

ORAL PRESENTATIONS

S1 - MODERN DIAGNOSTIC METHODS IN THE DETECTION AND FOLLOW-UP OF PATIENTS WITH MALIGNANT SKIN TUMORS

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Introduction: The incidence rates of melanoma and non-melanoma skin cancers are rising globally in most fair-skinned populations. Additional efforts in primary and secondary prevention are necessary.

Methods and results: Detection and excision of cutaneous malignancies, especially melanoma at early and still curable stages is an effective strategy to reduce skin cancer mortality rate.

Only a few examination strategies allow for a true screening of the whole integument, while the others are intended for application on preselected lesions:

1) Devices for large-scale screening purposes, eligible for screening in daily clinical routine intended for examination of many or all lesions of a patient within acceptable amount of time include: dermoscopy, sequential digital dermoscopy and total body photography. Correct interpretation of examination results requires a considerable amount of training that needs to be refreshed and updated regularly.

2) Device designed for assessment of a few atypical, preselected lesions:

a) Reflectance confocal microscopy and multiphoton tomography are intended for assessment of preselected lesions in specialised clinics by trained experts.

Teledermatology is a subspeciality of dermatology that uses the information and communications technologies to diagnose, monitor, treat, prevent, research and educate over a distance. It has become a routine procedure for skin cancer triage.

Artificial intelligence (AI) - new generation machines are using deep learning convolutional neural networks (CNN) and algorithms to compare the image with thousands images indicated the diagnosis for each image already archived. Study by Haensle et al. published in 2020. compared performance of a market-approved convolutional neural network in classifying a broad spectrum of skin lesions in comparison with 96 dermatologists working under less artificial conditions. The CNN and most dermatologists performed on the same level.

Modern machines for digital dermoscopy and total body photography use AI.

Mobile digital teledermoscopy applications for skin self-examinations are already on the market.

Conclusions: We are witnessing a constant improvement in early diagnosis and follow-up of malignant skin tumors. The primary focus should shift from human–computer competition to human–computer collaboration. Good quality AI-based support of clinical decision-making improves accuracy over that of either AI or physicians alone.

Keywords: digital dermoscopy, teledermatology, artificial intelligence

S2 - CLINICAL FEATURES AND DIFFERENTIAL DIAGNOSIS OF THE MOST COMMON MALIGNANT TUMORS OF THE SKIN

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The most common malignant tumors of the skin are non-melanoma skin cancers (NMSC) and melanoma.

NMSC mainly comprise two different entities: basal cell carcinoma (BCC) and squamous cell carcinoma (SCC).

Methods and Results: Basal cell carcinoma (BCC) is the most common skin cancer in fair-skinned individuals. Clinically, the vast majority of BCCs develop on the face. The most common clinical variants include: nodular, cystic, ulcerated, pigmented, morpheiform, and superficial BCC.

The classical dermoscopy algorithm for the diagnosis of BCC includes lack of pigment network and the presence of at least one of the following: ulceration, maple-leaf like structure, blue-grey globules, blue-void nests, arborizing vessels and spoke-wheel structures.

The main differential diagnoses include melanoma in pigmented lesions, Morbus Bowen and inflammatory skin diseases in superficial lesions, and adnexal tumors in non-pigmented nodular lesions.

Squamous cell carcinoma (SCC) is the second most common cutaneous malignancy. Clinically, most SCCs develop from a precursor lesion. Usually it presents as exophytic or endophytic often inflamed nodule.

The most important dermoscopic clues for SCC in situ are white circles, keratin, blood spots (hemorrhage), white structureless zones, and glomerular vessels. Hairpin vessels, linear irregular vessels, targetoid hair follicles, white structureless areas, a central mass of keratin, and ulceration are dermoscopic clues associated with invasive SCC.

Differential diagnosis includes precursor lesions, adnexal tumors, irritated seborrheic keratosis and amelanotic melanoma.

Melanoma is the most serious oncologic problem in dermatology. Its incidence and mortality are still on the rise. The most common clinical variants in whites are: superficial spreading melanoma (60-70%), nodular melanoma (15-30%), lentigo maligna melanoma (5-15%), and acral lentiginous melanoma (5-10%).

There are several dermoscopic algorithms for diagnosing melanoma including ABCD rule of dermoscopy, 7-point checklist and chaos and clues method.

Differential diagnosis includes: melanocytic tumors, epithelial tumors, vascular tumors, pigmented dermatofibromas, hemorrhage especially subungual.

Conclusions: Diagnosing malignant tumors of the skin at an early stage requires high level of expertise from the dermatologist. New diagnostic and therapeutic options are available today. Regular check-ups, early diagnosis, and timely treatment are essential for the prognosis and management of skin tumors.

Keywords: non-melanoma skin cancers, melanoma, dermoscopy

S3 - MEDICATION ERRORS IN THE TREATMENT OF PAIN IN CANCER PATIENTS

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Medication error is an unintentional event involving administration of medical drugs that results in unwanted and harmful consequences. Errors in prescribing the drug, giving the patient instructions on the proper use of therapy or in drug interactions can often be seen in the treatment of oncology patients, especially with supportive therapy. The pharmacist, primarily in his work in the outpatient pharmacy, has an important role in explaining how to apply the therapy when dispensing the drug to a patient or caregiver.

In this presentation we will present the treatment of patient's primary oncological disease, but also the pharmacotherapy prescribed to combat pain. Pain is a symptom that directly affects the quality of life of patients and, in addition to the correct choice of drugs, it is necessary to know how to use these drugs properly. We will also present the factors that influence the successful treatment of pain and the characteristics of the various drugs used in doing so.

The aim of this workshop is to remind the participants what needs to be clarified with the patient / caregiver regarding the dispensing of prescribed therapy. The patient / caregiver should know what the medicine is for, how to use it correctly, when to use it and what to do in case a single dose of the medicine is skipped. The patient / caregiver should understand the most common side effects, how to prevent them and how to take care of them in case they occur. In the last part of the presentation, we will pay attention to the disposal of unused drugs.

Keywords: medication error; pain treatment; supportive therapy

S4 - HOSPITAL PHARMACY IN 21ST CENTURY

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In the 21st century as patients evolve and this must follow hospital pharmacists in the age of digital health. They have to redefine their place in medicine as well. A simple drug dispenser will not be enough in a hospital-based economy. From adopting new approaches to letting go of older ones, the hospital pharmacy of the future will pack a different look and a different role. Hospital pharmacies should look to repurpose physical layout and optimize workflow processes to better support patient assessment and communication, including the use of eHealth technology, private rooms and interprofessional teamwork. They are well positioned to support better integration of patient care across the health care system. This also includes use of digital technology to improve working in multidisciplinary teams and collaboration with other care providers and with pharmacists in other care settings. The future of pharmacies will be human. Despite all the tech-talk, a constant element that will be an integral part of the hospital pharmacy of the future is the human element. With robots handling manual, routine tasks in hospital, pharmacists will have more time to dedicate to clinical needs of patients and tackle challenges requiring creativity.

Keywords: patient safety, hospital pharmacist, 21st century, digital technology, multidisciplinary teams

S5 - THE NCODA POSITIVE QUALITY INTERVENTION (PQI): EDUCATING YOUR MEDICALLY INTEGRATED TEAM WHILE SUPPORTING BETTER PATIENT CARE WITH A CONCISE, PEER-REVIEWED, PHARMACY-LED RESOURCE

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To promote higher quality patient care, NCODA created the Positive Quality Intervention (PQI) as a peer-reviewed clinical guidance document for healthcare providers. By providing Quality Standards and effective practices around a specific aspect of cancer care, PQIs equip the entire multidisciplinary care team with a sophisticated, yet simple-to-use resource for managing patients receiving oral or IV oncolytics. The PQI fosters better care for patients through appropriate patient identification, treatment selection, increased speed to therapy, reduced cost and hospitalization, and by improving adherence techniques for the patient and their medically integrated teams.

The treatment and management of oncology patients is continually changing and evolving. The growing complexity creates a need for healthcare professionals to have a quick resource to turn to for drug therapy management information. The medically integrated pharmacy team is in a unique position to ensure appropriate treatment, increase compliance, and maximize outcomes. PQIs, one of the four NCODA Quality Standards, are designed to operationalize and standardize best practices to achieve positive clinical outcomes.

As an expansion to the PQI, the PQI in Action incorporates opinions and experiences from oncology experts within the medically integrated teams at leading cancer care organizations. These professionals have successfully implemented medically integrated pharmacies as well as the use of PQIs throughout their care teams to improve the clinical outcomes of patients. Utilization of consistent clinical information, like that contained within NCODA's PQI, standardizes knowledge exchange and improves clinical communication within an organization.

In the lecture cemiplimab PQI will be presented. Cemiplimab is a programmed death receptor-1 (PD-1) monoclonal antibody which acts to block the PD-L1/PD-L2 pathway thereby removing inhibition of the immune response, potentially breaking peripheral tolerance and inducing immune-mediated adverse reactions.

Cemiplimab is indicated in:

- Locally advanced or metastatic basal cell carcinoma (laBCC or mBCC) previously treated with a hedgehog pathway inhibitor (HHI) or for whom an HHI is not appropriate.
- Locally advanced or metastatic cutaneous squamous cell carcinoma (laCSCC or mCSCC) who are not candidates for curative surgery or curative radiation.
- Locally advanced non-small cell lung cancer (NSCLC) where patients are not candidates for surgical resection or definitive chemoradiation or metastatic NSCLC whose tumors have high PD-L1 expression [≥50%] as determined by an FDA-approved test, with no EGFR, ALK, or ROS1 aberrations.

Keywords: PD-L1 expression, cemiplimab, positive quality intervention, cancer

S6 - CHALLENGES AND POSSIBILITIES IN THE PREVENTION AND TREATMENT OF FEBRILE NEUTROPENIA IN ONCOLOGY PATIENTS DURING THE COVID-19 PANDEMIC

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Introduction: Febrile neutropenia (FN) is one of the emergencies in working with cancer patients and only rapid identification and treatment can prevent the occurrence, complications, and possible consequent fatal outcome. The frequency and severity of FN are correlated with chemotherapy intensity, cancer type, and patient-related risk factors. Previous studies report that 50-75% of initial neutropenic complications occur in the first cycle, when most patients receive full-dose chemotherapy. FN is always accompanied by significant costs associated with hospitalization, additional outpatient treatment, and significant economic and psychological burden for patients and their caregivers. Cancer patients have a higher risk of severe COVID-19 infection. Therefore, prevention of COVID-19 infection is imperative, especially in the vulnerable population.

Material and methods: In order to obtain relevant information on a given topic, professional and scientific literature on the topic of febrile neutropenia, cancer and COVID-19 was used, as well as a search of bibliographic databases such as PubMed and Scopus.

Results: Oncology patients positive for SARS-CoV-2 without any or minimal symptoms can be monitored from home. Telemedicine is an option to aid in following patients without potential exposure. Treatment of neutropenic complications is of particular importance during the COVID-19 pandemic where clinicians seek to reduce the risk of patient infections and the need for hospital visits. Outpatient management of patients with low-risk FN is a safe and effective strategy. Risk stratification in patients with FN is a vital principle of the evolving strategy of sepsis and pandemic, requiring access to locally formulated services based on MASCC and other national and international guidelines.

Conclusion: The COVID-19 pandemic presents a challenge of global reach and significance which is unprecedented in the era of modern oncology. Modeling and innovation in oncology services will require the integration of a multidisciplinary team, telemedicine, a *home hospital* and outpatient services, not only to limit the number of hospital visits, but also to anticipate the complications of cancer treatment.

Keywords: cancer, febrile neutropenia, COVID -19, telemedicine

S7 - CANCER PAIN MANAGEMENT

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The presence and severity of pain has important clinical implications and significant impact on clinical outcomes. Health-related quality of life is a very important factor that provides prognostic information for survival. Malignant pain is caused by cancer growth, its treatment, various diagnostic procedures and poor condition of the organism in general. It is a serious public health problem because the prevalence in advanced disease is estimated to be more than 70%. Despite guidelines and the availability of opioids, undertreatment is common. In clinical practice, different pain assessment tools are used to assess pain intensity. The most common are: visual analogue scale, verbal rating scale and numerical pain scale. Guidelines for the treatment of carcinoma pain in adults of the Croatian Society for the Treatment of Pain follow the recommendations of the World Health Organization, which determines the treatment of pain according to the pain intensity. Thus, we distinguish three degrees of pain intensity: mild pain, mild to moderate, and moderate to severe pain. In each of these pain stages, it is possible to combine non-opioid and opioid analgesics as well as adjuvant therapy. The goal of malignant pain management is to achieve effective pain control and preserve the patients' quality of life without severe side effects. The first stage of analgesic therapy is paracetamol, nonsteroidal anti-inflammatory drugs, and cyclo-oxygenase-2 selective inhibitors. It is important to monitor and reassess the long-term use of NSAIDs or cyclo-oxygenase-2 (COX-2) selective inhibitors because of their significant toxicity (e.g. gastrointestinal bleeding, platelet dysfunction and renal failure). COX2-selective inhibitors should be carefully prescribed to patients with cardiovascular comorbidities. Weak opioids can be used to treat mild to moderate pain, and in severe pain, the drugs of choice are strong opioid analgesics. In case of rapid progression of the disease, some authors suggest eliminating the second step of the analgesic ladder, with weak opioids being replaced with low doses of oral morphine. Opioid analgesics should be titrated until achieving adequate analgesia. With the exception of transmucosal immediate release, a typical oral immediate release opioid will provide peak analgesic effect within 60-90 minutes and, in patient with normal renal and hepatic function, should provide pain relief for approximately 4 hours. The dose that serves as the base for the increase is the total dose of the opioid analgesic administered in the last 24 hours. The dose should be increased on demand (breakthrough pain), usually progressive dose increase correlates with disease progression. A different opioid should be considered in the absence of adequate analgesia (despite opioid dose escalation) or the presence of unacceptable opioid side effects. When rotating a patient to a new opioid, the clinician must calculate the equianalgesic dose of the new opioid and then decrease that dose by 25-50% to account for incomplete cross-tolerance. The oral route of administration is recommended whenever possible. If it not possible, there are transdermal, subcutaneous, intravenous and others routes of administration. Breakthrough pain is a special entity within chronic malignant pain, and represents episodes of moderate to severe pain in patients who otherwise have well-controlled background pain. Breakthrough pain should be treated with an additional dose of fast-acting analgesics that matches the pharmacokinetics of the breakthrough pain profile.

In conclusion, pain should be expected in all stages of malignancy. It should be treated multidisciplinary and assessed frequently in order to make the treatment as successful as possible.

Keywords: malignant pain, analgesics, breakthrough pain

S8 - ORAL ANTICANCER MEDICATION

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Over the last few decades, an increasing trend of oral anticancer drug usage can be observed. More than 20% of chemotherapy is currently administered orally and this number is likely to increase. Inconvenience of transportation, waiting time at the clinic and concerns regarding IV line are few negative attributes associated with parenteral administration of antineoplastic drugs and main reasons for the emergence of alternative administration routes. Because of its convenience, oral administration of antineoplastic treatment is preferred by patients but also health care professionals as they become more attuned to patient preferences and their quality of life during treatment. Unfortunately there are some barriers to safe and efficacious administration of oral antineoplastic medicines that need to be addressed. Oral anticancer therapy introduces a new factor which influences outcomes in cancer patients: adherence. Unlike traditional iv administration where healthcare professionals monitor their patients, oral administration shifts responsibility and requires more patient effort. WHO reports a 50% adherence rate regarding chronic diseases therapy in developed countries. It is commonly assumed that adherence rates among cancer patients are better due to their higher motivation and severity of the disease. However, research is suggesting that adherence among cancer patients isn't that good. Results regarding adherence to oral anticancer drugs vary, ranging from less than 20% to 100%. For example, Hershman et al. report that only 49% of 8769 breast cancer patients treated with adjuvant hormonal therapy took their medication for the full duration at the optimal schedule. Limited bioavailability of orally administered anticancer drugs is another issue which is stimulating the pharmaceutical industry to develop more efficient formulations. Oral paclitaxel+encequidar is such a formulation. It showed statistically significant improved ORR (overall response rate) and PFS (progression free survival) when compared with iv paclitaxel in a phase 3 RCT (randomized controlled trial). Recently paclitaxel+encequidar received CRL (complete response letter) from the FDA (Food and Drug Administration) for the treatment of metastatic breast cancer.

In the recently published AMBORA trial 202 patients receiving oral anticancer medication were evaluated for drug-related problems (ie, side effects and unresolved medication errors) and patient satisfaction. The intervention group which received clinical pharmaceutical care experienced significantly lesser drug related problems and the treatment satisfaction was higher among those patients when compared to control (patients receiving standard of care). This findings resolve some serious issues regarding oral anticancer drug administration with implementation of clinical pharmacy counseling in routine clinical practice.

In conclusion, oral anticancer therapy is a valid option for selected, highly motivated and health-literate patients who can adhere to oral regimens which can be very complex in this population of patients since most of them are polymedicated. In addition, those patients should be able to manage potential complications and store the medicines properly to avoid any harm to their family members, especially children. Since oral administration of anticancer medication increases patient satisfaction and quality of life every effort contributing to patient wellbeing should be made.

Keywords: oral anticancer medication, oral chemotherapy, adherence, clinical pharmacy

S9 - ASEPTIC MANUFACTURE (COMPOUNDING)/ PREPARATION OF ANTINEOPLASTIC DRUGS – REQUIREMENTS, STANDARDS AND GUIDELINES

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Today's pharmacotherapy in oncological medicine often cannot be performed without individualized, specially adapted, and pharmacy-prepared sterile drugs that have a targeted and good therapeutic effect on the disease and the expected good treatment outcome.

Much such complex liquid and solid forms of sterile magistral and galenic drugs for parenteral and other therapeutic applications are not suitable for sterilization by the classical terminal (thermal) sterilization process.

This leads to the increasing use of the aseptic process for the manufacture or preparation of medicinal products with a modified sterilization process under the conditions of a hospital and in certain cases of a public pharmacy.

Sterile magistral and galenic antineoplastic drugs are among the drugs whose preparation and use are associated with high risk due to the complexity of their preparation and toxicity.

The aim of this work and presentation is to present the main characteristics, requirements, standards, and guidelines for the manufacture of sterile antineoplastic drugs, based on the specifications and standards for asepsis. International and Croatian regulatory practice in the field of pharmacy will also be presented.

Aseptic production and preparation of sterile medicinal products is a unique professional challenge for pharmacy due to its complexity and high demands on safety and quality. Antiseptics first require careful and rational planning and evaluation of the cost-effectiveness of all resources and material requirements for such a specific type of manufacture, as well as complete definition, standardization, and validation of procedures and prescribed workflows in the procurement, manufacture, equipment, and dispensing of these drugs.

An important prerequisite for high-quality asepsis is the functional design and execution of technological work and auxiliary rooms with controlled and conditioned conditions. The equipment and professional aids used in manufacturing must be validated and approved.

Aseptic production requires the establishment of a quality management system in all processes.

The required basic aseptic technique ensures safe manufacturing and filling of the drug product into the primary tank in a laminar flow device of air purity class A, and the device itself must be located in a cleanroom - air purity class B - C. Today, more and more isolators are used as more technically sophisticated devices located in a cleanroom of air purity class D, but with a mandatory inlet chamber for decontamination of materials and equipment.

Asepsis in pharmacy today requires constant investment and renewal of specialized equipment, technological processes, and the adoption of new knowledge in the field. It also requires a constant professional review of the safety and risk assessment system, a review of its own development strategy, and

specific pharmaceutical activities. This requires constant interdisciplinary cooperation of all those involved in pharmacotherapy with complex sterile drugs.

Owners and persons responsible for such modern and high-quality antiseptic drug production in our pharmacy should be masters of pharmacy and specialists in pharmaceutical technology.

The presented requirements, standards, and guidelines provide a safe professional way for rational and effective pharmacotherapy in oncology. They help to optimize treatment outcomes with the most therapeutically sophisticated sterile antineoplastic biological and immunological drugs.

Keywords: aseptic manufacture/ compounding, antineoplastic drugs, hazardous drugs, pharmaceutical standards and guidelines.

S10 - SEXUAL PROBLEMS IN PATIENTS WITH ONCOLOGICAL PROBLEMS: ARE THEY THE CONSEQUENCE OF A DISEASE OR OF A TREATMENT?

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Patients with cancers have a higher prevalence of sexual problems (the prevalence is 40-100%) compared to general population. There are many reasons for such a distribution: the disease itself (a carcinoma) can lead to sexual problems via biological, psychological (e.g. depression, anxiety) and relational (e.g. relationship discord) mechanisms. On the other hands, treatment methods can lead to sexual side-effects. The highest prevalence of sexual problems (>80%) is among the patients who underwent radical pelvic surgery.

There are some gender differences in cancer survivors, regarding sexual functions. Women want to restore the relationship, and therefore have more desire problems and body image problems, whereas men want to restore function and have more erection/orgasm problems. Furthermore, there are some differences in sexual consequences of homosexual and heterosexual man and women (not just in prevalence of different cancers, but even in prognosis of sexual side-effects).

Unfortunately, less than 15% of patients with different cancers talk about sexuality with their doctors.

All methods of cancer treatments can lead to sexual side effects. Mastectomy reduces eroticism (because of absent erotic areas, such as nipples) and produces feelings of unattractiveness and loss of femininity. Bilateral salpingo oophorectomy adversely affects sexuality due to hormonal changes. fibrosis, scarring and lymphoedema produce reactions in both the patient and their partners. Chemotherapy can lead to ovarian failure, menopausal symptoms, erythrodysesthesia, alopecia, nausea. Radiation produces fatigue, dryness of skin, loss of sensation, alopecia. Affected sexual self-confidence can also be due to missing parts, loss of bleeding, loss of sexual sensations, loss of womanhood or manhood.

Treatment options for sexual problems in cancer survivors are multiple. Mindfulness techniques have been shown to have positive effects on desire and arousal problems. Local vaginal treatments (hormonal creams, lubricants, moisturizers) may treat vaginal atrophy and consequent dyspareunia. Different antidepressants which address levels of noradrenaline and dopamine (such as bupropion) increase sexual responsiveness and orgasmic capacity.

There are some specific problems, specific to the location of the cancer. Breast cancer directly affects the essence of the cultural sign of womanhood. Lung cancer can lead to dyspnoea, colorectal cancers to diarrhoea or incontinence, endometrial cancers to loss of reproduction, and each of these have specific consequences in the area of sexuality. Prostate cancers lead to erectile dysfunction due to surgery and to loss of desire due to antiandrogen therapy. Bladder cancer produce specific effects due to its location and surgery techniques.

One of the well-known techniques to address sexual problems in people with oncology problems is a DESIRE approach. Desire is an acronym of the following steps: discuss (sexual problems and a consequent distress), evaluate (for depression, sexual problems and relationship problems), screen for, intervene (with stress reduction, specific pharmacological agents, prioritizing intimacy), refer (to a specific professional) and educate.

Each and every health care professional (i.e. medical doctors, nurses, pharmacists, physiotherapists etc.) should have basic knowledge in sexual anatomy and physiology and should be able to take sexual

history and give basic counselling in the arena of sexuality. Pharmacists should be especially aware of possible adverse sexual effects of drugs and medicines used for the treatment of cancers. Hence, they should be familiar with counselling techniques and should provide education of patients regarding iatrogenic sexual problems.

Keywords: sexual problems, sexual side-effects, iatrogenic sexual problems, sexual counselling

S11 - CLINICAL SIGNIFICANCE OF REMDESIVIR ASSOCIATED BRADYCARDIA

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It was recently observed that use of remdesivir in Coronavirus disease 2019 (COVID-19) might be associated with higher occurrence of transitory bradycardia. However, the clinical significance of this phenomenon is unknown. We have retrospectively investigated a cohort of 473 COVID-19 patients hospitalized in our institution from 9/2020 to 4/2021 who received remdesivir for acute COVID-19 infection.

Median age was 65 years IQR (56-72.3). A total of 312 (66%) patients were male, 53 (11.2%) had atrial fibrillation (AF) and 141 (29.8%) used beta blockers (BB), respectively. Median Charlson comorbidity index (CCI) was 3 IQR (2-4). At the time of hospital admission, a total of 382 (80.8%) patients presented with severe and 83 (17.5%) with critical COVID-19 symptoms. Median C-reactive protein and Interleukin-6 levels on admission were 110.7 mg/L and 44.2 pg/ml, respectively.

Bradycardia (heart rate <60 beats per minute) was present in only 1.3% patients before remdesivir treatment. The rate of bradycardia steadily increased up to day 5 of remdesivir treatment on which 16.8% patients experienced bradycardia that subsequently diminished after remdesivir discontinuation. Occurrence of bradycardia on day 5 of remdesivir treatment was significantly associated with lower odds of high flow oxygen therapy use (OR 0.33 95% CI (0.16-0.7); P=0.004), intensive care treatment (OR 0.43 (0.2-0.91); P=0.027) and death during hospitalization (OR 0.33 95% CI (0.14-0.79); P=0.014).

In the multivariate logistic regression analysis, absence of remdesivir day 5 bradycardia occurrence (OR 0.39; P=0.043), more severe WHO COVID-19 severity on admission (OR 3.32; P<0.001), older age (OR 1.01; P=0.012) and higher Charlson comorbidity index (OR 1.16; P=0.047) were independently associated with death during hospitalization.

Our data suggest that remdesivir associated bradycardia might reflect more favorable disease course and has a substantial potential for improving prognostication of COVID-19 patients.

Thus, the most frequent cardiovascular “adverse drug reaction” to remdesivir seems to be the sign of good prognosis. Underlying mechanisms of these phenomena are unknown at the moment.

Keywords: SARS-CoV-2; COVID; cardiovascular side effects; adenosine; remdesivir

S12 - ONCOLOGY PHARMACIST AND RATIONALIZATION OF RESOURCES IN HOSPITAL

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Introduction: Current trends in healthcare expenditures suggest an increase at alarmingly high rates. Many EU Member States recorded overall increases of expenses for more than 20 %: Romania, Estonia, Lithuania, Bulgaria, Luxembourg, Germany, Portugal, Austria, Hungary, Latvia, Malta, Czechia, Poland and Croatia between 2012 (for some states 2013 or 2014 have been used for comparison) and 2018. The pharmaceutical expenditure accounts roughly for one-quarter of all healthcare expenditure, and it is a significant driver of rising healthcare cost. In Croatia average increase in expenditure for medicines from 2015 to 2019 was 9.8% annually. Even more worrisome is the increase in expenses of 15.5% in 2019 compared with 2018.

Oncology pharmacists are still insufficiently recognized healthcare professionals in Croatian healthcare system. Therefore, we have presented its economic value in rationalization of resources for medicines.

Methods: We have searched through scientific and professional literature for pharmacoeconomic analyses describing economic impact, rationalization of resources, oncology pharmacist and clinical pharmacist. We have used our own data regarding pharmacoeconomic analysis of the involvement of clinical pharmacist in the hospital medicines policy in a rural area.

Results: Oncology pharmacist is recognized in the European cancer organization (ECO) and involved as a team member in designing the Essential Requirements for Quality Cancer Care guidelines. Oncology pharmacist services are cost beneficial. The involvement of a clinical pharmacist in the hospital medicines policy in a rural area hospital results with an optimisation of investment in medicines and leads to substantial cost savings for the healthcare system.

Conclusion: As a part of the multidisciplinary team an oncology pharmacist can make a significant contribution to rationalization of resources for medicines. Released resources can be used for further investment in medical profession and healthcare quality for oncology patients. Oncology pharmacist is still an underutilized healthcare professional, expert for drugs, in the Croatian healthcare system. Through our joint work we can achieve a better positioning of the oncology pharmacist in the care of oncology patients.

Keywords: oncology pharmacist, rationalisation of resources, cost benefit

S13 - DIGITAL THERAPY IN ONCOLOGY

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Introduction: DTx (Digital Therapeutics) products represent a new category of evidenced-based therapeutic technologies that support clinicians in the delivery of high-quality patient care and consequently improve patient outcomes. DTx delivers evidence-based therapies via software, like mobile health apps, that replace or complement the existing treatment of a disease. Last year (2020), Insider Intelligence expected the DTx space to hit nearly \$9 billion by 2025, but its new forecasts expect DTx to be a \$56 billion global opportunity by 2025.

Methods: We have searched through scientific and professional literature for Digital Therapeutics and its effect on clinical outcomes and pharmacoeconomic analyses in oncology.

Results: From all registered clinical trials over the past 10 years involving DTx around 6% are in oncology therapeutic area. Seventy-seven percent of DTx trials have been sponsored by academia, but there is trend in increase in industry sponsored trials. To address the challenge posed by adaptive software-as-a-medical-device (SaMD) products, the US Food & Drug Administration (FDA) released a discussion paper in April 2019, describing a possible regulatory approach for premarket review regarding machine-learning-driven modifications in SaMD. Cross-industry stakeholders at the Digital Medicine Society (DiMe) and the FDA synthesized best practices from the digital health field, and created *The Playbook*, the comprehensive and accessible *how-to* guide to support all stakeholders working to advance the safe, effective, ethical, and equitable use of digital clinical measures to improve outcomes. Nevertheless, besides regulatory advancements in the DTx area the most important benefit of DTx are its effect on the patient centred outcomes. DTx prolonged overall survival in cancer patients with metastatic solid tumors and nonprogressive patients treated for metastatic lung cancers.

Conclusion: DTx emerge as great technologies that can directly impact disease state measures and clinical outcomes, expand access to safe, confidential, and effective medical treatments, extend clinicians' ability to care for patients, maximize patient engagement, and lower overall healthcare costs.

Because of their easy accessibility, record of improving outcomes and ability to integrate into care management workflows, DTx products are becoming critically important tools for the healthcare.

Keywords: digital therapy, oncology, accessibility, improving outcomes

S14 - EDUCATION OF PHARMACY TECHNICIANS IN ONCOLOGY PHARMACY

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A pharmacy technician is a health worker, a direct associate of a pharmacist and is a part of a pharmacy team. The integration of pharmacists into the health care system, while providing more services in the context of the development of pharmacy care, necessarily expands the field of work and responsibilities of a pharmacy technician.

The development of oncology pharmacy and the central preparation of antineoplastics in Croatian hospitals incorporates the work of a pharmacy technician, which has to acquire a new set of skills and knowledge. The only way to achieve this is through formal and organized education, which is still not the case. Up until now, the pharmacist responsible for the central preparation of antineoplastics at the hospital pharmacy conducted the training.

Recommendations *Quality Standard for the Oncology Pharmacy Service – QuapoS*, clearly emphasize the need that employees must be adequately educated and trained in aseptic working procedures and in the handling of hazardous substances before they start working. This also in accordance with the *Law on the Quality of Health Care and Social Welfare*.

Practical training consist of, for example, aseptic working techniques and their verification in working process simulations during the preparation, handling of disposable products, simulation of accidents and their management, packaging, distribution and disposal of contaminated material, handling of protective equipment in case of spillage. Each training must be properly recorded and stored in the pharmacy, in accordance with the quality documentation.

There is no special education for safe handling of antineoplastics for pharmacy technician at the level of public pharmacy.

Accordingly, it is necessary to regulate the professional development of pharmacy technicians at the state level. This the responsibility of Croatian Chamber of Pharmacist and it can be achieved by incorporating professional development into the Pharmacy Act, through which all pharmacy technicians would have the right and obligation to acquire a new set of skills and knowledge.

Keywords: pharmacy technician, education, practical training, the professional development of pharmacy technicians

S15 - CENTRAL PREPARATION OF CYTOTOXIC DRUGS – ESTONIAN EXPERIENCE

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Centralized preparation of anticancer drugs was started in Estonia in 2008 when the first centralized preparation unit was opened in North Estonian Medical Centre in Tallinn. Since then several other hospitals have started to prepare anticancer drugs in hospital pharmacy and currently there are 6 different hospital pharmacies all-around Estonia that are preparing anticancer drugs.

North Estonian Medical Centre is one of the biggest oncology centers in Estonia and last year we prepared over 32 000 patient based anticancer drugs (including monoclonal antibodies) compared to over 14 000 preparation in 2008 when we started. Over the past 13 years we as pharmacists have progressed and developed our processes and right now we are also providing preparation service to other hospitals - Tallinn Children's Hospital and West Tallinn Central Hospital. When we began, we started in *full package* meaning we had all the necessary tools and devices necessary and it was done by all the participating parties – pharmacy, wards. We started with computerized ordering and preparation program (Cato) and it was agreed that all the user groups would start using it at once and it was one of the key attributes for our early success. As the workload has increased over the years, there was need of change in our daily workflow. One of the issues we are facing is prolonged waiting times for patients and it was clear that the actual workflow is not suitable for current situation. To provide continuous service and decrease waiting times we started analyzing our workflow and made corresponding changes to our clean room routine. We changed the working shifts and agreed with the physicians that they order therapies in advance so that we can master our preparation workflow better. Currently our daily workflow is organized with three pairs working in shifts and there are two pairs preparing and covering the busiest time. The next step in the process of optimizing preparation and patient waiting time we looked for another practice that is used – dose banding. Before implementing dose-band analyze of drugs, dosages, stability data and NHS dose-band guidelines was done together with the physicians. The choice of most commonly used drugs in most common dose ranges such as oxaliplatin, carboplatin etc. was chosen and step-by-step implemented into everyday practice in March 2021.

Keywords: centralized preparation unit, workflow, everyday practice, dose-band

S16 - ROLE OF A PHARMACY TECHNICIAN IN CENTRALIZED PREPARATION OF ANTINEOPLASTIC AGENTS

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Pharmacy technician is a part of team in centralized preparation of antineoplastic agents, as defined by QuapoS - Quality Standard for Oncology Pharmacy Service. General Hospital Varazdin began with the central preparation in January 2009, and the team consists of two pharmacists and three pharmacy technicians.

Pharmacy technicians in General Hospital Varazdin were educated and trained by MPharm Ana Toplak, who was in charge of the centralized preparation. The centralized preparations are made in a dedicated room within the pharmacy specially equipped for work in aseptic terms. Preparations are made based on the physicians prescription for a single patient.

Tasks of a pharmacy technician in handling cytostatics include : acceptance of drug deliveries, transporting the deliveries (to the cytostatics unpacking site without opening), removing secondary and cleaning the primary packaging, transport to the storage location (cytostatics safe or refrigerator), production, labeling, release, cleaning the laboratory including cytostatic isolator, decontamination after inadvertent release of cytostatics, action in the case of incidents or accidents and waste disposal. Proper use of the personal protective equipment is necessary when preparing cytostatic products to protect the staff, product and the working environment.

The staff assigned to the preparation of cytostatics must have adequate knowledge of drugs, solutions and technical equipment used in the process. Continual training in preparing cytostatics, working in aseptic procedures and using new techniques is needed.

Pharmacy technician role in centralized preparation of antineoplastic agents is very demanding and responsible. It is necessary to work as a team with a pharmacist. The employees must be sufficiently educated with regard to aseptic procedures and handling of hazardous substances before assuming work.

Keywords: pharmacy technician, centralized preparation of antineoplastic agents, the team, General Hospital Varazdin, education

S17 - MULTIPROFESSIONAL AND INTERDISCIPLINARITY - TWO SIDES OF THE SAME COIN

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The common description of cooperation with patients has been given the term interdisciplinary for decades. It has become common practice to subsume all professions under this term.

When all well-known professional groups began to work together, in addition to various medical disciplines, nursing staff, psychologists and pharmacists at the ERQCC, it quickly became clear that the term had to be expanded and that we would have to speak of multi-professional action in the future.

However, if we look at the accompaniment and care of cancer patients, intensive treatment in clinics only takes place for a short period of time. Outpatient support, particularly through public pharmaceutical services, is required to a greater extent.

It seems appropriate to perceive the various disciplines of our profession as part of the overall process and to provide them with appropriate information so that there are no treatment breaks for cancer patients.

Keywords: multiprofessional, interdisciplinarity, outpatients, care, cancer patients

S18 - IMACT OF DIGITAL TRANSFORMATION ON SAFETY, QUALITY AND COMMUNICATION IN THE FIELD ON ONCOLOGY PHARMACY

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Digitalisation can be considered as the first step to digital transformation of any organisation. Once we have digitised our business documentation, whether it is changed from physical to a digital form or created digitally in the very beginning of the working process, it is possible to store, share and dynamically reuse information that opens almost unprecedented opportunities. Digital transformation appears to be continuous and endless process in which we transform our business models and processes thus achieving better quality, safety and communication by intensive adaptation of digital technology solutions.

New disruptive technologies will have significant influence on health sector in order to improve health care services. It is expected that technologies such as Advanced Genomic Analysis, Big Data, Artificial intelligence, Internet of Medical Things (IoMT), Robotics, 3D printing will also have a great impact on oncology pharmacy. New faster, more comprehensive and affordable DNA method of analysis enables detecting genetic changes connected with specific diseases of specific patient, leading to the personalised medicine. IoMT smart solutions with sensors integrated in various types of wearable and implantable devices enables collecting different patient health parameters, monitor patient condition remotely and adjust more precisely regular therapy application without necessary need that patient visit a hospital. Engaging of Big Data and Artificial intelligence capabilities by gathering health data from different non-clinical and clinical sources (Real World Data) and conducting real time analysis of health data, will significantly improve new drugs production and enhance time to market processes.

Automation of business processes in oncology pharmacy can be supported with software and technical solutions in order to improve procurement processes, drugs and medical material distribution management, production of antineoplastic drugs and other preparations and also many other daily repetitive tasks. In addition, full automation of some working processes is done by implementing smart robotics systems.

Digital transformation brings almost unprecedented opportunities for improvement and in the same time faces organisations with many challenges by having a comprehensive influence on changes in organisations including business processes, people and technology. It is expected that new technologies in oncology pharmacy will improve accessibility and quality of health care, improve working processes and make it easier to medical professionals, improve safety, quality and patient health outcomes.

Keywords: digital transformation, disruptive technologies, business processes, oncology pharmacy

S19 - THE IMPACT OF PATIENTS' CHARACTERISTICS AND DISEASE-SPECIFIC FACTORS ON THE FIRST-LINE TREATMENT DECISIONS FOR METASTATIC BRAF-MUTATED MELANOMA

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Overview: Melanoma is aggressive cancer with a historically poor prognosis for patients with unresectable or metastatic disease. Before 2011, systemic treatment had little impact on survival for metastatic melanoma. Since then, several targeted therapies (BRAF- and MEK-inhibitors for patients with BRAF V600 genetic mutation) and immunotherapies (immune checkpoint inhibitors, ICI) have been developed and approved for the treatment of melanoma. With new therapies available and introduced into clinical practice, treatment decisions have become increasingly complex and multifactorial.

Many guidelines, both international and national, on the management of advanced melanoma are available. However, while a helpful tool, they are of limited value because, due to the rapidly changing treatment landscape, it is difficult to update the information frequently enough, so they quickly become outdated. Additionally, they could be difficult to interpret and implement in clinical practice because some terms used (e.g., tumor burden) are not clearly or consistently defined. Some national guidelines have limited relevance when selecting a type of treatment if they only include funded or reimbursed drugs in a specific country.

Due to the lack of clinical evidence for many specific treatment decisions, the guidelines should only be, as the name says, a guide or direction for clinical decision-making, not the ultimate tool. There is no consensus on the factors that should guide the choice of first-line treatment (targeted therapy or immunotherapy) in clinical practice. However, there is a general agreement that no single treatment algorithm can or should be followed in all patients.

We focus on the patients' characteristics and disease-specific factors that influence first-line treatment choices in advanced (unresectable or metastatic) BRAF V600-positive melanoma patients and their use in clinical practice.

Influence of disease-specific factors (tumor burden, disease tempo, brain metastases or critical visceral metastases, LDH, PD-L1) on first-line treatment decisions:

The concepts of tumor burden and disease tempo or pace are difficult to define and measure because they involve multiple interrelated components. The thresholds for defining high or low tumor burden are not clear nor universally accepted. For instance, NCCN guidelines state quite simplistically that tumor burden can be defined by the size and number of tumor deposits but without clear thresholds. The presence of brain metastases or metastases in critical visceral sites (e.g., heart) is a negative prognostic factor and urges for quick treatment response. In these patients with *a single shot* chance of therapy to be effective, it is even more crucial to choose well. The choice between targeted therapy and immunotherapy, especially if combo-immunotherapy is available, can be difficult.

LDH level is an important factor that relates to both tumor burden and disease tempo. LDH is a surrogate for tumor burden and an important prognostic and predictive indicator of worse clinical outcomes

and lower response to therapy with higher mortality rates. PD-L1 status in melanoma is not routinely measured because even patients with low PD-L1 expression in tumor tissue can benefit from immunotherapy.

Influence of patient characteristics in first-line treatment decisions:

Patients characteristics, namely age, comorbidities, concomitant medications, performance status, treatment expectations, view on potential treatment toxicities and their impact on quality of life, preferences of drug application mode (oral versus parenteral), all play an important role in the decision-making process and should not be minimized.

Influence of drug-related characteristics in first-line treatment decisions:

Drug-related adverse events are utterly different in targeted therapy and immunotherapy and play an important part in the choice of first-line treatment. Parameters that should be considered in the context of toxicity are patient comorbidities (e.g., autoimmune diseases, immunosuppressive therapy) and patients' preferences; the informed patient decision should be achieved regarding the willingness to accept risks of specific drug toxicities.

Socioeconomic factors, including the reimbursement status and funding of different therapies, also influence the treatment choice in some cases.

The choice of first-line treatment in BRAF-positive advanced/metastatic melanoma patients is a complex task that should be discussed within the multidisciplinary tumor board to seek consensus.

Further clinical research on advanced melanoma is necessary to refine treatment decisions and personalize treatment based on patients' characteristics and disease-specific factors. The results of trials that would directly compare BRAF/MEK-targeted therapies with anti-PD-1 immunotherapies, *head to head*, would be necessary in this context.

Clinical trials that include patients with unfavorable prognostic indicators (i.e., bulky disease, brain and/or visceral metastases, elevated LDH...), as well as patients who generally do not qualify for inclusion in trials, for instance, those with poor performance status (ECOG status ≥ 2), will also be important for understanding appropriate treatment decision-making in a more clinically relevant patient population. However, until further clinical evidence is available, clinical judgment will remain the essential element of first-line decision-making.

Conclusion: First-line treatment decisions in advanced melanoma are complex and multidimensional. It is difficult to apply an algorithm that would be relevant to all patients. Multiple interrelated factors must be considered, and treatment must be personalized, individualized to the patient.

Choosing a first-line treatment for advanced/metastatic melanoma is a complex, multifactorial procedure that requires a multidisciplinary approach. Clinical judgment, taking into account numerous patient-related and disease-related parameters, remains the most crucial element of decision-making until research can provide clinicians with better scientific parameters and tools for first-line decision-making.

Keywords: advanced/metastatic melanoma, BRAF/MEK inhibitors, checkpoint inhibitors, factors, first-line treatment decision, selecting therapy

S20 - PROFESSIONAL EXPOSURE TO ANTINEOPLASTIC DRUGS – TOXICITY CLASSIFICATION

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Professional exposure to hazardous drugs is something that medical personnel meets in everyday work especially in units dedicated to compounding and administration of antineoplastic therapy.

Hazardous drugs are identified as being carcinogenic, teratogenic, genotoxic or as having other developmental, reproductive or organ toxicity regardless of dose; or a similar profile to drugs already considered hazardous. Therefore, in occupational terms, they are defined as agents that, due to their inherent toxicity, present a danger to healthcare personnel.

As a class, hazardous drugs may include cytotoxic drugs, certain antiviral drugs and hormones as well as other drugs fitting the term of hazardous drugs.

The term *cytotoxic drug* is frequently used as a synonym for oncology or antineoplastic drugs and it is used in a variety of regulations for pharmaceutical development and manufacturing of drugs as well as in regulations for protecting medical personnel from occupational exposure in pharmacy, hospital, and other healthcare settings. Also, regulations relating to health protection of employees occupationally exposed to cytostatics are not synchronised as they are derived from different areas of the law. Therefore a classification of hazardous drugs plays an essential role in determining suitable handling procedures for certain product.

In Europe there is no one common classification for hazardous drugs. Suggestion is up to each hospital to develop its own list with reference to available literature. These requirements are difficult to follow as the list of new antineoplastic drugs increases rapidly each year. For example, monoclonal antibodies are a novel class of agents and therefore lack information concerning hazards for healthcare workers. Since they are drugs used in cancer treatment they have been included in hospital hazardous drug lists. However, it was recently reported that they do not represent a significant risk to healthcare personnel because of their large molecular weight that would be expected to limit bioavailability and toxic potential.

In the United States the National Institute of Occupational Safety and Health (NIOSH) has developed a list of hazardous drugs that is updated regularly. NIOSH classifies drug as hazardous when it poses any one of the following six characteristics: carcinogenicity, teratogenicity or other developmental toxicity, reproductive toxicity, organ toxicity at low doses, genotoxicity, structure and toxicity profiles of new drugs that mimic existing drugs

Keywords: antineoplastic, classification, cytotoxic, NIOSH, professional exposure

S21 - UPDATES IN THE MANAGEMENT OF CHEMOTHERAPY INDUCED NAUSEA AND VOMITING

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Nausea and vomiting are common symptoms in cancer patients and may occur together, separately, in the acute or delayed phase after administration.

Actually, we have a good number of antiemetics approved or in clinical studies but the use depends on emetogenic potential of single antineoplastic agents and depends on age, sex, general conditions and interactions with other drugs.

We can divide the antineoplastic agents in three groups: high risk, moderate risk and low risk to generate emesis; we can use a specific drug, alone or in combination for each group.

Drug-drug interactions are not to be underestimated: we have to be careful with antiemetics interacting with several drugs such as diuretics, warfarin and even chemotherapy drugs.

The best way to use antiemetics is to follow the guidelines of the most important Scientific Societies such as National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO), Multinational Association of Supportive Care in Cancer (MASCC) and European Society of Medical Oncology (ESMO): the guidelines are always being updated and are very helpful in clinical practice.

Management of chemotherapy induced nausea and vomiting (CINV) is important both for the patient's quality of life and to ensure the best possible anticancer treatment.

It is very decisive to know the characteristics of the patient and concomitant therapies: the importance of always being updated on the guidelines combined with sharing experience with colleagues represent the key to being able to assist patients throughout the care process.

Keywords: nausea, vomiting, chemotherapy

S22 - COVID-19 VACCINES IN CANCER PATIENTS

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Clinical trials prior to licensing of COVID-19 vaccines collected key information on effectiveness and safety in general population. During rollout of COVID 19 vaccines, larger and diverse populations is vaccinated. Certain groups, e.g. immunocompromised patients or pregnant women, have not been included in pivotal clinical trials or number of patients included was small. Only approximately 4 percent of the patients enrolled in the phase III trial of Pfizer COVID-19 vaccine had a malignancy of any type, and these patients were not analyzed separately to assess vaccine efficacy; patients with cancer were not enrolled on the Moderna COVID-19 vaccine trial. In the Janssen COVID-19 vaccine phase III trial, only 0.5 percent of patients had cancer. Licensure of a vaccine that is rolled out to a large population in a short time requires not only regular spontaneous reporting but also cohort event monitoring to obtain more in-depth information on the safety of the vaccines.

A large-scale cohort event monitoring system is very useful for newly introduced vaccines or for new target groups, in addition to existing spontaneous reporting systems and healthcare database studies (i.e. secondary data), as it is complementary to these systems in several ways. It generates more comprehensive safety data, e.g. on disease course and impact of the adverse events. Moreover, in contrast to spontaneously reported data, the denominator of the studied cohort is known (in real time) so that adverse drug reactions frequencies can be calculated. Therefore, European medicines agency started study *Cohort event monitoring to assess safety of COVID-19 vaccines using patient reported event* in several European countries including Croatia to collect more data especially in immunocompromised patient, pregnant woman and patients with allergy in medical history. In Croatia all vaccinated adults can be included up to 6 days after the first or the third dose (more info: <http://www.halmed.hr>).

Clinical Guidances suggest that all individuals with active or prior cancer who are eligible for vaccination according to local allocation priorities be fully vaccinated to prevent SARS-CoV-2 infection. Immunocompromised patients may have attenuated immunogenicity to the COVID vaccines, but vaccination is still recommended in immunocompromised populations. For individuals undergoing hematopoietic cell transplantation (HCT) or cellular therapies such as chimeric antigen receptor (CAR)-T-cell therapy, clinical guidances usually suggest waiting at least three months for vaccination, if possible. Given the potential for a blunted immune response to vaccination, it is important to counsel immunocompromised patients on maintaining personal protective measures despite vaccination.

Keywords: COVID 19 vaccines, cancer, safety

S23 - ESMO GUIDELINES FOR USE OF NEXT GENERATION SEQUENCING FOR PATIENTS WITH METASTATIC CANCERS

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Based on the current evidence, ESMO recommends routine use of next-generation sequencing (NGS) on tumour samples in advanced non-squamous non-small-cell lung cancer, prostate cancers, ovarian cancers and cholangiocarcinoma. In these tumours, large multigene panels could be used if they add acceptable extra cost compared with small panels. In colon cancers, NGS could be an alternative to PCR.

Based on the KN158 trial it is recommended to test tumour mutational burden (TMB) in cervical cancers, well- and moderately-differentiated neuroendocrine tumours, salivary cancers, thyroid cancers and vulvar cancers, as TMB-high predicted response to pembrolizumab in these cancers. Study was not agnostic but limited to few cancers, additional studies are needed before implementing TMB in all cancers where anti - PD(L) 1 antibodies are not approved.

Outside the indications of multigene panels, and considering that the use of large panels of genes could lead to few clinically meaningful responders, ESMO acknowledges that a patient and a doctor could decide together to order a large panel of genes, pending no extra cost for the public health care system and if the patient is informed about the low likelihood of benefit.

ESMO recommends that clinical research centres develop multigene sequencing as a tool to screen patients eligible for clinical trials and to accelerate drug development.

Keywords: ESMO recommendations, next-generation sequencing (NGS), metastatic cancers

S24 - NEWS IN THE TREATMENT OF SOLID TUMORS - ASCO, ESMO HIGHLIGHTS

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Although cancer is one of the major public health problems worldwide and one of the leading causes of death, cancer mortality projections for 2021 confirm the persistent declines in cancer mortality in EU and US for many specific cancers. Despite the many problems and health challenges the last two years, we have seen impressive progress in many areas of cancer research. Many new drugs, new combinations and indications were approved in oncology in the last year as : antibody drugs conjugates (ADC) sacituzumab govitecan in TNBC and advanced urothelial cancer, fam-trastuzumab deruxtecan-nxki (T-DXd) in metastatic HER2 positive BC, tucatinib, a small kinase inhibitor in BC, lorlatinib - the third generation of ALK-inhibitors in the treatment of advanced NSCLC, osimertinib in adjuvant therapy in patients with non-small cell lung cancer (NSCLC), new immunological drugs and their combinations in different types of tumors and many others. With increasing advancements in biomarkers and personalized medicine genomic-guided trials have been developed. Many of this trial are included in the group of basket or umbrella trials under the master protocols framework based on the genomic alterations or technique such as NSG. There are many examples of such randomized studies that have been reported to date, for example French Shiva trial, MOSCATO 01 study, MyPathway study, TAPUR study, and some newly designed studies like WINTHER, I-PREDICT study and many more. During the virtual 2021 ASCO Annual Meeting and ESMO Congress important results from many clinical trials and potentially practice-changing studies in both solid tumors and hematologic malignancies were presented. Among such interesting studies presented at 2021 ASCO meeting and ESMO Congress are results in genitourinary cancers (STAMPEDE trial, PEACE 1 and 3, VISION, NORSE), breast cancer (DESTINY Breast03, KEYNOTE-355, TULIP, MONA-LEESA-02), gastrointestinal cancer (DESTINY CRC01, CheckMate 648, CheckMate 649, EPOCH) and lung cancer (DESTINY Lung01, Impower010, CheckMate 816, CheckMate 9LA, CodeBreak 100).

Keywords: oncology news, systemic therapy, ASCO 2021 highlights, ESMO2021 highlights

S25 - PHARMACY TECHNICIAN IN COMMUNITY PHARMACY – SUPPORT FOR ONCOLOGY PATIENTS

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Introduction: According to valid Pharmacy Law (NN 117/08), pharmacy technicians who have passed the professional exam participate in performing pharmacy activities. Pharmacy technicians can work in pharmacy activities only in presence of the pharmacist in accordance with the scope of work for pharmacy technicians. They can't dispense prescriptions medicines, medicines with opioid ingredients or compound medicines that include substances of strong or very strong action.

According to Croatian Health Insurance Institute, personnel norm for the pharmacy team in community pharmacy that provides service in 2 shifts has to consist of 2 pharmacists and 1 pharmacy technician.

Therefore, pharmacy technicians are essential in the primary health care and they assist pharmacists in providing pharmaceutical care, including oncology patients.

Methods: Oncology patients visit community pharmacy for various reasons. They either come to pick up their prescription medication for further treatment of the disease in their home setting or to pick up prescribed enteral nutrition or orthopedic aids. Likewise, oncology patients at community pharmacy are asking numerous questions about dietary supplements that they believe can help them treat cancer. Also, they are seeking for professional advice in skincare after chemotherapy or radiotherapy or other supportive treatments that do not include prescribing from the oncologist.

Considering the Pharmacy Law, pharmacy technicians are allowed to inform patients about orthopedic aids, dietary supplements and dermatological skincare that will improve the side effects of oncology treatment.

Pharmacy technicians in the community pharmacy laboratories have the opportunity to produce extemporaneous and galenic preparations with a minimum number of components of proven quality and controlled origin, which are compounded under the professional supervision of a pharmacist, the only highly educated health professional with education in that field. Extemporaneous preparations are made in collaboration with doctors and are tailored to the individual needs of patients.

With proper training, pharmacy technicians can take on an expanded role to aid pharmacists with advanced pharmacy care services like care for the oncology patients. Pharmacy technician in community pharmacy in their scope of work has to be able to recognize and identify different needs of oncology patients in order to improve their quality of life.

Consistent training of pharmacy technicians through continuing education or taking advantage of on-the-job learning opportunities could improve their job performance. However, continuing education after passing professional exam is not required among pharmacy technicians in Croatia and on-the-job training may be inconsistent and depend on the availability and ambition of the pharmacy technician.

Croatian society of pharmacy technicians as the only organized institution for pharmacy technicians rarely organizes educations that are not available for all pharmacy technicians in Croatia, because educations are mainly based in the capital of Zagreb. Also, educations are product oriented because they are sponsored by pharmaceutical industry, instead of being competency developing.

In the presence, only Farmacia Community Pharmacy Chain has in-house education in the field of oncology in community pharmacy that includes pharmacy technicians and there are not regional and national courses and qualifications available.

It is needed for pharmacy technicians nationally to keep their skills and knowledge up to date with annual continuing professional development (CPD) and hopefully it is going to be regulated in the new version of Pharmaceutical Law.

Results: Previous studies have reported that education level, continuing education and training of pharmacy technicians have been associated with impacting patient safety outcomes in community pharmacies, including oncology patients.

Conclusion: Pharmacy technicians with proper training, in their scope of work, can be support for oncology patients in community pharmacies, improving quality of life for the patients by providing them proper information for supportive treatments without prescription.

Keywords: pharmacy technician, oncology patient, community pharmacy

S26 - PHARMACEUTICAL CARE FOR ONCOLOGY PATIENTS IN COMMUNITY PHARMACY

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Introduction: Community pharmacy plays an important role in the care of oncology patients, with contact throughout the pathway from prevention and treatment to living with and beyond cancer. Primary health care pharmacies provide an accessible place for patients to get not just their prescribed medicine, but important advice and support during the treatment.

The importance of community pharmacy in oncology continues to grow, with an increase in the number of oral anti-cancer therapies that can be dispensed, as well as improvements in therapy leading to more patients living with cancer as chronic condition.

By 2020, nearly half the population in the Europe will be estimated to get cancer at some point during their lifetime – that's 50% or more of all patients walking through the doors of a community pharmacy.

There is a high demand and pressure across the healthcare system – the long-term plan emphasises the importance of shifting care where appropriate to the primary health care sector to improve patient experience and outcomes.

Methods: Community pharmacists are healthcare professionals who need to take on more specialist knowledge in order to facilitate delivery of optimised and integrated care for oncology patients.

Education and training are necessary providing up-to-date knowledge and relevant training to community pharmacists. Transfer of knowledge has to be provided by clinical care specialist in the oncology field.

Community pharmacists who finish oncology education need to get accreditation for providing oncology patient service. Education also needs to be delivered publicly to other healthcare professionals and patients to increase their understanding of the services community pharmacies can offer.

Pharmacists in primary health care need to fully understand the safety, efficacy, pharmacologic and financial components of care for oncology patients. Their extensive education and training has to prepare them with an in-depth knowledge of treatment medicines as well as the ways these medicines and targeted therapies can affect patients. They have to understand treatments' impact on patients in terms of interactions with other prescribed medicines, OTC and dietary supplements. Also, impact on patients' other diseases or health issues, as well as spotting and managing side effects.

European Society of Oncology Pharmacy (ESOP) is empowering pharmacists to improve health care for oral chemotherapy patients. Therefore, ESOP established a project named European best-practice model (EPIC) that is targeting pharmacists in community and hospital pharmacies and empowering them to significantly address the issue of patient safety for cancer patients on oral anticancer therapy. EPIC is available only in Estonia and Slovenia as e-learning course and as face-to-face one day educational event in Slovenia. The programme is divided to three modules and every part is completed by passing a test.

Farmacia community chain through its Educational centre established their education in oncology on monthly basis, started in 2019 and from 2020 it is available as on-line education. The programme includes etiology, epidemiology, cancer biology (disease development, staging etc.), basic principles of solid cancer and most common malignancies treatment (surgery, radiation, medical therapy), the princi-

ples of chemotherapy, hormonal therapy, targeted therapy and immunotherapy, overview of most common side effects of cytotoxic drugs, hormonal drugs and other oral anticancer drugs. Directions of use, how to find information (both pharmacists and patients), evidence of using alternative medicines, dietary supplements, herbal medicine, drug-drug and drug-food interactions, introduction of case reports. As well it includes principles of safe handling of medicines in a pharmacy and at the patient's home, support of patients in the treatment with oncologic medicines by pharmacists and counselling the patients.

There are a variety of services that could be delivered by community pharmacies to address: prevention of cancer, management of chemotherapy related toxicities through providing of OTC treatment and advice, counselling for patients on oral antineoplastic treatment and well-being services for patients living with and beyond cancer.

These services have to be arranged at national level through Pharmacy Law and counselling oncology patients in community pharmacies has to be accredited.

Collaboration between community pharmacies, patients and physicians is a key enabler to managing care effectively.

Results: In Farmacia community chain, in total 67 pharmacists are attending education in oncology on monthly basis which makes 39% of all employed pharmacists that makes base for quality oncology patient care after finishing the programme.

Conclusion: It is essential to establish national quality standards, best practice benchmarks, standard operating procedures, education and other processes for community pharmacies to enhance oncology patient care and to achieve their better quality of life.

Keywords: community pharmacy, oncology patient, pharmaceutical care

S27 - METASTATIC BREAST CANCER - CHRONIC DISEASE?

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Metastatic breast cancer means the spread of malignant cells from primary tumor to other organs in the body. Today, it is still deadly malignant disease and treatment is approached with the aim of prolonging survival and preserving quality of life, achieving as long as possible control of the disease. This ultimately strives for such a long control of disease that the lifespan of the patient is shortened less and less. Are we on the right track? When we look at breast cancer as a heterogeneous disease, with several subtypes, such as hormone-dependent cancers (HR +), HER2 positive, and triple-negative breast cancer (TNBC), it is really difficult to answer that question unequivocally. Situation with metastatic TNBC, which affects about 15-20% of patients, is the worst. Survival results of contemporary cohort of these patients show median of only 15 months overall survival. Causes probably lie in the fact that it is a very heterogeneous disease, and therapeutic possibilities are narrowed. Basis of treatment is chemotherapy. New drugs in the field of immunotherapy bring somewhat of the benefit in survival, but only in case of adequately expressed immune marker. For a small proportion of patients with BRCA inherited mutation, some benefit was demonstrated with PARP inhibitors. TNBC is still an unmet need and hope is being placed in new drugs, such as antibody-drug conjugates, which conceptually mean chemotherapy in specific intensified doses. In HR + breast cancers, which are also the most common subtype (over 2/3 of patients), there has been tangible progress in recent years. In addition to antihormonal therapy, which is the basic mechanism of disease control, CDK4 / 6 inhibitors are now standardly used as a targeted effect on cell cycle, which significantly extended time of disease control and overall survival of these patients. Unfortunately, today we still do not have equally good therapeutic options after first-line treatment, but some benefit in further disease control is achieved by other targeted drugs, such as mTOR inhibitors or PI3K inhibitors, if there is a mutation, and at some point it is necessary to introduce chemotherapy. With the described therapeutic choices, today these patients achieve median close to four years of survival. Longest survival is achieved in patients with HER2 + breast cancer. It is in nature very aggressive disease, but also a good example of how targeted sequencing of therapeutic choice, which always retains the basic – targeted, antiHER2 therapy, achieves very significant prolongation of overall survival of these patients, with median up to five years. Those are the drugs such as dual HER2 blockade by trastuzumab and pertuzumab, antibody-drug conjugate trastuzumab-emtansin and trastuzumab-deruxtecan, and a number of small molecules, anti-HER2 tyrosine kinase inhibitors. Targeted antiHER2 therapy, which remains the basis for treatment of HER2 positive breast cancer in combination with chemotherapy, antihormonal therapy, and less likely in the future with immunotherapy, has almost completely changed the natural course of an aggressive malignancy and thus achieved most in the pursuit of metastatic breast cancer to become chronic disease.

Keywords: breast cancer, metastatic disease, luminal breast cancer, HER2 positive breast cancer, triple negative breast cancer

S28 - ROLE OF COMMUNITY PHARMACIST IN PREVENTION AND TREATMENT OF MELANOMA PATIENTS

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Introduction: Skin cancer incidence is increasing alarmingly, despite current efforts trying to improve its early detection. In the last 30 years, the number of patients with malignant melanoma in the European Union has doubled, but although the number of diagnosed cases in Croatia is at the European average, the fact that the mortality rate is even 50% higher than the average mortality rate for EU countries is worrying.

The World Health Organisation recognises that community pharmacists are the most accessible healthcare professionals to the general public. Studies have shown that community pharmacies provide easy and equitable access to healthcare. Most patients regularly visit community pharmacies for health information and also seek advice from pharmacists with respect to signs and symptoms of cancer.

Methods: Community pharmacists are in a good position to raise awareness when they counsel people who buy over-the-counter medication and dermocosmetic products for the prevention of possible cancer-related symptoms. To be able to achieve this, as healthcare providers in the community, pharmacist must be able to differentiate between conditions that require self-medication and those that need the attention of a physician. They must be able to identify the common signs and symptoms of cancer. As readily accessible health care professionals, community pharmacists are in the best position to include skin cancer-preventing initiatives into their practice.

As one group of health professionals, pharmacists have great potential as skin cancer prevention educators because they are viewed as credible, have the opportunity to help the patient select an appropriate sunscreen product, come into contact with large numbers of individuals, and routinely counsel patients on prescription and over-the-counter medications and other health topics.

Risk factors for skin cancer are skin type, number of moles, genetic predisposition, age, but a key and most important risk factor is exposure to UV rays. The Sun Protection Factor (SPF) is the primary measure of the effectiveness of a sunscreen. The SPF factor is the ratio of the minimum UV dose required to produce erythema (MED-minimum erythema dose) on skin protected by a specific product and unprotected skin. The PPD (Persistent Pigment Darkening) estimates the pigmentation that occurs two hours after the end of exposure to UVA rays.

Scientific studies have shown that certain biological damage to the skin can be prevented and reduced if the ratio of UVA to UVB is 1/3. Proper application of sunscreen is extremely important to protect the skin from UV rays. Sunscreen acts as a filter for UV rays, preventing their penetration into the skin and thus cell damage caused by the sun.

Research has found that many people do not understand how to read labels on sunscreen products and how the product protects the skin. Only 43 percent of respondents understood the meaning of SPF values.

Pharmacists can be a valuable source of information about sun protection because many sell a range of related products. Pharmacy-based information on skin cancer prevention raises awareness, but more research is needed to see whether this heightened awareness has a positive effect on behaviour patterns. Pharmaceutical sunscreen preparations contain a minimum of chemical and mineral filters to reduce the

incidence of allergic reactions while providing adequate sun protection and are intended for the most sensitive skin.

Pharmacists in community pharmacies most commonly encounter the side effects of melanoma therapy such as dry skin, itching, hand–foot skin reaction, desquamation, or acne/acneiform eruptions.

Results: Pharmacies are becoming a place recognized by oncology patients as a professional corner for skin care advices that can be corrected and / or mitigated by appropriate care. At the same time, there is an awareness that dermocosmetic lines found in pharmacies, have a measurable difference from those in perfumeries or drugstores, have a significantly higher concentration of active ingredients with clinically proven results, that they are made to the high requirements of the pharmaceutical industry, and that there are formulations that they do not have preservatives and emulsifiers in their composition and are indeed hypoallergenic with 0% chemical ingredients.

Conclusions: Expanding the health promotion role of pharmacists in regard to sun protection and establishing appropriate infrastructure support to enable community pharmacies to contribute effectively in co-operation with other health professionals and related services is necessary to improve melanoma incidence.

Keywords: community pharmacy, melanoma prevention, side effects of melanoma treatment

S29 - PHARMACOGENOMICS IN COMMUNITY PHARMACY – PRESENT OR FUTURE?

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Introduction: The International Pharmaceutical Federation (FIP) in their Community Pharmacy Vision 2020 – 2025 presents that pharmacogenomics testing is going to be an available service for the patients in community pharmacies.

In addition to our age, gender, lifestyle, and health status, our genes also affect our response to medications. The influence of genetic factors on how we respond to drugs is very high, up to 95%.

A modern branch of personalized medicine called pharmacogenomics studies this relationship. Personalized medicine is the medicine of the future and aims to tailor healthcare to decisions and treatments tailored to each individual in the best possible way.

Although genomic testing is still relatively new when deciding to prescribe drugs, this area is expanding rapidly. Currently, more than 350 drugs have data related to pharmacogenomic biomarkers that identify genetic information useful for individualizing drug prescribing, and the list of drugs is constantly updated.

Methods: Knowing exactly which medicine to use for a patient and which to avoid can be a challenging task in clinical practice. However, pharmacogenomics can provide the prescriber with additional information on some of the unobserved patient characteristics that affect drug response — this can assist with both drug selection and safety. Therefore, the combination of this pharmacogenomic information along with other factors influencing pharmaceutical care may provide an opportunity to deliver more *personalised* medicine, facilitating better selection and reducing the need for *trial and error* prescribing.

One of the main barriers to the implementation of pharmacogenomics in clinical practice has been the translation of pharmacogenomic knowledge to that which is actionable and usable in the clinic. As pharmacogenomics develops, community pharmacists are likely to have a role in providing services to ascertain if people are on the best medicines or them as individuals, using their genomic data.

Sampling is simple, quick and painless, and it involves wiping the mucosa from the inside of the cheek. The DNA sample is sent to the laboratory after which comes the test result with detailed explanations.

The result describes gene interactions with drugs that the patient is currently using, occasionally, or have been prescribed as a previous therapy. The activities of enzymes for metabolizing drugs encoded by certain genes are also described, which provides information on which drugs should have an adjusted dose in the future or should not be prescribed.

Given that pharmacists are drug experts, who help patients interpret the results of this type of testing, and thus doctors in prescribing drugs tailored to the patient's genetic profile, this service is recognized in pharmacies in the US, Canada and began to spread in European countries.

In the Netherlands, the Royal Dutch Pharmacists Association (KNMP) initiated a pilot in community pharmacies with the aim of demonstrating the impact of Pharmacogenomics (PGx) testing by community pharmacists on individual patients. Following development of evidence-based guidelines and having undergone appropriate training, pharmacists collected and interpreted PGx test results, discussed therapy

optimization with other healthcare providers and advised on changes to patients' pharmacotherapy. This led to interventions such as dose adjustments and therapy switches.

Education and training are essential to the delivery of pharmacogenomic testing. Pharmacist training can come in the form of formal postgraduate programmes and online modules designed by the company performing the testing.

As part of the service set-up, pharmacists are encouraged to get in touch with local practices to educate them on pharmacogenomic testing. This is important because the pharmacogenomic test results need to be reviewed by a clinician if the results are to be actioned.

Experience shows that doctors are receptive to pharmacogenomic advice offered by community pharmacists. However, it is important that these relationships are built early, especially if the report results are sent directly to the patient's doctor.

This model of testing carried out in Australia, Canada and the United States is not publicly funded and typically requires payment from the patient.

Results: There is evidence that suggests pharmacogenomic testing could have an effect on improving medicines adherence, improving confidence in deprescribing and facilitating shared decision making. These are all mechanisms that could support medicines optimisation.

Conclusion: Wide application of pharmacogenomic testing and application of personalized medicine will reduce the number of side effects and interactions and improve patient treatment outcomes.

Keywords: pharmacogenomic testing, community pharmacy, adherence, patient outcomes

S30 - ORAL ANTINEOPLASTIC AGENTS IN COMMUNITY PHARMACY

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Introduction: Croatian Health Insurance Institute has approved 302 oral antineoplastic drugs from which 85 of them have different mechanism of action. These agents are used for the treatment of a broad spectrum of solid tumors and hematological diseases. Oral chemotherapy agents are no longer limited to cytotoxic drugs but include tyrosine kinase inhibitors and hormonal treatments now becoming available.

The majority of literature currently states that 25% of all antineoplastic drugs in development are oral medications. This trend is linked to the fact that these treatments are being used for chronic or palliative therapy rather than adjuvant treatment.

Methods: To improve access and affordability of cancer treatments which can be administered at home, such as oral chemotherapy and self-administrable biological medicines, it is important to make use of the highly accessible network of community pharmacies.

European countries where oral antineoplastic drugs are dispensed only in hospital pharmacies are United Kingdom, Poland and Belgium. Countries in which they are dispensed in public pharmacies are Germany, Spain, France, Ireland, Slovenia and Croatia. Community pharmacists in all countries require additional education and training on oral anticancer agents.

Oral anti-cancer agents prevent many people with cancer from numerous hospital visits, allowing them to obtain their medicines from their local community pharmacy. People taking these oral medicines still require support, as many of these agents can cause significant side effects and interactions.

Oral anticancer medication does require the patient to be able to self-manage. Adherence becomes a significant issue here. The World Health Organisation estimates that 50% of medicines taken for chronic conditions are not taken as prescribed. A large number of patients who receive oral anticancer medication are older and often have multiple co-morbidities and consequently need more support because of this. Managing toxicities is also a significant challenge for these patients and the teams supporting them.

About 50% of all oral anti-cancer drugs come with instructions regarding intake in relation to meal-times, as substance absorption can be increased or decreased by food. The patient has a special responsibility to follow the instructions accurately.

Moreover, attention must be paid to a variety of potential drug–drug interactions. Many oral anti-cancer drugs are metabolized by CYP3A4. Inhibitors or inducers of CYP3A4 may reduce the therapeutic effect or elevate the risk of side effects. A retrospective study in the Netherlands found potential drug–drug interactions in 46% of around 900 patients treated with oral anti-cancer drugs; in 16% of patients these were classified as potentially major events. The potential consequences of interactions most frequently noted in this study were QT interval prolongation, gastrointestinal effects, or complications affecting the central nervous system.

Characteristic side effects (affecting, for example, the skin, the cardiovascular system, and the gastrointestinal system) must be anticipated whenever oral anti-cancer drugs are used. The wide variety of possible side effects means that the health care team must be experienced in their prevention and management; also, patients must be fully informed. A study noted that more than half of ambulatory patients with cancer had at least one potential drug interaction. One-third of ambulatory patients with cancer had a major potential drug interaction that could result in serious clinical consequences.

Today, we see however that in some European countries these medicines are still not accessible for patients through their local community pharmacy, which puts an unnecessary burden on patients.

Results: Community pharmacies are ideally placed within the community to help oncology patients and can explain any concerning signs and symptoms and explain how their medicines should be taken.

They can provide reassurance as many people are worried about the use of these medicines and counsel people on safe handling and storage of anti-cancer medicines. Lastly, they can review side effects that might occur and help people manage these alongside their symptoms utilization of healthcare resources.

Conclusion: Community pharmacists can supply these treatments close to patients' homes accompanied with expert guidance on their optimal use, safety and adherence. Several models of pharmacists' interventions in oncology outpatient care have already proven to be successful, have been consistently efficacious, and have positively influenced patient outcomes.

Keywords: oral antineoplastic drugs, community pharmacy, safety, adherence, side-effects

S31 - IMMUNOTHERAPY IN BREAST CANCER

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Modern immunotherapy is represented by drugs from the category of inhibitors of immune checkpoints. For some years now, they have been significantly present in clinical practice, in the treatment of a number of solid tumors, such as lung cancer and melanoma, achieving unprecedented results in disease control and maintaining a long-term response. In the treatment of breast cancer the situation is somewhat different. Until very recently, breast cancer was considered a non-immunogenic tumor, and as such an uninteresting target for immunotherapy. However, work on dissecting the molecular background of different subtypes of breast cancer has shown that triple-negative breast cancer (TNBC) however is an immunogenic disease and has the ability, sometimes significant, to accumulate immune infiltrate as a signal of intrinsic response. Not surprisingly, most immunotherapy research in breast cancer has focused on TNBC. In the early stage of TNBC, most significant results were achieved by pembrolizumab and atezolizumab, which, when administered with chemotherapy in a neoadjuvant context, ie preoperatively, achieved a significantly higher rate of complete pathological response. What has been shown to be significant is both the question of study design and selection of a chemotherapeutic partner, such as anthracyclines, because of their potent immunomodulatory effect. On the other hand, durvalumab showed results without post-operative continuation of durvalumab maintenance therapy. In the metastatic stage of disease, pembrolizumab and atezolizumab again showed best results. Applied with standard chemotherapy in first-line treatment, they achieved significantly longer disease control, but also overall survival, in patients with metastatic TNBC. In contrast to the early stage, in metastatic TNBC results were achieved exclusively in the PD-L1 positive population of patients. In the HER2 positive and hormone-dependent HER2 negative subtype of breast cancer, results with immunotherapy are much more modest. Thus, in the case of hormone-dependent HER2 negative breast cancer, studies are currently being conducted at an early stage, in terms of neoadjuvant immunotherapy with chemotherapy in those very high-risk cases, and in metastatic disease there are no significant results so far. In the HER2 positive subtype, studies of the addition of atezolizumab to chemotherapy and targeted antiHER2 therapy administered neoadjuvantly did not show satisfactory results, while in the metastatic stage of HER2 positive breast cancer the situation is somewhat better and studies with the addition of atezolizumab to chemobiotherapy promise positive result at this time. Immunotherapy in breast cancer is currently limited to TNBC in clinical practice, and significant changes are not expected in the near future. Nevertheless, advances in the treatment of this subtype of breast cancer, which is still an unmet need, with very poor results of previous therapeutic efforts, give hope for a new era and potentially very good and long-term disease control in at least some of these patients.

Keywords: immunotherapy, immune - checkpoint inhibitors, TNBC, HR+HER2- BC, HER2+ BC, pembrolizumab, atezolizumab

S32 - TREATMENT OF CASTRATION-RESISTANT PROSTATE CANCER - NEW GUIDELINES

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Prostate cancer is the most common malignant neoplasm in men in Croatia. It manifests clinically without symptoms and it is detected due to elevated serum PSA values either in a regular examination or a systematic examination of primary care physicians based on age as screening or due to a positive family history. The decision on treatment is made on the basis of the degree group. Gleason score based on pathological findings resulting from prostate biopsy and PSA values, which is a major factor for prostate biopsy indication and TNM classification. Clinically localized disease is very successfully treated with surgical treatment of the prostate or radical radiotherapy with or without hormone therapy. Clinically locally advanced disease is treated by the use of radiation and hormone therapy with either LHRH agonists and androgen deprivation therapy. Metastatic disease can be controlled by androgen deprivation therapy and after the development of castration-resistant disease, which is defined as reduced testosterone levels below 50ng / dl, chemotherapy or additional forms of hormone therapy are justified, which is now becoming the gold standard.

Keywords: prostate cancer, castration resistant prostate cancer, localized prostate cancer, metastatic prostate cancer, androgen deprivation therapy

S33 - THE UNIQUE ROLE OF NATURAL PRODUCTS IN THE ONCOLOGY DRUG RESEARCH AND DEVELOPMENT

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Natural products comprise a significant portion of modern pharmaceuticals, most notably in cancer therapy. Among the anticancer drugs currently used, about 60% are naturally occurring molecules or derived from a natural product lead. In the last half century, enormous efforts have been made to isolate novel natural products from plants, microbial and marine organisms to assess their anticancer therapeutic properties and to elucidate their mechanisms of action. These efforts have led to the development of clinically effective drugs. The first plant-derived agents to enter clinical use were the vinca alkaloids isolated from the Madagascar periwinkle (*Catharanthus roseus* G. Don) in 1958. Both vincristine and vinblastine proved to be potent mitotic inhibitors in the treatment of various types of lymphoma and leukaemia ailments. Paclitaxel and camptothecin, discovered over 60 years ago, are the two most successful examples of natural products that remain the mainstay in cancer treatment. Paclitaxel, originally isolated from the bark of Pacific yew (*Taxus brevifolia* Nutt.), was the first microtubule targeting agent described in the literature. Due to the limited natural resources, paclitaxel has been obtained by a commercially feasible semi-synthetic procedure, starting from 10-deacetylbaccatin III isolated from the leaves of European yew (*Taxus baccata* L.). Additionally, most of the analogues and new formulations have been created for the purpose of overcoming clinical limitations of paclitaxel, including poor solubility, dose-limiting toxic effects, allergic reactions, and development of drug resistance. Camptothecin, alkaloid from wood and bark of Chinese happy tree (*Camptotheca accuminata* Decne.), has been found to act with a unique mechanism of action, targeting the nuclear enzyme topoisomerase I which is critically involved in DNA replication and transcription processes. Extensive research aimed to improve its solubility, reduce toxicity, and retain anticancer effects led to the development of semi-synthetic derivatives approved for clinical use, such as topotecan and irinotecan. Chemotherapeutic agents derived from bacteria and fungi have also been utilized as clinically valuable drugs for cancer treatment. The anthracycline doxorubicin, as one of the most widely used agents in the treatment of several types of cancers, was initially obtained from the soil bacteria *Streptomyces peucetius*. Intercalation of doxorubicin into DNA, inhibition of topoisomerase II, generation of free radicals and oxidative damage of biomolecules have been proposed to explain the mode of action of this drug in cancer cells. Although effective, doxorubicin-based chemotherapy is associated with serious side effects, such as irreversible cardiotoxicity or nephrotoxicity. Consequently, several attempts have been made to decrease the side effects, including the production of doxorubicin analogues and development of efficacious delivery systems. In addition to terrestrial plants and microorganisms, diverse marine organisms have been indicated as another potential source of new anticancer agents. The first marine natural product to become a successful drug was cytarabine as a potent antineoplastic and antiviral agent. Cytarabine is a synthetic analogue of arabinose-containing bioactive nucleosides isolated from the Caribbean sponge *Tectitethya crypta*. Following all the above, it is undisputed that natural products and their structural analogues have historically made a major contribution to cancer therapy. Due to their unique biological activities and chemical features, natural products are remaining the main source of lead molecules in modern drug discovery.

Keywords: natural products, drug discovery, anticancer drugs

S34 - THE APPLICATION AND SIDE EFFECTS OF IMMUNOTHERAPY - EXPERIENCE OF SESTRE MILOSRDNICE UNIVERSITY HOSPITAL CENTER

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Introduction: A growing number of oncology patients have, in the last years, been treated with immunotherapy - immune checkpoint inhibitors. We are currently witnessing the extension of medical indications for this group of medicines. Immunotherapy, however, the same as any other drug, can cause side effects, including rare complications that could prove fatal for some patients.

Method: A search of scientific and professional databases with the keywords immunotherapy, immune checkpoint inhibitors and side effects was conducted.

Results: The side effects, related to immune system, point out the basic difference between these drugs and other drugs used in treating malignant diseases.

The most frequent side effects resulting from the affected immune system include colitis, dermatitis, hepatitis, nephritis, pneumonitis and endocrinopathies. Most of these appear in the course of the first 12 weeks of treatment, but can as well appear at any point in the treatment. The form is mild to moderate and patients generally tolerate them well. These side effects are usually reversible and react to fast beginning of corticosteroid treatment.

Patients who develop endocrinopathies, such as hypothyreosis and hypopituitarism, usually do not regain function and need a long-term replacement hormone therapy.

Other side effects, such as neurological disorders and myocarditis are relatively rare, but can be very serious, even lethal.

Treatment with check point inhibitors can be discontinued for a short period, depending on the gravity of side effects, to be continued after toxicity withdraws and corticosteroid treatment is stopped.

Conclusion: It is currently not possible to predict the side effects a patient might develop as a result of the affected immune system, but the patients with already existing autoimmune disorders, may be exposed to a higher risk.

It is of great importance to raise awareness in patients and educate them and their carers, and health care workers, that it is crucial, in the appearance and taking care of side effects, to stress that an oncology treatment with immunotherapy is under way.

Keywords: immunotherapy, immune checkpoint inhibitors and side effects

S35 - CDK4/6 INHIBITORS IN THE TREATMENT OF BREAST CANCER – NOTES FOR ONCOLOGY PHARMACIST

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Metastatic breast cancer remains an incurable disease, deadly for about 30% of new cases, of which there are about 2,700 in Croatia every year. Most patients, regardless of stage and menopausal status, will have hormone receptors expressed in the tumor cells. We can count that about $\frac{3}{4}$ of patients at some point in their illness will have the opportunity to be treated with some form of antihormonal treatment. If we analyze the results of the effectiveness of our treatment, until about 10 years ago, the only progress was visible in the treatment of HER2 + breast cancer, while the effectiveness of treatment in HR + and triple-negative breast cancer stagnated. However, with the advent of CDK 4/6 inhibitors, significant changes are also beginning to occur in the HR + breast cancer population. It is a therapy that we add to antihormonal therapy, which is still the basis for the treatment of HR + breast cancer. CDK 4/6 inhibitors include abemaciclib, palbociclib and ribociclib. All three drugs are of similar but again sufficiently different structure, which consequently affects the side effect profile. Most common side effects are associated with neutropenia, increased transaminases, diarrhea, prolongation of the QTc interval, and the occurrence of thromboembolic events. Neutropenia is the most common side effect, especially with palbo and ribociclib, less common with abemaciclib. Since this is a cell cycle arrest and not a cytotoxic effect, such as the effect of chemotherapy on the bone marrow, discontinuation of therapy and dose reduction can very easily manage this side effect without fear of developing febrile neutropenia, despite the high incidence of neutropenia grade III and IV. The occurrence of diarrheal stools (usually grades I and II) is related to all three drugs, but especially to the use of abemaciclib, and consequently quality of life of the patient can be significantly impaired. This is also the most important position of the oncology pharmacist during the application of ciclib treatment, both advisory and therapeutic. The pharmacist in most cases will not have available information about the increase in transaminases, but already knowing about this possibility is very important in terms of educating patients about the importance of avoiding untested alternative preparations that can further aggravate the situation which will result in discontinuation of the oncological treatment. The proarrhythmogenic effect of ribociclib is very rare both in the study and in real life, as is the thromboembolic effect of abemaciclib. The addition of CDK 4/6 inhibitors is today also associated with a clear prolongation of overall survival, so that today we have a significant number of patients taking therapy for more than three years, which is a great success in treatment compared to the period before their onset. However, despite these successes and side effects of CDK 4/6 inhibitors, we must not forget that the basis of treatment of HR + metastatic breast cancer continues to be antihormonal therapy (aromatase inhibitors, fulvestrant and tamoxifen) whose use is also associated with a number of side effects, fortunately, well known to most oncology pharmacists.

Keywords: oncology pharmacist, CDK4/6 inhibitors, abemaciclib, palbociclib, ribociclib, neutropenia, diarrhoea

S36 - THE INFLUENCE OF DIGITAL COMMUNICATION ON EMOTIONS AND ATTITUDES (USE OF ARTIFICIAL INTELLIGENCE FOR SENTIMENT ANALYSIS AND HATE SPEECH DETECTION)

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Citizen's competence is of crucial importance for active social participation, which is one of the main components of good governance and sustainable democracy. In many parts of EU, social participation is stagnating. Particularly worrisome are the apathy and lack of interest on the side of younger population. Furthermore, in the last years, we witness social developments that result in deterioration of standards in many parts of the EU. The core element of the citizen's competence is high level of media literacy. It is necessary for citizens' reflection of social reality and their resilience to negative media phenomena, like hate speech and fake news. The main objective of the presentation is to point out importance of digital literacy and to present recent project, Media Literacy Observatory for Active Citizenship and Sustainable Democracy. Project aim is to improve transnational governance by developing transnational media literacy observatory, based on digital platform able to identify hate speech on five EU languages (Croatian, Slovenian, English, Romanian and Hungarian) and to serve as a mechanism for increasing media literacy and thus strengthening citizens' competences what will contribute to development of sustainable democracy. The main target groups are the youth and the people who work with them.

Keywords: emotions and attitudes, artificial intelligence for sentiment analysis, hate speech detection

S37 - INFLUENCE OF DRUG INTERACTIONS ON TREATMENT OUTCOMES: A CASE REPORT FROM A PHARMACY

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Introduction: Whenever two or more drugs are being taken, there is a chance that there will be an interaction among the drugs. The interaction may increase or decrease the effectiveness of the drugs or their side effects. The likelihood of drug interactions increases in parallel with the increase of the number of drugs being taken. Therefore, people who take many drugs are at the greatest risk for interactions. Polypharmacy is the leading cause of drug interactions. Drug interactions contribute to the cost of healthcare because of the costs of medical care required to treat problems caused by changes in effectiveness or side effects. Interactions can also lead to psychological suffering. This review discusses the issue of drug interactions and several ways to avoid them.

A drug interaction can be defined as an interaction between a drug and another substance that prevents the drug from performing as expected. This definition applies to interactions of drugs with other drugs (drug-drug interactions), as well as drugs with food (drug-food interactions) and other substances, such as supplements. Drugs may also interact with laboratory tests, changing the proper results of the laboratory test.

A drug–drug interaction (DDI) is an event that occurs when the effects of a drug are modified by another drug that is taken concomitantly. DDIs can be classified, according to the mechanisms by which drugs interact with each other, as pharmaceutical, pharmacokinetic and pharmacodynamic. DDIs may result in either increase or decrease in efficacy, in treatment failure, or in an increased toxicity of medications. However, not all potential DDIs are clinically significant.

Methods: The case-study of a female patient, taken from everyday practice, using the interaction determining application, will show the most frequent interactions. Health-care professionals such as community pharmacy pharmacists, general practitioners, a pharmacologist a psychiatrist and internal medicine oncology intern will give their opinions concerning the prescribed therapy.

Results: Although the concurrent use of multiple drugs often increases therapeutic effectiveness, certain combinations are harmful. Most interactions go unnoticed by physicians due to the absence of new clinical signs and symptoms and because they often produce a worsening of already existing symptoms. DDIs sometimes go undetected because of a lack of knowledge and training, low motivation and poor attitude. The incidence of potential DDIs may be affected by different factors, such as a higher number of concomitant drugs, presence of comorbidities and advanced age.

Conclusion: Effective interprofessional collaboration is critical for sustaining high quality care in the context of the increasing burden on primary healthcare services. Despite this, there is limited understanding of the factors contributing to effective collaboration between general practitioners and community pharmacists.

The role of the family physician as the leader and gatekeeper to health care access is evolving in the new culture of medicine. Community pharmacists can align more closely with family physicians to bring a more integrated health care system to the local community level, thereby enhancing improved outcomes to patients and communities across the nation. Drug interactions are common in the primary care setting and are usually predictable. Identifying the most important and clinically relevant drug interactions in primary care is essential to patient safety. Strategies for reducing the risk of drug-drug interactions include minimizing the number of drugs prescribed, re-evaluating therapy on a regular basis, considering non-pharmacologic options, monitoring for signs and symptoms of toxicity or effectiveness, adjusting dosages of medications when indicated, and adjusting administration times

Keywords: community pharmacists, family doctor, interaction drug-drug, pharmacotherapy analysis

S38 - PRECISION MEDICINE - A NEW DEVELOPMENT AREA FOR ONCOLOGY PHARMACISTS

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Introduction: The way we treat cancer is changing. Scientific and technological advances such as tumor profiling, big data, and an increasing number of targeted therapies and combined regimens will result in a paradigm shift away from a *one-size-fits-all* concept toward personalised, on-demand, precision medicine, which will result in smaller, more defined patient populations.

Methods: For the purpose of preparing this paper, a search of scientific and professional literature was made using the PubMed database.

Precision medicine is the concept of tailoring disease treatment and modifying prevention to account for differences in genetic, environmental, or even lifestyle factors specific to groups of people.¹ Precision medicine takes genetic and biochemical information unique to a group of patients and uses that information to develop more specific and streamlined medication or treatments. The goal is to ensure that each medication or treatment is best suited to treat the individual, resulting in decreased side effects and increased effectiveness.

Results: Precision medicine incorporates biomarkers to help make informed decisions and to select optimal treatment for complex disease states. With this approach, physicians and pharmacists can also identify patients susceptible to adverse effects; be aware of dangerous drug-drug, drug-gene and drug-drug-gene interactions; and provide care in a whole new way so that it is completely individualised. The goal of precision medicine is simply to deliver the right cancer treatment to the right patient, the right dose at the right time. The goal of precision testing is to identify the optimal therapy for patients that will maximise their survival and quality of life. Pharmacogenomics (PGx) is the use of genetic information to guide the choice of drug and dose based on an individual's genetic makeup. PGx plays an important role in identifying responders and non-responders to medication, avoiding adverse events, and optimising drug dose. Precision medicine (PM) is an approach to disease treatment and prevention that takes into account differences in people's genes, environment, and lifestyles.

Conclusion: Pharmacy is a constantly changing profession that requires pharmacists to adapt their skills as scientific advances continue to transform the practice of medicine. Over the last 100 years, the profession of pharmacy has evolved from a dispensing model focused on the formulation and delivery of a drug product to a patient care model focused on individualising drug therapy and delivering direct patient care.

In the light of evolving medical landscape, the role of pharmacist is also expanding as they transition toward a consultation-based, patient-centric and collaborative model of care, with increased responsibility and accountability for medicines management

Today pharmacy is facing a new challenge – precision medicine.

The field of precision medicine affords multiple opportunities to pharmacists. Pharmacists have specific knowledge, skills and abilities that make them uniquely suited to advance the use of precision medicine as a clinical tool. Pharmacists are the only health care professionals who are specifically trained to

understand and apply the fundamental sciences of pharmacokinetics, pharmacodynamics and clinical pharmacology in patient care.

One of the greatest barriers toward advancing pharmacogenetics across the profession is the lack of clearly defined roles and responsibilities for which current and future pharmacists can prepare.

With respect to individual factors, education and training are perhaps the biggest

Keywords: pharmacogenomics, pharmacogenetics, oncology pharmacy.