

POSTER PRESENTATIONS

P1 - ADVERSE DRUG REACTIONS OF IBRUTINIB REPORTED TO AGENCY FOR MEDICINAL PRODUCTS AND MEDICAL DEVICES

Ivana Ljubičić¹, Nikica Mirošević Skvrce¹, Siniša Tomić¹, Ivona Bahnik Biševac¹

¹Agency for Medicinal Products and Medical Devices, Zagreb, Croatia

Introduction: Ibrutinib is a potent, small-molecule inhibitor of Bruton's tyrosine kinase (BTK) approved in EU for the treatment of chronic lymphocytic leukaemia (CLL), mantle cell lymphoma (MCL) and Waldenström's macroglobulinaemia (WM). Ibrutinib is first-in-class oral Bruton's tyrosine kinase (BTK) inhibitor.

Ibrutinib forms a covalent bond with a cysteine residue (Cys-481) in the BTK active site, leading to sustained inhibition of BTK enzymatic activity. BTK, a member of the Tec kinase family, is an important signaling molecule of the B-cell antigen receptor (BCR) and cytokine receptor pathways. The BCR pathway is implicated in the pathogenesis of several B-cell malignancies, including MCL, diffuse large B-cell lymphoma (DLBCL), follicular lymphoma, and CLL. BTK's pivotal role in signalling through the

B-cell surface receptors results in activation of pathways necessary for B-cell trafficking, chemotaxis and adhesion.

Chronic lymphocytic leukemia (CLL) is a progressive hematologic disease characterized by an accumulation of monoclonal mature B cells in the blood, bone marrow, and secondary lymph organs. It is the most common form of adult leukemia in the Western world.

Mantle cell lymphoma (MCL) is a subtype of non-Hodgkin lymphoma (NHL) which represents approximately 6% of all new NHL cases per year.

The most commonly occurring adverse reactions ($\geq 20\%$) of ibrutinib are diarrhoea, neutropenia, musculoskeletal pain, rash, haemorrhage (e.g., bruising), thrombocytopenia, nausea, pyrexia, arthralgia, and upper respiratory tract infection. The most common grade 3/4 adverse reactions ($\geq 5\%$) were neutropenia, lymphocytosis, thrombocytopenia, pneumonia, and hypertension.

The aim of our study is to describe adverse drug reactions of ibrutinib (Imbruvica) reported to the Agency for Medicinal Products and Medical Devices of Croatia (HALMED) until September 29, 2021.

Methods: Data was analyzed in respect to the total number of reports, demographic characteristics of the patients, suspected drug, reporter qualification, System Organ Class (SOC), MedDRA Preferred Terms, seriousness and suspected/interacting active compounds.

Results: HALMED received 114 reports related to ibrutinib. In cases in which age was reported most patients belonged to 65 – 74 age group. Most ADRs belonged to the infections and infestations followed by skin and subcutaneous tissue disorders, cardiac disorders, blood and lymphatic system disorders, gastrointestinal disorders and respiratory, thoracic and mediastinal disorders. Most frequently reported MedDRA Preferred Term was atrial fibrillation followed by sepsis, pneumonia, diarrhoea, thrombocytopenia, haematoma and haematuria. There were 80 serious ADRs (70,2%) (23 of them caused death and 19 of them led to hospitalization) and 34 non-serious ADRs (29,8%). 113 reports were reported by physicians and 2 reports were reported by consumer/non health professional. 77 reports (67,5%) were reported in males and 37 reports (32,5%) were reported in females. In the highest number of cases rivaroxaban (n=5) was reported as the suspected/interacting drug. Atrial fibrillation is known and common ADR of ibrutinib and therefore many patients are taking anticoagulants. On the other hand, ibrutinib is associated with bleeding includ-

ing minor bleeding events and major bleeding events and concomitant use of anticoagulants can contribute to the risk of bleeding.

Conclusion: The knowledge of ADRs enables prevention and adequate management of the ADRs of this effective treatment for hematological malignancies.

Keywords: ibrutinib, ADRs, CLL

P2 - INCIDENCE OF HYPOKALEMIA DURING THERAPY WITH ABIRATERON ACETATE – REAL CLINICAL PRACTICE DATA

Ljubica Vazdar¹, Petra Linarić¹, Mirjana Pavlović¹, Ana Tečić Vuger¹, Robert Šeparović^{1,2}, Andreja Jurić¹

¹*Division for Medical Oncology, University Hospital for Tumors, Sestre milosrdnice University Hospital Center, Zagreb, Croatia*

²*Juraj Dobrila University of Pula, Pula, Croatia*

Abirateron acetate (AA) selectively inhibits the CYP17 enzyme resulting in a decrease in androgen synthesis in the adrenal glands, testicles and prostate tissue. Inhibition of CYP17 reduces serum cortisol levels and increases ACTH secretion through negative feedback loop, which can lead to mineralocorticoid excess and cause hypokalemia, fluid retention and hypertension. Coadministration of prednisone 10 mg per day, divided into two doses, reduces the return secretion of ACTH and the increase in mineralocorticoids.

Objective: To analyze the frequency and degree of hypokalemia during the treatment with abiraterone acetate (AA) for metastatic castration resistant prostate cancer (mCRPC).

Methods: Retrospective analysis of medical records of patients with mCRPC treated with AA available in the information system of the University hospital for tumors.

Results: A total of 36 patients (5 after and 31 before chemotherapy with docetaxel) were treated with AA for mCRPC in period between 03/2018 and 09/2021. Patient age was 52 to 85 years (median 75 years). Total duration of treatment with AA was 2-34 months (median 15 months). The median duration of treatment in the group of patients treated with AA after docetaxel was 15 months, and in the group of patients treated with AA before the docetaxel was 14 months (therapy is still ongoing in 14 out of 31 patients, or in 45% of patients).

Serum potassium levels were monitored before the start of each cycle, monthly. Out of a total of 36 patients, three (8.3%), in the pre-docetaxel group, developed milder grade hypokalemia (grade I) in one occasion, the median time of occurrence was 6 months. No severe cases of hypokalemia have been reported. Treatment with AA was continued with nutritional recommendations, without medication intervention.

Conclusion: The results of the hypokalemia analysis during AA therapy for mCRPC show a significantly lower incidence of hypokalemia compared to two prospective Phase III studies in mCRPC (COU-AA-301 and COU-AA-302) where in post chemotherapy treatment (COU-301) all degrees of hypokalemia were found in 18% of patients (placebo 8%), and pre-chemotherapy (COU-AA-302) in 16.6% (placebo 13%). These results show that in real clinical practice, AA therapy with prednisone coadministration does not lead to a significant suppression of serum cortisol levels and recurrent mineralocorticoid excess. On the other hand, a possible influence on the low incidence of hypokalemia is an angiotensin converting enzyme inhibitor (ACEi) therapy that was present in 13 (36%) patients due to comorbidity. In view of possible more severe forms of hypokalemia, especially in patients after docetaxel therapy and coadministration of ACEi and/or diuretics, serum potassium value should be monitored according to recommendations.

Keywords: abirateron acetate, metastatic castration-resistant prostate cancer, hypokalemia

P3 - THROMBOCYTOPENIA INDUCED BY IMMUNE CHECKPOINT INHIBITORS IN TRIPLE NEGATIVE BREAST CANCER PATIENT – CASE REPORT

Petra Linarić¹, Ljubica Vazdar¹, Ana Tečić Vuger¹, Mirjana Pavlović¹, Petra Lepetić¹, Robert Šeparović^{1,2}

¹Division for Medical Oncology, University Hospital for Tumors, Sestre milosrdnice University Hospital Center, Zagreb, Croatia

²Juraj Dobrila University of Pula, Pula, Croatia

Introduction: triple negative breast cancer (TNBC) accounts for about 12-17% of all breast cancers. It is a heterogeneous disease that is estrogen receptor (ER) negative, progesterone receptor (PR) negative and human epidermal growth factor receptor 2 (HER2) negative. It has aggressive behaviour and worst prognosis of all breast cancer subtypes, and occurs more often in younger, premenopausal women with higher early recurrence rate and fast progression. It is mainly treated with cytotoxic chemotherapy due to the lack of biomarkers or valid treatment targets. In the last decade, immunotherapy, particularly with immune checkpoint inhibitors has had an important role in metastatic TNBC treatment. Immune checkpoint inhibitors (ICIs), such as monoclonal antibodies atezolizumab and pembrolizumab, are targeted agents which enhance the immune response against cancer cells. Despite clinical benefit, there are various immune-related adverse effects (irAEs) linked to ICIs, such as dermatological, gastrointestinal, hepatic and endocrine toxicities. Although irAEs are generally confirmed to be less severe than toxicities caused by conventional chemotherapy and targeted therapy, uncommon irAEs, such as immune thrombocytopenia, may sometimes be severe or fatal.

Case report: 47-year-old female was initially treated at our Clinic in 2011 for early triple-negative left sided breast cancer. Considering tumour size (T3), radical mastectomy and axillary dissection were performed, followed by adjuvant chemotherapy (combination chemotherapy regimen consisting of docetaxel, doxorubicin and cyclophosphamide) and irradiation. In 2018, early cancer of the contralateral breast has been verified, followed by right sided mastectomy and sentinel axillary lymph node (SLNB) biopsy, and the final pathology report indicated a non-luminal, HER2-positive tumour. Patient was treated with additional adjuvant chemotherapy according to the APT regimen (paclitaxel + trastuzumab) for up to a total of one year. During regular follow-up in 2021, breast MRI verified the hypoechoic mass in the parasternal area. Cytopuncture was performed which confirmed the presence of malignant cells. Additionally, PET/CT confirmed metastases in parasternal mammary lymph nodes. Surgical extirpation of parasternal lymph node was done, and the final pathology report indicated an advanced, triple-negative, PD-L1 positive breast cancer. Treatment started in February 2021, with combination therapy - nab-paclitaxel chemotherapy and atezolizumab immunotherapy. CT scans done in April 2021 showed tumour pseudo progression and treatment continued according to the same regimen.

In May 2021, 3rd therapy cycle was administered, and the same day, in the afternoon, the patient developed symptoms in the form of bleeding gums, leg petechiae and epistaxis, for which she reported to the nearest emergency room. Severe thrombocytopenia (platelet count $28 \times 10^3/\mu\text{L}$) was verified with normal values of red blood cell count, normal liver panel and renal function tests. Coagulation tests were without deviations. Laboratory findings made next day early in the morning showed even lower platelet counts (platelet count $11 \times 10^3/\mu\text{L}$), and the patient was referred to urgent hospitalization at Division for Medical Oncology, University Hospital for Tumours. After being admitted, the patient was hemodynamically

cally stable, with no signs of acute bleeding. Treatment started with parenteral corticosteroid infusions, and after haematological workup, it was concluded that immune thrombocytopenia was precipitated by atezolizumab. After corticosteroid therapy platelet count slowly recovered (platelet count $89 \times 10^3/\mu\text{L}$). According to the clinical pharmacologist, given the life-threatening immunotherapy adverse effect with the possibility of recurrence up to 20-30%, atezolizumab treatment continuation was contraindicated. In this patient, after complete platelet count recovery, other cytotoxic regimens will be reconsidered, respecting the patient's wishes.

Conclusion: immune checkpoint inhibitors can induce immune-mediated adverse effects with specific toxicity profile and potential detrimental effects on several organ systems. Although mostly mild and manageable, sometimes severe and even life-threatening adverse effects can occur that require prompt treatment in a hospital setting and discontinuation of immunotherapy, as in the case described by our patient. It is important to know the toxicity profile, as well as early recognition of the immune precipitated adverse effects symptoms and signs in order to start early treatment.

Keywords: immune thrombocytopenia, TNBC, immune checkpoint inhibitors

P4 - MANAGEMENT OF ABEMACICLIB SIDE EFFECTS IN CLINICAL PRACTICE – CASE REPORT

Kristina Kanceljak¹, Petra Lepetić², Petra Linarić², Ana Tečić Vuger², Ljubica Vazdar²,
Mirjana Pavlović², Robert Šeparović^{2,3}

¹*School of Medicine, University of Zagreb, Zagreb, Croatia*

²*Division for Medical Oncology, University Hospital for Tumors, Sestre milosrdnice University Hospital Center, Zagreb, Croatia*

³*Juraj Dobrila University of Pula, Pula, Croatia*

Introduction: CDK4/6 inhibitors have shown very good results in combination with antihormonal therapy in advanced breast cancer - leading to FDA approval of palbociclib, ribociclib and most recently abemaciclib. MONARCH 2 was a global, multicenter, double-blind, randomized (2:1), placebo-controlled phase 3 study of abemaciclib plus fulvestrant vs placebo plus fulvestrant in women with HR-positive and HER2-negative advanced breast cancer who progressed during antihormonal therapy. This study demonstrated that the addition of abemaciclib to fulvestrant resulted in a statistically significant improvement in overall survival (median OS improvement of 9.4 months). Common hematologic adverse events graded 3 or higher in the abemaciclib arm included neutropenia (29.9%), anemia (9.1%), and leukopenia (11.1%). Diarrhea was the most frequent nonhematologic adverse effect reported in the abemaciclib arm (14.5 %) and the most cases occurred during the first 4 weeks of abemaciclib initiation (peaking at cycle 3 and subsequently decreasing over time) and were effectively managed using loperamide or dose adjustments. We report a case of advanced breast cancer treated with abemaciclib plus fulvestrant resulting in reducing the dose due to severe side effects. Patient has provided informed consent.

Case report: A 71-year-old, postmenopausal female patient was diagnosed with breast cancer in 2012 and underwent right breast segmentectomy and sentinel lymph node biopsy. Postoperative patohistological finding showed luminal B like HER2 negative biology, and a stage IA disease. She was treated adjuvantly with six cycles of standard chemotherapy with doxorubicin and cyclophosphamide (AC) followed by adjuvant irradiation and introduction of adjuvant antihormonal treatment. Six months after the initiation of adjuvant treatment with anastrozole she developed intense side effects and was switched to letrozole treatment which lasted until January 2018 when right axillary relapse was detected. After excluding the possibility of surgical treatment, antihormonal treatment with tamoxifen was commenced. In October 2019 bone scan showed osteolytic bone metastasis at the 3rd lumbar vertebra as PET/CT scan showed enlarged focus of FDG uptake in a right axillary lymph nodes. Patient also had increased levels of Ca 15-3 tumor marker. In November 2019 tamoxifen was discontinued and the patient started treatment with fulvestrant 500 mg by intramuscular injection on days 1 and 15 of the first cycle and on day 1 of each cycle thereafter in combination with abemaciclib 150 mg (dosed on a continuous, twice-daily schedule). We used EORTC QLQ-C30 and EORTC QLQ-BR23 to assess QoL of our patient during initial period of abemaciclib treatment. In this period of abemaciclib initiation the most common registered symptoms were diarrhea and fatigue (scored 2 and 3) whereas other parameters in Global Health Scale and Functional Scale were well tolerable and maintained. Furthermore, during the 2nd cycle (December 2019) of abemaciclib, patient developed about 4 stools per day which is according to CTCAE moderate grade II. The patient was fatigued and exhausted so therefore, abemaciclib treatment was stopped for 7 days until toxicity resolved. Throughout 3rd cycle the patient got managed GI symptoms by diet recommendations and hydration. In the course of next treatment cycle, main adverse event appearing was again the repeated

diarrhea but now graded as severe (grade III) AE, which is according to CTCAE seven or more stools per day. Loperamide was introduced during this 4th cycle but without resolving and diarrhea repeated in form of 6-7 liquid stools per day. Considering that, the dose of abemaciclib was reduced to 100 mg. Since March 2020 (5th cycle) diarrhea issue has resolved and the patient continued treatment successfully in the mentioned reduced dose of abemaciclib, together with fulvestrant which was not discontinued during the management of AE due to abemaciclib. She maintained ECOG 0 performance status and good overall activities, and a satisfying quality of life.

Conclusion: Our case shows how good communication and tools assessing patient needs as well as prompt reaction to debilitating AEs can result in a stabilization of situation and good, prolonged treatment duration, in order to reach for a maximum of a life-prolonging treatment.

Keywords: breast cancer, CDK4/6 inhibitors, abemaciclib, diarrhea

P5 - A SINGLE INSTITUTIONAL EXPERIENCE WITH CETUXIMAB IN METASTATIC COLORECTAL CANCER

Biljana Grozdanovska¹, Nenad Mitreski¹, Bojana Petresk¹, Olivera Spasovska², Faik Misimi¹

¹University Clinic of Radiotherapy and Oncology, Skopje, North Macedonia

²University Clinic of Abdominal Surgery, Skopje, North Macedonia

Introduction: Cetuximab is an IgG1 monoclonal antibody (mAb) against epidermal growth factor receptor (EGFR) with limited efficacy in the subset of patients with RAS wild type metastatic colorectal cancer (mCRC).

Purpose of this study is to present our Institution's experience in patients with wild type metastatic CRC treated with Cetuximab.

Methods: We collected data for 18 patients with wild-type RAS mCRC. Patients received Cetuximab (500mg/m²) in combination with oxaliplatin and irinotecan-based chemotherapy. The treatment has been continued until unacceptable toxicity or disease progression (PD). Tumour response has been evaluated every 12 weeks using Response Evaluation Criteria in Solid Tumors (RECIST 1.1) and toxicity was assessed according to the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0.

Results: Eighteen patients with median age 55 years (range 41-67 y) were identified. Most patients were in good ECOG Performance Status (0-2). The primary location of cancer was the rectum (11 patients), and colon (7 patients). The most common metastatic sites were liver and lungs with more than 50% of patients (72.2%) having 2 or 3 metastatic sites.

Most patients (55.56%) received ≥ 1 prior lines of chemotherapy and 44.44% of patients received Cetuximab as 1st line treatment. Six patients (33.33%) received it in combination with Oxaliplatin and 12 patients (66.67%) received it in combination with Irinotecan-based chemotherapy. In the majority of cases (77.77%) good response to treatment was reported (stable disease in 44.44% (8) and partial response in 33.33% (6)).

In regards to toxicity, rash grade 1 was the most common adverse effect. Ocular toxicity (conjunctivitis) was reported in only one patient. The 12-month survival rate was 94% and the 24-month survival rate was 46%.

Conclusion: Over the last decades, the incorporation of novel agents in the management of mCRC is associated with improvement in survival. Anti EGFR mab is an effective and well-tolerated treatment option in RAS wt mCRC. Nowadays, molecular profiling with the identification of prognostic and predictive biomarkers provides a personalized treatment approach, with the potential of improved treatment efficacy. To assess value of adding Cetuximab to mCRC treatment, longer follow-up is needed.

Keywords: Cetuximab; EGFR inhibitor; metastatic colorectal cancer

P6 - ELEMENTS OF QUALITY ASSURANCE IN THE PREPARATION OF ANTINEOPLASTIC DRUGS IN HOSPITAL PHARMACIES

Anni Mikić

Hospital Pharmacy, University Hospital of Split, Split, Croatia

Introduction: Antineoplastic drugs are a group of drugs used for the treatment of malignant diseases and their consumption is continuously increasing mainly due to the use of new biologic and biosimilar drugs. Such medicines are mainly administered intravenously and require reconstitution and preparation. However, antineoplastic drugs are potentially hazardous to personnel and patients, so special procedure is required working with these chemical substances. Centralized preparation of antineoplastic drugs reduces these risks and problems, improves overall safety for patients and personnel. Centralized preparation means safe production of the medicinal product in aseptic conditions that will minimize the possibility of contamination of the preparation, in accordance with the “Good Manufacturing Practice regulations for medicinal products”. Dosing and handling errors in this kind of system are reduced together with the costs and amount of hazardous waste. The consequences of this work have led to the standardization of techniques and the implementation of quality system. The concept of quality system or quality management system includes quality assurance, good manufacturing practice and quality control. A key element of quality assurance in the preparation of antineoplastic drugs in hospital pharmacies is the quality control of critical parameters before, during and after the completion of antineoplastic drugs.

Methods: Review of professional literature on the topic of quality assurance in the preparation of antineoplastic drugs and good pharmacy and manufacturing practices.

Results: Preliminary controls include checking the prescription and medicine used in preparation. The pharmacist controls prescription by checking the dosage and provides the necessary documentation of medicine (production sheet, labeling, delivery note, etc.). When it is confirmed that the patient can receive therapy, the required doses of the drug are prepared according to the therapeutic protocol, in an infusion bottle with an infusion system, a syringe or other appropriate packaging as prescribed. This kind of preparation is carried out in a specially qualified area (clean rooms with controlled conditions for working without contamination) of environment class B or C in which a biohazard safety cabinet with laminar air flow or closed isolator class A is located. The cabinets must be qualified and parameters such as pressure (for isolator), air flow rate (for cabinet with laminar air flow) and temperature must be monitored daily. Storage conditions and shelf life are also checked for medicine used in preparation. Preparation can be controlled throughout the preparation process using a smart video system that allows automatic verification during critical phases combined with subsequent video control to monitor whether the right patient is given the right dose in a good drug carrier. Human error can be reduced by robotics according to the special criteria of the robot. Before preparation, it can recognize all the necessary items: drugs, drug dissolution containers, bar code and digital images. In addition to video surveillance and robotics, gravimetric control helps in process control as a simple method that compares the observed (weighed) weight of the preparation with the expected weight obtained by summing the real mass of manufacture drug, mass of infusion bag and medical devices combining the mass with drug density. The control of the final product can be analyzed visually and / or instrumentally. Basic visual inspection includes checking the drug labeling, sediment formation, color, visible particles or bubbles. More complex control is instrumental, which uses analytical methods for identification and determination of the content of active substance,

qualitative and quantitative determination of impurities or identification of excipients. Among the most precise, and often used analytical methods in the quality control of the final product are sophisticated chromatographic methods (High performance liquid chromatography- HPLC, Gas chromatography- GC) followed by spectroscopic methods (UV/VIS, infrared, Raman, NMR, fluorescence spectroscopy, etc.).

Conclusion: There is no legal document in the Republic of Croatia that completely includes quality assurance of antineoplastic drugs prepared in the hospital pharmacy, so in their daily work pharmacists use international recognized standards, expert guidelines in aseptic preparation of anticancer drugs. One of such are guidelines to Good Manufacturing Practice and Good Pharmacy Practice as a part of quality assurance system that ensures uniformity of manufactured products and supervision to the standard of quality that is appropriate for their application according to valid regulation. The quality assurance system of antineoplastics is a complex system that requires a wide range of knowledge of pharmacist, specific equipment, continuous education of all personnel who are in any way involved in the work and handling of antineoplastic drugs. The best way to implement a relevant quality assurance strategy is to carry out a risk analysis considering local preparation conditions (drug quantity, target patients, analytical instruments, etc.), employee skills, required level of information and financial income.

Keywords: antineoplastic drugs, centralized preparation, quality assurance

P7 - NEW INSIGHTS INTO THE POTENTIAL USE OF MEDICAL CANNABIS IN CANCER CARE

Sanda Vladimir-Knežević¹, Biljana Blažeković¹, Maja Bival Štefan¹, Marija Kindl¹, Mateja Mervić¹

¹Department of Pharmacognosy, Faculty of Pharmacy and Biochemistry, University of Zagreb, Zagreb, Croatia

Cannabis sativa L. (Cannabaceae) is one of the earliest known medicinal plants. Despite long-standing controversial and limited medical use by unavoidable psychotropic effects, lately it is receiving renewed scientific interest. The last two decades have brought a new evidence of cannabis therapeutic potential, especially in cancer care. Cannabis is a source of over 100 active compounds known as phytocannabinoids whose numerous effects on the human body are primarily exerted through interactions with cannabinoid receptor types 1 (CB1) and 2 (CB2). Delta-9-tetrahydrocannabinol (THC) having psychoactive properties and non-psychotropic cannabidiol (CBD) are the principal plant constituents. The therapeutic value of cannabis and cannabinoid-based medicines has been evaluated in numerous clinical trials, several of them are still ongoing. Obtained results indicated that cannabis, its main components, and their synthetic analogues may have a meaningful clinical impact on several common cancer-related symptoms, including chemotherapy-induced nausea and vomiting, pain, cachexia, and anorexia. Nausea and vomiting are the chemotherapy side effects considered by patients as the most stressful. Cannabis extracts and synthetic THC (dronabinol) added to standard antiemetic therapy were well tolerated and provided better protection against these chemotherapy-induced symptoms. Cancer-related pain is often multidimensional and can affect all aspects of a patient's life. At this time, data supporting the effectiveness of cannabis and cannabinoids in the treatment of cancer-related pain is limited. However, available studies indicate that the cannabis extract containing THC and CBD may be an effective addition to cancer pain treatment in those who are not optimized by opioid therapy, but the effectiveness varies widely between patients. Great number of cancer patients also suffer from anorexia which can lead to poor chemotherapy response and decreased survival. In contrast to cannabis extracts and THC, synthetic cannabinoids dronabinol and nabilone showed appetite improvement properties. In addition, surveys collected data implicated the potential use of cannabis for palliative indications in oncology as well-tolerated, effective and a safe option to help patients cope with the malignancy related symptoms. In conclusion, the current evidence for the use of cannabis-based medical products in cancer patients is still weak because of clinical trials with small populations, multiple dosage forms and products, and inconsistent results. Given the increased use of cannabis and cannabinoids in oncology patients, it is needed to conduct larger, high quality randomised controlled trials including patients with similar cancer diagnoses and medical conditions to elucidate their efficiency and safety in cancer care.

Keywords: *cannabis sativa*, cannabinoids, THC, CBD, chemotherapy side effects, cancer-related pain

P8 - NIVOLUMAB INDUCED HYPOPITUITARISM – CASE REPORT

Petra Lepetić¹, Petra Linarić¹, Dejana Jezernik², Kristina Kanceljak², Ana Tečić Vuger¹,
Mirjana Pavlović¹, Ljubica Vazdar¹, Robert Šeparović^{1,3}

¹*Division for Medical Oncology, University Hospital for Tumors Zagreb, Sestre milosrdnice University Hospital Center, Zagreb, Croatia*

²*School of Medicine, University of Zagreb, Zagreb, Croatia*

³*Juraj Dobrila University of Pula, Pula, Croatia*

Intro: Nowadays, immune checkpoint inhibitors (ICI) are a treatment of choice in a wide array of malignancies such as RCC, melanoma, or non - small cell lung carcinoma with significantly improved survival rates. Nivolumab targets programmed death 1 receptor (PD-1) - an effector ligand of immune checkpoint pathways, thus promoting an immunological reaction against cancer cells. Many immune-related adverse effects are due to specific mechanisms of action. The most frequent adverse reactions are fatigue, musculoskeletal pain, nausea. Common endocrine disorders are hypo/hyperthyroidism, while uncommon are adrenal insufficiency, hypopituitarism, hypophysitis, and diabetes mellitus. The majority of adverse reactions were mild to moderate

Case: A 62 – year – old caucasian man, in 2016, was diagnosed with left renal cancer and was committed to radical nephrectomy. Postoperative PET/CT scan revealed disseminated disease, wherefore, due to his frail general clinical state and PS, he was treated with temsirolimus for one year and five months. Immunotherapy with nivolumab, as a second-line treatment choice, was introduced in June 2018, considering the progression of the disease. He was admitted to the hospital because of fatigue, inappetence, and worsening of performance status, after six months of treatment with nivolumab. Diagnosis of secondary adrenal insufficiency was made by biochemical assessment of adrenal, gonadal, and thyroid axes along with electrolyte and prolactin levels. Also, an MR scan of hypophysis was performed; scans indicated partial empty sella. According to one study, endocrine abnormalities such as hypopituitarism have occurred in approximately 20% of patients with partial or complete empty sella. The patient began replacement therapy with hydrocortisone and experienced improvement in fatigue and general weakness. Treatment with nivolumab was continued in the next five months.

Conclusion: Although hypopituitarism is more frequent following combo therapy (ipilimumab with nivolumab), it rarely occurs in monotherapy with nivolumab. This care report aims to demonstrate occasional, but potentially severe entity that requires appropriate prompt diagnostic and therapeutic interventions. Patients should be closely monitored for a wide range of adverse events, keeping in mind that a wide range of immune-related adverse events can occur. Some of them are potentially severe, deferring treatment and compromising outcomes. At that point, prompt and focused care is needed to resolve the complications and to achieve maximum therapeutic potential.

Keywords: immune checkpoint inhibitors (ICI), programmed death 1(PD-1) receptor, renal cell carcinoma (RCC), hypopituitarism