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ORAL PRESENTATIONS

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ANUŠKA BUDISAVLJEVIĆ[1]

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The triple negative breast cancer (TNBC) had been known for the worst survival rates among all breast cancer subtypes and, from historical point of view, systemic chemotherapy improved median overall survival (OS) for advanced/metastatic TNBC (a/mTNBC) from 5.9 to 12.9 months, making it still the most *uncurable* subtype of breast cancer(1). Considering the early TNBC (eTNBC) the constant challenge are high recurrence rates after primary treatment - surgery and adjuvant/neoadjuvant systemic chemotherapy along with the locoregional radiotherapy(2).

The immune checkpoint inhibitors have been introduced in clinical practise for the treatment of a/mTNBC in 2018 along with the publication of the results of the IMpassion 130 study(3). This study showed significantly longer PFS for the a/mTNBC patients with PD-L1>1%, treated in the first line setting with atezolizumab + nab-paclitaxel compared with nab-paclitaxel alone, PFS 7.5 vs 5.0 months with HR 0.62 (95%CI 0.49-0.8). Moreover, median OS improved from 15.5 to 25.0 months with the addition of atezolizumab with HR 0.62 (95%CI 0.45-0.86) for PD-L1 positive group. In 2020 FDA granted fast approval for another ICI, pembrolizumab, due to primary analysis of KEYNOTE-355 study(4). In this study pembrolizumab was combined with chemotherapy in first line setting for a/mTNBC for the patients with CSP >10, in combination with different chemotherapy back-bone (nab-paclitaxel/paclitaxel/gem-carbo). Patients treated with pembrolizumab + chemotherapy achieved median PFS 9.7 months compared to control treated with chemotherapy alone with PFS 5.6 months HR 0.66 (95% CI, 0.50-0.88). In 2022 final results of the study showed significantly better OS results for pembrolizumab CPS>10 group, 23.0 vs 16.0 months, respectively, with HR 0.73 (95% CI, 0.55-0.95). Today, NCCN guidelines recommend pembrolizumab with chemotherapy as the first line therapy for a/mTNBC while ESMO guidelines recommend both atezolizumab and pembrolizumab in combination with chemotherapy for selected a/mTNBC with positive PD-L1 status(5).

There are numerous ongoing studies exploring further the potential benefit of treatment with ICI in a/mTNBC mostly in combination with antibody drug conjugates (ADC). Particularly noteworthy are the results of the phase 1b/2 BEGONIA study. The study was evaluating combinations of durvalumab (D) with other novel therapies in the first line treatment of a/mTNBC. At the last ESMO meeting the results for Arm 7 were presented where durvalumab was combined with ADC datopotamab-deruxtecan (Dato-DXd). Primary endpoints of the study were safety and tolerability and secondary endpoints were overall response rates (ORR), PFS and duration of response (DoR). At median follow up of 7.2 months ORR was 74%, median PFS was 13.8 months (95% CI, 11.0-NC) and median DoR was 15.5 months (95% CI, 9.92-NC). Although, it was a phase 1b/2 study the results were very promising. In line with the results of BEGONIA Arm 7, TROPION-BREAS-05 study was created, which will compare the standard first line a/mTNBC therapy, pembrolizumab with chemotherapy, versus the combination of Dato-DXd/D. Primary analysis of the study is expected in September 2026.

Quite differently from the mTNBC studies exploring ICI treatment in eTNBC showed positive PD-L1 status in not required nor predictive for ICI treatment response. Many studies with different ICI in different treatment scenarios explored whether addition of ICI to chemotherapy could lead to better event free

survival (EFS) or OS outcomes. In the IMpassion031 study atezolizumab was administered in neoadjuvant setting with nab-pacli/ddAC and then continued after the surgery as adjuvant therapy for one year, versus neoadjuvant chemotherapy(6). The pathologic complete response (pCR) rates for atezolizumab group were 58% vs 44%, 2-EFS years rates for ITT population were 85% vs 80%, numerically improved, but without significant statistical difference. On the other hand, in the NeoTRIPaPDL1 study atezolizumab was given in combination with neoadjuvant chemotherapy (carboplatin + nab-pacli) with control group receiving only neoadjuvant chemotherapy. After the surgery both groups received adjuvant chemotherapy (AC/EC/FEC)(7). The study did not meet endpoints: pCR rates and 5-year EFS rates. Different approach was taken in the GeparNuevo, phase II study, where durvalumab was applied 2 weeks before the start of neoadjuvant chemotherapy and then continued as addition to neoadjuvant chemotherapy (nab-paclitaxel/ddEC), but durvalumab was not given after the surgery in adjuvant setting, the control group was treated with neoadjuvant chemotherapy only(8).The study showed pCR rates of 53% vs 44%, and impressive results of OS; 3-year OS 95% vs 83%, HR 0.24 (95% CI 0.08-0.72). And last but not least, the KEYNOTE-522 study with pembrolizumab along with the neoadjuvant chemotherapy (paclitaxel + carboplatin/AC) and adjuvant pembrolizumab after the surgery for one year, versus control treated with neoadjuvant chemotherapy only(9). The study included T2N0 and T1-T4N+ patients. The pCR rates in this study were 64.8% vs 51.2% and 3-EFS rates were 84% vs 76.8%, respectively, with HR 0.63 $p<0.001$. The result of KEYNOTE-522 made pembrolizumab, in combination with neoadjuvant chemotherapy + adjuvant pembrolizumab, the new standard of care treatment for high risk eTNBC.

There are still many unanswered questions considering eTNBC treatment with ICI. Firstly, taking into account immune related adverse events, which can appear long after the treatment with ICI finished, the question raised how to select patients and which is optimal sequencing, duration and combination to maximise potential benefit from ICI? Ongoing studies are addressing the questions of therapy de-escalation. For example, the Optimice-pCR study is recruiting the patients with pCR after neoadjuvant pembrolizumab + chemotherapy treatment, continuing adjuvant pembrolizumab versus placebo(10). On the other hand, The NeoSTAR, phase 2 study, is questioning de-escalation by omitting anthracyclines from chemotherapy back-bone. The study explores the efficacy of Sacituzumab-govitecan in combination with pembrolizumab in neoadjuvant setting with adjuvant pembrolizumab + chemotherapy that does not contain anthracyclines (paclitaxel/carboplatin)(10). Secondly, what about the patients treated with neoadjuvant pembrolizumab + chemotherapy but without pCR and RCB III? Current studies with adjuvant Sacituzumab-govitecan, datopotamid-deruxtecan or durvalumab will give us valuable information regarding that question(10). Thirdly, we still do not have reliable predictive biomarkers for the treatment of eTNBC with ICI. Hopefully, near future will give us all the answers needed and help us improve furthermore the treatment outcomes for TNBC patients.

Keywords: immune checkpoint inhibitors, triple negative breast cancer

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S2 – NEOADJUVANT AND ADJUVANT TREATMENT OF MUSCLE-INVASIVE BLADDER CANCER

MIRELA ŠAMBIĆ PENC[1,2], Maja Kovač Barić[1], Josipa Flam[1,2], Zdravka Krivdić Dupan[2,3], Silva Gulja[2,3], Luka Perić[1,2], Tara Cvijić[1,2], Dino Belić[1,2], Sebastijan Spajić[1,2], Dominik Seletković[1], Ivana Canjko[1]

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Urothelial carcinoma of the bladder is one of the most prevalent cancers worldwide, diagnosed as muscle invasive in 25% of cases.

Muscle-invasive bladder cancer (MIBC) is a highly aggressive chemo-sensitive disease with nearly 50% of patients developing metastatic disease, likely owing to the presence of micrometastases at diagnosis and is characterized by an overall poor prognosis with a 5-year overall survival (OS) of ~50%.

Radical cystectomy (RC) with cisplatin-based neoadjuvant chemotherapy (NAC) has demonstrated improved survival in eligible patients and is the current guideline-recommended treatment. This is based on the randomized Phase III study by Grossman et al, showing a survival advantage for patients treated with neoadjuvant MVAC (methotrexate, vinblastine, adriamycin, cisplatin) followed by RC, compared with RC alone.

Other, more commonly used protocols today are ddMVAC and GC protocol. Dose dense MVAC (ddMVAC), which is similar to MVAC, but administered every 2 weeks with growth factor support, has also been studied in phase II clinical trials in the neoadjuvant setting, and has shown comparable efficacy, shorter duration of administration and better tolerance when indirectly compared with classic MVAC.

Extrapolating from the metastatic setting, another commonly used neoadjuvant regimen is gemcitabine and cisplatin (GC). GC showed similar efficacy but better tolerability compared to classic MVAC. In the neoadjuvant setting, a retrospective multicenter study has shown that neoadjuvant GC and MVAC achieved comparable pCR rates providing further evidence to support its use in this setting.

The first and only prospective randomized Phase 3 study in the perioperative setting to directly compare ddMVAC (6 cycles) and GC (4 cycles) is the GETUG/AFU V05 VESPER study. This study showed a statistically significant overall survival benefit for ddMVAC compared to GC, in the subset of patients treated in the neoadjuvant setting although ddMVAC was associated with a higher toxicity. Recently published results of a randomized trial in almost 500 patients with localized MIBC, ddMVAC improved five-years OS relative to GC (66 versus 57 percent) with a nonsignificant trend toward improvement among those receiving both neoadjuvant and adjuvant treatment (64 versus 56 percent).

Currently all guidelines on the management of MIBC recommend neoadjuvant cisplatin-based combination chemotherapy (ddMVAC or GC) for patients who are eligible for cisplatin, followed by radical cystectomy (RC).

For select patients who are not candidates for radical cystectomy or desire preservation of their native bladder, radiation therapy (RT) plus concurrent chemotherapy known as trimodality therapy (TMT) incorporating maximal TURBT followed by radiation therapy with concurrent radiosensitizing chemotherapy) is indicated rather then chemotherapy or RT as single-modality treatment which is not recommended to be used alone in neoadjuvant setting.

There is an efforts to develop predictive molecular signatures for chemosensitivity in bladder cancer. Studies are investigating gene expression profiling to predict individual responsiveness to neoadjuvant chemotherapy. For example, in a randomized phase II trial (S1314) is evaluated the utility od Co-expression Extrapolation (COXEN) biomarker. In this trial, COXEN score for Gc or ddMVAC were not associated with improved overall survivel within their respective treatment arms. So the role of gene expression profiling in the molecular prognostication of invasive bladder cancer remains experimental.

In recent years, there is interest in investigating the use of checkpoint inhibitor immunotherapy as neoadjuvant treatment, given its efficacy in the treatment of metastatic urothelial cancer. Most studies investigating neoadjuvant immunotherapy in patients who are ineligible for cisplatin-based chemotherapy. Complete pathologic response rates between 30- 40 percent have been reported in early phase studies using neoadjuvant atezolizumab (ABACUS), pembrolizumab (PURE-01) and in the combination of durvalumab and tremelimumab and nivolumab and ipilimumab. Also complete pathologic response rates have been seen in patients receiving immunotherapy in combination with chemotherapy in neoadjuvant setting (pembrolizumab plus GC, nivolumab plus GC and durvalumab plus GC).

For some patients who did not received neoadjuvant therapy, but undergo radical cystectomy, adjuvant treatment is recommended for those with high -risk tumor features as long as no contraindications to cisplatin are present. Although studies suggest that adjuvant chemotherapy is efficacious in such patients, as it may delay recurrences and improve overall survival such data are controversial. The preferred chemotherapy protocol is also cisplatin -based combination therapy (ddMVAC or GC). For patients who did not received neoadjuvant chemotherapy and are ineligible or decline adjuvant cisplatin-based chemotherapy or for those who received neoadjuvant chemotherapy and had persistent muscle invasive or nodal disease FDA approved adjuvant immunotherapy (nivolumab) based on results of randomized study phase III (CheckMate 274) who showed that adjuvant nivolumab improved disease free survival (DFS) over placebo.

This year on ASCO meeting the results of the AMBASSADOR trial was published. AMBASSADOR is phase III randomized adjuvant study of pembrolizumab in muscle-invasive and locally advanced urothelial carcinoma versus observation. The trial showed that adjuvant pembrolizumab demonstrated a statistically significant and clinically meaningful improvement in disease-free survival compared to observation alone in patients with high-risk muscle invasive urothelial carcinoma after radical surgery, regardless of PD-L1 status and these results support adjuvant pembrolizumab as a new therapeutic option for patients with muscle invasive urothelial carcinoma with high risk for recurrence.

There are many drugs such as ADC, alone or in combinations with ICI that are currently being tested in this setting with encouraging results.

The future of patients with muscle-invasive bladder cancer is promising because neoadjuvant therapy in MIBC is rapidly evolving as novel agents previously approved in the metastatic setting are being used and tested in earlier disease states. While cisplatin based neoadjuvant chemotherapy remains an gold standard, either alone or in combination with other agents, ICI and ADCs have shown significant activity in patients who are cisplatin ineligible or intolerant. The use of biomarkers to predict response to cisplatin-based NAC or ICIs is largely investigational, but molecular signatures are showing promise in reshaping selection for treatment and disease monitoring.

Keywords: neoadjuvant therapy, adjuvant therapy, radical cystectomy, immunotherapy, muscle-invasive bladder cancer

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S3 – INTEGRATION OF SBRT AND IMMUNOTHERAPY IN THE TREATMENT OF EARLY STAGE LUNG CANCER

IVANA CANJKO[1], Maja Kovač Barić[1], Luka Perić[1,2], Zdravka Krivdić Dupan[2,3], Tara Cvijić[1,2], Sebastijan Spajić[1,2], Dominik Seletković[1], Dino Belić[1,2], Josipa Flam[1,2], Mirela Šambić Penc[1]

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Approximately 30% of non-small cell lung cancers are diagnosed at an early stage (stage I and II). It is expected that, by implementing the national prevention programme, there will be an increase in a number of patients diagnosed at an early stage of the disease. Surgical resection is „the gold standard" for treatment of early stage non-small cell lung cancers. However, if there are contraindications for surgical resection or considering the patient's preferences, recommended treatment is stereotactic radiation therapy (SBRT) that can provide high rates of local control, preserved quality of life with minimal therapy-specific side effects. Nonetheless, the rates of locoregional and/or distant reccurence are high in these patients. Currently, there are no randomized clinical trials comparing stereotactic radiation therapy and surgical resection in patients with early stage, resectable non-small cell lung cancer. Combination of immunotherapy and stereotactic body radiation therapy is currently being tested in several phase II and III trials in patients with early-stage non-small cell lung cancer. The rationale for this combination is the immunomodulatory effects of radiotherapy and, as we are already familiar with, significantly improved survival in patients with stage III non-small cell lung cancer treated with immunotherapy after concomitant chemoradioterapy. Results from a phase II trial showed a significant improvement in 4-years EFS with I-SBRT compared to SBRT alone in patients with de novo early-stage or lung reccurent, node negative non-small cell lung cancer. Durvalumab after SBRT is currently being tested in a phase 3 trial (PACIFIC 4) versus placebo after SBRT in an early, non-resectable, non-small cell lung cancer. Minimal residual disease is one of the risk factors for recurrence in an early stage non-small cell lung cancer and thus can be used for the selection of patients suitable for new adjuvant strategies. Preliminary clinical results of combination of immunotherapy and SBRT are promising however phase III trial levels of evidence are required to form a definitive conclusion.

Keywords: early stage of lung cancer, immunotherapy, SBRT

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S4 – IMMUNOTHERAPY IN TREATMENT OF ADVANCED GASTRIC AND EGJ CANCER

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Gastric cancer is the 4th most common cancer and the 4th leading cause of cancer death globally. in the moment of diagnosis it is usually in a advanced stage. the standard of care is the first-line platinum doubled treatment, with trastuzumab in her two positive disease. In the second line but with the cell with or without ramucirumab is usually used for unresectable or metastatic we gastric cancer. however median of survival in this patient is 12 to 15 months so we need a new treatment possibilities. In the last few years immunotherapy become a new standard of treatment in a lot of malignant tumours including advanced ventricular cancer which significant clinical benefit in this population.

Biomarkers for immunotherapy can be categorized into three major groups immunological genetic and virological. The expression of PDL one before treatment can be used as an immunological biomarker that is predictive of of tumor shrinkage. Tumor mutation burden might also be used to predict the benefit of immunotherapy. Ventricular cancer in ancient population has a lower expression of this cell markers and the higher expression of immunosuppressive T cells so we need further investigation to compare benefit and toxicity of immunotherapy in Asian and a non Asian population.

In a phase III ATTRACTION-2 trial nivolumab has shown a better overall survival compared to placebo in patients with advanced ventricular cancer after two and more lines of chemotherapy. These patients had a hazard ratio of 0.67. it also shown a benefit in the overall response rate as in progression free survival.

According to this result nivolumab was approved for a treatment of advanced ventricular cancer in Asian population.

In April 2021 FDA approved nivolumab in combination with fluoropyrimidine and platinum based chemotherapy for the first line of treatment for a patient with metastatic ventricular cancer. as a provent was based on the results of phase III Checkmate-649 trial actions with untreated, her two negative unresectable ventricular cancer, EGJ cancer and eosophageal adenocarcinoma. in this trial patients received chemotherapy with or without nivolumab, end addition of nivolumab resulted in a significant benefit in overall survival and progression free survival. So the combination of nivolumab and chemotherapy become a standard of the first line treatment in a patient with a her two negative advanced ventricular cancer with the CPS score higher or equal 5.

Pembrolizumab is approved in 2017 for patients with unresectable or metastatic solid tumors who had a high microsatellite instability. This approval was based on 5 multicentric global trials with 149 patients who had our overall response rate of 39%.

In June 2020 Pembrolizumab is approved for a treatment of patients with metastatic solid tumors who had a high TMB. Disapproved is based on a retrospective analysis of a 102 patients included in KEYNOTE 358 trial, and they had a response rate of 29% with 4% of complete responses. 50% of patients had duration both response longer then 24 months. According to this pembrolizumab can be used for patients in a second or later lines of therapy who has tumors MSI-H/dMMR, or TMB-H. pembrolizumab also shown or response rate of 11.6% in a third or later lines in a KEYNOTE-059 trial.

In the meantime avelumab didn't show better overall survival compared to chemotherapy in JAVELIN 300 trial.

Dostarlimab-gxly was approved by the FDA in August 2021 for the treatment of patients with dMMR solid tumors who have progressed on or following prior treatments. The majority of patients had endometrial or gastrointestinal cancers overall response rate was 42% with 9% of complete response rate, and the median duration of response was 35 months. Based on this data does sterling mob may be used to treat patients with MSI-H/dMMR tumors.

KEYNOTE-811 trial shown a significant improvement in response rate in combination of pembrolizumab trastuzumab and chemotherapy in patients with healthy positive advanced ventricular cance

In conclusion we can say that addition of immunotherapy in the first line shone a clinical benefit for patients with Her2 negative advanced ventricular cancer. In HER-2 positive disease combination of pembrolizumab trastuzumab and chemotherapy have indicated promising effects. A novel immunotherapy approach using CAR-T cell therapies might be used as a personalized treatment for advanced gastric cancer. Despite these breakthroughs, there is still an urgent need to establish novel biomarkers for immunotherapy and develop new immunotherapies.

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S5 – TARGETED THERAPY IN THE TREATMENT OF GYNECOLOGICAL CANCERS

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During the past decade, considerable progress has been made in the treatment of gynecological cancers.

Endometrial cancer (EC) is the most common gynecological cancer. In recent years, there is a new classification system based on molecular phenotype. The four different molecular subclasses have been identified: POLE- mutant, microsatellite-unstable (MSI), p53 positive (copy-number high) and no specific molecular profile (NSMR or copy-number low). Several studies have reported the strong prognostic value of molecular subgroups, and the PORTEC 3 trial also reported their predictive value. Patients in the POLE-mutant subgroup have an excellent prognosis and do not require to receive adjuvant treatment in the early stages of disease regardless of the unfavorable pathohistological characteristics of the tumor. Copy-number high patients have the worst prognosis and generally benefit from adjuvant chemotherapy. Patients in MSI or NSMR subgroups have intermediate prognosis and little benefit from adjuvant chemotherapy.

Currently, the standard chemotherapy regimen for advanced, metastatic or recurrent disease is paclitaxel/carboplatin with or without immunotherapy, but there is no standard second line therapy. New therapies have been investigated, and molecular profiling of the tumor is being used to try to find new predictive biomarkers for targeted therapy.

Mismatch repair-deficiency (dMMR), high MSI and high tumor mutation burden (≥ 10 mut/Mb) are effective biomarkers for immunotherapy with checkpoint inhibitors. In patients who are MMR proficient (pMMR) or microsatellite stable (MSS)., the combination of lenvatinib and pembrolizumab is an effective option.

For patient with EC overexpressing human epidermal growth factor receptor 2 (HER2), addition of trastuzumab to front line chemotherapy and continuing it as maintenance therapy is an option. In those patients with recurrent disease, an excellent results were achieved with trastuzumab deruxtecan.

In hormone receptor positive tumors, the combination of endocrine therapy and mTOR inhibitor has been shown to be effective, especially in chemotherapy-naive patients. Another novel combination with hormone therapy that has made recent advances is the cyclin dependent kinase (CDK) 4/6 inhibitors.

In patients with T53, therapy with PARP inhibitors has been investigating. In patients with recurrent uterine serous cancer, an oral Wee1 inhibitor (adavosertib) has shown clinical activity and demonstrated reduction in disease progression. Selinexor is an option for the treatment of patients with p53 wild type tumors.

The most commonly used targeted drug for the treatment of cervical cancer is bevacizumab which attaches vascular endothelial growth factor (VEGF). The addition of bevacizumab to chemotherapy in patients with metastatic, persistent or recurrent disease improves tumor response and survival.

Recently, immunotherapy has an increasingly important role in the treatment of metastatic, persistent or recurrent cervical cancer, especially in patients with PD-L1 positive tumors. New trials have also demonstrated the benefit of immunotherapy in locally advanced disease.

The first antibody-drug conjugate targeting tissue factor (TF) is tisotumab vedotin. TF is abnormally expressed in several solid tumors including cervical cancer. The InnovaTV 301 trial demonstrated clini-

cally meaningful and durable antitumor activity with tisotumab vedotin in woman with previously treated recurrent or metastatic cervical cancer. In combination with bevacizumab, carboplatin or pembrolizumab, tisotumab vedotin have also showed encouraging antitumor activity in treatment-naïve and previously treated recurrent and metastatic cervical cancer.

Trastuzumab deruxtecan showed clinical benefit in pretreated patients with HER2-expressing cervical and ovarian tumors.

Ovarian cancer is the leading cause of death from gynecological malignancies. The most important treatment method is still optimal surgery, followed by platinum-based chemotherapy. All patients with advanced disease should receive maintenance therapy. The two most promising targeted agents are anti-angiogenic agents (bevacizumab) and molecular targeting agents (poly-ADP ribose polymerase (PARP) inhibitors. The status of BRCA mutation and homologous recombination deficiency (HRD) must be known before a decision is made. All patients with BRCA mutation or HRD and who have objective response to platinum-based chemotherapy, should receive maintenance therapy with PARP inhibitors or a combination of olaparib and bevacizumab. In HRD-negative tumors, maintenance treatment with bevacizumab or niraparib can be recommended. The choice of treatment should be based on disease and clinical characteristics of the patients.

The treatment of the first recurrence depends on many factors, including duration of initial treatment response, residual toxic effects from previous therapy, performance status, tumor genomics and the preferences of patient herself. Patients, in whom platinum is an option, should be treated with either a platinum-based doublet with bevacizumab or a platinum based doublet followed by maintenance with PARP inhibitors if a response to chemotherapy is achieved and the patient has not been previously exposed to PARP inhibitors. In patients in whom platinum is not an option, single-agent non-platinum chemotherapy is recommended and bevacizumab should be offered if patient has not previously exposed to bevacizumab.

For patients with recurrent low grade serous ovarian cancer, treatment with the MEK inhibitor should be consider.

Keywords: endometrial cancer, ovarian cancer, cervical cancer, targeted therapy

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S6 – LOCALLY ADVANCED PANCREATIC CANCER – MULTIDISCIPLINARITY ON THE TEST

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Pancreatic ductal adenocarcinoma (PC) is the 12th most common malignancy and 7th cause of cancer mortality in the world with the projection to become the 2nd leading cause of cancer deaths in the United States and 3rd in Europe by 2025. Despite significant progress in the understanding of this disease in recent years, the prognosis is still poor with 5-year survival of only 3-11%. Unfortunately, around 50% of patients have metastatic disease already at the time of diagnosis, and potentially curable primary surgical resection is feasible in merely 15-20% of patients. Median overall survival (mOS) of patients treated with upfront surgery followed with 6 months adjuvant chemotherapy is about 34 months or even more but with frequent relapses.

Metastasis-free patients are often divided into 3 groups: resectable, borderline resectable and locally advanced prostate cancer (LAPC). Resectability is defined by several different systems based on the relationship between tumour and blood vessels, among which the National Comprehensive Cancer Network (NCCN) definition is the most commonly used. LAPC is considered tumour encasement greater than 180 degrees of circumference of the superior mesenteric artery (SMA) or celiac artery (CA), an unreconstructable superior mesenteric vein (SMV) or portal vein (PV). However, apart from anatomical criteria resectability, performance status and Ca 19/9 levels are also important. About one third of patients have LAPC. Median survival of treated LAPC patients is 12-25 months. Around 20% of patients with LAPC become eligible for resection after neoadjuvant therapy even in the absence of a clear radiological response. They have similar outcomes to those who were resectable at diagnosis.

Since LAPC patient have subclinical metastases in up to 50% of cases, chemotherapy is the pillar of treatment. mFOLFIRINOX is the preferred regimen for patients with ECOG 0-1 with the pooled mOS in a

meta-analysis 24 months and the resection rate of approximately 30%. In the LAPACT trial (phase II) patients treated with nab-paclitaxel and gemcitabine (NG) had overall response rate (ORR) 33.6%, disease control rate (DCR) 77.6%, mOS 18.8 months and 16% resection rate. NEOLAP trial (phase II) compared 4 cycles of NG with 2 cycles of NG followed by FOLFIRINOX. There was no difference in efficacy and safety. FOLFIRINOX and NG had also comparable efficacy and safety in JCOG1407, while in PRODIGE 29 trial FOLFIRINOX showed significantly prolonged progression-free survival (PFS) (9.7 vs. 7.5 months, $p = 0.03$) in comparison with gemcitabine alone but without difference in mOS (15.6 vs. 15.1 months).

Chemoradiation (CRT) prolonged the OS in clinical trials in comparison to best supportive care. However, the results of randomised trials comparing CRT with chemotherapy are conflicting (FFCD/SFRO 2000-01, ECOG trial). In the LAP-07 trial patients were treated with 4 months of gemcitabine with or without erlotinib and then randomised to continue with 2 more months of gemcitabine or CRT. Although mOS was not improved in the CRT group, CRT was associated with a decreased risk of local progression (32% vs. 46%, $p = 0.03$). The effect of the addition of radiotherapy to neoadjuvant chemotherapy was also investigated in the phase III CONKO-007 trial. Patients were enrolled between 2013 and 2021 to receive 3 months of chemotherapy (85% FOLFIRINOX, 15% gemcitabine) followed by CRT or continuation of chemotherapy in those without progression of the disease. The primary endpoint was changed from OS to R0 resection due to insufficient recruitment. R0 resection rate was significantly higher in CRT group (69% vs. 50%, $p = 0.04$) as well as pathological complete response rate (pCR) (18% vs. 2%, $p = 0.004$). The mOS was significantly improved in resected patients (19 vs. 14 months, $p < 0.001$) but the mOS did not differ between the randomised groups (15 months in both arms).

Therefore, radiotherapy in LAPC is controversial but it is recommended according to the guidelines after up to 6 months of chemotherapy for selected patients without distant metastasis. However, in some randomised trials outdated radiation techniques were performed. In small retrospective cohorts intensity modulated radiotherapy with biologically effective dose more than 70 Gy and high-dose magnetic resonance image-guided radiotherapy improved survival of treated patients.

Numerous randomised trials with stereotactic body radiotherapy (SBRT) are ongoing (MASTERPLAN, SABER, STEREOPAC, LAP-ABLATE, ARCADE) since retrospective data showed previously improved local control along with significantly shorter duration of treatment. Locoregional percutaneous interventional techniques (radiofrequency ablation, microwave ablation, cryoablation, irreversible electroporation, brachytherapy, intra-arterial infusion of chemotherapy, transarterial chemoembolization, intratumoral immunotherapy) are used in specialized centres in the treatment of LAPC. These techniques showed the potential to increase survival as well as the immunomodulatory capacities.

Surgical exploration is the option for patients with a decrease in serum Ca 19/9 level to < 50% of the baseline value and substantial clinical improvement. Imaging can be unreliable in the assessment of resectability due to fibrosis and scar tissue after neoadjuvant therapy. Experienced multidisciplinary tumour board is of paramount importance in the treatment of LAPC.

Finally, PC is genetically and biologically heterogeneous disease. New therapeutic strategies based on the distinct molecular features of the tumour are needed.

Keywords: pancreatic cancer, neoadjuvant, chemotherapy, chemoradiotherapy

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S7 – IMMUNOTHERAPY IN GYNECOLOGICAL CANCERS

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The leading cause of cancer death for women varies significantly depending on geographic location, socioeconomic factors, and access to healthcare. Gynecological cancers significantly contribute to female cancer mortality worldwide. Carcinomas of the uterus, cervix, and ovary in advanced and metastatic stages have poor five-year survival rates, presenting a significant clinical challenge. Immunotherapy using checkpoint inhibitors (ICI) has revolutionized cancer treatment, demonstrating remarkable effectiveness against various tumor types. Immunotherapy shows promising results for treating endometrial and cervical cancers, while research on its efficacy in ovarian cancer is not satisfactory.

The Cancer Genome Atlas (TCGA) identified four molecular subtypes of endometrial cancer. Among these, microsatellite instability (MSI), present in approximately 25-30% of cases, serves as a potential biomarker for immunotherapy response. After progression on platinum-based chemotherapy, two approved treatment options are available for MSI high or mismatch repair-deficient (dMMR) endometrial cancer, pembrolizumab and dostarlimab, both of which are anti-programmed cell death-1 (PD-1) inhibitors. Pembrolizumab received approval based on the phase 2 KEYNOTE 158 study, which demonstrated an objective response rate (ORR) of 48% and not reached duration of response (DOR). Dostarlimab was approved based on the results of the GARNET study with similar ORR and DOR like in KEYNOTE 158 study. Following platinum-based chemotherapy progression, the combination of dostarlimab and lenvatinib (anti VEGF) is currently approved as a second-line treatment for microsatellite stable (MSS) or mismatch repair-proficient (pMMR) endometrial cancer. This approval is based on a phase 3 KEYNOTE 775 study demonstrating its superiority over standard chemotherapy options (doxorubicin or paclitaxel) in ORR, progression-free survival (PFS), and overall survival (OS). Dostarlimab received approval for the first line treatment of advanced or recurrent endometrial cancer with MSI-high/dMMR based on the results of the phase 3 RUBY study. This trial demonstrated the superiority of dostarlimab compared to standard chemotherapy with paclitaxel and carboplatin in terms of ORR, PFS (HR 0.28), and OS (HR 0.30) and change standard of care in first line treatment for MSI-high/dMMR status endometrial cancer.

Pembrolizumab offers a promising option for second-line treatment of advanced cervical cancer. The phase 2 KEYNOTE 158 study demonstrated an ORR of 14.3% in previously treated advanced cervical cancer with PD-L1 positive tumor. The phase 3 EMPOWER study established cemiplimab (anti PD-1) as a second-line treatment option for recurrent or metastatic cervical cancer, demonstrating a survival benefit

over chemotherapy regardless of PD-L1 status. The pivotal phase 3 KEYNOTE 826 study showed that the addition of pembrolizumab to first-line platinum-based chemotherapy, with or without bevacizumab (anti-VEGF), led to a significant improvement in PFS among patients diagnosed with PD-L1 positive persistent, recurrent or metastatic cervical cancer. Consequently, pembrolizumab has approval for this specific indication. The phase 3 KEYNOTE-A18 study investigated pembrolizumab potential in locally advanced cervical cancer. The addition of pembrolizumab to chemoradiotherapy followed by maintenance of pembrolizumab showed promising results in improvement of PFS compared to chemoradiotherapy alone. While pembrolizumab isn't yet approved for this specific use case, and overall survival data is pending, these findings suggest a potential new approach.

Disappointingly, clinical trials published to date haven't demonstrated significant benefit from immunotherapy in advanced ovarian cancer. This includes ICI monotherapy and combinations with chemotherapy, bevacizumab, or PARP inhibitors. Further research is needed for better patient selection, biomarker identification, and novel treatment strategies to improve the efficacy of immunotherapy for ovarian cancer.

Keywords: immunotherapy, gynecologic cancers, endometrial cancer, cervical cancer, ovarian cancer

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S8 - IMPORTANCE OF PROGNOSTIC AND PREDICTIVE TESTS IN ADJUVANT BREAST CANCER THERAPY

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Breast cancer is most frequent cancer in women. Due large number of patients and large heterogeneity of the disease, it's clear that treatment of early breast cancer (BC) has to be more efficacious and less toxic. New technologies identify today a number of biomarkers in BC prognosis and risk prediction. Prognostic factors are used to estimate risk of recurrence and possible benefit of systemic therapy, factors that influence survival and can be changed by therapy. Predictive factors are used to determine optimal therapy for each patient. Prognostic and predictive markers can overlap. These biomarkers enable us to apply optimal treatment for each patient- not to over treat or under treat, improving prognosis and survival of

patients with early BC. Till recently, we used traditional prognostic features (tumour size and grade, lymph node status) and traditional predictive markers: A/ER-the most common predictive marker; B/PR-related to better survival and lower recurrence rates if positive C/ HER2 status, both prognostic and predictive, of which overexpression is connected with aggressive disease and lower survival; D/ Ki67 status that discriminates luminal A and B BCs. Newer markers show potential as markers of survival and risk assessment, as well predisposition to BC. PI3KCA regulates proliferation and protein synthesis and is associated with chemoresistance and reduced survival.TP53 is related to cell cycle, differentiation and apoptosis as well as to predisposition to BC, a feature that shares with BRCA1/2 tumour suppressor genes involved in DNA repair. PTEN, tumour suppressor gene related to cancer cell survival. Its downregulation is associated with worse outcomes, lower sensitivity to CDK4/6 inhibitors and immunotherapy. CHEK2, ATM and PALB genes are involved in cell cycle regulation, DNA repair, apoptosis and increased risk of BC development. CDH1 suppresses spread of tumour cells and is associated with worse prognosis, though its hypermethylation can be reversed. by DNA methylation inhibitors. PD-1/PD-L1 regulate immune response against tumour cells by inhibiting T-cell activation. Antibody mediated PD-L1 degradation enhances effects of radiotherapy and cisplatin. MSI microsatellite instability is associated with malignant tumours development, and is a possible marker for immunotherapy.

Genomic test have changed treatment paradigms with patients with HR+ BC, sparing substantial number of patients of unnecessary chemotherapy and overtreatment. It is emerging strategy of risk prediction and treatment decision based on genomic data. MammaPrint defines 5-10 year recurrence risk and potential benefit from chemotherapy, regardless of ER and HER2 status. Oncotype DX evaluates expression of 21 genes to predict recurrence risk at 10 years. Its use reduced prescription of chemotherapy in low and intermediate risk patients. Prosigna (PAM50) predicts 10-year distant recurrence survival assuming five years of ET. Endopredict assay determines 10-year risk of distant recurrence and to determine benefit of chemotherapy. Breast Cancer Index (BCI) assesses early and late distant recurrence risk and predicts which patients could benefit from extended ET. Single-cell-based genomic technologies and in situ spatial methods provide more personalized therapy approach- a serial monitoring of cell heterogeneity, spatial and temporal cell mapping, epigenetic mechanisms of resistance..., identifying potential treatment targets for new drugs

Keywords: breast cancer biomarkers, personalized therapy, genetics of breast cancer

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S9 – ANTIBODY-DRUG CONJUGATES IN THE TREATMENT OF BLADDER CANCER

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Despite introduction of immune checkpoint inhibitors in the treatment armamentarium for advanced urothelial cancer (aUC), only a minority of patients respond to this therapy. Even in the era of immune checkpoint inhibitors, aUC is still characterized by rapid disease progression and poor survival. Antibody drug-conjugates (ADC) represent the novel concept of targeted therapy for urothelial carcinoma that can overcome resistance mechanisms associated with immunotherapy failure. ADC therapy can be considered as a breakthrough as it allows the combination of a target-specific monoclonal antibody covalently conjugated via a linker to a cytotoxic agent (payload) to be directed against tumor cells. aUC is a perfect candidate for this therapeutic approach since it is particularly enriched in antigen expression on its surface and each specific antigen can represent a potential therapeutic target. ADCs can deliver chemotherapy drugs to a specific target with greater therapeutic efficacy and less toxicity.

Enfortumab Vedotin (EV) is an ADC developed to target nectin-4. The open-label, single-arm phase II trial (EV-201) evaluated the efficacy of EV in patients pretreated with immunotherapy enrolled in two cohorts: cohort 1 enrolled patients previously treated with platinum-containing therapy; and cohort 2 platinum-ineligible patients. The ORR in cohort 1 (125 patients) was 44% and the median duration of response (mDOR) was 7.6 months. The estimated median PFS was 5.8 months and the median OS was 11.7. Responses were observed in all subgroups, including patients unresponsive to ICI. Adverse events (AEs) seen in more than 20% of patients included fatigue (50%), alopecia (49%), rash (48%), loss of appetite (44%), peripheral sensory neuropathy (40%), and dysgeusia (40%). The EV-301 study, a randomized, open-arm phase III trial of EV versus investigator-choice chemotherapy (docetaxel, paclitaxel, and vinflunine) enrolled 608 patients progressing after platinum-containing chemotherapy and ICI. The study reached its primary endpoint, obtaining a median OS of 12.9 and 9.0 months respectively for EV and chemotherapy (hazard ratio (HR): 0.70; 95% confidence interval (CI) 0.56 to 0.89; p = 0.001). Based on these data, EV received FDA and EMA approval for the treatment of patients previously treated with platinum-containing chemotherapy and ICI. In first-line setting, EV has also been shown to have a synergistic effect when combined with ICI in the cohort A of the ongoing phase Ib/2 EV-103 trial, showing an ORR of 73%, with 15.6% of CR and median PFS of 12.3 months, in cisplatin-unfit patients.

Sacituzumab Govitecan Sacituzumab Govitecan (SG) is an ADC conceived to specifically target human trophoblastic cell surface antigen 2 (Trop-2). SG consists of a monoclonal antibody against Trop-2 conjugated to SN-38, an active metabolite of irinotecan, through a hydrolysable linker.

In a phase I/II study 45 patients with metastatic urothelial carcinoma who progressed after ≥1 prior systemic therapy were treated with SG at 10 mg per kg on days 1 and 8 of 21-day cycles, until progression or unacceptable toxicity. The ORR was 31% with a clinical benefit rate of 47%. The median DOR was 12.6 months. The mPFS and mOS were 7.3 and 18.9 months, respectively. The most common grade 3 or higher reported side effects were neutropenia (38%), anemia (11%), hypophosphatemia (11%), diarrhea (9%) fatigue (9%), and febrile neutropenia (7%). The TROPHY-U-01 study is an open-label, single-arm phase II

study evaluating the efficacy of SG in patients progressing after platinum-containing chemotherapy and a checkpoint inhibitor. Preliminary data from cohort 1, including 113 patients with locally advanced or unresectable or metastatic UC who had progressed after prior platinum therapy and ICI, showed an ORR of 27% with a mPFS and mOS of 5.4 months and 10.9 months, respectively.

Disitamab Vedotin is a novel ADC consisting of a humanized monoclonal antibody directed against HER-2 conjugated to MMAE through a cleavable linker with a DAR of 4. A recent phase II study reported encouraging results in 43 patients with HER-2+ metastatic urothelial cancer previously treated with at least one line of systemic treatment platinum-based chemotherapy. The ORR was 51%, mPFS and mOS were 6.9 and 13.9 months, respectively. Another phase II trial enrolling a larger population is starting to test the efficacy of this agent in HER-2+ UC metastatic patients.

Trastuzumab Deruxtecan (DS-8201a) is an ADC consisting of a monoclonal antibody targeting HER-2 conjugated to a topoisomerase I inhibitor (DXd) at a DAR of 7–8. This ADC has shown significant activity even in tumor cells expressing low levels of HER-2. In early trials conducted in heavily pretreated metastatic breast cancer patients DS-8201 showed a high response rate. A phase II trial evaluating the efficacy of DS-8201 in several tumors including metastatic UC is currently ongoing (NCT04482309). Some preclinical data have also shown the role of DS-8201 in the immunogenic modulation of the tumor microenvironment. Trials testing the association of DS-8201 and ICIs such as Nivolumab are ongoing to evaluate the safety and efficacy of combinations.

Keywords: urothelial carcinoma, antibody-drug conjugates, ADC, Enfortumab vedotin, ADC resistance mechanism

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S10 – TREATMENT OF UNRESECTABLE STAGE III NON-SMALL CELL LUNG CANCER IN CROATIA

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Stage III non-small cell lung cancer (NSCLC) comprises a highly heterogenous group of patients regarding patient fitness and tumour size and distribution, resulting in a wide range of treatment goals and therapy options. Curative-intent treatment for stage III NSCLC is multimodal, consisting of a combination of chemotherapy, radiotherapy (RT), and/or surgical resection, although the optimal sequence and modality is debated and highly case-specific. The extensive staging work-up required to assess the feasibility for curative-intent treatment, and the need for consultation with a multidisciplinary team further complicates the optimal, individualized management of stage III patients. In patients with unresectable disease who are fit (ECOG 0–1), have adequate lung function, and have a disease that can be encompassed within a radical radiation volume, chemoradiotherapy (CRT) using platinum-based chemotherapy is the standard of care. Concurrent CRT (cCRT) is typically favoured for these patients, owing to its superiority to sequential CRT. As cCRT can be curative in 20–30% of patients with stage III NSCLC, it is critical that newly diagnosed patients be assessed for cCRT treatment eligibility. Within the last few years, immunotherapy has been introduced into stage III treatment regimens as a consolidation therapy following cCRT and substantially improved survival outcomes. In the 5-year update of the phase III PACIFIC trial, durvalumab following cCRT led to a significant improvement in overall survival and progression- free survival versus placebo in patients with stage III NSCLC with only a 4% increase in grade 3/4 adverse events from the addition of durvalumab. Consolidation durvalumab is nowadays a standard of care for patients with stage III unresectable NSCLC whose disease has not progressed following platinum-based cCRT. Despite the practice-changing results of the PACIFIC trial and availability of durvalumab, real- world data show that the percentage of patients receiving optimal treatment is low, with many country- related factors contributing to the underusage of cCRT in clinical practice.

In Croatia there are approximately 3200 newly diagnosed patients with lung cancer each year. Population registries do not show accurate distribution by stage and histology, but according to the world lung cancer statistics, 20-25% of patients have stage III, of which up to 80% are unresectable. Thus, we can

assume that unresectable stage III NSCLC is diagnosed in at least 400 patients. For the purpose of this work, data about management of patients with stage III NSCLC in year 2023 have been collected from five academic centers in Croatia.

Clinicians in Croatia are facing many challenges regarding timely and accurate diagnostics for stage III NSCLC. Comprehensive diagnostic procedures including endoscopies, invasive mediastinal staging, imaging (including PET/CT and brain MRI), pathological and molecular diagnostics, as well as the multidisciplinary evaluation are mainly performed in five university hospital centers, but there is no established oncological network which could enable fast patient flow from general hospitals to academic centers. Other factors contributing to delay in diagnosis at some institutions include insufficient number of endoscopy facilities, as well as the availability of specialists, such as radiologists, pathologists, pulmonologists performing endoscopic procedures (EBUS, rEBUS, EUS, etc). Some lung cancer guidelines suggest diagnostic work-up should be completed within 26–30 days of referral, with an additional 7–15 days before treatment initiation. In Croatia, average time to establish diagnosis is often longer than recommended due to above mentioned reasons. Multidisciplinary teams are functional in all academic centers, but there are differences in the extent of suggested staging procedures (especially invasive mediastinal staging and PET/CT).

Regarding treatment, there are different approaches among institutions, but ≥ 50% of patients undergo cCRT (others, mostly fragile or patients with comorbidities are treated with sequential chemotherapy followed by hypofractionated RT or RT alone). In patients undergoing cCRT, some centers begin treatment with two induction cycles of chemotherapy (with other two given concurrently with RT); this is the case in institutions with longer waiting- time for initiation of RT.

The main challenge in timely delivery of cCRT in Croatia is related to insufficient number of linear accelerators; there are only ten LINACs in five university hospitals and most of these machines are older than 10 years, so treatment disruptions or delays are very common. Accordingly, modern treatment planning (4D CT, respiratory gating) and radiotherapy delivery (IMRT/VMAT) techniques which reduce severe cCRT toxicities, have not been implemented as a standard of care; in most institutions 3D- conformal RT is still dominant RT technique. Concurrent chemoradiotherapy poses many other challenges; approximately 15% of patients do not complete the treatment for reasons like distance from treatment centres, lack of logistical support, management of adverse events during treatment, poor coordination between institutions delivering chemo- and RT, etc.

Durvalumab is reimbursed in Croatia since September 2020 for all patients with stage III NSCLC (PD-L1 positive) with non- progressive disease after cCRT. Penetrance of consolidation treatment with durvalumab is lower than expected due to reasons such as non- completion of cCRT, adverse events, disease progression or death. The main reasons for interruption of maintenance immunotherapy are adverse events (mainly pneumonitis) and disease progression.

In conclusion, there is a need for regional- and institutional-level evaluation of care pathways in Croatia. Better organized referral system, access to timely assessments, increased capacities of daily hospitals and radiotherapy facilities for delivery of modern, high quality radiotherapy are key to ensure more eligible patients with stage III NSCLC can receive curative treatment options. In context of upcoming adoption of new TNM classification and perioperative chemoimmunotherapy, multidisciplinary team collaboration will be crucial in optimizing outcomes for these patients.

Keywords: stage III non- small cell lung cancer, unresectable, treatment, Croatian practice

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S11 – OPEN QUESTIONS IN TARGETED THERAPY OF NON-SMALL CELL LUNG CANCER

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Targeted therapies have greatly improved the survival in non-small cell lung cancer (NSCLC) patients with actionable mutations. Despite that, there are still many unresolved questions and a lot of possibilities for further progress.

The main obstacles for a more comprehensive and even more efficient application of targeted therapy are drug resistance, toxicity and high costs of the therapy itself that limit the access for the NSCLC patients. Essential for improving treatment results is better understanding of resistance mechanisms and developing combination therapies.

The efficacy of combination therapy has been shown in the first-line treatment of patients with advanced EGFR mutation positive NSCLC in two phase III studies.

In FLAURA study, combination of osimertinib and chemotherapy resulted in a significantly better progression-free survival (PFS) in comparison with osimertinib monotherapy (median PFS 25,5 vs 16,7 mo; HR 0.62; P<0.001).

Combination of amivantanab and lazertinib also resulted in a significantly better efficiency than osimertinib in MARIPOSA study (median PFS 23,7 vs 16,6 mo; HR 0.70; P<0.00).

However, considering higher toxicity of combined treatment in comparison to osimertinib monotherapy and immature survival data, it is still unclear what the optimal first-line treatment is for the majority of these patients.

Another challenge which, without doubt, requires better solutions is the further treatment of patients who progressed on all available (EGFR) tyrosine kinase inhibitors (TKIs). Subsequent treatment depends on patient and disease characteristics, genomic findings and the patient's possibilities to access the treatment. Therefore, a precondition for improvement in treatment efficacy is to provide an environment in which retesting (tissue or liquid biopsy) can easily be carried out for all patients who progressed on TKIs.

Unfortunately, at least for now, the majority of these patients continues to be treated only with chemotherapy.

Recently published phase III study MARIPOSA 2 provides new treatment options for these patients: combination of amivantanab and chemotherapy, with or without lazertinib, in patients who progressed on EGFR TKIs including osimertinib, significantly improved PFS in comparison with chemotherapy treatment.

It is very important to define whether the application of checkpoint inhibitor immunotherapy is reasonable in patients with targetable mutations.

In CheckMate 722 and KEYNOTE-789 phase III studies, which compared the efficacy of adding nivolumab or pembrolizumab to chemotherapy in patients with advanced EGFR mutation positive NSCLC who progressed on TKIs, immunotherapy did not result in significant improvement of neither PFS nor overall survival (OS). One of the possible explanations for negative results of these studies is an immunosuppressive tumor microenvironment associated with EGFR mutation positive NSCLC. Therefore, it is reasonable to investigate whether combining chemoimmunotherapy with immunomodulatory drugs, like those targeting vascular endothelial growth factors (VEGFs), can improve efficacy.

Exploratory analysis of patient subpopulation with EGFR mutation positive NSCLC in IMpower150 study showed that combination of atezolizumab, bevacizumab and chemotherapy provides OS and PFS benefit in comparison with combination of bevacizumab and chemotherapy.

The phase III IMpower151 study compared two almost the same drug regimens in a similar patient population with EGFR mutation. Unfortunately, the trial did not meet its primary endpoint – significant improvement of PFS.

On the other hand, in ORIENT 31 study with a similar patient population, adding immunotherapy or immunotherapy with anti-VEGF to chemotherapy significantly improved PFS but, for now, without improvement in OS.

Based on the data in the resectable and metastatic setting, there is a rationale to believe that EGFR TKIs may improve outcomes in patients with unresectable EGFR mutation positive stage III NSCLC. Unfortunately, for now there are no approved targeted treatments for these patients due to lack of robust evidence from the existing clinical trials. Meta-analysis showed that combination of radiotherapy (RT) and TKIs and combination of chemo-radiotherapy (CRT) and TKIs have significantly longer PFS than CRT ± immunotherapy, with uncertainty regarding the tolerability.

Keywords: non-small cell lung cancer, targeted therapy, treatment strategy, treatment outcomes

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S12 – NEOADJUVANT MELANOMA TREATMENT – THE IMMINENT FUTURE

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Clinical stage III melanoma encompasses approximately 15% of new melanoma cases, with additional patients presenting with recurrent nodal disease. The current standard of care for these resectable clinical stage III melanoma patients is surgical resection, consisting of therapeutic lymph node dissection (and/or resection of in-transit metastases) and subsequent adjuvant systemic therapy, either targeted or immunotherapy, and occasionally adjuvant radiotherapy.

However, even with adjuvant systemic therapies applied, these patients have suboptimal long-term outcomes and are at high risk of regional recurrence and/or progression to metastatic disease, highlighting the need for better treatment options.

With the success of targeted therapy and immunotherapy in the adjuvant and metastatic settings, the use of these agents in the neoadjuvant setting has been an emerging area of research interest.

Neoadjuvant therapy involves administering systemic treatment before the primary treatment, in the case of melanoma, before surgical intervention.

The neoadjuvant approach has multiple potential advantages. Early systemic intervention can reduce the tumor size and potentially downstage it, thus facilitating subsequent less invasive surgical resection and reducing perioperative morbidity. By shrinking the tumor before surgery, neoadjuvant therapy may increase the likelihood of achieving clear surgical margins, which is crucial for minimizing the risk of recurrence.

Moreover, by treating the systemic disease upfront, neoadjuvant therapy addresses potential micrometastases, thereby reducing the risk of distant metastasis and improving long-term outcomes.

Initiating treatment before surgery provides an opportunity to assess treatment response at an early stage, enabling clinicians to tailor adjuvant therapy accordingly (or omit it altogether), thus maximizing therapeutic efficacy and minimizing toxicity.

The ability to early evaluate response or resistance to treatment in the neoadjuvant setting is an ideal platform for quick evaluation and development of new treatment approaches.

Neoadjuvant immunotherapy provides an opportunity to better understand the tumor microenvironment while the patient is on active treatment; it also allows for gathering and exploring biomarkers predictive of therapy response/resistance, which is still a great unmet need in melanoma treatment.

The rationale for neoadjuvant immunotherapy arises from the concept that the administration of immune checkpoint inhibitors (ICIs), while the primary tumor is still present, will lead to a more robust systemic antitumor immune response compared to the one in the adjuvant setting due to more numerous and more various tumor antigens presented to the immune system. This theoretic concept was proven preclinically as well as in several clinical trials, demonstrating the increased ability to generate tumor-specific CD8 T-cells, greater expansion of the existing clones of tumor-specific T-cells, and detection of the higher number of new clones of T-cells in comparison to adjuvant therapy.

With neoadjuvant therapy, the assessment of response to treatment is feasible after surgical resection, which provides valuable prognostic data from tissue pathology, including intratumoral T-cell expansion, presence of tertiary lymphoid structures, and percentage of viable tumor cells.

In a pooled analysis, Menzies et al. showed that pathologic complete response (pCR) correlated with improved recurrence-free survival (RFS) and disease-free survival (DFS) and suggested that pCR should be an early surrogate primary endpoint for clinical trials. Moreover, detecting poor response enables altering the planned adjuvant therapeutic regimen, and obtaining pCR can potentially de-escalate further treatment.

However, there are still potential pitfalls and challenges in the neoadjuvant setting. One significant concern is the potential for disease progression during the neoadjuvant period, leading to delayed surgery or compromised resectability. Furthermore, adverse effects of neoadjuvant immunotherapy can also postpone surgery. Neoadjuvant therapy is more demanding logistically, requiring precise coordination of systemic therapy, diagnostic procedures, and surgery. Pseudoprogression due to neoadjuvant therapy can be misinterpreted as a progressive disease and remains difficult to evaluate.

Additionally, not all patients respond favorably to neoadjuvant treatment, highlighting the need for predictive biomarkers to identify responders and non-responders accurately.

The optimal duration and sequencing of neoadjuvant therapy remain areas of ongoing research, requiring prospective studies to elucidate.

Neoadjuvant targeted therapy with dabrafenib and trametinib in BRAF-V600-positive stage III. melanoma patients, although having high overall response rates (ORR) and a high percentage of pathologic complete response (pCR) of almost 50%, has proven to be of short duration, with high percentages of patients recurring shortly after the neoadjuvant treatment and subsequent surgery.

In contrast, immunotherapy, either dual/combined anti-PD-1 antibody and anti-CTLA-4 antibody (primarily nivolumab and ipilimumab) or monoimmunotherapy with anti-PD-1 antibody pembrolizumab, has emerged as a cornerstone in melanoma treatment.

The efficacy of neoadjuvant therapy in melanoma has been supported by a growing body of clinical evidence, including prospective trials, retrospective studies, and meta-analyses.

Several landmark trials have demonstrated impressive response rates and favorable outcomes with neoadjuvant targeted therapy and immunotherapy.

OpACIN clinical trial was the first to show significant benefit and improved patients' outcomes by applying neoadjuvant immunotherapy with two standard doses for melanoma (ipilimumab 1 mg/kg + nivolumab 3 mg/kg) versus adjuvant nivolumab monoimmunotherapy.

The opACIN-neo clinical trial was designed to explore different schedules of dual neoadjuvant immunotherapy with ipilimumab and nivolumab, aiming to identify the schedule with the best efficacy-to-toxicity ratio. Modified dosing (ipilimumab 1 mg/kg + nivolumab 3 mg/kg) was identified as the best, with maintained efficacy (pathologic response rate of 77%), but twice lower the incidence of grade 3 or 4 adverse effects (20%) in comparison to standard dosing (40%).

PRADO clinical trial further explored the personalization of neoadjuvant therapy by excising and analyzing the so-called "index lymph node" (the largest regional metastatic lymph node) as the representative for the whole regional lymph node basin after the application of neoadjuvant dual immunotherapy. Based on the achieved pathologic response to treatment in the index lymph node, further activities were stratified as – observation only (if pCR or near-pCR was achieved); total lymph node dissection (TLND) followed by observation if pathologic partial response (pPR) was achieved; or TLND and subsequent adjuvant therapy if pathologic no response (pNR) occurred. Patients in the PRADO – trial had 71% of pRR, with an impressive 61% of pCR or near-pCR.

SWOG1801 trial in 2022, surprisingly, showed PFS benefit by moving three cycles of monoimmunotherapy with pembrolizumab from the adjuvant to the neoadjuvant setting (while the remaining 15 cycles were applied adjuvantly) in comparison to 18 cycles of adjuvant pembrolizumab (HR=0.58; p=0.004).

Eagerly awaited are the results of the ongoing stage III neoadjuvant NADINA trial, which is comparing response-driven neo-adjuvant combination of ipilimumab + nivolumab versus adjuvant nivolumab.

The ongoing clinical trials further explore new therapeutic combinations in the neoadjuvant setting, such as the combination of nivolumab and relatlimab.

Based on these results, neoadjuvant immunotherapy has already been included in clinical practice guidelines for melanoma treatment, although it is still not formally registered for this indication.

In conclusion, neoadjuvant melanoma treatment represents a paradigm shift in the management of melanoma, offering the potential to improve outcomes through early intervention, tumor downstaging, and systemic disease control.

It is most likely the imminent future in the management of patients with clinical stage III melanoma.

Keywords: neoadjuvant treatment, melanoma, immunotherapy, anti-PD-1 therapy

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S13 – BREAST CANCER AND PREGNANCY

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Breast cancer is the most commonly diagnosed cancer during pregnancy. An estimated incidence is of 1 case every 1000 pregnancies(1). The incidence is likely to rise due to later maternal age at first pregnancy.

Breast cancer during pregnancy is associated with a lower prevalence of hormone receptor expression, thus with a predominance of more aggressive subtypes that are peculiar for younger ages, such as triple-negative or HER2-positive(2,3). The diagnosis occurs more frequently at more advanced stages in comparison with non-pregnant patients, potentially due to the teratogenicity of most radiological imaging procedures, and suboptimal staging and management.

Breast cancer during pregnancy is a challenging and delicate situation requiring a multidisciplinary team work to establish the best strategy for assuring safe care for both the mother and the child(4).

To date, data regarding breast cancer care occurring during pregnancy are mostly derived from retrospective reports, thus the inclusion of patients in dedicated registries is advisable.

The different treatment strategies can be combined according to the gestational age.

Breast surgery is feasible throughout the pregnancy while radiotherapy should be postponed after delivery.

Patients diagnosed with breast cancer during pregnancy can be safely treated with chemotherapy starting from the second trimester while it is contraindicated in the first trimester due to the high risk of fetal malformations(4,5). The choice of the regimen should follow the guidelines for non-pregnant patients, anthracyclines and taxanes being the standard of care after the first trimester(5).

Endocrine therapy and targeted therapies are not indicated in pregnant patients and should be postponed after delivery(5).

Targeted therapies for the treatment of breast cancer have been increasingly used in the last few years. Current guidelines contraindicate the use of trastuzumab during pregnancy, mainly due to the increased risk of developing oligo- and/or anhydramnios. Up to now, no data available for administration of newer

anti HER therapy, pertuzumab, trastuzumab-emtansine (T-DM1) and neratinib, in early breast cancer during pregnancy, thus they are contraindicated.

To date, no data on the safety of CDK4/6i during pregnancy are available, so currently their use is contraindicated during pregnancy(5).

Patients with breast cancer during pregnancy should undergo a close fetal monitoring, and a full-term delivery should be reached to reduce the risk of long-term complications(4).

Immunotherapy with antibodies directed against programmed cell death protein 1 (PD-1) or its ligand (PD-L1) is becoming a relevant option for triple-negative subtype. During pregnancy, the mother develops an immune tolerance towards the fetus, involving the PD-1/PD-L1 pathway; therefore, its inhibition could potentially result in an immune response against the fetus(6,7,8).

The treatment landscape of breast cancer is rapidly evolving, but very few data have been reported about the safety of new compounds during pregnancy. The collection of prospective data regarding patients with breast cancer during pregnancy into dedicated registries is highly recommended, in order to enrich current knowledge on this topic and to improve the counseling of patients and their caregivers.

Considering the young age of patients with breast cancer during pregnancy, proper genetic counselling should be offered.

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POSTER PRESENTATIONS

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

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

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

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

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

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

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

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

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

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

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

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

VESNA BIŠOF[1], Florian Lordick[2], Manish Shah A[3], Shitara Kohei[4], Ajani Jaffer A[5], Bang Yung Jue[6], Peter Enzinger[7], David Ilson[8], Eric Van Cutsem[9], Javier Gallego Plazas[10], Jing Huang[11], Shen Lin[12], Oh Sang Cheul[13], Sunpaweravong Patrapim[14], Soo Hoo Hwoei Fen[15], Turk Haci Mehmet[16], Park Jung Wook[17], Moran Diarmuid[18], Bhattacharya Pranob[19], Cao Ying[20], Xu Rui Hua[21]

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Keywords: Dysphagia Bioimpedance electrical analysis, Radiotherapy, Phase Angle

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

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

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

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

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

Keywords: BIA, chemotherapy, side effects

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

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

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

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

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

Keywords: abemaciclib, diarrhea, toxicity, dose modification

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

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

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

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

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

Keywords: urothelial cancer, avelumab maintenance

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

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

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

Results: There were overall 4630 ED visits, and 5,3% were cancer patients (250 visits). Our research included 105 males (42%) and 145 (58%) females with a median age of 70 years (range 30-89). The main symptoms of cancer patients referred to ED were: dyspnea (27,2%), abdominal pain (20,8%), fever (10%), weakness and fatigue (9,6%), peripheral edema (7,6%) and nausea (6%), and other identified symptoms were chest pain (4,8%), hemorrhage of any kind (4,4%), arterial hypertension (2%) and rash (1,6%), in much lower prevalence. Out of a total number of visits, there were 69,2% (173) cancer patients in active treatment, and they were stratified based on the type of treatment – chemotherapy, endocrine therapy, immunotherapy, radiotherapy and other specific therapy subtypes, as well as various combination therapy regimens. Palliative patients visited in 16% of cases, and 14,4% were patients who hadn`t yet started active treatment for various reasons. Out of all visits, 70,4% were patients with metastatic disease, 22,8% with early stage, and 4,8% with locally advanced disease. The most common cancer sites were breast cancer (20%), lung cancer (16,4%), colorectal cancer (16,4%), pancreatic cancer (6,4%), ovarian cancer (6,4%), and prostate cancer (6%). Hospitalization rate was 38%, and almost half of those patients eventually died in the hospital (17,8%).

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

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

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

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

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

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

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

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

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

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

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

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

Keywords: Luminal B subtype of breast cancer, neoadjuvant therapy

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Keywords: breast cancer, radiotherapy, NAFLD, thyroid gland

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

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

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

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

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

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

Keywords: breast cancer radiotherapy, cardiotoxicity, HER2 targeted therapy

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Keywords: lung cancer, elderly patients, immunotherapy

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

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

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

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

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

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

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

Keywords: breast cancer, survival outcomes

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

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

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

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

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

Keywords: breast cancer, neoadjuvant therapy, complete pathological response

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

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

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

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

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

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

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

Keywords: comprehensive genomic profiling, metastatic colorectal cancer, Croatia

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

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

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

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

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

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

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

Keywords: melanoma, diagnosis, Covid-19, pandemia

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

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

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

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

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

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

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

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

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

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

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

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

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P23 - MY SURVIVORSHIP PLAN - WHAT WORKS FOR ME?

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Keywords: olaparib, ovarian cancer. maintenance therapy, outcome

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Keywords: comprehensive genomic profiling, metastatis gastric cancer

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

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

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

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

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

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

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

Keywords: Radium-223, prostate cancer, retrospective analysis

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

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Introduction: Small cell lung cancer (SCLC) is an aggressive subtype of lung tumor that accounts for 15% of all lung tumors. The first line of treatment for extensive stage (ES) SCLC consists of a combination of platinum and etoposide chemotherapy, along with the immune checkpoint inhibitor (ICI) atezolizumab (anti-PD-L1) or durvalumab (anti-PD-L1). While standard chemotherapy alone yields a median overall survival (OS) of around 10 months for SCLC patients, the addition of immunotherapy to chemotherapy can extend OS to 12 months1, 2. In our abstract, we will present the results of the first-line chemotherapy administered to patients with ES-SCLC at our institution.

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

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

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

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

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

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

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

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

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

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

Keywords: metastatic melanoma, pembrolizumab, retrospective analysis

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

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

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

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

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

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

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

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

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

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

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

Keywords: renal cancer, immune checkpoint inhibitors, hemodialysis,

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Keywords: lung cancer, lung cancer screening, artificial intelligence

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Keywords: ultrasound, breast, lymph node, reliability

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

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

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

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

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

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

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

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

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

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

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

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

Keywords: salivary gland, radiotherapy, retrospective analysis

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

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

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

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

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

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

Keywords: sarcopenia, phase angle, BIA

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Keywords: ALK inhibitors, lung cancer, OS, PFS

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

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

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

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

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

Keywords: Melanoma, Immunotherapy, adjuvant, targeted therapy

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

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

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

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

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

Keywords: TFD, endometrial cancer, myometrial invasion

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

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

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

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

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

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

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

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

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