POSTER PRESENTATIONS

P1 - APPLICATION OF ARTEFICIAL INTELLIGENCE IN PERSONALIZED TREATMENT OF ONCOLOGY PATIENTS

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Objective: Oncology is one of the most dynamic branches of medicine. As a result of numerous oncology studies, there has been a significant increase in scientific and clinical data that the human brain cannot store. Advances in artificial intelligence (AI) technology have led to its rapid clinical application. In this paper, we wanted to see the role of the use of artificial intelligence (AI) in oncology.

Methods: We conducted a comprehensive database search (Pub Med, MEDLINE, and Google Scholar) using the keywords: artificial intelligence, deep learning, machine learning, oncology, personalized medicine. We supplemented the database search with reference list checks. The primary objectives were clarity and innovation regarding the use of artificial intelligence in oncology and the ability to apply the results in everyday clinical work. Exclusion criteria were: not about cancer and AI, lack of relevance after reviewing of the title and abstract, papers not written in English, publications before 2015, studies not reviewed, not applicable in everyday clinical work. From a large number of articles available to us, we have selected review articles and results of clinical trials according to their clarity and innovation in terms of the use of artificial intelligence in oncology.

Results: The possibilities of using artificial intelligence in oncology are innumerable. It can be used for diagnostic purposes (screening programs, histopathology, and molecular diagnostics), therapeutic purposes (personalized treatment, anticipation of treatment side effects and response to therapy, treatment decisions), as well as for prognostic purposes (risk stratification, survival prediction, monitoring). For example, the use of stored mammograms can help us identify breast cancer, the use of stored digital pathology images can help us diagnose cancer and the analysis of stored dermoscopy images can identify skin lesions, such as melanoma. In general, we can say that AI is already used to perform various tasks in oncology at a level equal to or sometimes greater than the level of clinicians. The goal of modern oncology is personalized treatment. Given the large amount of data that oncologists are daily exposed if we want to personalize oncology, we need the help of AI. Namely, the prerequisite for personalized treatment is knowledge of the genomic data of the tumour, i.e. whether there are possible genomic mutations in the tumour as target points of oncological treatment. Hundreds of thousands of articles are published annually on genomic mutations and cancer. Therefore, databases are being created that aim to help clinicians (e.g. COSMIC, ExPecto, The Cancer Imaging Archive [http://www.cancerimagingarchive.net], and Genomic Data Commons Data Portal [https://portal.gdc. rak.gov]). Genomic tests in oncology also play an important role. Thus, only in 2017., the FDA approved several such tests (Oncotype Dx, Praxis Extended RAS Panel, MSK-IMPACT, and FoundationOne CDx). They help us predict the prognosis of cancer so we can avoid over-treating cancer patients. Although the application of AI in oncology seems very complex and still inaccessible to all oncology centres, given the required infrastructure and skills of clinicians, some segments of AI can already be used in everyday clinical practice. Thus, AI can help us make decisions about cancer treatment. Namely, decisions on oncology treatment are based on the assessment of the patient's clinical condition (PS = performance status). It is a subjective assessment made by the clinician by observing the patient's condition and based on data obtained in conversation with the patient. An objective assessment of the patient's clinical condition (PS) is difficult because patients spend most of their time

outside the hospital. But objective real-time activity data that we can collect with physical activity tracking devices, such as smartphones or smartwatches, can help. A prospective study by Gresham et al (2018) showed us that monitoring patient activity (steps, distance, stairs) can help not only in assessing the clinical condition of patients with metastatic cancer but also in assessing clinical outcomes (side effects, hospitalization, survival). These findings should be confirmed in larger, randomized trials.

Conclusions: The application of AI in clinical practice presents new challenges for clinicians. Namely, in the era of evidence-based and patient-centered medicine, they will have to master statistical as well as computer skills, in addition to clinical ones. Therefore, it is necessary to start educating future doctors about the importance of artificial intelligence as soon as possible.

Keywords: artificial intelligence, oncology, personalized medicine

P2 - APPLICATION OF CHEMOTHERAPY VIA ELASTOMERIC PUMP IN AN OUTPATIENT SETTING: PATIENT SATISFACTION SURVEY

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The use of elastomeric pumps to administer chemotherapy in protocols that require 48 hours continuous infusion was recently introduced in Pula General Hospital. This allows the application to be administered at hospital day center and continued at patients home as opposed to in hospital stay. We conducted a research among patients who had the experience of receiving chemotherapy via an elastomeric pump and also used to receive the same therapeutic protocol while admitted in our oncology department. We carried out a telephone survey on 19 patients who answered a questionnaire prepared for this research. One subject received application via the peripheral venous route, and the other eighteen used a central venous port catheter. There were ten questions prompting general satisfaction and perceived safety during the use of elastomeric pumps, as well as comparing the experience of receiving the chemotherapy at home with being admitted in hospital. The responses in the survey indicate that application of chemotherapy at home via the elastomeric pump improves some aspects of daily life. Specifically the most pronounced improvements were reported in the quality of social relationships with loved ones, increased energy levels and feelings of optimism. Better sleep quality and diet were also noted. One respondent described his negative experience during the application of chemotherapy at home. It was a patient that received the therapy through peripheral venous line and developed a local complication with soft tissue necrosis. All others reported very high satisfaction and feeling of safety while receiving chemotherapy at home. These results suggest an improvement in quality of life and provide strong support for further implementation of methods that allow patients to receive chemotherapy at home.

Keywords: elastomeric pump, patient satisfaction survey, chemotherapy, outpatient care

P3 - ASSESSMENT OF FATIGUE IN CANCER PATIENTS TREATED WITH RIBOCICLIB AND ENDOCRINE THERAPY ACCORDING TO PATIENT REPORTED OUTCOMES AT THE UNIVERSITY HOSPITAL FOR TUMORS

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Around 70% of metastatic breast cancers have hormone receptor (HR) positive, HER2-negative biology and selective cyclin-dependent kinases 4/6 (CDK 4/6) inhibitors, in addition to endocrine therapy (ET), are standard of care in the first line, and effective treatment option in subsequent lines of therapy. One of the main purposes of treatment in a metastatic setting is maintaining a good quality of life. These agents have shown acceptable and easily manageable toxicity profile. It has been described that health care professionals underestimate side effects of specific antineoplastic treatment, such as endocrine therapy, compared with patients themselves. Fatigue is indistinct, not well defined, multidimensional symptom which is not easily measurable. It is well known that menopause also can cause fatigue, as well as endocrine treatment so it's challenging to determine if this symptom is predominantly caused by menopausal status or specific oncological treatment, but it is most likely that the impact of these factors overlap. Nevertheless, fatigue is a symptom that negatively impacts patients' quality of life. This analysis evaluated patient-reported outcomes (PROs) to assess fatigue and its impact on health-related quality of life in patients with HR-positive, HER-2 negative metastatic disease treated at University hospital for tumors. We obtained data from 99 patients with HR-positive HER2- negative breast cancer who were treated at the Division of Medical Oncology with ribociclib and endocrine therapy, in the period from 08/2018 to 12/2020 and had reported fatigue as an adverse event. Patients had to complete at least one four-week cycle of therapy and fill in the questionnaires. PRO assessments were evaluable for 87 female patients, median age of 60 years, all postmenopausal. Endocrine partners in treatment with ribociclib were aromatase inhibitors in around 65%, predominantly anastrozole, while in around 35% of patients partner was fulvestrant. During therapy with ribociclib, 80% of patients reported fatigue as an adverse effect of this specific antineoplastic treatment. We have shown that fatigue is common in this observed population, and with this analysis from real clinical practice, we indicate the requirement for a better understanding of symptoms experienced by patients on this precise therapy. Since this symptom is not easy to define, we consider that it is necessary to carefully plan further researches to better identify and objectify it. Although not a life-threatening adverse event this is challenging symptom for patients, because of its feasible severe distress potential.

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

P4 - ATEZOLIZUMAB IN THE SECOND LINE TREATMENT OF METASTATIC UROTHELIAL CANCER THE FIRST EXPERIENCE OUTSIDE OF CLINICAL TRIAL

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Introduction: Checkpoint inhibitors have dramatically changed the landscape of treatment for patients with metastatic urothelial cancer. Since 2016 PD-1 inhibitors (pembrolizumab and nivolumab), as well as PD-L1 inhibitors (atezolizumab, durvalumab and avelumab) had been approved for the treatment of patients who progressed after the first line platinum based chemotherapy. Before this the only approved therapeutic option was vinflunin with median overall survival (OS) of 7 months.

Patients and methods: We present data for 17 metastatic urothelial cancer patients treated with second line atezolizumab at Oncology Institute of Vojvodina, Serbia from 2018 to 2021. Progression free survival (PFS) and OS curves were calculated using Kaplan –Meier method.

Results: Median age was 67. There were four female and 13 male patients. In the first line two patients were treated with carboplatin, 15 patients received cisplatin. Seven patients (53,8%) had visceral metastases, five (29,4%) had bone metastases, 6 (35,3%) had lymph node metastases. Majority of the patients (59%) had one metastatic site. Majority of the patients (88%) were in good clinical shape with ECOG performance status 0 or 1. Median number of immunotherapy cycles was 4 (1-17). Adverse events were recorded in three patients: one patient had hypothyroidism, one patient had neurologic symptoms of undetermined cause and one patient had hyperprogressive disease. Median PFS was 3 months (1-26). Median OS was 5 months (1-26). Best objective response rates are as follows: two patients (12,5%) had partial response, three (18,7%) had stable disease while 11 (68,7%) patients had progressive disease.

Conclusion: Patients with metastatic urothelial cancer who progress on the first line platinum based chemotherapy have poor prognosis. Our data are in consistence with the results of randomized prospective phase 3 trial IMVigor 211: median OS was 8,6 months, while PFS was 2,1 months. Patients that were in good PS with low tumor burden and no visceral metastases had numerically longer PFS and OS.

Keywords*:* atezolizumab, metastatic urothelial cancer, second line treatment

P5 - BODY COMPOSITION OF BREAST CANCER PATIENTS TREATED WITH ADJUVANT CHEMOTHERAPY AND ITS INFLUENCE ON QUALITY OF LIFE

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Body composition has been studied relatively recently as part of oncology trials in different types of tumours in the context of the metabolism of different anticancer drugs, the assessment of response to treatment and its toxicity, and consequently the overall prognosis of the disease depending on the proportion of each body component. 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 (study allowed inclusion of patients who have had their last menstrual cycle within one year before the start of treatment). All patients received four cycles of AC chemotherapy (doxorubicin + cyclophosphamide) every three weeks, before or after the surgery. The total dose of doxorubicin administered was 240 mg/m2 and cyclophosphamide 2400 mg/m2 for all patients. During the each visit patients filled standardized quality od 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 46,6 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 treatment, the most pronounced was the connection between body composition and physical and sexual functioning and hair loss. In the second cycle, significant quality-of-life result included financial problems, while in subsequent treatment cycles other variables begin to significantly affect subdomaines of quality of life, in particular fatigue and diarrhoea. 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 chemotherapy. 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. This research has some limitations including unrandomized design, which could have led to significant deviation of the results, small sample size and most importantly individual characteristics of each patient which may significantly affect the studied parameters.

Keywords: body composition, bioelectric impedance, breast cancer, adjuvant chemotherapy, quality of life

P6 - BRAF POSITIVE MALIGNANT MELANOMA: CASE REPORT

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Background: Melanoma regularly exhibits extremely aggressive biological behavior, and resistance to therapy causes 80% mortality from all skin tumors. Pathohistological findings should also include data on the presence or absence of ulceration, number of mitoses per mm, Clark level (especially for lesions <1 mm), edge data. Molecular and genetic understanding of melanoma tumor cells has led to the development of targeted therapy as one of the ways to treat this disease. Therefore, the determination and analysis of genetic changes in melanoma samples becomes an indispensable part of diagnosis, prognosis and prediction of response to therapy. Mutation of the BRAF gene most commonly occurs at 600 codons.

Case report: The patient is 54 years old. In May 2011, a dermatoscopically suspicious lesion on the skin of the left forearm was surgically removed. The histopathological finding was melanoma cutis, Breslow 2 mm thick, with stage pT3. According to the recommendation of the multidisciplinary team, re-excision was performed with a sentinel lymph node biopsy and the final stage of the disease was III a. According to the protocol, regular monitoring is indicated. Regular follow-up was performed until 2013, after which the patient did not come for check-ups for paramedical reasons. In that period in 2012, another skin lesion appeared on the same forearm, was surgically removed and melanoma was diagnosed histologically. Only after 5 years does the patient come for an oncologist examination. Clinical examination revealed a 15 mm diameter nodule on the left forearm, immobile without surface changes. After ultrasound examination, excision was performed and histologically diagnosed metastatic melanoma of the skin and subcutaneous tissue. Due to the resection of R1, a re-excision was performed. Subsequently, an assessment was performed based on ultrasound and chest X-ray, as well as a complete laboratory test involving LDH. All findings were orderly. According to the protocol, BRAF testing and PET CT scan were performed. A mutation in V600E was found on the BRAF gene, and PET CT had no pathological findings. According to the guidelines, adj. therapy. iBRAF / MEK. However, at that time the therapy was not funded by the Fund. In June 2018, during a regular examination, a protrusion of the right bulb was clinically detected. An MRI scan was performed that showed inhomogeneous tumor formation in the retrobulbar right muscle. This was consistent with the primary diagnosis that it was most likely a metastasis of melanoma. A multidisciplinary team with an ophthalmologist decided to surgically remove the tumor ex tempore by biopsy. Histological diagnosis of ex tempore biopsy was benign muscle tumor, but after examination of the entire tumor and immunohistochemical analysis, the final diagnosis was metastatic melanoma to the retrobulbar muscle. Subsequently, therapy for metastatic BRAF-positive melanoma was initiated. All subsequent examinations showed normal findings, including CT and PET CT scans, ultrasound examinations, ophthalmological and dermatological examinations. The patient was without signs of illness and without symptoms and adverse events. But in laboratory tests, LDH began to show an increase in value. Control CT scanner in January 2019 and CT scanner in April 2019, which were without pathological findings. A reassessment of treatments in May 2019 revealed the following: LDH findings continue to vary with values up to 25 percent higher than normal. And the last PET CT showed two small 6 mm diameter changes in the right lung lobe without FDG accumulation. In November 2020, the CT finding indicates the still present irregularity of pleural thickening in the lower right pulmonary lobe, and a pair of small subpleural thickenings in the lower left pulmonary lobe, which appears on the right in discrete regression

compared to the previous finding. dg. may correspond to changes in the procedural etiology, although given the reference diagnosis, another etiology cannot be ruled out with certainty. CT finding of neurocranium and CT of abdomen and pelvis: still without evident CT signs of pathological changes.

Conclusion: Time from diagnosis of primary disease to metastatic disease more than 7 years. Therapy is indicated for metastatic melanoma BRAF positive. Therapy received after complete surgical removal of retrobulbar metastasis. (June 2018). Dabrafenib / Trametinib therapy has been administered for the last 32 months. Last 32nd cycle issued on 29.03.2021. Reassessment planned with findings: CT of the thorax, abdomen and small pelvis, and MRI of the head.

Keywords: malignant melanoma, retrobulbar right muscle metastasis, BRAF mutation.

P7 - CARDIAC SAFETY OF PALBOCICLIB IN BREAST CANCER PATIENTS WITH CARDIAC RISK

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According to the results of randomised clinical studies, cardiac toxicity of palbociclib is clinically irrelevant compared to other CDK4/6 inhibitor ribociclib. Data from real world studies showed a significant difference in incidence of cardiac toxicity (atrial fibrillation, cardiac failure, myocardial infarction) between two drugs – 2.2% with palbociclib compared to 7.7% with ribociclib. We conducted retrospective analysis of data collected for four advanced breast cancer patients, median age 64 (52-78 years) with history of cardiovascular diseases and significant heart risk factors (dilatative cardiomyopathy NYHA II/III, atrial fibrillation, hypertension, implantation of pacemaker), treated with combination of palbociclib and fulvestrant in first line treatment of metastatic hormon sensitive HER2 negative breast cancer. Initial cardial status showed no clinical signs of cardial failure, average heart frequency was 60-75/min, systolic function of left ventricle was reduced with ejection fraction (LVEF) of 45-53%, QTcF was 415-450 msec. Beside perscribed cardiac therapy patients had no comedication which could influence QTcF interval. During the treatment period (3-15 months) LVEF was stabile, no changes in the ECG record, in terms of emerging repolarisation disorders with changes in QTcF interval, and no clinically significant deterioration in cardiac function were observed while all patients benefited from therapy in terms of disease control. Combination therapy of palbociclib and fulvestrant showed no safety concerns in patients with significant cardiac comorbidity and increased cardiac risk.

Keywords: palbociclib, cardiotoxicity, breast cancer

P8 - CASE OF RECCURENT UTERINE ADENOSARCOMA WITH SARCOMATOUS OVERGROWTH (ASSO)

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Background: Adenosarcomas are rare malignancies of the female genital tract, accounting for approximately 5 % of uterine sarcomas. It is defined as a biphasic tumour composed of both sarcomatous stroma and benign epithelium. The majority of patients present with stage I disease, with a 5-year overall survival of 60 to 80 %. Standard of care treatment is total hysterectomy with bilateral salpingo-oophorectomy without lymphadenectomy, as the incidence of lymph node metastasis is rare. There is no defined role for adjuvant or neoadjuvant chemotherapy or radiation. Although uterine adenosarcomas are typically low-grade tumours with a good prognosis, uterine adenosarcoma with sarcomatous overgrowth (ASSO) is a rare and aggressive disease and results in a higher rate of death and recurrence.

Case report: A 65-years old patient with previous history of uterine fibroids presented with painful pressure in the lower abdomen without signs of vaginal bleeding or discharge. She had a past medical history of cervical conisation because of cervical dysplasia 30 years ago. Ultrasound showed enlarged uterus and multidisciplinary team recommended radical hysterectomy with bilateral adnexectomy. Patient underwent surgical treatment in the November of 2019. Patohistological analysis revealed high grade uterine adenosarcoma with sarcomatous overgrowth, pT1bNxMx FIGO IC. The proliferation index – Ki67 was over 30%. Postoperative abdominal and pelvic MRI and thoracic CT scan performed in the December, 2019 showed no signs of residual or metastatic disease. Adjuvant chemotherapy was initiated (6 cycles of mesna, doxorubicin, and ifosfamide – MAI) in the January, 2020. In the April, 2020 patient felt a sudden pain in the lower abdomen. Attending gynaecologist performed ultrasound examination which revealed anechoic zone with characteristics of liquid collection with a diameter of 29x18 mm located on the right side of urinary bladder, in the projection of the right ovary. Based on the ultrasound examination it was suspected that described, anechoic zone was abscess, but further diagnostic evaluation was recommended. In the early May of 2020 patient underwent abdominal and pelvic CT scan which revealed oval area with a diameter of 45x26 mm located on the right side of the urinary bladder. Based on radiologic characteristics described area corresponded to the recurrence of adenosarcoma. In the July of 2020 patient underwent surgical resection of suspicious mass. Patohistological analysis confirmed that the resected mass represents recurrence of the primary disease. Tumour tissue was dominantly composed of mesenchimal component, without epithelial tissue. Immunohistochemical status of the tumour was SMA and h-Caldesmon positive, but desmin negative. In order to define plan of treatment PET/CT was performed in August of 2020. It showed solitary lesion, probably residual tumour located along craniodorsal wall of bladder with diameter of 15mm. NGS genomic testing of the tumour was performed in the October, 2020. Analysis showed that genomic profile of tumour is MS stable, TMB 6 mut/Mb, KIT, PDGFRA, EPHB1, JUN, KDR amplification, CDKN2A/B loss, PT53 P278T but without available therapies with proven clinical benefit for this kind of tumour. Based on the results of NGS testing (KIT and PDGFRA amplification) possible therapies with clinical benefit in other tumour type were: imatinib, nilotinib, sorafenib, sunitinib. After the patient consulted several centres for a second opinion, it was jointly decided to start SBRT of the target area in the small pelvis. During the period from November 30 to December 4, 2020, the patient received a TD 25Gy/5 fr on the target lesion representing residual tumour. In the January of 2021 reevalu-

ation was done with MRI and it showed stable disease, stationary size of residual tumour with radiologic signs of postiradiational fibrosis.

Conclusion: Uterine adenosarcoma with sarcomatoid overgrowth is rare variant of uterine sarcomas with aggressive clinical course. Therapeutic options and benefit of chemotherapy and radiotherapy is still unclear. We presented a case of 65 years-old patient with recurrence of the disease during the adjuvant chemotherapy. Comprehensive genomic profile could not reveal potential targeted therapy with proven clinical benefit for this type of tumour. SBRT was performed to the area of residual tumour which resulted with stable disease and stationary size of the residual tumour one month after the therapy. Regular follow-up of our patient is planned as defined per protocol. Systemic progression of the disease could impose challenge for therapeutic decision regarding possible therapies with clinical benefit in other tumour type based on KIT and PDGFRA amplification proven in the genomic profile analysis. There is an obvious lack of information about rare types of uterine sarcomas. Future similar abstracts and case reports should be encouraged.

Keywords: uterine adenosarcoma, sarcomatoid overgrowth, SBRT

P9 - CLINICAL VALUE OF ANDROGEN RECEPTORS IN TRIPLE NEGATIVE BREAST CANCER

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Today, there is still no clear and unambiguous view on the role of androgen receptors (AR) in breast cancer, nor in triple-negative breast cancer (TNBC). A series of studies over the years have shown very heterogeneous results. Given the lack of a valid biomarker in TNBC, much hope is placed in the prognostic and predictive potential of AR in this aggressive disease. We performed a retrospective cohort study on the consecutive sample of 151 early TNBC patients diagnosed and treated at the University Hospital for Tumors in 2009-2012. We analyzed AR using immunohistochemistry (IHC), with the cutoff value for positivity of ≥1%, referring to current ASCO/CAP recommendations on hormone receptor (ER and PR) analysis. The analysis was adjusted for age, comorbidities, menopausal status, histological type of tumor, tumor size, number of positive lymph nodes, stage of disease, Ki-67 proliferation index, type of surgery of the breast and axilla, and treatment with adjuvant chemotherapy and radiotherapy. Correlations of AR with all parameters were calculated, as well as 5 - year disease – free survival (DFS) and overall survival (OS). Incidence of AR (≥1%) in patients with early TNBC in our analysis was 31.1%, of which 85% of patients had AR≥10% and as many as 60% had AR>50%. AR were found to be statistically significantly positively correlated with age and menopausal status, and statistically significantly negatively correlated with tumor size, grade and Ki67, as well as disease stage. AR≥1% showed no statistically significant association with DFS, median DFS was not reached for both groups of patients, those with AR≥1% as well as those without AR, with HR for disease recurrence or death of 1.08. AR were not statistically significantly associated with OS, there was no difference in the 5-year OS of patients with AR≥1%, compared with those with AR <1%, and median OS was not reached in either group. In this analysis, AR proved to be significantly correlated to more indolent, favorable disease characteristics, as expected and seen in many other analyses. However, AR did not prove to be an independent factor in the prognosis of patients with early TNBC in this cohort. Taking into consideration that there have been some of the larger studies confirming the role of AR as a good prognostic factor in this population of patients (although still with many controversies), further analyses should consider larger sample size, but also additional molecular markers in TNBC that might be in the background of forming the ultimate disease behaviour.

Keywords: triple-negative breast cancer, androgen receptors, biomarker, prognostic biomarker

P10 - COMPARISON OF PATHOLOGICAL RESPONSE IN HER2 POSITIVE BREAST CANCER, MONO VERSUS DUAL ANTI-HER2 BLOCKADE, DATA FROM CLINICAL PRACTICE

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Background: Untreated human epidermal growth factor receptor 2 positive (HER2+) breast cancer (BC) is aggressive disease, but its prognosis has been improved by HER2-directing drugs. In neoadjuvant setting the first generation of promising targeting HER2 treatment was chemotherapy plustrastuzumab and recently the standard first line therapy has become chemo plus dual anti-HER2 blockade (trastuzumab and pertuzumab). The pathological complete response (pCR) at time of surgery has been shown to predict clinical benefit in patients with early-stage HER2-positive BC, improving disease-free survival, event-free survival and overall survival. Across the studies the definition of pCR varies. The most common used definitions are: 1) eradication of in-situ cancer and invasive cancer in the breast and axillary nodes (ypT0 ypN0) or 2) eradication of only invasivecancer in the breast and axillary nodes (ypT0/is ypN0) or 3) eradication of only invasive cancer inthe breast (ypT0/is).

Methods: In this retrospective study 178 consecutive patients with invasive HER2+BC were diagnosed in clinical stage IA – IIIC and they received neoadjuvant therapy (antracyclines plus taxanes with mono vs dual anti-HER2 blockade) in period from 2010 to 2020 at the Institute for Oncology andRadiology of Serbia in Daily chemotherapy hospital. The primary end point was to compare pCRin two group of patients, mono versus (vs) dual anti-HER2 therapy. We strongly defined pCR as absence of in-situ cancer and invasive cancer in both the breast and the axillary lymph nodes. The Second aims of the study were to compare the pCR rates in different subpopulation based on age, initial clinical stage, hormone receptor (HR) status and type of second line chemotherapy paclitaxel vs docetaxel.

Results: At this point we analyzed patients with unilateral BC who received anthracycline-taxane–based chemo plus trastuzumab (N=84) or trastuzumab and pertuzumab (N=94). The median age in our cohort was 52.5 years (range 26-79). The majority of women had clinical stage IIIA 43.8%, followed by IIIB (27.0%), IIA (12.9%), IIB (11.8%), IIIC (3.9%) and only one patient had stage IA (0.6%). The most frequent hystomorphological tumor type were ductal IC 54.5%, undefined IC 32.0% and lobular IC 6.7%. The histological tumor grade 2 was the most common 77%, with the missing data for 16.8% of patients. The overall observed pCR rate was 42.7%. We found improved pCR in dual versus mono anti-HER2 therapy (49.5% vs 34.5%, $p<0.05$). The patient with HR negative status had higher pCR rate 49.3% (34/69) comparing with positive HR status 38.5% (42/109) without statistical significance, $p=0.17$. Although pCR rates were numerically higher in women older than 50 years versus younger women (47.0% vs 37.2, $p = 0.22$) and in group with the initial clinical stages IA-IIB versus more advanced stages IIIA-IIIC (51.1% vs 39.8%, $p=0.22$), differences were not statistically significant. The choice of taxane drug (paclitaxelvs docetaxel) did not influence pCR (43.0% vs 38.8%, $p=0.73$).

Conclusion: In accordance with previous neoadjuvant studies in patients with HER2-positive BC dual anti- HER2 blockade increases pCR compared with mono anti-HER2 treatment. The more frequent pCR was achieved in subgroup with HR negative tumor than with HR positive tumor.

Keywords: HER2 positive breast cancer, neoadjuvant therapy, anti-HER2 therapy, pathological complete response

P11 - COVID-19 VACCINATION IN PATIENTS WITH CANCER – SINGLE INSTITUTIONAL EXPRERIANCE

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Introduction: COVID-19 infection is the biggest global health treats worldwide, which has now infected over 150 million people with death range over 3 million. Cancer patients are usually more sensitive to infective diseases than people in overall population especially those receiving highly myelosuppressive chemotherapies. Coronavirus pneumonia led to 24% mortality with frequently extended viral shedding in cancer patients compared to 3% in noncancer patients. Because of its rapid spread in human population, the most effective management strategies are protective measures for preventing further transmission of the virus. Therefore, vaccines against SARS-CoV-2 are the promising solution to minimize the spreading of the virus. There are still limitations to be considered, including the efficacy of COVID vaccines for immunocompromised individuals. Patients with an active cancer should be considered for priority access to COVID-19 vaccination. The aim of our study was to examine number of patients vaccinated against SARS-CoV-2 virus, type of vaccines they received and side effects of the vaccination.

Methods: Between February and April 2021. we collected data from 87 oncology patients that have received vaccine against SARS-CoV-2 virus. All of the patients, at the time of the vaccination, were actively treated at the Daily Chemotherapy hospital at IORS, Institute for Oncology and Radiology of Serbia. Demographic data, oncology diagnosis, current treatment modality and co-morbidities were collected from patients' electronic records. Information's of the vaccination such as date of the first and second dose of received vaccine, type of the received vaccine and side effects were collected by questionnaire which was previously approved by the Ethics Committee of the IORS.

Results: Out of 87 patients, 67 (77%) are female, and 20 (23%) are male. Patients' mean age at the time of the first dose of vaccine received was 62.2 ± 13.4 years. The youngest patient was 39.8 years old, and the oldest one was 83.9 years old at the time of the vaccination. Out of 87 patients, 81 of them received both doses of the vaccine. 6 patients are still waiting to receive the second dose of the vaccine. 33 patients (37.9%) didn't have any co-morbidities. 28 of them (32.2%) had one and 26 (29.9%) had 2 or more co-morbidities requiring active therapy. In our group, 39 patients (44.8%) had non-metastatic disease and 48 (55.2%) had metastatic disease, out of whom 29 patients have one organ affected with metastasis and 19 have two or more affected sites. At the time of the vaccination, 28 patients (32.2%) was receiving cytotoxic chemotherapy. Out of 87 vaccinated patients, only 5 of them (5.7%) had previously COVID-19 infection. One patient had COVID-19 infection 5 days after receiving second dose of vaccine. Patient had mild symptoms with normal chest X-ray findings. She has fully recovered and continue her oncology treatment. 63 patients (72.4%) received vaccine made by Sinopharm company, followed by Pfizer-BioNtech vaccine (11 patients, 12.6%), Sputnik V (8 patients, 9.2%) and Oxford/AstraZeneca vaccine (5 patients, 5.7%). Out of 87 patients, 66 of them (75.9%) didn't have any side effects after receiving the vaccine. Only 11 patients (12.6%) had 2 or more different symptoms. The most common side effect was pain at the injection site of the vaccine and it was present in 10 patients (11.5%). 9 patients (10.3%) reported chills and shivering. Fever was present in 8 patients (9.2%). Only two patients had allergic-like reactions that was present with skin rush. None of the patients had severe allergic reactions.

Conclusion(s): In our study 87 patients with solid tumors and active oncology treatment had been vaccinated against SARS-CoV-2 virus without severe side effects. Although our study has a small number of patients vaccination against SARS-CoV-2 is safe. We will follow further our patients for possible COVID-19 infection. Our study support current guidelines which promote vaccination in oncology patients as priority.

Keywords: oncology patients, SARS-CoV-2 virus, vaccination

P12 - CURRENT STRATEGIES TO IMPROVE RESECTABILITY OF COLORECTAL LIVER METASTASES

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Around 25% of colorectal cancers manifest with liver metastases (CRLM) during the course of the illness, and surgical resection offers the only hope of cure and long-term survival. However, at the time of diagnosis, most patients have irresectable tumors due to inadequate healthy liver parenchyma that could be spared with standard liver resections. FLR of >30% is required for safe resection of healthy liver and >40% for the cirrhotic liver. Neoadjuvant chemotherapy can reduce the size and number of CRLMs, converting 10-20% of patients into resectable ones, but in case of failure, the prognosis is poor. Regenerative liver surgery was developed in order to prevent post hepatectomy failure by promoting liver hypertrophy prior to a definitive surgical procedure. Different approaches are available, including portal vein embolization (PVE), *2-stage hepatectomy* and novel method: *Associating liver partition and portal vein ligation for staged hepatectomy* (ALPPS). In the first stage of ALPPS, the liver is transected between the healthy and diseased lobe along with the ligation of the portal vein that supplies the part to be removed. After 1-2 weeks and adequate FLR hypertrophy, a second stage which includes the removal of the diseased liver lobe, is performed. The main advantage of ALPPS over other methods is faster and more intensive liver hypertrophy (mean FLR increase is 75%). Improvement in operative technique and postoperative care allowed the performance of ALPPS with acceptable mortality (7%) and morbidity rate (25%). In addition, these patients achieved an appealing long-term oncologic outcome (1-year disease free rate of 70%). The management of CRLM should always be based on a multidisciplinary paradigm with emphasis on tumor biology and personalized approach. The role of liver transplantation, hepatic vein embolization, and standard loco-regional therapies is yet to be addressed.

Keywords: liver, colorectal, cancer, regeneration

P13 - DUAL BLOCKADE WITH PERTUZUMAB/TRASTUZUMAB VERSUS TRASTUZUMAB IN NEOADJUVANT TREATMENT OF HER2 POSITIVE BREAST CANCER

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We present data of HER2 positive early breast cancer patients treated with neoadjuvant chemotherapy at Oncology Institute of Vojvodina from 2015 until 2020. The first anti HER2 standard of treatment were neoadjuvant antracycilnes followed by trastuzumab and taxanes (AC/HT) until October 2018, when dual HER2 blockade (AC/PHT) became available in Serbia.

Results: We identified 108 patients treated with neoadjuvant chemotherapy in this period. Total pathologic complete response (pCR) was defined as the absence of residual invasive and in situ cancer after neoadjuvant treatment. Median age was 54 (27-79). Among HER2 positive patients there were 41 (37.9%) hormone receptor negative patients (ER value 0), 21 (19,4%) intermediate hormone receptor positive patients (ER value 1 to 6), and 46 (42,5%) hormone receptor positive patients (ER value 7 and 8). Thirtyeight (38) patients were treated with AC/HT regimen, 94% of them were clinicaly node positive, 27,5% had tumor smaller than 3cm. Seventy (70) patients were treated with AC/PHT, 60% of them were clinicaly node positive, 52,2% had tumor smaller than 3cm. Total pCR rate in AC/HT group was 17,9%, and 50,7% in AC/PHT group p=0,0008. Breast pCR rate in AC/HT group was 41%, and 52,2% in AC/PHT group. In the hormone receptor negative group total pCR rates were: 35,7% for AC/HT regimen, and 65,2% for AC/PHT. In the intermediate hormone receptor positive group tpCR rates were 25% for AC/HT regimen and 53,3% for AC/PHT regimen. In the hormone receptor positive group tpCR rates were: 6,6% for AC/HT, and 33,3% for AC/PHT p=0.049. In the hormone receptor negative group pCR rates in breast were: 50% for AC/HT regimen, and 65,2% for AC/PHT. In the intermediate hormone receptor positive group pCR rates in breast were 42,8% for AC/HT regimen and 53,3% for AC/PHT regimen. In the hormone receptor positive group pCR rates in breast were: 33,3 % for AC/HT, and 40% for AC/PHT.

Conclusion: These results are in consistence with large prospective phase 3 clinical trials that led to approval of trastuzumab and later pertuzumab in the neoadjuvant treatment of HER2 postive breast cancer, as well as numerous real-world data published in the past years. Higher precent of node positive and large tumors in AC/HT group is in accordance with previously used criteria for neoadjuvant chemotherapy, while introduction of dual blocade led to a new standard of treatment that completely changed the mindset of oncology professionals.

Keywords: HER2+ breast cancer, neoadjuvant therapy, dual blockade, total pathological complete response

P14 - EFFICACY OF BIWEEKLY CETUXIMAB-IRINOTECAN COMBINATION IN THIRD LINE TREATMENT OF PATIENTS WITH METASTATIC COLORECTAL CANCER

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Introduction: Cetuximab is an IgG1 chimeric monoclonal antibody directed against the extracellular domain of epidermal growth factor receptor (EGFR). It has antitumor activity in patients without mutations of the RAS gene. Its combination with irinotecan is widely used in heavily pretreated patients progressing on at least two lines of systemic chemotherapy. Weekly Cetuximab administration is the standard regimen in patients with metastatic colorectal cancer (mCRC), but bi-weekly regimen is more convenient for the patients. Cetuximab has been reimbursed by the Serbian Health Insurance Fund from 2009.

Method: This is a retrospective study of Cetuximab-Irinotecan combination every two weeks in patients with KRAS wild type gen who previously progressed on oxaliplatin and irinotecan based regimens. Genomic DNA was extracted from formalin-fixed paraffin embedded tumor tissue samples and real-time PCR was used for RAS mutation detection. Cetuximab was used in dose of 500mg/m^2 and Irinotecan in dose of 180mg/m$^{2.}$ Response was evaluated every 2 months. Treatment was applied until disease progression or unacceptable toxicity.

Results: 204 patients were treated with Cetuximab-Irinotecan combination, after disease progression on at least two lines of systemic treatment. 132 patients were male (65%) and 72 female (35%), with median age at diagnosis 61 years (range 24 to 81). Median number of Cetuximab was 10 (range 1-50). Best therapy response was a partial response in 40 patients (19%), stable disease in 113 patients (56%), and progression in 51 patients (25%). Median progression-free survival (PFS) was 6.67 months (CI 95% 5.95-7.38). Median overall survival (OS) was 10.4 months. There was no statistically significant difference in PFS regarding gender, age, sidedness of primary tumor (left vs right), and localization of metastatic sites.

Conclusion: In our experience, Cetuximab given every other week is an optimal treatment choice in chemotherapy pretreated patients with wild type RAS gene. It showed a good response rate as well as progression free and overall survival.

Keywords: biweekly cetuximab, third line treatment, metastatic colorectal cancer

P15 - ENDOCRINE VERSUS CHEMOTHERAPY IN METASTATIC HR+/HER2- BREAST CANCER

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Background: Just a few years ago chemotherapy or endocrine therapy were the only possible treatment options of HER2 negative (HER2-), endocrine dependent (HR+) metastatic breast cancer. Guidelines were favoring endocrine therapy over chemotherapy, and oncology practitioners were following guidelines to a greater or lesser extent.

Patients and Methods: We have conducted a retrospective observational study in order to investigate the first line treatment choices for 425 metastatic HER2-/HR+ breast cancer patients diagnosed and treated from 2014 until 2018 at Oncology Institute of Vojvodina, Serbia. We have assessed the potential parameters that may influenced the treatment choice. Progression free survival (PFS) curves were calculated using Kaplan –Meier method.

Results: Patients' median age was 63 (28-85), majority were postmenopausal (86,5%), 114/425 (27%) patients had de novo metastatic disease. Almost half of the patients were treated with chemotherapy in the first line 218/425 (48,6%). These patients were significantly younger, had less comorbidities, had more metastatic sites, had visceral disease and were less likely to have bone only metastases in comparison to patients treated with endocrine therapy in the first line. Primary endocrine resistance (relapse during the first 24 months of adjuvant hormonal treatment) did not influence the first line choice of treatment (p=0,65). Median PFS for initial chemotherapy was 6 months versus 12 months for initial endocrine therapy p<0.0001 HR 0.57 (0.45-0.73). First line chemotherapy was not associated with better outcome in comparison to endocrine therapy even in patients with primary endocrine resistance: mPFS was 6 vs 12 months: p<0.0032 HR 0.47 (0.26-0.85). First line choices have been evolving through the years: in 2014 and 2015 35% of the patients were treated with endocrine therapy in comparison to 55% in 2016 and 2017.

Conclusion: Although guidelines have recommended endocrine therapy in the first line treatment of metastatic HER2-/HR+ breast cancer, our data are in consistency with other real-world data, suggesting that high percentage of patients have been treated with first line chemotherapy. This strategy is not associated with better outcomes even in patients with primary endocrine resistance.

Keywords: breast cancer, metastatic, chemotherapy, endocrine therapy, progression-free survival

P16 - GASTRIC METASTASIS 15 YEARS AFTER RADICAL MASTECTOMY FOR PRIMARY BREAST CANCER: CASE REPORT

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Background: Breast cancer is one of the leading cause of cancer-associated mortality worldwide, and its incidence is continuously increasing**.** The most common metastatic sites of breast cancer are the bone, brain, liver and lungs, but patterns of metastasis are affected by the breast cancer subtype. Gastrointestinal metastases from breast cancer are rare. The incidence of gastrointestinal metastases from breast cancer in long-term series and autopsies ranges between 2% and 18%. However, the rate of gastrointestinal (GI) metastasis from breast cancer is considered to be <1% in the clinical setting.

Case report: A 63-years old female patient underwent mammography and FNA biopsy after she discovered a suspicious lump in her left breast during self-examination. After patohistological confirmation of malignant disease, radical mastectomy was performed in the May of 2006. Pathologic analysis showed G1 tubular invasive breast cancer pT4 N0 (0/25) M0. Immunohistochemistry analysis revealed that tumour is ER-positive, PR-positive, Her2-negative. Adjuvant chemotherapy was initiated (6 cycles of FEC protocole: 5-FU, Farmorubicin, Endoxan) followed by hormonal therapy based on the immunohistochemical status of the tumour. Because of febrile neutropenia after 5th cycle, chemotherapy was stopped and the patient underwent thoracic wall irradiation with TD 50 Gy. In the November of 2006 hormonal therapy – tamoxifen was initiated. In the November of 2007 transvaginal ultrasound revealed endometrial hyperplasia, tamoxifen was discontinued and letrozole was initiated as an adequate substitution. Adjuvant hormonal therapy was discontinued in the November of 2017. Regular follow up was suggested as defined per protocol. In the March, 2021 patient presented with haematemesis, anaemia and fatigue. She underwent proximal gastrointestinal endoscopy which revealed a tumour arising from the gastric wall. Patohistological analysis and imunohistochemical profile suggested Er-negative, Pr-negative, Her2-positive metastatic breast cancer. Abdominal CT scan showed infiltration of stomach with pathologically enlarged lymph nodes next to the lesser curve of the anterior gastric wall. Liver was enlarged with multiple focal areas (secondary deposits). CT also revealed multiple osteolytic lesions of lumbar spine. Multidisciplinary team decided to initiate weekly Paclitaxel for 12 weeks with dual Her2 blockade: trastuzumab + pertuzumab. Patient is currently undergoing the therapy. After 5 cycles of Paclitaxel and 2 cycles of trastuzumab + pertuzumab she is feeling better with significant clinical improvement.

Conclusion: We report a case of a female patient at the age of 78 presented with an acute episode of haematemesis with previous anaemia and fatigue. Diagnostic evaluation revealed gastric, liver and bone metastases 15 years after radical mastectomy and more than 3 years after ending the adjuvant hormonal therapy. Although primary tumour was luminal A, gastric metastasis underwent molecular subtype change. Systemic treatment was initiated based on immunohistochemical profile of the gastric metastasis. Gastrointestinal metastases from breast cancer are considered rare in the clinical setting. However, patients with anaemia and/or other gastrointestinal symptoms occuring many years after diagnosis of primary breast cancer should be properly evaluated with gastrointestinal endoscopy. Molecular subtype change in metastatic tumours should be considered.

Keywords: breast cancer, gastric metastasis, molecular subtype, subtype change

P17 - HYPERPROGRESSIVE DISEASE IN PATIENT WITH METASTATIC UROTHELIAL CARCINOMA TREATED WITH ATEZOLIZUMAB – CASE REPORT

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Introduction: Until recently, the only approved therapeutic option for second line treatment of metastatic urothelial cancer was vinflunin with median overall survival (OS) of 7 months. Since 2016 PD-1 inhibitors (pembrolizumab and nivolumab), as well as PD-L1 inhibitors (atezolizumab, durvalumab and avelumab) had been approved for the treatment of patients who progressed after the first line platinum-based chemotherapy.

Case report: Female patient, 71 years old, with history of arterial hypertension, was diagnosed with grade 3 transitiocellular carcinoma of the left kidney in december 2019. She was initially treated with left nephroureterectomy and partial cistectomy in december 2019, pT2NxMx. Initial CT scans after surgery showed dissemnation ot the disease in the lungs: solitary node 29x25mm localized in S9/10 right lung. She was treated with 3 cycles of gemcitabine/cisplatin protocol. CT scans showed partial response in the lungs: solitary node reduced in size 16x20mm. She was treated with 3 more cycles of gemcitabine/cisplatin protocol until August 2020. PET CT revealed solitary node in the lungs 17x21mm SUVmax 9,7. She received no further treatment. Follow up CT scans in January 2021 showed progressive disease: enlargement of solitary metastasis in the right lung 41x30mm and mediastinal lymphadenomegaly. Since the progression was confirmed five months after first line platinum-based chemotherapy, patient began treatment with atezolizumab in the second line. Six days after the first cycle of treatment she presented with weakness in her lower limbs, elevation of LHD and alkaline phosphatase 2xULN. Two weeks later she was admitted to the hospital due to paraparesis. MRI of spine was performed and showed massive progression of disease in all spinal vertebra with fracture of VTh10 and ekstraosseal propagation of neoplastic process and spinal stenosis. The immunotherapy was stopped, and patient was referred to radiation oncologist for palliative radiotherapy. Hyperprogressive disease is defined as tumor growth rate at least twice as high after immunotherapy in comparison to beginning of treatment. It is also defined as double increase of the sum of target lesions in comparison to the baseline values, and at least two new lesions. It is described in 4-29% patients treated with immunotherapy. It is more common in patients older than 65, previously treated with radiotherapy and certain gene alterations.

Keywords*:* hyperprogression, immunotherapy, metastatic urothelial cancer

P18 – KIDNEY CANCER: HOW COULD WE INTERPRET RADIOLOGIC RESPONSE TO IMMUNOTHERAPY?

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Introduction: Immunotherapy represents a significant progress in treatment of malignant disease. Considering the specific activity of immunotherapy, applying standard RECIST criteria could lead to discrepancies in radiologic and true stage of tumor disease, resulting in early and potentially unjustified therapy discontinuation. In order to circumvent these pitfalls, iRECIST criteria were developed. Their specificity comparing previous criteria, is that increase in tumor size at the first control is not unambiguously defined as progressive disease, but further radiologic evaluation is required, resulting in better utilization of immunotherapy potential.

Case report: A 66- year old patient had undergone left sided nephrectomy in year 2000, with patohistologic diagnosis of clear cell carcinoma. In 2015, lung and pancreas metastases were verified, and treatment with sunitinib was started, with discontinuation in 2016 due to nephrotic syndrome. During 2017, he underwent stereotactic radiotherapy of lung and pancreas metastases. In April, 2018 immunotherapy with nivolumab was started. After 5 cycles, CT reevaluation verified increase in size of lung and mediastinal lymph node metastases with slight regression in the size of pancreatic lesion, compared to radiomorphologic status 3 months before immunotherapy inception. In a 2 month interval without therapy, radiologic reevaluation showed a stationary constellation regarding lung metastases, with regressive dinamics of pancreatic lesion, so immunotherapy with nivolumab was continued. Subsequent CT reevaluation showed further metastases regression, and the patient remained in excellent clinical condition. Altogether, till April, 2021, the patient is 3 years on nivolumab immunotherapy, radiomorphologically and clinically with stable disease.

Conclusion: Considering the specific tumor morphological changes during immunotherapy, modified radiologic criteria of therapy response evaluation were developed. As presented in this case report, radiomorphologic tumor progression does not necessarily implement overall therapy failure. Although missing conclusive reccomendations regarding immunotherapy continuation, evidence exist that with favourable clinical status it is reasonable to wait even for several months for radiomorphologic tumor size regression.

Keywords: kidney cancer, immunotherapy, iRECIST

P19 - NEOADJUVANT TREATMENT FOR HER2 POSITIVE EARLY BREAST CANCER – DIFFERENCES BETWEEN TRASTUZUMAB MONOTHERAPY AND DUAL ANTI-HER2 BLOCKADE IN OUR CLINICAL PRACTICE

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Neoadjuvant systemic therapy is standard treatment option for the most of HER2 positive early breast cancer patients. Studies confirm that patients with pathological complete response (pCR) to neoadjuvant therapy have better disease free survival (DFS) and overall survival. It is generally used to downstage the tumor which leads to higher rates of breast-conserving surgery rather than mastectomy. The response to neoadjuvant treatment informs us of the efficacy of the used therapeutic regimen and, therefore, helps us to choose an appropriate treatment strategy. First significant results have been shown in NeoALTTO study, which enrolled women with HER2-positive early breast cancer treated with lapatinib and trastuzumab and confirmed that patients who achieve pathological complete response after neoadjuvant anti-HER2 therapy have longer event-free and overall survival. Hence, studies with pertuzumab, such as NeoSphere trial, show improved efficacy when combined with the established HER2-directed antibody trastuzumab in breast cancer therapy. According to NeoSphere trial, patients given pertuzumab and trastuzumab plus docetaxel had a significantly improved pathological complete response rate compared with those given trastuzumab plus docetaxel, with favourable safety profile. At University hospital for Tumors, Zagreb, neoadjuvant systemic treatment was officially introduced in May 2015. and during that time, over 400 patients were treated. Our pilot trial analyzed consecutive sample of first 50 HER2 positive patients treated in our Clinic. We've analyzed patients characteristics, and compared two cohorts, one treated with anti-HER2 monotherapy (trastuzumab) versus the one treated with dual anti-HER2 therapy (trastuzumab + pertuzumab), from the moment dual anti-HER2 therapy became available. In patient cohort who received only trastuzumab together with chemotherapy, we enrolled 25 patients, consecutively. This cohort included 13 patients with hormone dependent tumors, and 12 patients who had non-luminal tumors. One patient in this cohort had multifocal disease, with both luminal biology tumors. Second cohort of patients which was treated with dual anti-HER2 therapy (pertuzumab+trastuzumab) plus chemotherapy, included 13 patients with luminal disease, 11 patients with non-luminal disease, and again, one of the patients had two primary tumors, both luminal type. In the cohort treated only with trastuzumab, 8 patients achieved pCR (complete pathological response), 3 patients achieved RCB (residual cancer burden) class I response, 5 of them RCB class II response, and two patients RCB class III response. For 6 patients residual cancer burden was not calculated. In the cohort treated with dual anti-HER2 therapy, 10 patients had pCR, 2 patients had RCB class I response, 8 patients had RCB class II response, 3 had RCB class III response, and for 2 patients RCB class was not calculated. In conclusion, there were more patients who achieved complete pathological response in cohort treated with both trastuzumab and pertuzumab. Among the patients who achieved pCR with trastuzumab monotherapy, 3 patients had luminal disease, and 4 patients had non-luminal tumor. For comparison, in cohort treated with dual anti-HER2 therapy, 4 of patients who had complete response to neoadjuvant treatment had luminal and 6 had non-luminal disease. Most of the patients in both cohorts who had RCB class II or RCB class III response to treatment had luminal cancers. Statistically significant results were not obtained, likely due to the small number of patients included in

this preliminary study. However our data clearly showed a trend of improved response to treatment and higher pCR in patients treated with both trastuzumab and pertuzumab in contrast to trastuzumab monotherapy, as well as tendency for better response rate to neoadjuvant chemotherapy in patients with HER2 positive non-luminal subtypes, which is consistent with results showed in relevant studies.

Keywords: neoadjuvant treatment, early breast cancer, HER 2 positive

P20 - PATHOLOGICAL COMPLETE RESPONSE FOLLOWING NEOADJUVANT THERAPY FOR GASTRIC CARCINOMA

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Background: Gastric cancer is the fifth most common malignancy and the third most common cause of cancer-related deaths worldwide. The incidence has declined over the last decades, but still, there is a significant number of new cases per year. A high mortality rate could be contributed to the fact that gastric malignancies have a tendency to present in advanced stages, with patients that are usually asymptomatic. Surgical resection still remains the only curative treatment for gastric cancer. Even after potentially curative surgery, overall survival at 5 years for patients with gastric adenocarcinoma remains as low as 20%–30%. Survival rates in gastric cancer have improved since the implementation of a combined approach of surgery and perioperative chemotherapy versus a surgery up-front approach. Neoadjuvant therapy has shown various benefits including an improved tolerance of chemotherapy regimen, overall survival and disease-free survival, increased probability of achieving negative margins, as well as tumor downstaging. These advantages demonstrated in the MAGIC and FLOT4 trials caused a paradigm shift favoring neoadjuvant chemotherapy followed by surgery and then additional adjuvant chemotherapy as the standard of care for patients with locally advanced gastric cancer. MAGIC trial is the first landmark trial, which showed overall survival (OS) improvement with perioperative chemotherapy (3 cycles of ECF/ECX) in resectable gastric, GEJ junction, and lower esophageal adenocarcinoma. The experimental arm showed significant improvement in 5 year OS as compared to surgery alone. The FLOT trials compared two different perioperative chemotherapy regimens (FLOT vs ECF/ECX) and findings have shown that overall survival was increased in the FLOT group compared with the ECF/ECX group for locally advanced, resectable gastric carcinoma. The estimated 5-year OS was increased in FLOT group than in ECF/ECX group, as well as median OS. Thus, this standard of therapy has not only shown to downstage locally advanced tumors but can potentially result in pathological complete response (pCR), although it is rare ranging from 3 to 15%.

Case report: A 61-year old female patient has presented to the primary care physician complaining of abdomen pain and heartburn. Abdominal ultrasound had shown gastric mucosal edema and with prior history of heartburns, the patient underwent gastrointestinal endoscopy which revealed a defect in the mucosa. The pathohistological analysis identified a grade 3 invasive adenocarcinoma. Abdominal MR scan showed a significant infiltration of the stomach with pathologically enlarged lymph nodes without signs of pancreatic infiltration or other secondary deposits. A multidisciplinary team (MDT) decided on initiating a neoadjuvant chemotherapy prior to doing surgery in the duration of 4 cycles following FLOT protocol.

In March 2021, an abdominal CT scan showed infiltrative gastric wall thickening of the greater curvature of the stomach with signs of perigastric fat infiltration. Post-neoadjuvant chemotherapy gastrointestinal endoscopy showed a cobblestone-like appearance of gastric mucosa in place of ulcerative infiltration initially described. MDT decided to proceed with surgical treatment. Thus, in late March 2021. The patient underwent gastrectomy, omentectomy and lymphadenectomy. Pathohistological analysis confirmed the initial diagnosis. A total of 12 lymph nodes were extirpated and had shown only signs of inflammation, but no signs of neoplasia. The patient is currently undergoing adjuvant chemotherapy, with no signs of recurrence of the primary disease.

Conclusion: We report a case of a 61-year old female patient presenting with abdominal pain and heartburn. Diagnostic evaluation revealed grade 3 gastric adenocarcinoma with signs of local advancement. The patient underwent perioperative chemotherapy according to the FLOT4 trial, afterward following successful surgical treatment, with currently ongoing adjuvant chemotherapy. Gastric adenocarcinoma prognosis remains poor despite recent advances in therapies. The multimodal approach represents the standard of care for the treatment of resectable oesophageal and gastric cancer patients today. Various trials showed an improvement in overall survival by using a perioperative treatment in comparison to surgery alone. A combined approach of surgery and perioperative chemotherapy versus a surgery upfront approach should be implemented as a staple standard of care for patients with localized or locally advanced gastric carcinoma. This is giving a greater chance for a longer OS or even pCR.

Keywords: gastric carcinoma, complete response, neoadjuvant, chemotherapy

P21 - PATHOLOGICAL COMPLETE RESPONSE RATES WITH DUAL HER2 BLOCKADE ADDED TO NEOADJUVANT CHEMOTHERAPY IN BREAST CANCER: A SINGLE-CENTER EXPERIENCE

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Background: In human epidermal growth factor receptor 2 (HER2)-positive early and locally advanced breast cancer (BC) neoadjuvant treatment with a combination of sequential chemotherapy and HER2-targeted therapy is currently the standard of care. Studies have shown that patients who achieve pathological complete response (pCR) after neoadjuvant treatment have a better long-term outcome.

Objective: The aim of this study is to identify pCR rates in patients with early and locally advanced HER2-positive BC receiving neoadjuvant chemotherapy with trastuzumab plus pertuzumab.

Methods: A retrospective single-center review was conducted among HER2-positive early and locally advanced BC patients (stage II and III) who received neoadjuvant therapy for two years period (2019/2020). All the patients received 4 cycles of anthracycline-containing therapy followed by a taxane (4 cycles of docetaxel or 12 weekly application of paclitaxel) in combination with of trastuzumab and pertuzumab. Complete pathological response was defined as the absence of residual invasive cancer both in the breast tissue and lymph nodes.

Results: Thirty-four treatment-naive patients with early or locally advanced HER2-positive BC were included in the analysis. The median age of the patients was 49,5 (36-68). Thirteen out of 34 patients (38%) were diagnosed in stage II and 21 out of 34 pts (62%) were in stage III. After competition of neoadjuvant therapy, thirty-two patients underwent surgery, while two patients, due to the lack of response to neoadjuvant therapy, were treated with radiotherapy. Overall pCR was attained by 18 patients (56%), pCR 62% in stage II and pCR 57% in stage III. Tolerability of neoadjuvant chemotherapy with trastuzumab plus pertuzumab was generally good, without any patient discontinuing therapy due to toxicity.

Conclusion: pCR rates obtained among our patients are slightly lower than those reported from the majority of neoadjuvant studies with chemotherapy plus trastuzumab plus pertuzumab, mostly due to the high percentage of locally advanced stage of BC in our patient population. These findings support current recommendations of using dual HER2-targeted combination of trastuzumab and pertuzumab with chemotherapy in neoadjuvant setting for early and locally advanced HER2-positive BC.

Keywords: HER2-positive BC, neoadjuvant therapy, pCR, dual HER2 blockade

P22 - PATIENT WITH LIVER TUMORE BEFORE AND AFTER LIVER TRANSPLANTATION

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Introduction: Intraahepatic cholangiocarcinoma is generally a contraindication for liver transplantation, because of aggressive biology of the disease and poor long term prognosis. However, based on recent retrospective trials one question inserts itself. Is there a small group of patients with early ICC (tumor smaller than 2 cm) that would benefit from liver transplantation? Additional prospective trial are required to answer this question.

Case report: In this case report we will show patient, Š.V, born 1960. In February of 2011 patient underwent liver transplantation due to HCC. Patient was a long time alcoholic with liver cirrhosis, osteoporosis and arterial hypertension. Tumor was initially found on abdominal ultrasound, and diagnosis was confirmed by MSCT and high AFP values. Patient was a candidate for liver transplantation according to Milan criteria (solitary tumor less than 4cm in diameter, Child Pugh status B, and in good general condition, ECOG 1). After liver transplantation there was no sign of disease recurrence until August 2017 when two suspicious liver lesions were found on abdominal ultrasound. Additional diagnostic tests (MSCT and biopsy of liver) confirmed diagnosis of intrahepatal adenocarcinoma. Given the fact that this histology was different then primary tumor, additional molecular testing was done, and it was confirmed that second malignancy originated in donor liver (tumor tissue had XX chromosome, donor was a female, and patient is a male). Our patient was then discussed in MDT, and conclusion was reached that there is no indication for second liver transplantation (ICC, multiple tumor lesions). Our patient received systemic chemotherapy, 1 st line cisplatin and gemcitabine, 2 nd line 5fu mono, and 3 rd line irinotecan. At this moment patient is still alive, has only intrahepatal disease and is in good general condition.

Conclusion: A number of population and observation studies have shown that patients with transplanted liver have higher incidence of secondary malignancies, primary head and neck tumors, esophageal tumors, renal carcinomas and colorectal carcinomas. This fact is probably due to the immunosupression of these patients. In spite of all protocolar criteria for liver transplantation, there is always a risk of occult tumor in transplanted organ, which might become a new disease in patient on immunosupressive treatment.

Keywords: hepatocellular carcinoma, cholangicellular carcinoma, liver transplantation

P23 - PATTERNS OF LOCOREGIONAL RECURRENCE AFTER SURGERY AND RADIOTHERAPY OR CHEMORADIATION FOR SQUAMOCELLULAR HEAD AND NECK CANCER

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Background: Worldwide, head and neck squamous cell cancer (HNCSCC) are the sixth most common type of cancer. In Serbia, the incidence of oropharynx,oral cavity, hypopharynx and larynx cancer was estimated to 2000 new cases yearly. For patients diagnosed with HNSCC definitive treatment strategies consist of surgery upfornt followed by adjuvant radiotherapy with or without chemotherapy as indicated or chemoradiotherapy for patients with locally advanced head and neck cancer.

Patients and methods: This retrospective study included 20 patients with recurrent or metastatic HNSCC who had been treated in Institute for Oncology and Radiology of Serbia, Department of Medical Oncology, Department for Head and Neck tumors during the period from January 2019 to February 2021. Data were collected from medical documentation.

Results: Median age was 64 years (range 47-76 years) and all patients are men. Laryngeal cancer being the most common primary tumor manifestation in 50% and more than two thirds had stage III and IVA/B disease. Histologically, all of the treated tumors were squamous cell carcinoma. In the primary approach two patients were treated only with radiation therapy, 8 patients had upfront surgery with adjuvant radiotherapy, 6 patients received neoadjuvant chemotherapy (out of which 4 received with concomitant chemo), 2 received radiation therapy potentiation with weekly cisplatin and 2 with cetuximab. The majority of patients were, furthermore, treated with conventional radiotherapy (median 60 Gy, range 58-70 Gy) in daily fractions of 2 Gy. The median time to recurrence was 10 months (range 3-35). Among these 20 patients there were 11 local, 17 regional and 6 simultaneous local and regional recurrences, synchronous distant metastases occured in 3 out of 20 patients. One patient developed distant metastases in the absence of a locoregional recurrence. All of the patients received-platinum based chemotherapy with cetuximab with disease control in 13 out of 20 patients.

Conclusion: The majority of failure treatment for a locoregional advanced HNSCC were regional relapses. Improving a locoregional control remains a high priority to identify the patients with a radiation resistant tumor subpopulation and underline the rationale for dose escalation to the highest risk for relapse.

Keywords: head and neck squamous cell cancer, locoregional recurrence, radiation therapy

P24 - SIDE EFFECTS OF LHRH ANALOGUES IN THE TREATMENT OF EARLY BREAST CANCER PATIENTS: FREQUENCY AND TIMING

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Introduction: LHRH analogues (*analogues* of luteinizing hormone-releasing hormone) stop the signal that the body sends to the ovaries to make oestrogen, which causes temporary menopause. LHRH are given in adjuvant therapy for early breast cancer, premenopausal patients with hormone receptor positive disease based on the risk of relapse (REF vodic St Gallen2021). In hormone receptor negative breast cancer patients LHRH analogues are given concomitantly with chemotherapy with intention for fertility preservation.

Methods: Consecutive patients receiving LHRH analogue therapy in Daily Chemotherapy Hospital at the Institute for Oncology and Radiology were included in this analysis. We evaluated the frequency of symptoms during therapies at different time periods. Symptoms were reported by patients on monthly basis using the list of the most frequent side effects of LHRH based on the literature data. Patients were divided into 3 groups according to the LHRH therapy duration: 15, 10 and 5 months respectively. We evaluated 4 symptoms as the most frequent: hot flashes, night sweats, insomnia and anxiety.

Results: The first group consists of 50 patients with follow up of 15 months, from November 2019to April2021. The second group consist of 46 patients with follow up of 10 months, from June 2020 to April 2021. The third group consists of 25 patients with follow up of5 months, from December 2020 to April 2021. In every group median age was 42, age range from 30 to 53. 80% of total number of patients were node negative, 22% of patients have a node negative diseases and tumor size less than two centimetres. 10% of patients were HR+HER2+ positive and they received adjuvant Herceptin. LHRH analogues were combined with endocrine therapy: in 99,7 % of patients with tamoxifen and 0,3 % with aromatase inhibitors. In 47% of patients LHRH treatment were given concomitantly with sequential chemotherapy, anrtacycline and taxane based, due to fertility preservation reasons. In the first group of patients, with the longest follow up of 15 months, the most frequent side effects were hot flashes and night sweats been present in 90% of patients, while insomnia and anxiety were detected in 46% and 30% of patients respectively. In the second group, with the follow up of 10 months, the prevalence of hot flashes was lower seen in 83%, while night sweats were detected in 71%, insomnia in 66% and anxiety in 50% of patients. In the third group, with shortest follow up of 5 months the most frequent symptoms were hot flashes 92% and night sweats 80%.Insomnia was reported in 40% and anxiety in 28% of patients. Other symptoms reported by patients were the following: headaches 12%, nonspecific abdominal pain 5 %, nausea 2 % and fatigue 2%.None of the patients interrupted their treatment due to the side effects.

Conclusion: In this study, a considerable proportion of young women reported as the most frequent symptom hot flashes and night sweats in first 5, 10 and 15 months during LHRH treatment been given as part of adjuvant endocrine treatment for early breast cancer. Effective treatment to diminish these side effects are needed.

Keywords: breast, cancer, side-effects, LHRH

P25 - SINGLE CENTER EXPERIENCE STUDY WITH PEMBROLIZUMAB IN PATIENTS WITH UNRESECTABLE OR METASTATIC MELANOMA

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Until the introduction of novel agents, the prognosis of metastatic melanoma patients was poor. The first registered drug was BRAF inhibitor Vemurafenib in 2011, and since then palette of single and double agent therapeutics has been approved. Pillars of treatment nowadays are immune checkpoint inhibitors (PD-1 and CTLA-4) in both BRAF mutant and wild type melanoma patients, whereas in BRAF mutant melanomas combined targeted therapy (BRAF and MEK inhibitors) is a possible choice as the first line of treatment. We conducted a retrospective study among unresectable and metastatic melanoma patients treated with Pembrolizumab in University Clinical Center Nis from February 2017 to March 2021. We assessed the efficacy of Pembrolizumab in general, and among specific subgroups, the appearance of immune-related adverse events (irAEs), and also the appearance of irAEs as a predictive factor of prolonged response in the real clinical setting. Pembrolizumab efficacy was assessed through overall response rate (ORR) and progression-free survival (PFS), and toxicity with irAEs. A total of 63 patients, 44 male and 19 female, were included. The median age was 64 years. Most of the patients were treatment-naive (84.1%), but patients who received single-agent or combined targeted treatment in the first line, were also included. Patients were staged according to the AJCC 8th edition staging system. Almost half of the patients were M1c clinical stage (49.2%), followed by M1d (28.5), M1a (9.5%), and only one patient was CS III (1.6%). Elevated LDH level was observed in 57% of patients. As for the BRAF mutation status 17 patients (27%) had V600E mutation, 9 of them were treatment-naive and 8 previously received targeted therapy. A total number of administered cycles was 729, with an average of 11.5 cycles per patient. Among all 63 treated patients, 8 achieved complete response (CR, 12.7%), 9 partial remission(PR, 14.3%), and 19 stabile disease (SD, 30.2%), for a disease control rate (DCR) of 57.2%. The median time to response was 6 months (range, 2-8 months), and the median time to progression was between the 3rd and 4th cycle. At data cut off 29 patients (46%) were still receiving treatment, while 34 patients (54%) were discontinued due to disease progression (PD, n = 27, 42.9%), adverse events (n = 2, 3.17%), patient withdrawal (n = 3, 4.77%) or lost to follow-up (n = 2, 3.17%). Among the patients treated with Pembrolizumab 14 of them (22.2%) developed Immune-Related Adverse Events (irAEs). There were two therapy discontinuations due to recurrent grade III irAE in form of pemphigoid skin rash and grade III autoimmune hepatitis. Interestingly, seven out of nine patients that achieved complete response had irAEs during their course of treatment. As for the efficacy of Pembrolizumab ORR was 44.5%, with a median PFS of 33 months (CI 95%) achieved. There was no statistical difference among genders, but there was a statistically significant difference between treatment-naive and previously treated patients (p=0.002). There was also a statistically significant difference in PFS between patients with and without elevated levels of LDH (p=0.05). In conclusion, we observed a median PFS of 33 months which endorses long term response which is one of the main characteristics of immune checkpoint inhibitors. As for the subgroups, statistically significantly lower median PFS was observed among previously treated patients (p=0.002) and patients with elevated levels of LDH (p=0.05). Pembrolizumab showed a favorable safety profile, with only 3% high-grade irAEs which lead to discontinuation of treatment and also the resolution of symptoms.

Keywords: immunotherapy, advanced melanoma, real world data, adverse events.

P26 - THE MODEL OF A DIRECT COLLABORATION BETWEEN MULTIDISCIPLINARY TUMOR BOARD AND SUPPORTIVE CARE DEPARTMENT FOR PATIENTS WITH ADVANCED CANCER

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Introduction: Symptom burden as a result of cancer and its treatment is present across all disease types, stages and phases of care in cancer patients. Symptom management guided by patient's self-report of symptoms improves symptom management, quality of life and prolongs overall survival. The Edmonton Symptom Assessment System (ESAS) has been proposed as a screening tool in cancer patients and in the clinical setting, ESAS is most often used to identify patient's unmet needs by systematic screening. It consists of 11-point numerical rating scales (0-10) for self-report of nine common symptoms of cancer, with a 10th scale for a patient-specific symptom. Each symptom is assessed separately on a scale from 0 to 10, with 10 representing the greatest severity. Scores between 4 to 6 correspond to "moderate" symptoms, and scores between 7 to 10 reflect "severe" symptom burden. The goal of our study is to evaluate the model of a direct collaboration between multidisciplinary tumor board (MTB) and supportive care department (SCD) for patients with advanced cancer.

Methods: From November 2018 to December 2019, MTB referred advanced cancer patients with severe symptom burden to the SCD. ESAS was used to assess the symptom burden, and severity of symptoms was evaluated initially and after the SCD intervention. Assessment of symptom burden after the SCD intervention was scheduled 7 days after the initial visit. Descriptive statistics were used to evaluate frequencies, means and/or medians, and standard deviations (SDs) and/or ranges for patient's demographic and clinical information.

Results: ESAS records were collected from 54 patients with median age of 65 years (range 35 -85 years). Data were collected form 57.4 % female patients and 42.6 % male patients. The most common cancer type was genitourinary cancer (27.7%), followed by gastrointestinal (24.07%) and breast carcinoma (14.81%) while 11.1 % of patients had a cancer of unknown primary site. The most frequent patient performance status (PS), estimated by MTB, was 2 (31.48%) followed by PS 1 (29.6%) and PS 3 (27.7%). Moderate to severe pain and moderately to severely impaired well-being were most frequently reported symptoms (n=45, 83%, n=29, 53.7%, respectively). Severe nausea, loss of appetite, shortness of breath, fatigue, depression, drowsiness and anxiety were reported in 5.56%, 33.33%, 7.14%, 42.59%, 25.93%, 16.67%, 31.48% of patients, respectively. After seven days clinically meaningful (≤30%) pain relief and improvement of well-being was reported in 34 patients (62.9%) and 32 patients (59.25%), respectively.

Conclusions: Pain was the most frequent reason for referral from MTB to SCD. Among symptoms impaired well-being and pain were most frequently reported symptoms at the time of assessment by the supportive care team with the clinically meaningful improvement after SCD intervention. For advanced cancer patients with heavy symptom burden the direct collaboration between MTB and supportive care team can provide better symptom management and help to better assess and characterize symptom burden as well as to provide timely symptom management at the moment of presentation to the MTB. We are conducting further research to examine the impact of ESAS in the treatment decision-making process in advanced cancer patients.

Keywords: patients reported outcomes, Edmonton Symptom Assessment System (ESAS), advanced cancer patients

P27 - TOLERABILITY OF OLAPARIB IN PATIENTS WITH BRCA 1/2-MUTATED PLATINUM-SENSITIVE RECURRENT HIGH-GRADE SEROUS OVARIAN CANCER RECEIVING OLAPARIB MAINTENANCE MONOTHERAPY: A SINGLE INSTITUTION EXPERIENCE

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Background: Olaparib, a poly(adenosine diphosphate–ribose) polymerase (PARP) inhibitor, is approved in the maintenance setting for patients with platinum-sensitive relapsed ovarian cancer (who are in complete or partial response) with germline or somatic *BRCA1* and *BRCA2* mutations. Safety data from clinical trials in recurrent ovarian cancer (OC) patients have shown that olaparib monotherapy is generally well tolerated.

Aim: The aim of our study was to investigate the toxicity profile of olaparib used in daily clinical practice among patients with recurrent OC.

Methods: At our Medical Oncology Department, patients with *BRCA*-mutated recurrent OC received olaparib as maintenance monotherapy following response to platinum-based chemotherapy (800 mg daily, capsule formulation) from November 2019 to February 2021. Adverse events (AE) were closely monitored and recorded at least monthly, and graded according to CTCAE v.5.0.

Results: Sixteen patients were included in the study, median age 52.6 (39-63 age). Patients were stratified according to ECOG performance status: 5 pts (31.2%) were ECOG 0 and 11 pts (68.7%) were ECOG 1. The majority of adverse events had early onset, usually recorded within the first 3-6 months of drug administration. Registered toxicity was as follows: five pts (31,25%) had anemia gr 1, three pts (18,75%) had anemia gr 2, seven pts had anemia gr 3 (43,75%), three pts had thrombocytopenia gr 2 (18,75%) and three pts experienced neutopenia gr 2 (43,75%), Furthermore, four pts had nausea gr 1 (25%) and five pts had fatigue gr 1 (31,25%). One patient discontinued treatment due to prolonged pancytopenia (anemia, thrombocytopenia and neutropenia) gr 3/4, but there was no evidence of myelodysplastic syndrome/acute myeloid leukemia after a bone marrow biopsy. Due to registered high-grade anemia, the dose of the drug was reduced to the 1st level of dose reduction (400mg daily) in seven patients.

Conclusion: Our research showed that olaparib tolerability in platinum-sensitive recurrent OC is comparable to previously reported findings in prospective clinical trials. The most frequent high-grade AE in our analysis was anemia which was adequately corrected by dose modification and simple supportive measures. The most common non-haematological AEs (fatigue, nausea) were mild in severity and did not require treatment modification. Patient education and awareness of side effects can also be helpful in managing olaparib toxicity.

Keywords: recurrent *BRCA*-mutated ovarian cancer, olaparib, toxicity

P28 - TREATMENT OF A PATIENT WITH ADVANCED HEPATOCELLULAR CARCINOMA - CASE REPORT

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Background: The combination of atezolizumab and bevacizumab has been approved globally for patients with unresectable hepatocellular carcinoma (HCC) who have not received prior systemic therapy, based on results from IMbrave150 (NCT03434379).

Results: At the time of the primary analysis (August 29, 2019), the hazard ratio for death with atezolizumab–bevacizumab as compared with sorafenib was 0.58 (95% confidence interval [CI], 0.42 to 0.79, P<0.001). Overall survival at 12 months was 67.2% (95% CI, 61.3 to 73.1) with atezolizumab–bevacizumab and 54.6% (95% CI, 45.2 to 64.0) with sorafenib. Median progression-free survival was 6.8 months (95% CI, 5.7 to 8.3) and 4.3 months (95% CI, 4.0 to 5.6) in the respective groups (hazard ratio for disease progression or death, 0.59, 95% CI, 0.47 to 0.76, P<0.001). Grade 3 or 4 adverse events occurred in 56.5% of 329 patients who received at least one dose of atezolizumab–bevacizumab and in 55.1% of 156 patients who received at least one dose of sorafenib. Grade 3 or 4 hypertension occurred in 15.2% of patients in the atezolizumab–bevacizumab group, however, other high-grade toxic effects were infrequent.

Case report: A 62-year-old woman with a 4-month history of jaundice, dark urine and pale stools was presented to her family doctor in September 2019. She gave no history of chronic medical illnesses, there was no drug or allergy history of note. She had a positive family history of lung and brain cancer. The patient was a long-term smoker who has stopped smoking since the symptoms started. A Multi-Slice Computed Tomography (MSCT) of the abdomen showed inhomogeneous and unsharply marked tumor in the right lobe (segment V and VI) of liver, with a diameter of 5.5x7 cm. The patient was taken up for surgery in October 2019. She underwent a right hepatectomy, cholecystectomy, left hepaticojejunostomy and radical lymphadenectomy. Histopathology report showed HCC. Postoperative recovery was uneventful. She was seen in our oncology clinic for further management. Postoperative Magnetic Resonance Imaging (MRI) of the abdomen showed multiple hepatic satellite lesions (segment II-1.6x1.2 cm, segment IVa-1.2 cm, segment IVb-1.3 cm, with a few minor lesions in the remaining liver segments). Postoperative serum alpha-fetoprotein (AFP) level was 13.1 ng/ml. In February 2020 patient started treatment with a combination therapy of the atezolizumab (1200 mg iv) and bevacizumab (15 mg/kg iv) every 21 days. In April 2020, the tumor response was evaluated according to the modified Response Evaluation Criteria in Solid Tumors, and a complete response (CR) was identified. MRI of the abdomen showed complete regression of previously visible metastatic liver lesions. The serum levels of AFP decresead from 13.1 to 3.2 ng/ml. She continued to receive atezolizumab and bevacizumab combination therapy. Manageable toxicity included grade 2 hypertension and grade IA hypothyroidism. Until now, the patient received a total of 20 cycles of combination therapy and she had maintained CR.

Conclusions: IMbrave150 trial showed consistent clinically meaningful treatment benefit and safety with 12 months of additional follow-up. The combination provides the longest survival seen in a front-line Phase III study in advanced HCC, confirming atezolizumab and bevacizumab combination as a standard of care for previously untreated, unresectable HCC.

Keywords: hepatocellular carcinoma, HCC, atezolizumab, bevacizumab, IMbrave150

P29 - YOUNG-ONSET COLORETAL CANCER

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Background: In contrast to the decreasing incidence of colorectal cancer (CRC) in older populations, the incidence in younger adults has nearly doubled since the early 1990s. Increasing incidence of early-onset colorectal cancer is poorly understood and rising number of publication is trying to describe its clinical characteristics, pathogenesis, genetic background and potential risk factors. Differences in clinical behavior and tumor phenotypes have been observed, suggesting that early-onset CRC could be a different disease than the traditional CRC.

Methods: The records of patients with histologically confirmed colorectal carcinoma bellow 40 years of age at the time of diagnosis treated in a ten year period (between 2009 and 2018) at single institution were reviewed. Clinical and histopathology data were evaluated.

Results: In a 10 year period, 109 patients with colorectal cancer, younger than 40 years of age at the time of diagnosis have been treated at single institution (2.7% of all-age patients with diagnosed CRC). Median age was 35 (range 19-40), 49% were female, PS0 in 66.1%, PS0+1 in 98% of patients. Patient had mostly normal BMI (49.3%). Family history was positive for various malignancies in 26.6% cases with family history positive for colorectal cancer in 12.8% patients. Most of the patients experienced some disease specific symptoms, having one symptom in 55.9% patients and two or more symptoms in 37%. Acute bowel obstruction was a presenting symptom in 35% of patients with tumor perforation registered in 6.4%. There have been 57% of colon cancer and 46% of rectal cancer. Sigmoid carcinoma was most often diagnosed among patient with colon carcinoma (45.6%). Disease was mostly localized in a left colon, in 83.5% of patients. Mucinous tumors were diagnosed in 25.7% of patients. Initially patient were diagnosed in stage II, III and IV in 18.3%, 47.7% and 33.9%, respectively.

Conclusions: Colorectal cancer should no longer be considered a disease of older people. Patient have presenting symptoms, with high percentage of acute one. These tumors have a striking predilection for distal colon, particularly the sigmoid colon and rectum and are much more likely to demonstrate adverse factors, including mucinous differentiation and advanced disease.

Keywords: colorectal cancer, young-onset, adverse factors