusomaDB system (https://www.eusoma.db.org). QIs were calculated for CHC Rijeka and the results were compared with the minimum requirements and the target values benchmark QIs.

Results: Overall 342 patients had breast surgery in 2019 in CHC Rijeka; 62 for benign lesions and 280 for breast carcinoma. For 288 patients, surgery was the primary treatment and 54 patients were submitted to preoperative systemic treatment. Conservative surgical approach was predominant both in the breast (83% BCS) and in the axilla (94% SLNB, 77% SLNB-only).

According to the official EUSOMA report, CHC Rijeka has not only reached the conformity in 12 out of 14 mandatory benchmark QIs, but has exceeded even the target values in over 50% of cases. However, we have failed to achieve compliance with 2 mandatory benchmark QIs.

Conclusion: Multidisciplinary assessment in not only the recommendation, but the imperative in now-days breast cancer management, e.g., the standard of care. In comparison with EUSOMA benchmark QIs, our results imply high level of compliance with the EUSOMA requirements for setting up the BC as well as with the current guidelines for optimal multidisciplinary management of breast cancer patients. In our first successful database validation, we have failed in conformity with only two of fourteen mandatory benchmark QIs. However, we have already taken the appropriate corrective actions, that would improve our results in the near future, with the validation of already prepared 2020 dataset. But even more important, identification of our fails and their corrections would lead to improvements in the quality of care for our breast cancer patients.

Keywords: breast cancer, EUSOMA quality indicators, multidisciplinary management

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P23 - NEOADJUVANT CHEMOTHERAPY FOR MUSCLE-INVASIVE BLADDER CANCER: A PILOT FEASIBILITY BIOMARKER ANALYSIS

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Introduction: Cisplatin based neoadjuvant chemotherapy (NAC) is standard of care for muscle-invasive bladder cancer and is associated with overall survival benefit. However, only a patient (pt) subset derives benefit while a proportion of patients may not tolerate cisplatin. Retrospective data suggest basal subtype is associated with worse prognosis but responds better to NAC compared to luminal subtype.

Our aim was to assess potential association between immunohistochemically (IHC) assessed molecular subtypes, pathologic response to NAC and survival outcomes. Hypothesis of the study was that bladder cancer subtyping based on IHC panel is feasible at our institution. No clinical decisions were made based on these subtypes.

Patients and methods: A single-institution cohort of pts with localized muscle-invasive bladder cancer that received cisplatin-based NAC was evaluated. Consecutive pts were treated with NAC and parallel to formal histopathologic analysis of transurethral bladder tumor resection (TURBT) specimen, additional IHC analysis on the same specimen was performed using Choi consensus (Cancer Cell 2014) panel to classify bladder tumors into putative luminal and basal subtypes. Biomarkers included cytokeratin 5/6, 20 (CK 5/6, 20), CD44, GATA-3 and *p*53.

Results: Between March 2018 and December 2020, 25 pts were included and had TURBT specimen IHC analyzed; 23 completed NAC, in 2 patients NAC was still ongoing, 17 had radical cystectomy, 3 declined cystectomy and in 3 pts cystectomy was not pursued due to development of metastasis. In 17 patients who had cystectomy, median age was 62 years (range 48-73 years), and 14 were men. Distribution of clinical T stages (based on TURBT and CT investigations) was following: cT2, cT3, and cT4 in 10, 5, 2 patients, respectively. Twenty pts received dose-dense methotrexate, vincristine, doxorubicin, and cyclophosphamide (dd-MVAC) and 3 pts cisplatin/gemcitabine. In those 23 pts, based on our IHC panel, 15 pts were assigned to luminal subtype, 5 pts to basal subtype, 2 pts in p-53 like subtype, and 1 pt in mixed/equivocal subtypes (luminal+basal). After median follow-up of 22 months (range 4-33 months), 11 pts experienced progression and 8 died due to metastatic disease. Among 17 pts who had cystectomy, 5 (29%) experienced pCR; 4 had tumor luminal subtype and 1 tumor basal subtype. Median progression-free and overall survival were 16 months (95%CI 10-19 months), and 17 months (95%CI 13-17 months), respectively. Formal statistical comparisons were not feasible due to low sample size.

Conclusions: IHC-based classification of bladder cancer into putative molecular subtypes was found to be feasible in our clinic. However, it remains to be seen whether these molecular subtypes are associated with response to NAC and other clinical outcomes. We plan to prospectively compare IHC-based subtyping with NGS (next generation sequencing) approaches for molecular characterization of muscle-invasive bladder cancer.

Keywords: Bladder cancer, molecular subtype, neoadjuvant chemotherapy, immunohistochemistry, basal, luminal.

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P24 - NIVOLUMAB AND ATEZOLIZUMAB AS SECOND-LINE TREATMENT FOR NON-SMALL CELL LUNG CANCER - EXPERIENCE OF THE DEPARTMENT OF ONCOLOGY UNIVERSITY HOSPITAL OF SPLIT

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Background: Phase III clinical studies comparing immunotherapy (nivolumab, atezolizumab, and pembrolizumab) with docetaxel in patients with non-small cell lung cancer (NSCLC) that progressed during or after first-line platinum-based chemotherapy, showed improvement in overall survival and lower toxicity. Based on those results, immunotherapy become the new standard of care in second-line treatment of patients with locally advanced or metastatic NSCLC who are in good general condition and without driver mutations.

In this work we present the real world results of second-line treatment of patients with nivolumab and atezolizumab at the Department of Oncology, University Hospital of Split.

Methods: The analysis included all patients with locally advanced or metastatic NSCLC who received at least one cycle of second-line immunotherapy with nivolumab or atezolizumab in the period from November 2019 (when drugs were approved by the Croatian Health Insurance Fund in this indication) until March 1st, 2021. 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 IBM SPSS 13.0 for windows, SPSS Inc.

Results: 44 patients received immunotherapy (nivolumab 18 patients, atezolizumab 26 patients), of whom 26 were men and 18 women. The median age was 66 years.

39 patients (89%) had ECOG status 1, while 5 patients had ECOG status 0 (11%). Adenocarcinoma was present in 25 patients (57%) and 19 patients (43%) had squamous cell carcinoma. 8 patients (18%) had brain metastases.

Tumor-membrane expression of the PD-L1 was as follows: less than 1% in 22 patients (50%), 1-49% in 13 patients (29%), 50% or more in 3 patients (7%), while 6 patients had unknown PD L1 status (14%).

The median progression-free survival was 4,0 months (4,5 months in the nivolumab group and 4,0 months in the atezolizumab group). The median number of administered cycles of immunotherapy was 6 (range 1-26), 8 cycles in the nivolumab group and 6 cycles in the atezolizumab group.

The median overall survival was not reached (at the time of analysis 29 patients (66%) were alive).

The objective response rate was only 2.3% (one patient in the nivolumab group had a partial response). Stable disease was the best response to therapy in 28 patients (64%), disease progression was observed in 7 patients (16%), while 8 patients (18%) had not yet undergone control diagnostic process.

Of the 27 patients whose disease progressed, 10 (37%) received at least one additional line of systemic treatment.

The immune-related adverse events were observed in 9 patients (20%): thyroiditis (hypothyroidism, hyperthyroidism G I, thyrotoxicosis G I, II) in 6 patients (14%); rash (G I, II) in 2 patients; adrenal insuffi-

ciency G II in 1 patient; hepatitis G II in 1 patient. There were no adverse events leading to treatment discontinuation.

Conclusion: Immunotherapy with nivolumab and atezolizumab as second-line treatment of locally advanced or disseminated NSCLC in our institution had relatively similar efficacy and toxicity to that published in the registrational studies. The lower response rate compared to registration studies, in which it was 14-20%, might be explained by the fact that in our population a higher proportion of patients had brain metastases, ECOG performance status 1, and tumors with PD-L1 expression less than 1%, as well as with the fact that in the real world the quality of radiological follow-ups are lower than in the clinical trials. The weaknesses of this analysis are its retrospective nature, small number of patients and short follow-up period.

Key words: nivolumab, atezolizumab, non-small cell lung cancer, second-line treatment

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P25 - NUCLEAR EGFR STRONG EXPRESSION IN LARYNGEAL SQUAMOUS CELL CARCINOMA AFFECTS A MORE AGGRESSIVE BIOLOGICAL BEHAVIOUR

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Aim of the study: Membrane EGFR (mEGFR) protein overexpression is frequently found in the head and neck squamous cell carcinoma (HNSCC). It has been found that mEGFR upon stimulation translocates to nucleus and its nuclear localisation is associated with poor prognosis in many cancers. The main focus of this study is to asses if nuclear EGFR (nEGFR) expression affects biologically more aggressive tumor behaviour in comparison to mEGFR expression in laryngeal SCC.

Material and Methods: We examined 42 laryngeal squamous cell carcinomas (SCC) for nEGFR and mEGFR expression as well as cell cycle proliferative markers Ki-67, p53, cyclin D1 using immunohistochemistry.

Results: In our study group, we found in 28.57% (12/42) SCC cases a strong (3+) nEGFR expression, 64.28% (27/42) SCC had weak to moderate (1+/2+) nEGFR expression while 7.14% (3/42) cases were negative for nEGFR. The majority of patients with SCC had strong (3+) mEGFR (52.38% or 22/42) expression and 45.23% (19/42) had weak to moderate (1+/2+) mEGFR expression and one case (1/42) was negative for mEGFR. The mean values ± standard deviation (%) of Ki-67, p53 and cyclin D1 expression in our study group were 39.04 ± 18.08, 38.88 ± 32.22 and 43.82 ± 18.34, respectively.

When assessing the association of nEGFR with mEGFR and cell cycle proliferation markers there was statistically significant negative correlation between nEGFR and mEGFR expression (τ = -0.389; P = 0.002) and statistically significant negative correlation between nEGFR and cyclin D1 (τ = -0.274; P = 0.032). In the analysis of mEGFR correlations with the examined cell proliferation markers there were no statistically significant associations.

We also observed that higher number of patients with strong nEGFR expression and concomitant negative/weak to moderate mEGFR expression died (70% or 7/10 patients) in comparison to number of patients with strong mEGFR expression and negative/weak to moderate nEGFR expression (40% or 8/20 patients). Moreover, univariate statistical analysis showed a statistically significant correlation between strong nEGFR protein expression with worse overall survival in laryngeal SCC, alone or in co-expression with strong cyclin D1 and high Ki-67 (P=0.025, P=0.046, P=0.043, respectively). However, there was no statistically significant difference in the overall survival, when we analyzed strong mEGFR expression, alone or in co-expression with cyclin D1 and Ki-67 cell cycle proteins (P=0.953, P=0.731, P=0.647, respectively).

Conclusion: Our data indicate that nuclear EGFR cellular localization with strong expression might influence the more aggressive biological behaviour of laryngeal SCC carcinoma with poor patient survival.

Keywords: Immunohistochemistry; Epidermal Growth Factor Receptor; Laryngeal Cancer; Carcinogenesis.

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P26 - PD-L1 EXPRESSION IS REGULATED BY MICROPHTHALMIA TRANSCRIPTION FACTOR (MITF) IN NODULAR MELANOMA

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Backround: A recent meta-analysis of anti-PD1 and anti-PDL1 therapy (nivolumab and pembrolizumab) examined twenty trials, seven in melanoma patients, and reported that overall response was significantly higher in tumors positive for PD- L1. The question that arises is how PD-L1 expression is regulated in malignant melanoma cells. Recent researches introduce MITF (microphthalmia transcription factor) as an immunohistochemical marker for the diagnosis of melanoma. MITF amplification was found in 10-15% of melanomas. Studies on in vitro melanoma cell lines link MITF with the regulation of the PD-L1 molecule. Furthermore, several MITF target genes such as BCL2, CDK2, CDKN1A link MITF to the regulation of cell survival and growth. The Bcl2 protein regulates apoptosis while cyclin D1 gene regulates the transition from G1 to the S phase of the cell cycle.

The aim of our study is to assess the relationship between MITF, Bcl2 and cyclin D1 protein expression and the expression of the PD-L1 molecule. We will examine the expression in clinical samples of nodular melanoma in the relation to invasive growth, tendency to early metastasize and a higher degree of resistance to therapy.

Methods: For this study, we selected fifty-two formalin-fixed, paraffin-embedded tumor samples from patients surgically treated at our hospital between 2007 and 2011 and diagnosed with nodular melanoma. Immunohistochemical (IHC) stains were performed on tissue samples of nodular melanoma by the tissue microarray method (TMA). The number of stained cells was presented as a percentage. IHC staining for Bcl2 protein was expressed in the cytoplasm, IHC staining for cyclin D1 and MITF proteins were expressed in cell nuclei while PD-L1 molecule was expressed on the cell membrane. For the purposes of statistical analysis, IHC positivity was subsequently classified into the categories of weakly positive (<25%), moderately positive (25 - 50, 20-60%) and strongly positive (> 50 or > 60%). Statistical significance was measured by the Chi-square test. For the parameters with fewer observations or measurements, Fisher's exact test was used.

Results: According to Breslow thickness grades, 15 (28.8%) samples were less than 4 mm thick, and 37 (71.2%) samples were more than 4 mm thick (median 6.3; range 0.5 - 18 mm). By comparing the correlation of Breslow grade and other analysed parameters, the connection with Clark level and categorized expression of MITF protein was confirmed ($p = 0.067$). By comparing the expression of the tested proteins and the PD-L1 status, the following correlations were confirmed: a statistically significant inverse proportional correlation ($p= 0.001$) between cyclin D1 protein expression and PD-L1 expression. We did not find a statistically significant correlation between the expression of Bcl2 and PD-L1 ($p = 0.117$). There was a statistically significant correlation between PD-L1 expression and MITF protein expression ($p = 0.023$).

Conclusion: Our results suggest that it is possible that PD-L1 expression is precisely regulated by MITF. Understanding how immune regulation interacts with the MITF pathway may help differentiate between the characteristics of melanoma that portend susceptibility and those that portend resistance to checkpoint inhibitor therapy.

Key words: microphthalmia transcription factor; melanoma; PD-L1

P27 - POSSIBLE PREDICTIVE FACTORS FOR THE EFFECTIVENESS OF TRIFLURIDINE/TIPIRACIL IN REFRACTORY METASTATIC COLORECTAL CANCER. A MULTICENTER EXPLORATORY ANALYSIS

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Background: Trifluridine/tipiracil (TAS-102) is an orally administered cytotoxic agent approved for treatment of patients with metastatic colorectal cancer (mCRC) after progression to at least two prior regimens of standard therapy with survival benefit demonstrated in two phase 3 trials. Recent exploratory analysis of RECOURSE trial revealed that patients with low tumor burden and indolent disease derive greater benefit from TAS102 in terms of progression-free survival (PFS) and overall survival (OS). Nevertheless, the final answer on the TAS102 real impact on well-being of a patients with late stage mCRC will come from a real-world data, especially on the national level.

Methods: The aim of this retrospective exploratory study was to investigate the effectiveness of TAS102 in refractory mCRC with regard to different duration of standard treatment (ST) defined as time from the beginning of the first-line chemotherapy until progression to second line. Two separate analyses were done, each comparing the effect of TAS102 depending on the duration of ST in which the time difference between aggressive and indolent disease was set at 12 and 18 months, respectively.

We included patients who began treatment with TAS102 between Jun 2017 and Oct 2020, from three university hospitals: University Hospital Centre Zagreb (Zagreb), University Hospital Split (Split), and Sestre milosrdnice University Hospital Center (Zagreb). TAS-102 was introduced after progression to ST. Outcomes, measured as PFS and OS, were estimated using the Kaplan-Meier method and curves were compared using the log-rank test. Patients lost to folllow-up were censored at their last hospital visit.

Cox regression analysis was used to examine the association between survival, sex, age, location of the primary tumor, ECOG performance status, RAS status, previous biological therapy, and treatment sequence (TAS102 in 3rd or 4th line). Data on OS and PFS were censored at 12 months cutoff.

Results: In total, data on 138 patients (92 men, 46 women) were analyzed. For the entire cohort, the median age was 65, the mST was 21.05 months with mPFS and mOS for the treatment with TAS102 being

2.57 and 6.08 months, respectively. Groups were well balanced regarding baseline characteristics in each comparison.

In the first analysis, 27 patients in the group with more aggressive disease (ST duration less than 12 months) had significantly worse mPFS than 111 patients with ST over 12 months, 2.33 vs. 2.67 months (P=0.015), respectively.

Similar results were obtained from the second analysis in which the groups were defined as ST being shorter or longer than 18 months (ST<18 vs. ST≥18). mPFS for ST<18 (n=57) was 2.37 months compared to 2.67 months in ST≥18 (n=81), P=0.591. No significant differences were observed in response rate and OS between the two groups, albeit there was a tendency towards better OS in ST≥18, 6.53 months compared to 5.42 months in ST<18 group. Cox regression analysis revealed no influence on survival from other covariates.

Conclusion: We used two different time standards in ST for mCRC to distinguish a more from the less aggressive course of the disease. Based on both, our results demonstrate that patients with more indolent clinical course derive significantly greater PFS benefit from TAS102 regardless of patient or tumor characteristics, or previous therapy.

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P28 - PRECISION ONCOLOGY THROUGHOUT THE COMPREHENSIVE GENOMIC PROFILING (CGP) - A SINGLE INSTITUTION CROSS-SECTIONAL DATA FOR THE 2020

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Background: Nowadays, due to the development of different genetic testings such as next generation sequencing that enables comprehensive genomic profiling (CGP), approaches such as *one size fits all* or *hit or miss* are becoming part of the history and precision medicine is accentuated, in which treatment is tailored individually for every patient. As a result, molecular targeted therapy and immunotherapy are now standard treatment in many cancer types.

CGP is gradually being introduced in everyday clinical practice and Croatia is among first ones in the World to have entered into force a country-level based project of precision medicine throughout the CGP

analysis in 2019. The aim of this abstract is to present the first-year results of the CGP analyzed patients in a single institution in Croatia.

Methods: The observational retrospective study was conducted at the Department of Oncology and Radiotherapy, University Hospital of Split. It included all analyzed patients in 2020. who were eligible for the CGP analysis (advanced or metastatic stage with at least 6-12 months of life-expectancy, depending on the tumor site, with ECOG performance status ≤2 and sufficient tissue for the analysis). CGP was performed via FoundationOneCDx, FoundationOneLiquid (two patients without available tissue) or FoundationOneHeme (one patient with sarcoma). The data were analyzed with methods of descriptive statistics using Microsoft Excel tools.

Results: There was 89 tumor specimens sent for the analysis in 2020. The results have arrived for 85 (95.5%) patients the and for 4 (4.5%) patients the CGP could not be completed or there was not sufficient tissue. Median age of patients was 61 year (range from 28-79 years). The most common tumor sites tested were ovarian (18, 21.2%), uterine (16, 18.8%), breast (9, 10.6%) and colorectal (8, 9.4%) cancer. CGP reports showed that every specimen analyzed had at least one genomic alteration (GA), divided into clinically relevant (CRGA) with approved targeted therapy in patients' (on-label) or in other tumor type (off-label), or with existing clinical trials available, and GA without clinical significance (GAwCS), meaning no reportable therapeutic or clinical trials options. CRGA had 75 (88.2%) patient, while GAwCS had 76 (89.4%) patients.

Microsatellite status was not determined for 9 (10.6%) patients, determined as stable (MSS) for 72 (84.7%) and as high instability (MSI-high) for 4 (4.7%) patients. Tumor mutational burden (TMB) was not determined for 7 (8.2%) patients. Meanwhile, it was high (≥10) in 10 (11.8%) patients and the average of TMB was 5.4 Muts/Mb. Loss of heterozygosity (LOH) score was reported in 16 out of 18 patients with ovarian cancer and the average LOH was 7.5% with LOH ≥16 reported in 5 (27.8%) patients.

Some kind of targeted therapy was opted in 59 (69.4%) patients, of which on-label in 26 (30.6%) and off-label in 54 (63.5%) patients. Furthermore, targeted therapy without approval but also driven by patients GA was reported in 57 (67%) patients and for 16 (28%) patients it was the only suggested targeted therapy option. Due to disese progression on all standard systemic therapy options or as an addition to existing therapy, 21 (24.7%) patient has started treatment in accordance with CGP analysis during 2020.

Conclusion: Our results have shown that every tumor specimen analyzed had at least one genomic alteration with the majority of patients having CRGA. Also, for the majority of patients some kind of targeted therapy was opted and nearly one fourth of the patients have started treatment in accordance to the CGP but with rather short follow-up time to assess its impact on the outcomes. In addition to the above, our results from all patients included (chemotherapy-naïve and pretreated patients), all the more so, favor the utility of CGP in everyday clinical practice and show good compliance to the established criteria and protocol for the analysis.

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P29 - PRELIMINARY RESULTS OF PIK3CA MUTATION ANALYSIS IN ADVANCED BREAST CANCER

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Based on the SOLAR-1 trial in 2019 FDA approved therapy with PIK3CA inhibitors for patients with HR-positive and HER2-negative advanced breast cancer previously treated with aromatase inhibitors. Patients with mutation treated with PIK3CA-targeted inhibitors had improved progression-free survival of an average of 11 months compared with 5.7 months of an average in patients without PIK3CA inhibitor therapy. PIK3-kinase (phosphoinositide-3-kinase) activates diverse cellular processes (cell growth, differentiation, proliferation, survival). Activating somatic mutations in its catalytic subunit p110α (PIK3CA) are present in about 40% of BC, and via the AKT/mTOR signaling pathway are involved in oncogenesis and cancer growth.

Material and method: Qualitative detection of somatic PIK3CA mutations was performed on DNA isolated from formalin-fixed paraffin-embedded (FFPE) tissue of 159 patients with advanced BC who met the criteria for treatment with PIK3CA inhibitors. The tissue available for analysis was a primary tumor or metastasis. PIK3CA mutations were detected by real-time PCR using Roche Cobas® PIK3CA mutation assay that can detect 17 hotspot single amino acid substitutions in five exons (ex1, ex4, ex7, ex9, and ex20), provided by Roche Company.

Results: Median age of patients with advanced BC included in our study was 63 years (range from 34-89 years). Patients without mutation in the PIK3CA gene (wild type) were somewhat older than patients with detected mutation (64 *vs.* 62 years). PIK3CA mutation was detected in 56 patients (36.1%). In only four cases, the result was invalid due to poor material. As expected, most mutations were in exons 9 and 20 (87.5%) while less frequent mutations in ex1, ex4 and ex7 were detected in 12.5% of cases. Hotspot mutations were detected as follows: in ex4 N345K (six cases); ex7 C420R (one case); ex9 codons E542K (six cases) and E545A/D/G/K (19 cases), and ex20 codon H1047L/R/Y (24 cases). It remains to be seen whether cancers show different effects of therapy depending on hotspot mutations. 57.4% of the analysis was performed on metastatic lesions with 31.4% of mutations detected compared to 40.3% of mutations in primary breast cancer (χ^2=2.38, P=0.123). In 31% of cases, the tissue used for analysis (FFPE) was older than three years, but this did not affect the detection itself, and PIK3CA mutations were detected in 39.3% of such cases.

Conclusion: Frequencies of PIK3CA mutations were as expected, and both primary and metastatic lesions were acceptable for analysis. We will continue to monitor our patients to obtain more information about their course of the disease, treatment response, and outcomes.

Keywords: breast cancer, PIK3CA mutations

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P30 - PROGNOSTIC RELEVANCE OF LACTATE DEHYDROGENASE IN STAGE IV MELANOMA WITH KNOWN BRAF MUTATION STATUS

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Introduction: Serum lactate dehydrogenase (LDH) is a well-known biomarker for metastatic melanoma patients. Elevated LDH is one of the strongest independent prognostic factors in metastatic melanoma independent of site and number of metastases, that correlates well with decreased survival in patients with advanced disease. Given the hypoxic environment of melanoma cells with resultant inability to produce adenosine triphosphate from glucose through oxidative phosphorylation, LDH catalyzes the conversion of pyruvate to lactate when oxygen supply is low or absent. It is not a secreted enzyme; thus, an elevated serum level is thought to be secondary to spillage of LDH when melanoma cells outgrow their blood supply. It is relevant to confirm its prognostic role in patients treated with targeted therapies [BRAF inhibitors (BRAFi) and MEK inhibitors (MEKi)].

Methods: Median time to progression and overall survival were assessed according to LDH levels for patients with stage IV melanoma treated with BRAFi and MEKi, between March 1, 2017 and December 31, 2020. Three LDH categories were considered: ≤1 × ULN, >1 to ≤ 2,5 × ULN and >2,5 × ULN.

Results: We retrospectively analyzed 81 metastatic melanoma patients (46 males and 35 females) treated with BRAFi and MEKi. The median follow-up of our patients was 29 months (95% CI 24–78). 47

(58%) patients with normal LDH (≤1 × ULN) had a median progression free survival (PFS) of 10 months (95% CI 8-14), and median overall survival (OS) of 34 months (95% CI 20-50). For 20 (24%) patients with elevated LDH >1 to ≤ 2,5 × ULN a median PFS was 6 months (95% CI 4-11) with median OS of 33 months (95% CI 8-38). 14 (18%) patients with elevated LDH >2,5 × ULN had a median PFS of 3 months (95% CI 1-16) and median OS of 4 months (95% CI 14-36). The median PFS of the entire cohort was 9 months (95% confidence interval 5 months-11 months with median OS of 22 months (95% confidence interval 14 months-36 months). Kaplan Meier log rank test showed a statistically significant difference in PFS and OS with respect to LDH levels stratified into 3 categorical variables.

Conclusion: In advanced melanoma treated with BRAFi±MEKi, elevated LDH level at baseline represents a poor prognostic factor. However, patients with increased LDH levels and treated with these drugs gain significant benefits in terms of PFS and OS. Our results are consistent with literature data.

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P31 - RADIOTHERAPY INDUCED HYPOTHYROIDISM PREDICTS PROGRESSION-FREE SURVIVAL IN HEAD AND NECK CANCER PATIENTS

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Introduction: Hypothyroidism is well known side effect of head and neck cancer treatment. The relationship between hypothyroidism and cancer is complex, and the data about impact of hypothyroidism on survival in head and neck cancer patients are scarce. The aim of this study was to determine the possible impact of hypothyroidism on outcomes in patients with squamous cell head and neck carcinoma (HNSCC) treated with (chemo) radiotherapy.

Patients and Methods: This study included 142 patients with HNSCC who were treated with (chemo) radiotherapy in a primary or postoperative setting between August 2012 and September 2017. After the completion of therapy, the patients' hormone status was regularly assessed during follow-up using thyroid-stimulating hormone (TSH) and free thyroxine (fT4) assays. Thyroid hormone evaluation was done every 3 months for the first two years, and every 6 months afterwards. Hypothyroidism was defined as a

thyroid stimulating hormone (TSH) level ≥ 5 uIU/mL..The analysis of relationship between radiation induced hypothyroidism and outcomes like progression-free survival (PFS), and overall survival was performed. Outcomes (PFS and OS) were assessed using Kaplan-Meier method. Association of hypothyroidism (categorical variable) with survival outcomes was assessed using Cox regression model

Results: Hypothyroidism was detected in 62% (88/142) of patients during the follow up period. After median follow-up of 50 months (95% CI 47-95 months, range 5-95 months) we observed 25 local events, 10 regional events and 11 distant events, and 17 patients died. Presence of hypothyroidism was associated with longer PFS compared with patients who did not develop hypothyroidism. Median PFS for patients with hypothyroidism vs patients without hypothyroidism was 65 months (95%CI 24-65 months) vs not reached, p=0.03. For OS there was no difference.

Conclusion: Development of radiotherapy induced hypothyroidism is associated with longer progression-free survival. However, we did not observe impact on overall survival, yet. This hypothesis needs to be tested in larger prospective studies.

Keywords: Chemoradiation, head-and-neck cancer, hypothyroidism, survival, thyroid

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P32 - REAL WORLD EXPERIENCE IN TREATMENT OF PATIENTS WITH ADVANCED KIDNEY CANCER ACROSS THERAPY LINES: SINGLE INSTITUTION ANALYSIS FROM LARGE TERTIARY CENTER

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Introduction: The treatment of renal cell carcinoma (RCC) represents one of the great success stories in translational cancer research, with the development of novel therapies targeting key oncogenic pathways. However, given broader treated population, treatment results in every day real-world practice may differ from results of landmark randomized trials. The aim of this study was to compare efficacy and toxicity of established first and subsequent therapy lines in our unselected population of patients with advanced RCC with results of landmark randomized trials.

Patients and methods: Retrospective analysis of institution's database of all patients with advanced RCC who received active anticancer treatment between 2008 and 2021 was undertaken. Data on specific agents, dose, schedule and patients' clinical characteristics were retrieved for first and subsequent therapy lines. Progression-free survival (PFS) and overall survival (OS) was estimated by the Kaplan-Meier log-rank method for each therapy line. Cox regression analysis was used to assess association of known prognostic factors and PFS and OS.

Results: A total of 180 patients were treated in first line; 171 (95%) patients had clear cell histology, 151 (84%) patients had nephrectomy. The risk status of 81% of the patients could be stratified using the Heng criteria into favorable (17%), intermediate (61%), and poor risk (22%) categories. In first line 122, 45, 4, and 9 patients were treated with sunitinib, pazopanib, sorafenib, and temsirolimus, respectively. After median follow-up time of 48 months (95%CI 39-54 months) for living patients, for patients receiving first line TKI (N=171) PFS and OS were 10 months (95%CI 8-96 months), and 23 months (95%CI 15-122 months), respectively. The median OS of the favorable, intermediate, and poor risk groups were 36, 21, and 9 months, respectively ($p<0.0001$). Patients who had TKI dose reduction (49/171, 29%) experienced significantly better PFS (27 vs 7 months) and OS (44 vs 16 months) compared to patients who remained on standard TKI dose (both $p<0.001$). We build prognostic model for PFS and OS. Variables that were significant on multivariate analysis were TKI dose reduction, history of nephrectomy and IMDC risk group (both Wald $p<0.001$). Second line treatment received 83 patients (63%), stratified as follows: nivolumab, sorafenib, axitinib, everolimus, and vinblastine in 31, 22, 14, 11, and 5 patients, respectively. There was no statistically significant difference observed in median second-line PFS, however numerically was longest for nivolumab (nivolumab 13 months, axitinib 9, sorafenib and everolimus 3, and vinblastine 2 months, respectively). Third line treatment received 36 patients (21%): 23, 5, 4, 2, 2 patients received vinblastine, sorafenib, everolimus, nivolumab, and megesterol-acetate, respectively. Eleven patients (6%) received forth-line treatment: 6, 4, and 1 patient received megesterol-acetate, vinblastine and everolimus, respectively.

Conclusions: Real world data of efficacy of the first line TKI and second line immune checkpoint inhibitor therapy in unselected patients with metastatic kidney cancer are similar to landmark clinical trials. Management of TKI-related toxicity is crucial to derive utmost benefit of first line TKI treatment and to allow patients uninterrupted transition to subsequent therapy lines upon progression. Second line immune checkpoint inhibitor therapy might offer long-term disease control.

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P33 - RESULTS OF TREATMENT OF MUSCLE-INVASIVE BLADDER CANCER IN UNIVERSITY HOSPITAL OF SPLIT: 2014.-2021.

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Introduction: Neoadjuvant chemotherapy (NAC) based on cisplatin, given prior radical surgical treatment, is the golden standard of therapy for localised and locally advanced muscle-invasive bladder cancer (MIBC) (1–4). In our everyday practice unfortunately, NAC has still not become part of standard approach to these patients.

In this study we present the retrospectively collected data on value of NAC in the multidisciplinary treatment of MIBC.

Materials and Methods: We have treated 48 patients with MIBC with NAC in period between 1.1.2014. until 1.3.2021. by the desicion of Multidisciplinary team for urogenital cancers of University Hospital of Split. A retrospective analysis of data collected from the patients' medical charts was performed. Study was approved by Ethical Comittee of University Hospital of Split.

Results: Median age of patients vas 69 years, there were 34 (71%) males, and 14 (29%) female patients. Forty-one patients (85%) were diagnosed with clinical T2 tumor, 6 patients (13%) had T3 tumor, and one patient (2%) had T4a tumor. Forty-six patients had high grade urothelial cancer, and 2 patients had urothelial cancer with small cell neuroendocrine component. Clinically positive lymph nodes were found in 8 (17%) patients. Fifteen patients (31%) received 4 cycles of cisplatin –gemcitabine combination, 30 (62%) patients got 3 cycles of same chemotherapy, one patient (2%) was treated with carboplatin-gemcitabine and 2 (4%) patients with small cell neuroendocrine tumor component with cisplatin-etoposide.

In two patients (4%) NAC had to be stopped due to side effects (anasarca and high-grade prolonoged pancytopenia).

Surgery was performed in 39 (81%) patients, of whom 37 (95%) had radical cystectomy, and 2 (5%) patients had partial cystectomy. One patient (2%) refused operation, in 2 patients (4%) surgery was canceled due to worsening of general condition and progression of the disease, and 5 patients (10%) were lost from follow- up after NAC. One patient (2%) undergone adjuvant radiation.

Pathological complete response was achieved in 8 (20.5%) patients. Median follow-up for our patients was 23.2 months. In group of surgically treated patients, 4 patients (10%) had died (median survival in this group was 16.6 months).

Conclusion: The results of this study confirm succesfull implementation of NAC in standard clinical practice of MIBC treatment. The pathological response rate is in accordance to published real - world data (5). Lack of this study is its' retrospective design, low number of treated patients and short follow-up period.

Keywords: bladder cancer, neoadjuvant chemotherapy, cystectomy, muscle-invasive bladder cancer

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P34 - RETROPERITONEAL CASTELMAN'S DISEASE

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Introduction: Castleman's disease (CD), or angiofollicular lymphnode hyperplasia is uncommon condition distinguished by development of benign lymph node masses. It is pathological diagnosis, and it rarely diagnosed before surgery.

Case report: A 67-year-old man was admitted to hospital for planned surgery on the *MultiSlice Computed Tomography (*MSCT)-verified intrabdominal mass. The patient was diagnosed with tumor mass two years earlier but the patient then refused the surgery. He is now coming to the hospital for an enlargement of the tumor and a feeling of pressure and abdominal pain. Repeated MSCT indicates an increase in tumor mass now measuring 10 cm in diameter with an increase in paraortal and aortocaval lymph nodes up to 4 cm in diameter. The tumor did not show invasion to the surrounding structures. The abdominal organs are of neat structure and size. MSCT of the chest showed no enlargement of the lymph nodes. An exploratory laparotomy was performed in the patient whereby a retropeitonal located sharply circumscribed tumor was removed in toto. One enlarged lymph node is removed at the same time. Based on the histologic and immunohistochemical findings, the diagnosis of Castelman's hyaline vascular disease is made. The patient endured the surgery well and is discharged home for 14-postoperative days.

Conclusion: In the retroperitoneal space, numerous benign and malignant tumors can occur, with a differential diagnostic of Castelman's disease always being suspected in hypervascular heterogeneous tumors. Retroperitoneal localization of Castelman's disease, although rare, has been reported in the literature, with the most common unicentric form of disease for which surgical treatment is also the therapy.

Keywords: Castelman's disease, retroperitoneal tumor, localised type, surgery

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P35 - RETROSPECTIVE GAMMA ANALYSIS OF PATIENT ABSORBED DOSE DISTRIBUTIONS IN A VIEW OF NEW TOLERANCE CRITERIA RECOMMENDATIONS

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Introduction: In radiation oncology, uncertainties in treatment delivery should be kept as low as possible. Establishment of a comprehensive quality assurance (QA) program is a crucial step of uncertainties reduction. Important part of a QA program is verification of calculated patient absorbed dose distributions, also known as *patient specific dosimetry* (PSD).

At Medical Physics Department, PSD verification is undertaken for each advanced radiation oncology treatment. Calculated absorbed dose distributions are validated using gamma method. Since 2018 international tolerance criteria for gamma passing rate calculation have become more stringent. This was a motivation for a retrospective verification of calculated dose distributions validated before 2018 according to new tolerance criteria.

Methods and materials: Two different treatment planning system's dose calculation algorithms were used for absorbed dose calculation. Standard Superposition algorithm (Elekta XiO ver. 5.10) for "field in field" (FiF) technique and Monte Carlo based algorithm (Elekta Monaco ver. 5.11) for intensity modulated radiation therapy (IMRT) technique. Detector IBA Matrixx, along with MultiCube phantom, was used for measurement of absorbed dose distributions. Linear accelerators Siemens Oncor Impression and Siemens Oncor Expression were used for dose delivery. Calculated and measured absorbed doses were compared using IBA OmniPro I'mRT. Up to 2018, recommended tolerance criteria were 3% dose-difference and 3mm distance-to-agreement (DTA). Gamma passing rate was set to ≥95%. In 2018, these criteria were changed to be 3% dose-difference and 2mm DTA. Retrospectively, absorbed dose distributions calculated using the 3%/3mm criteria were re-validated using more stringent criteria. Over 1800 FiF and over 250 IMRT dose distributions were validated. The results were presented per anatomical sites: breast, rectum, H&N, CNS, prostate, lung (FiF) and H&N, CNS, prostate (IMRT).

Results and discussion: Applying the 3mm/2% criteria, for FiF, average gamma passing rates for anatomical sites, along with their standard deviation, were as follows (in %): 96.99 (1.67) for breast, 95.22 (4.12) for rectum, 96.98 (1.98) for H&N, 98.39 (2.01) for CNS, 98.17 (1.13) for prostate and 99.22 (2.32) for lung. Correspondingly, for IMRT, average gamma passing rates for anatomical sites, along with their standard deviation, were as follows (in %): 96.35 (3.95) for H&N, 97.09 (1.87) for CNS and 95.78 (1.89) for prostate.

Presented results shows that despite the validation according to more stringent tolerance criteria, average gamma passing rates exceed the ≥95% tolerance limit for all observed treatment sites for both treatment planning modalities.

Conclusion: Validated average gamma passing rates exceeded the ≥95% tolerance criteria when new recommendations were followed. This shows that a prerequisite to deliver prescribed absorbed dose to the patient was fulfilled and calculated absorbed dose distributions were optimized in a very good manner.

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Keywords: dose calculation algorithm, pre-treatment dosimetric verification, new tolerance criteria

P36 - TDM-1 FOR HER2-POSITIVE ADVANCED BREAST CANCER – CLINICAL PRACTICE EXPERIENCE AT UNIVERSITY HOSPITAL FOR TUMORS

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Trastuzumab emtansine (TDM-1) in monotherapy is standardised second line treatment option for HER2-positive advanced breast cancer patients, who had previously been treated with trastuzumab and a taxane. The EMILIA study assessed the efficacy and safety of T-DM1, as compared to lapatinib plus capecitabine, and has shown significantly improved progression-free and overall survival with median duration of response 12,6 months in comparison to 6,5 months with lapatinib plus capecitabine. In this trial, more patients had luminal breast cancer (282), whereas 202 patients had non-luminal breast cancer.

Also, there were 334 patients included with visceral disease involvement compared to 161 patients with non-visceral site of disease.

Everyday clinical practice results often differ from study results. We wanted to share TDM-1 treatment results from our clinic, from March 2017 through March 2020, with 36 patients included, who received at least 4 cycles of TDM-1.

From 36 enrolled patients, there were 26 patients with hormone dependent breast cancer, related to 10 patients with non-luminal disease. Overall 19 patients had visceral disease only, 17 patients had visceral and bone disease involvement, and there was no patient with solitary bone disease involvement.

After initial four cycles of treatment with TDM-1, control diagnostic evaluation was performed. Analysis has shown that 26 patients had positive response to treatment, which was assessed by either stable disease or improving disease burden (evaluated by RECIST criteria), with clear clinical benefit. Unfortunately, disease progression with clinical deterioration has been registered in 10 patients.

In the group of patients who had positive response to treatment, there were 19 patients with hormone-dependent disease and seven with non-luminal type of breast cancer. There was no significant difference in subgroups according to sites of disease involvement. In the group of patients who had disease progression, there were seven patients with luminal breast cancer and three patients with non-luminal breast cancer. The above group was dominated by patients with exclusively visceral disease, seven of them, while three patients had both bone and visceral disease involvement.

In our clinical practice experience study, median duration of treatment was 7,5 months.

Our data evaluation, as reflected in referent study, did not show significant differences in the median duration of treatment, within subgroups of patients based on tumor characteristics such as site of disease and hormone receptor status.

Although, in reference to EMILIA trial results, our analysis indicates shorter duration of treatment in real-life conditions, a fact that is often shown in everyday clinical practice. For further analysis and clarification of the observed pattern causes, longer patient follow-up should be performed, however, this pilot project and preliminary findings clearly show a tendency which should be worked on for improvement.

P37 - THE ACCURACY OF BREAST MAGNETIC RESONANCE IMAGING IN PREDICTING PATHOLOGIC RESPONSE TO NEOADJUVANT CHEMOTHERAPY

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Objective: This study aimed to evaluate our results with preoperative contrast-enhanced magnetic resonance imaging (CE-MRI) in predicting pathologic complete response (pCR) or residual disease in the breast and axilla after neoadjuvant chemotherapy (NACT), for locally advanced breast cancer.

Materials and methods: In this retrospective study, we included 119 patients treated for locally advanced breast cancer with an indication of NACT, between January 2019 and December 2020.

All patients had CE-MRI before, after 4 cycles of NACT and at the end of completed NACT. The findings of post-NACT MRI in the breast and axilla were correlated with findings on the final pathology of the surgical specimen.

Pathologic complete response (pCR) was defined as absence of invasive and in situ disease in breast. Radiologic complete response (rCR) was applied when MRI images revealed no contrast enhancement in the tumor bed.

The axillary nodes were considered abnormal on MRI if they had a round shape, loss of the fatty hilum and/or thickened or irregular cortex (> 4 mm). Enhancement of the axillary nodes on MRI cannot be considered as a criterion of malignancy, as benign nodes normally enhance.

Results: We evaluated CE-MRI findings of 119 breast cancers before, after 4 cycles and at the end of NACT. The average patient age was 57 years. According to tumor subtypes there were 13/119 (11%) HER 2 positive; 12/119 (10%) luminal B HER 2 positive; 58/119 (49%) luminal B; 10/119 (8%) luminal A and 26/119 (22%) triple-negative cancers, with respective pCR rates of: 26% 22%, 23% and 29%, respectively. Overall, pCR was 26% and rCR was 28%. 63% (21/33) of rCR corresponded to pCR. Contrarily, in 87% (75/86) of patients, residual tumor observed on MRI was pathologically confirmed. Sensitivity of MRI to detect pCR and residual tumor was 68% and 85%, respectively.

Axillary nodes were abnormal on pre-NACT MRI in 63 cases, they were all biopsy-confirmed metastases. The axillary rCR on post-NACT MRI was found in 31/63 (49%); axillary pCR was present in 25/63 (40%). In cases where axillary rCR was achieved, axillary pCR was present in 23 cases (23/31, 74%). Among those patients with abnormal axillary nodes on post-NACT MRI 32/63 (51%), 29 had confirmed residual disease on final pathology (90%).

Conclusions: Consistent with relevant literature, our study confirmed that preoperative CE-MRE is not the best predictor of pathologic complete response in breast and axillary lymph nodes. Therefore, surgical resection post-NACT MRI is still the gold standard. Sensitivity and specificity of detecting residual disease in axillae in our study is above average, probably since all patients who were node positive were confirmed prior to NACT.

MRI has low sensitivity but high specificity in predicting pCR in breast. Different factors such as tumor subtypes and treatment regimen, can influence the accuracy of MRI. Nevertheless, it is still the most sensitive diagnostic method for monitoring patient response to NACT. With the addition of specific MRI sequences like DWI and MR spectroscopy according to some authors, we can improve the sensitivity and specificity of MRI in detecting a PCR.

Keywords: CE-MR imaging, breast cancer, neoadjuvant chemotherapy, pathologic complete response, radiologic complete response, tumor subtypes

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P38 - THE FIRST EXPERIENCE OF PIK3CA TESTING IN CLINICAL HOSPITAL CENTER SPLIT – WHAT OUR RESULTS ARE?

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Introduction: Breast cancer is the most commonly diagnosed cancer in women worldwide. It represents 24.5% of all cancers in women with estimated 684,996 deaths from breast cancer in 2020. More than 80% of breast cancer is classified as hormone receptor-positive (*HR+*) breast cancer. *PIK3CA* mutations occur in approximately 40% of patients with HR +, human epidermal growth factor receptor 2 (HER2)–negative breast cancer. Endocrine therapy, with or without cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitor is the standard treatment for patients with HR-positive, HER2-negative advanced breast cancer. However, acquired resistance to endocrine-based therapy still remains a challenge. Moreover, the truth is that breast cancer outcomes lie in the treatment opportunities as well as system organization. Recently, PIK3CA inhibitor alpelisib became a new standard of care for a second line therapy. Its penetration in the everyday care depends on diagnostic of the biomarker - PIK3CA mutation. Here, we describe the first experience of ours in the process of diagnostics of PIK3CA mutation on the cohort of our advanced HR+, HER2- breast cancer patients.

Methods: We did a retrospective analysis of data from all patients with HR+, HER2- metastatic breast cancer who were tested on presence of PIK3CA mutation in Clinical Hospital Split until December 2020. The cobas® PIK3CA Mutation Test was used. This is a real-time polymerase chain reaction (PCR) test used to identify patients with advanced or metastatic breast cancer with PIK3CA mutation.

Results: From September 2019 until December 2020, we have tested 50 patients on presence of PIK3CA mutation. In all cases PCR method was used and the sample was archival tissue. Only two of all tested patients were male and the rest were female. The average age of patients was 61.13 years. The eldest patient was 81 and the youngest 32 years old at the time they were tested. The PIK3CA mutation was established in 21/50 (42%) of patients. Determined hotspot mutations were: E545 in 3/21 (14.28%), E545X in 4/21 (19.04%), E542 in 2/21 (9.53%), E542K in 2/21 (9.53%), H1047 in 2/21 (9.53%), H1047X in 4/21 (19.04%), N345K in 2/21 (9.53%) cases. In two cases (2/21, 9.53%) hotspot mutations H1047X and N345K were presented concurrently.

Conclusion: Our results coincide with data from previous world studies. In our hands PIK3CA testing proves to be easily established and run. Given the situation with COVID-19 pandemic, the number of

tested patients is not overly high. Additional efforts are needed to fully state testing and to test as many patients as possible so that patients who result positive could potentially have benefits from therapies directed against PIK3CA.

P39 - THE FIRST INSIGHT IN IMMUNOTHERAPY WITH CHECKPOINT INHIBITORS FOR METASTATIC COLORECTAL CANCER IN OUR DAILY PRACTICE

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Immunotherapy with check point inhibitors significantly improved outcomes in many solid tumors. Efficacy and safety of those drugs have been investigated in many clinical trials that involved a broad spectrum of solid tumors including metastatic colorectal cancer (mCRC). Based on the results from KEYNOTE-164 trial and CheckMate-142 trial, pembrolizumab and nivolumab, targeting PD-1, have been approved for previously treated patients with microsatellite instability-high (MSI-H) mCRC. KEYNOTE-164 investigated the efficacy of pembrolizmab in 124 patients with MSI-H. The patients were divided into two cohorts based on whether they received two or more prior lines of standard therapy (including fluoropyrimidine, oxaliplatin and irinotecan (cohort A)) or one or more prior lines of standard therapy (cohort B). ORR was 33% for both cohorts. Median PFS was 2,3 months for cohort A and 4,1 months for cohort B. Median OS was 31,5 months for cohort A and had not been reached for cohort B. In the CheckMate-142 multicohort, phase II trial nivolumab was studied with or without ipilimumab. One cohort of this trial included 74 patients with deficient mismatch repair-dMMR CRC who were treated with nivolumab. ORR for these patients was 31,1% with 69% of patients having disease control for at least 12 weeks. PFS and OS were 50% and 73% at 1 year. Another cohort of this trial included 119 patients with dMMR CRC who were treated with nivolumab in combination with ipilimumab. For this cohort ORR was 55% and the disease control rate for at least 12 weeks was 80%. PFS and OS were 71% and 85% at 1 year.

After analyzing the results of those clinical trials, as well as assuming a relatively small number of MSI-H mCRC, our multidisciplinary team decided to treat this group of patients without other valuable therapy options with check point inhibitors. Of note, all patients with mCRC are routinely tested on MSI status.

Methods: After approval of local authorities, retrospective analysis of patient charts was done. Results: In our database we found 5 patients with mCRC treated with pembrolizumab (N=3) and nivolumab (N=2). Three patients received immunotherapy as a second, and 2 as the third line of treatment. Average number of cycles was 17 (5-34). Among the patients who progressed, duration of treatment was 7.5 and 11.5 months. Three patients are still on treatment for a 7, 13 and 25 months. One patient died. Partial response was observed in 3 patients and stable disease in 2 of them. Grade III adverse events included hypothyreosis in 1 patient and arthritis in 3 patients was observed.

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 treatment is relatively well tolerated and efficacy of treatment comparable with results of previously mentioned clinical trials. We consider this short report valuable, due the fact that is our first experience with checkpoint inhibitors in mCRC in our daily practice.

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P40 - THE IMPACT OF MULTIDISCIPLINARITY IN PATTERNS OF CARE IN NEWLY DIAGNOSED BREAST CANCER PATIENTS

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Introduction: Since long time ago, neoadjuvant therapy is standard therapeutic approach for locally advanced breast cancer.1 Recently it is also considered as new standard of care in earlier stage of HER2+ or triple negative breast cancer (TNBC) due to better outcomes with additional adjuvant chemotherapy (capecitabine in TNBC) and immunotherapy (TDM-1 in HER2+) as well as to reduce the impact of surgery and to allow conservative treatment.2-4 Multidisciplinarity has a huge impact on the implementation of neoadjuvant approach. There is no one single definition of a tumor size or clinical characteristic that can establish whether the patient will benefit from neoadjuvant therapy, although some centres favour those cases in which a breast carcinoma is either larger than 2 cm or has clinically involved axillary nodes. In our analysis, we focused on stage migration in neoadjuvant approach due to better penetration of multidisciplinarity, presentation of great majority of newly diagnosed breast cancer patients on the multidisciplinary team before surgery.

Methods: We did the analysis of medical data for 169 consecutive patients with breast cancer treated with neoadjuvant therapy during the period 2017-2020 at our institution.

Results: From January 2017 until December 2020, 169 patients recieved neoadjuvant therapy. 21(12%) of patients recieved neoadjuvant endocrine therapy, and 148 (85) recieved neoadjuvant chemotherapy or chemoimmunotherapy. From 2017 to 2020, by incorporating a mulitdisciplinarity approach, a proportion of patients who were treated neoadjuvant has increased. In 2017, 7% (32/423) od newly diagnosed breast cancer patients recieved neoadjuvant therapy, in 2018 7% (30/380) patients. In 2019, we doubled the number of patients who were treated with neoadjuvant therapy to 15.9% (39/244). Following an significant increase in percentage of neoadjuvant approach, in 2020., 39% (69/362) of patients have recieved neoadjuvant therapy.

According to initial clinical staging, data from 2017 shows that 3% of them had stage IIA disease, 36% had stage IIB, 22% stage IIIA, 31% IIIB and 3% were diagnosed with stage IIIC disease.In 2018, 31% of patients had stage IIB, 10% had stage IIIA, and 58% had stage IIIB.

Data from 2019 showed that 39/244 (15.9%) patients recieved neoadjuvant treatment. 20/39 patients had stage II disease (2% stage IIA, and 31% stage IIB), and 19/29 had stage III (31% stage IIIA, and 34% stage IIIB). In 2020 there were 29/69 (42%) with stage IIA, 17/69 (24%) stage IIB, 6/69 (8%) IIIA, 16/69 (23%) IIIB, and 1/69 (1%) stage IIIC.

Conclusion: Our analysis showed that by implementing multidisciplinarity we are moving forward to neoadjuvant approach in patients with newly diagnosed, locally advanced or early breast cancer. In 4 years we almost tripeled the number of patients who were treated neoadjuvantly. The fact that we are significantly increasing the proportion of patients with earlier stage disease who are receiving neoadjuvant therapy defines better compliance with newly established guidelines, all based on the results of CREATE-X and KATHERINE studies.

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P41 - THE ROLE OF HORMONAL THERAPY AS TREATMENT OPTION FOR NEOADJUVANT BREAST CANCER – IS LESS MORE?

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Introduction: For patients diagnosed with locally advanced luminal A or luminal B breast cancer, neoadjuvant endocrine therapy (NET) could facilitate down-staging of the tumor and increased rates of breast-conserving surgery. The choice of patients who would benefit the most from this approach is still not well defined. There are limited clinical guidelines for best choice of treatment agent and for optimal duration of therapy applied. Several phase III randomised clinical trials (IMPACT, PROACT, STAGE) addressed this question were comparing different endocrine agents and optimal duration of treatment in the neoadjuvant setting. Meta-analysis of this trials showed that aromatase inhibitors provide somewhat better efficacy than tamoxifen. The optimal duration of NET is still not well defined, suggesting that at least 6 months should be obtained to achieve maximum reduction in tumor volume. Aim of our analysis was to provide single institution experience about this unfortunately often underrepresented approach of neoadjuvant treatment.

Methods: We did retrospective analysis of collective data from January 2017 until December 2020 for 169 patients who had been treated with neoadjuvant therapy. 21/169 (12%) of patients recieved neoadjuvant endocrine therapy. Patients have signed informed consent and medical data was analysed.

Results: Our analysis included 21 patients treated with neoadjuvant endocrine therapy, with median age of 81. 10 patients (47%) had luminal A immunophenotype breast cancer, 11 patients (52%) had luminal B disease. Majority of patients, 12 (57%) of them, had disease stage 3B. 5 (23%) patients were diagnosed with clinical stage 2A. There were 2 (9%) patients diagnosed with stage 3C, and 2 (9%) with stage 2B disease. Only 2 patients were premenopausal at the time of diagnosis, while 19 (90%) of them were postmenopausal at treatment beginning. Two patients who were premenopausal recieved neoadjuvant hormonal therapy with aromatase inhibitors and LHRH. 12 (57%) of postmenopausal patients recieved aromatase inhibitors, 1 (4%) received tamoxifen, and 6 (28%) of patients were treated with combination of aromatase inhibitors and fulvestrant. At the data analysis, February 2nd 2021, 9 patients finished preplaned neoadjuvant treatment. Average duration of hormonal therapy in these patients was 6.8 months. All of these patients had an operation after completion of neoadjuvant therapy. Pathologic analysis of response to treatment showed that 1 patient had residual cancer burden (RCB) score 1, 6 (28%) of patients had RCB score 2, and 2 patients (9%) had RCB score 3. 12/21 (57%) of patients didn't have an operation. 8 of them refused operation, or were unfit for surgery because of age or comorbidities. At the time of data analysis, 8 (38%) of them were still recieving hormonal therapy, with no patients stopping the treatment because of toxicity. 4 (19%) patients had died during follow up period.

Conclusion: Our analysis showed that NET is safe an effective treatment option. Offering NET can reduce the number of patients exposed to significant and unnecessary chemotherapy-related toxicities, in particular the elderly and frail patients, but still providing significant clinical benefit and efficacy similar or better to more toxic therapeutic options for low grade luminal breast cancers. Future perspectives in defining of biomarkers of response to NET is a matter of great interest.

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P42 - THERMAL ABLATION IN OLIGOMETASTATIC LUNG DISEASE

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Introduction: Percutaneous thermal ablation is a very efficient therapeutic method in metastatic lesions of the lung measuring up to 3,5 cm in size. Local reccurence rates in lesions smaller then 2 cm is 5 %, which puts this method in the same category with surgical resection. Ablation is most efficient in perifferally located lesions surrounded by lung parenchima, and located at least 3 mm from the bronchovascular bundle. Thermal ablation and SBRT have similar indications when lung oligometastatic disease of the lungs is involved, but the advantage of lung ablation is the possibility to repeat the procedure multiple times without radiation restrictions. Lung ablation has shown to reduce lung capacity less then SBRT.

Complications of lung ablations are rare, with pneumothorax being the most common one, with an incidence of up to 40%, but only 10% of those require any additional procedures such as chest tube placement. Pneumonia and other inflamatory reactions occur in less then 2 % of patients after ablation. Small pleural effusions can be seen often but are asymptomatic and self limited.

Lung ablation allows for great preservation of lung parenchima, which is especially important in patients, who are often expected to have reccurent metastatic lesions during the course of their life. Compared to surgical segmentectomy or lobectomy, which reduce %FEV1 for 10-16%, percutaneous ablation reduces %FEV1 for only 2,5 % 3 months after therapy. Bilateral metastatic lesions in the lungs present a problem and risk for surgery, while ablation mostly has no restrictions when treating ipsilateral or bilateral lesions.

Primary lung cancer can also be treated with percutaneous ablation, but in this indication patients are candidates only when they have a contraindication for surgery. This is usually the case in patients with severe comorbidities and reduced lung capacity, which also effects possible outcomes after lung ablations with complications beeing more frequent and the procedure beeing more chalenging.

Purpose: To investigate the safety and effectiveness of percutaneous microwave ablation for lung metastasis (CRLM) with evaluation of factors influencing the efficacy of the method.

Methods: From July 2017 to September 2020, 36 patients with lung metastases treated with percutaneous MWA were included in our study. All patients were followed up for at least 6 months. We assessed primary technical success, local tumor progression (LTP) and complications. Most patients were diagnosed with metastatic colorectal carcinoma(22).

Results: Median followup was 13 months. Mean tumor diameter was 17.4 ± 6.2 mm, range 8-67 mm. Primary technical success was achieved in 76% (27/36) of lesions. LTP occurred in 8,1% (2/24) of lesions smaller than 3 cm and 42% (5/12) of lesion larger the 3 cm in diameter. LTP was more likely to occur in lesions larger than 3 cm in diameter, near a large vascular structure (<5 mm). All patients were treated using sedation and local anesthesia. Major complication rate was 8,2%, minor complication rate of 25 % and a mortality rate of 0%.

Conclusions: Percutaneous MWA of lung metastases is a safe and effective method that is a valuable option and should be considered more often in oligometastatic lung disease for patients who are not ideal surgery candidates.

P43 - TOMOSYNTHESIS GUIDED VACUUM-ASSISTED BREAST BIOPSY IS A SAFE ALTERNATIVE TO DIAGNOSTIC SURGICAL BIOPSY IN THE SETTING OF MAMMOGRAPHY-SUSPICIOUS, ULTRASOUND-OCCULT BREAST LESIONS

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Introduction: Breast cancer (BC) is the most common cancer diagnosed and the second most common cause of cancer-related mortality among women worldwide, with a lifetime risk of 12 % (1/8 women). 20-25 % of all newly diagnosed BC and 17-34 % of all mammographically detected BC are ductal in situ carcinoma (DCIS). Following the introduction of screening mammography, 80-85 % of DCIS are screen-detected. Suspicious calcifications (BI-RADS 4 and 5) obligates to tissue diagnosis. High rates of radiological-pathological discordance in literature, as well as in our study, results in a high rate of unnecessary surgical breast biopsies. Vacuum-assisted breast biopsy (VABB) emerges as a safe alternative to open biopsy in the setting of mammographically suspicious, ultrasound occult breast lesions.

Methods: From March 2018 to June 2020, 235 ultrasound-occult breast lesions scored as 4 or 5 by mammography or/and magnification were submitted to DBT-guided VABB in the institutional Breast Division of the Radiology Department Clinical Hospital center Rijeka (CHCR). During the study period, 233 patients underwent VABB at our hospital: mean age 59.7 years (range 40 – 85 years). All biopsies were performed by specialized breast radiologists with a 9-Gauge needle (Eviva® Breast Biopsy system), guided by tomosynthesis device Hologic Selenia Dimensions (Hologic, Bedford, Massachusetts). All VABB procedures were performed on sterile skin, in prone position using compressive plates with vertical needle breast approach. A total of 235 consecutive breast lesions were submitted to tomosynthesis guided VABB. All tissue samples were pathologically evaluated and classified according to the College of American Pathologists. All B2 and 38 % of B3 lesions were recommended for surveillance, while all B5a and B5b, as well as 54 % of B3 lesions, were submitted to surgical biopsy and pathological reevaluation in addition to VABB.

Results: Following VABB, radiological-pathological discordance was 72.3 %, predominantly due to radiological overestimation. Therefore, 69.4 % of patients were spared by VABB of unnecessary surgical procedures. However, 72 lesions were excised and pathological reevaluation exposed an underestimation rate of 19.4 %, mostly due to underestimation of DCIS. At median follow-up time of 18 months, we did not detect a single case of progression although surgery was omitted in 163 patients with B2 and B3 lesions diagnosed on VABB.

Conclusion: DBT-guided VABB is a safe and secure biopsy method for mammographically detected suspicious lesions that are ultrasound occult. With a low-false negative rate and no signs of progression detected in our surveillance subgroup, the omission of surgery may be safely recommended for all B2 lesions and low-risk B3 lesions selected in a multidisciplinary fashion. We strongly recommend a careful radiological-pathological-surgical approach with deep analysis of all medical data to accurately decide whether a surgical biopsy or follow-up should be recommended in the selected group of patients.

Key Messages: While waiting for new morphological markers that might decrease the radiological-pathological discordance rate, VABB emerges as a preferred method of breast tissue biopsy in the setting of mammographically suspicious, ultrasound occult lesions.

P44 - TREATMENT OUTCOMES AND PATTERNS OF RELAPSE FOLLOWING ACTIVE SURVEILLANCE FOR STAGE I TESTICULAR GERM-CELL CANCER USING MRI-BASED SURVEILLANCE STRATEGY: SINGLE CENTER EXPERIENCE

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Introduction: Active surveillance (AS) is guidelines-recommended management strategy for clinical stage I testicular germ-cell cancer (CSI TGCC). Computed tomography (CT) is currently the reference standard in AS protocols, although there is emerging data that support use of magnetic resonance imaging (MRI) in order to reduce the radiation dose. The aim of this study was to report treatment outcomes, and recurrence rates, for patients with CSI TGCC undergoing AS with MRI.

Material and methods: From our institutional TGCC database, 115 patients with CSI TGCC diagnosed between January 2012, and December 2019 were retrospectively identified. The criteria for inclusion were patients who had previously undergone inguinal orchidectomy as the primary treatment and were enrolled in AS program. Patients were followed-up every third or fourth month for the first two years, every six months in the third year, and thereafter, at increasing intervals. Follow-up included serum tumor markers and chest roentgenograms for non-seminomas. Abdominal 1.5 T MRI was repeated two times the first year, one to two times the second year, and every 12 months in the third year. Standard follow-up for these patients lasted approximately 5 years after achievement of disease-free status. Clinical data on patients, relapses, and possible prognostic factors were collected through review of patient files and pathology reports. Association of known risk factors with relapses were tested using Cox hazard regression model.

Results: Out of 115 patients with CSI TGCC, 62 patients (53.9%) underwent AS with MRI as their preferred management strategy. Ten patients (8.7%), with newly detected small pulmonary nodules, with low probability of malignancy, underwent AS with MSCT of the chest, abdomen, and pelvis. Remaining CSI patients, 37 (32.17%) received adjuvant chemotherapy, one patient was treated with radiotherapy, and five patients (4.34%) were lost from follow-up. The median follow-up time was 27 months (range, 6 to 375 months). Eight relapses (8/62, 12.9%) were detected using MRI, all eight were in patients with seminomas (8/50, 16%), and median time to relapse was 19.1 months (range, 5 to 72 months). Aditional five relapses were detected among 10 CSI patients who were followed by CT. In all CSI AS cohort (N=72), relapse rate was 18% (13/72); 18.5% (10/54) for seminomas, and 16.7% (3/18) for non-seminomas. In total, ten patients were treated for relapse with BEP (one received two cycles, and nine three cycles), and three patients refused treatment. From ten patients who received chemotherapy for relapse, in eight patients no evidence of disease was observed at latest disease assessment, and two patients were lost from follow-up. Due to low sample size and low number of events, no statistically significant association of known risk factors (tumor size, LVI, rete testis invasion) with occurrence of relapse were found.

Conclusions: Our initial results suggest that MRI is acceptable imaging surveillance modality for man with CSI TGCC on AS and results in similar relapse detection rate comparable to historical controls based on CT-only or other MRI-only protocols. In the setting of AS, MRI has the potential to markedly

reduce ionizing radiation exposure in this young patient group. Longer follow-up period and more enrolled patients are needed to confirm our initial observations.

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P45 - VERTEBRAL AUGMENTATION AS A TREATMENT OPTION IN METASTATIC DISEASE OF THE SPINE

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Europe consists 1/8 of the world population, however 1/4 of all new carcinoma cases are discovered in Europe, with 3,7 million new cases yearly. 10% of those patients will develop symptomatic metastatic lesions in the spine. Up to 85% of patients with breast, kidney, lung and prostate cancer have proven bone metastasis at the time of death. The spine is the single most common location for bone metastasis, 30-70%, due to high haematopoietic activity and vascularization.

With the development of oncologic treatment the life expectancy of patients with metastatic disease has been prolonged. Consequently, the patients with bone metastases live a longer life, which demands adequate therapy and pain control. Even though radiation therapy still presents the main treatment option for bone metastasis, along with systematic therapy, up to 30% of bone lesions are resistant to radiation. Surgical resection of bone metastasis, especially in the spine, is difficult and associated with prolonged recovery.

Vertebroplasty of osteolytic vertebral lesions can be an ideal method to treat painfull vertbral metastatic disease. At the same time it reduces the risk for vertebral collapse or in case of earlier compression fracture presents a valuable tool for bone consolidation. The medical cement used in the procedure, PMMA, also has chemoablative effect on tumor tissue, which can lead to local tumor control and prevent progression of the disease.

In certain situations procedural complications, which include cement leak due to the destruction of normal vertebral anatomy, can be avoided with the use of more complex augmentation techniques, such as kyphoplasty, where a baloon is first inflated in the vertebra to create space for the cement.

Along with vertebral augmentation, oligometastatic disease with lytic lesions of the spine can be additionally treated with thermal ablation such as radiofrequency, microwave or cryoablation. These minimaly invasive methods can help achieve great local tumor control, with not only palliative but also currative intent.

At our center we treated 87 oncological patients with vertebral augmentation methods (79 vertebroplasty, 8 kyphoplasty) since November 2016 to February 2021. A median of 2,1 segments were treated (1-6). Major complication rate was 1,2 % (1 clinically insignificant pulmonary embolism) and minor complication rate was 13,8 % (localized pain). 86,2% patients reported a significant reduction in pain (VAS score > 3). 23 patients were treated with spinal RFA or MWA due to osteolytic metastases. 12 were refractory to radiation therapy and 11 with primary indication for biopsy and ablation, with a mean tumor size of 2,3 cm. There were no major complication after ablation. Local tumor progression was noted in 3 patients.

Oncology patients with spinal metastasis in Croatia are very rarely treated with vertebral augmentation and percutaneous ablation, compared to other European countries, and most patients lack therapeutic options after radiation therapy is exhausted. Despite proven efficacy and safety of vertebral augmentation and thermal ablation, these methods are underutilized.