20.02. - 22.02.2026.

VODICE, HRVATSKA

KNJIGA SAŽETAKA

Young experts;
a new era of medicine!

3. ŠKOLA RACIONALNE I SIGURNE
FARMAKOTERAPIJE
S MEĐUNARODNIM SUDJELOVANJEM

3rd SCHOOL OF RATIONAL AND SAFE
PHARMACOTHERAPY
WITH INTERNATIONAL PARTICIPATION

KNJIGA SAŽETAKA

Digitalno izdanje / Digital edition

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

Organizator: Hrvatska ljekarnička komora
Organizer: Croatian Chamber of Pharmacists

Hotel Olympia, Vodice, Hrvatska, 20.–22. veljače 2026.
Hotel Olympia, Vodice, Croatia, 20 –22 February 2026.
Izdavač: Hrvatska ljekarnička komora, 2026., www.hljk.hr
Publisher: Croatian Chamber of Pharmacists, 2026, www.hljk.hr

Urednik / Editor: Doc. dr. sc. Ivan Krečak, dr. med.

TABLICA SADRŽAJA:

POSTER PREZENTACIJE:

UVODNA RIJEČ

Poštovane kolegice, poštovani kolege, dragi prijatelji,

zahvaljujemo na sudjelovanju na 3. školi racionalne i sigurne farmakoterapije s međunarodnim sudjelovanjem, koja se održala od 20. do 22. veljače 2026. u osunčanim Vodicama, u Hotelu Olympia, u organizaciji Hrvatske ljekarničke komore (HLJK).

Vaše prisustvo i aktivno sudjelovanje doprinijeli su ostvarenju glavnog cilja ove škole – promicanju racionalne i sigurne farmakoterapije te unaprjeđenju kvalitete zdravstvene skrbi kroz bolju suradnju između liječnika i farmaceuta.

Škola je bila posebno usmjerena prema specijalistima i specijalizantima raznih grana interne medicine, farmakologije, kliničke farmacije, liječnicima opće prakse, farmaceutima u bolničkim i javnim ljekarnama i studentima završnih godina medicine i farmacije.

Zahvaljujemo i svim predavačima i sudionicima koji su pridonijeli bogatom i kvalitetnom programu, koji je obuhvatio tematska područja:

- Nove spoznaje u upalnim bolestima crijeva
- Farmakoterapija hematoloških bolesti
- Nove spoznaje u liječenju solidnih tumora
- Enteralna prehrana
- Praćenje ishoda liječenja u javnim ljekarnama
- Sigurna primjena lijekova i farmakovigilancija

Hvala vam na doprinosu i entuzijazmu. Radujemo se budućim susretima.

S poštovanjem, Organizatori

Doc. dr. sc. Marko Skelin mag. pharm.
Ana Soldo, mag. pharm.
Dr. sc. Marko Lucijanić, dr. med.

INTRODUCTORY SPEECH

Dear Esteemed Colleaguesand Friends,

We would like to thank you for your participation in the 3th School of Rational and Safe Pharmacotherapy with International Participation, held from 20 to 22 Ferburary 2026 in the beautiful city of Vodice at the Hotel Olympia, organized by the Croatian Chamber of Pharmacists (HLJK).

Your presence and active engagement significantly contributed to achieving the main goal of this event – the promotionof rational and safe pharmacotherapy and the improvement of healthcare quality through enhanced collaboration between physicians and pharmacists. The programme was particularly tailored to specialists and students specializing in various branches of internal medicine, pharmacology, clinical pharmacology, primary doctors and pharmacists in both hospital and public pharmacies.

We also extend our gratitude to all lecturers and participants who contributed to a rich and high-quality programme, which covered the following key topics:

- New Insights in Inflammatory Bowel Disease
- Pharmacotherapy of Hematological Disease
- New Insights in the Treatment of Solid Tumors
- Enteral Nutrition
- Monitoring of Treatment Outcomes in Community Pharmacies
- Safe Use of Medicines and Pharmacovigilance

Thank you for your contribution and enthusiasm. We look forward to future gatherings and continued collaboration.

Respectfully, The Organizers

Asst. Prof. Marko Skelin, MPharm, PhD
Ana Soldo, MPharm
Marko Lucijanić, MD, PhD

USMENA IZLAGANJA

3. ŠKOLA RACIONALNE I SIGURNE
FARMAKOTERAPIJE
S MEĐUNARODNIM SUDJELOVANJEM

3rd SCHOOL OF RATIONAL AND SAFE
PHARMACOTHERAPY
WITH INTERNATIONAL PARTICIPATION

ULOGA CRIJEVNE MIKROBIOTE U UPALNIM BOLESTIMA CRIJEVA – KLINIČKA PERSPEKTIVA

Prof. dr. sc. Goran Hauser, dr. med. [1]
[1] *KBC Rijeka, Rijeka*

O-1

Upalne bolesti crijeva (IBD), Crohnova bolest i ulcerozni kolitis, kronične su imunološki posredovane bolesti čija patogeneza uključuje međudjelovanje genetske predispozicije, okolišnih čimbenika, poremećenog imunološkog odgovora i crijevne mikrobiote. Genetske studije identificirale su brojne lokuse povezane s prepoznavanjem mikroorganizama i regulacijom imunološke reakcije, čime se dodatno naglašava klinička važnost mikrobiote u nastanku i tijeku IBD-a. Međutim, ostaje otvoreno pitanje predstavlja li disbioza primarni patogenetski čimbenik ili sekundarnu posljedicu kronične crijevne upale.

U fiziološkim uvjetima, crijevna mikrobiota ima ključnu ulogu u održavanju crijevne barijere, modulaciji mukoznog imuniteta, produkciji kratkolančanih masnih kiselina te zaštiti od patogenih mikroorganizama. U bolesnika s IBD-om dosljedno se bilježi smanjena mikrobna raznolikost, smanjenje protektivnih bakterijskih sojeva, osobito proizvođača butirata poput Faecalibacterium prausnitzii, te porast potencijalno proinflamatornih bakterija iz skupine Proteobacteria. Takve promjene povezane su s povećanom propusnošću epitelne barijere, pojačanom aktivacijom imunološkog sustava i težim kliničkim tijekom bolesti.

Eksperimentalni modeli potvrđuju da prisutnost mikrobiote predstavlja preduvjet za razvoj crijevne upale, dok kliničke studije pokazuju da uspješno protuupalno liječenje može djelomično normalizirati sastav mikrobiote. Ovi nalazi upućuju na dvosmjernu povezanost između upale i disbioze, s jasnim kliničkim implikacijama. U posljednjem desetljeću razvijaju se terapijski pristupi usmjereni na mikrobiotu, uključujući probiotike, selektirane bakterijske konzorcije i fekalnu mikrobiota transplantaciju. Iako su rezultati pojedinih studija obećavajući, heterogenost bolesnika i bolesti trenutačno ograničava rutinsku kliničku primjenu.
Daljnja istraživanja trebala bi omogućiti identifikaciju klinički relevantnih mikrobnih profila i razvoj personaliziranih terapijskih strategija usmjerenih na mikrobiotu.

Ključne riječi: upalne bolesti crijeva; crijevna mikrobiota; disbioza; mikrobiota-usmjerena terapija

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

THE ROLE OF THE GUT MICROBIOTA IN INFLAMMATORY BOWEL DISEASE – A CLINICAL PERSPECTIVE

Prof. Goran Hauser, MD, PhD [1]
[1] *University Hospital Centre Rijeka, Rijeka*

O-1

Inflammatory bowel diseases (IBD), including Crohn's disease and ulcerative colitis, are chronic immune-mediated disorders whose pathogenesis involves complex interactions among genetic susceptibility, environmental factors, dysregulated host immune responses, and the gut microbiota. Genetic association studies have identified numerous loci related to microbial recognition and immune regulation, further emphasising the clinical relevance of the gut microbiota in the development and progression of IBD. However, it remains unclear whether intestinal dysbiosis is a primary pathogenic factor or a secondary consequence of chronic intestinal inflammation.

Under physiological conditions, the gut microbiota plays a central role in maintaining intestinal barrier integrity, modulating mucosal immunity, producing short-chain fatty acids, and providing colonisation resistance against pathogenic microorganisms. In patients with IBD, a consistent reduction in microbial diversity has been observed, along with depletion of protective bacterial taxa – particularly butyrate-producing species such as *Faecalibacterium prausnitzii*—and an expansion of potentially proinflammatory bacteria belonging to the Proteobacteria phylum. These alterations are associated with increased epithelial permeability, enhanced immune activation, and a more severe clinical disease course.

Experimental models demonstrate that the presence of the gut microbiota is a prerequisite for the development of intestinal inflammation, while clinical studies indicate that effective anti-inflammatory therapy may lead to partial normalisation of microbial composition. These findings support a bidirectional relationship between intestinal inflammation and dysbiosis, with important clinical implications. Over the past decade, microbiota-targeted therapeutic strategies – including probiotics, rationally designed bacterial consortia, and faecal microbiota transplantation – have been increasingly explored. Although results from selected studies are promising, disease and patient heterogeneity currently limit routine clinical application.

Future research should focus on identifying clinically relevant microbial signatures and developing personalised microbiota-targeted therapies for patients with inflammatory bowel disease.

Keywords: inflammatory bowel disease; gut microbiota; dysbiosis; microbiota-targeted therapy

UNAPRJEĐENJE SIGURNOG RUKOVANJA SISTEMSKOM ONKOLOŠKOM TERAPIJOM I PROPISIVANJE TERAPIJE OD STRANE FARMACEUTA: NOVOSTI U REGULATIVI I UTJECAJ NA ZDRAVSTVENI KADAR U UJEDINJENOM KRALJEVSTVU

Joseph Thomas David Williams MPharm, FRPharmS, PG Dip GPP, mBOPA, IPresc.[1, 2, 3]

[1] *The Christie NHS Foundation Trust, Manchester, UK*
[2] *The University of Manchester*
[3] *The British Oncology Pharmacy Association (BOPA)*

O-2

Ova prezentacija pruža ažuriran pregled promjenjivog okvira u Ujedinjenom Kraljevstvu i na međunarodnoj razini vezano uz sigurno rukovanje sistemskom antikancerogenom terapijom (SACT) te rastuću ulogu farmaceuta s pravom samostalnog propisivanja. Objedinjuje regulatorne novosti, dokaze o opasnim lijekovima (HMP – hazardous medicinal products) te implikacije za radnu snagu u onkološkim farmaceutskim službama.

Prvi dio sažima međunarodne regulatorne okvire koji utječu na sigurno rukovanje opasnim lijekovima, uspoređujući britanska tijela poput Health and Safety Executivea (HSE), MHRA-e i Royal Pharmaceutical Societyja (RPS) s američkim strukturama kao što su OSHA, NIOSH, USP 800 i Joint Commission. Ključna tema je širenje baze dokaza o riziku profesionalne izloženosti, okolišnoj kontaminaciji i ulozi zatvorenih sustava za prijenos lijekova (CSTD). Globalna literatura pokazuje smanjenje kontaminacije pri primjeni CSTD-ova, iako i dalje postoje zabrinutosti vezane uz kompatibilnost, agregaciju proteina, zadržavanje para te potencijalni gubitak volumena — osobito kod monoklonskih protutijela (mAb). Nedavne smjernice ISOPP-a i Specialist Pharmacy Servicea (SPS) naglašavaju potrebu za robusnim procjenama rizika, dosljednom edukacijom te centraliziranom pripremom gdje god je to moguće. Važan istaknuti razvoj događaja jest jačanje europskog zakonodavstva vezanog uz opasne lijekove, nasuprot trenutačnom nedostatku nacionalnih definicija, obveznih popisa i zahtjeva za praćenje okolišne kontaminacije u Ujedinjenom Kraljevstvu. Stajalište RCN-a za razdoblje 2025.–2026. poziva na obveznu primjenu CSTD-ova, bolju usklađenost s COSHH-om, uvođenje nacionalnih popisa HMP-ova te ažuriranje smjernica kroz cijeli životni ciklus opasnih lijekova. Paralelno s tim, zajednička izjava BOPA-e i PASG-a iz 2025. naglašava potrebu za dokazima utemeljenim nacionalnim konsenzusom o sigurnom rukovanju, uz uravnoteženje sigurnosti, provedivosti, održivosti i troškova.

Drugi dio prezentacije bavi se propisivanjem lijekova od strane farmaceuta u kontekstu šire krize kapaciteta NHS-a, oslanjajući se na podatke UK SACT Boarda, nalaze lorda Darzija iz 2024. godine te Desetogodišnji plan zdravstvene skrbi NHS-a. Rastuća potražnja za SACT-om, kašnjenja u dijagnostici i pritisci na radnu snagu naglašavaju potrebu za proširenjem uloga farmaceuta. S obzirom na to da će samostalno propisivanje postati standard pri registraciji od 2026. godine, farmaceuti će sve više doprinositi provedbi SACT-a, dijagnostici i skrbi u zajednici.

Predstavljen je strukturirani kompetencijski okvir za propisivanje SACT-a, koji obuhvaća put od promatranja do samostalnog započinjanja i prilagodbe složenih terapijskih režima. Upravljanje, obrazovni putovi i prošireni opseg prakse istaknuti su kao ključni pokretači transformacije usluga te osiguravanja sigurne i održive provedbe SACT-a — kako u bolničkom okruženju, tako i u kućnim modelima skrbi poput programa The Christie at Home.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

ADVANCING SAFE SACT HANDLING AND PHARMACIST PRESCRIBING: UK REGULATORY UPDATES AND WORKFORCE IMPLICATIONS

Joseph Thomas David Williams MPharm, FRPharmS, PG Dip GPP, mBOPA, IPresc.[1, 2, 3]

[1] *The Christie NHS Foundation Trust, Manchester, UK*
[2] *The University of Manchester*
[3] *The British Oncology Pharmacy Association (BOPA)*

O-2

This presentation provides an up-to-date overview of the evolving UK and international landscape surrounding the safe handling of systemic anti-cancer therapy (SACT) and the expanding role of pharmacist independent prescribers. It brings together regulatory updates, evidence on hazardous medicinal products (HMPs), and workforce implications for oncology pharmacy services.

The first section summarises international regulatory frameworks influencing safe handling of hazardous drugs, contrasting UK bodies such as the Health and Safety Executive (HSE), MHRA and Royal Pharmaceutical Society (RPS) with the US structures of OSHA, NIOSH, USP 800 and the Joint Commission. A key theme is the widening evidence base around occupational exposure risk, environmental contamination, and the role of closed system transfer devices (CSTDs). Global literature demonstrates reductions in contamination when CSTDs are implemented, although concerns remain regarding compatibility, protein aggregation, vapour containment and potential volume loss—particularly with monoclonal antibodies (mAbs). Recent guidance from ISOPP and the Specialist Pharmacy Service (SPS) underscores the need for robust risk assessments, consistent training, and centralised preparation where possible.
A major development highlighted is the strengthening of European legislation on hazardous medicinal products, contrasted with the current gap in UK national definitions, mandatory lists, and environmental monitoring requirements. The 2025–26 RCN position statement calls for mandated CSTD use, improved COSHH alignment, national HMP lists, and updated guidance across the whole hazardous drug lifecycle. In parallel, BOPA and PASG's joint 2025 position statement emphasises the need for an evidence-informed UK consensus on safe handling, balancing safety, feasibility, sustainability and cost.

The second half of the presentation examines pharmacist prescribing within the wider NHS capacity crisis, drawing on UK SACT Board data, Lord Darzi's 2024 findings and the 10-Year NHS Health Plan. Rising SACT demand, delayed diagnostics and workforce pressures underscore the need for expanded pharmacist roles. With independent prescribing becoming the default on registration from 2026, pharmacists will increasingly contribute to SACT delivery, diagnostics, and community-based care.

A structured competency framework is outlined for SACT prescribing, from observation through to initiation and customisation of complex regimens. Governance, training pathways, and enhanced scope of practice are positioned as essential levers to support service transformation and ensure safe, sustainable SACT delivery—both in hospital and at home through models such as The Christie at Home.

STANIČNA TERAPIJA U LIJEČENJU HEMATOLOŠKIH BOLESTI

Izv. prof. dr. sc. Zinaida Perić, dr. med. [1]
[1] *KBC Rijeka, Rijeka*

O-3

Stanična terapija se pojavila kao transformativni pristup u liječenju malignih hematoloških bolesti. Ova terapijska metoda uključuje transplantaciju ili modificiranje živih stanica kako bi se obnovila, zamijenila ili poboljšala funkcija hematopoetskog i imunološkog sustava. Ključne primjene uključuju transplantaciju hematopoetskih matičnih stanica, adoptivne terapije imunološkim stanicama poput CAR-T stanica i bispecifična antitijela.

Ovi pristupi pokazali su značajnu učinkovitost u stanjima poput leukemije, limfoma i multiplog mijeloma. Unatoč izvanrednom kliničkom napretku, postoje izazovi, uključujući toksičnost povezanu s liječenjem, recidiv, složenost proizvodnje i dostupnost.

Trenutna istraživanja usmjerena su na poboljšanje sigurnosti, trajnosti odgovora i proširenje indikacija. Sveukupno, stanična terapija predstavlja brzo evoluirajuće područje s velikim potencijalom za preoblikovanje liječenja zloćudnih hematoloških bolesti.

Ključne riječi: transplantacija krvnotvornih matičnih stanica; CAR-T; bispecifična antitijela; stanična terapija

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

CELLULAR THERAPY IN THE TREATMENT OF HEMATOLOGICAL DISEASES

Assoc. prof. Zinaida Perić, MD, PhD [1]
[1] *University Hospital Centre Rijeka, Rijeka*

O-3

Cellular therapy has emerged as a transformative approach in the treatment of hematological diseases, offering targeted and potentially curative strategies for malignant disorders. This therapeutic modality involves the transplantation or modification of living cells to restore, replace, or enhance hematopoietic and immune system function. Key applications include hematopoietic stem cell transplantation, adoptive immune cell therapies such as CAR-T cells, and bispecific antibodies.

These approaches have demonstrated significant efficacy in conditions such as leukemia, lymphoma, and multiple myeloma. Despite remarkable clinical progress, challenges remain, including treatment-related toxicity, relapse, manufacturing complexity, and accessibility. Ongoing research focuses on improving safety, durability of response, and expanding indications.

Overall, cellular therapy represents a rapidly evolving field with substantial potential to reshape the management of hematological diseases.

Keywords: bone marrow transplant; CAR-T; bispecific antibodies; celullar therapy

USPOREDBA INDEKSA TUMORA I DRUGIH KOMPETITIVNIH ČIMBENIKA KAO UZROKA SMRTI U OBOLJELIH OD KARCINOMA USNE ŠUPLJINE

Doc. dr. sc. Petar Suton, dr. med. [1]
[1] *KB Dubrava, Zagreb*

O-4

Preživjeli od planocelularnog karcinoma glave i vrata suočavaju se s povećanom smrtnošću od brojnih uzroka. Međutim, utjecaj i obrasci smrtnosti od drugih uzroka ostaju nepoznati kod bolesnika s rakom usne šupljine.

Cilj ove studije bio je analizirati te obrasce kod preživjelih od raka usne šupljine s dugogodišnjim praćenjem. Retrospektivno smo analizirali bolesnike s klinički negativnim vratom (cN0) i rakom usne šupljine koji su primarno kirurški liječeni u tercijarnom onkološkom centru.

Ukupno je identificirano 152 bolesnika. Medijan praćenja kohorte iznosio je 59 mjeseci. Ukupno je umrlo 76 pacijenata. Trideset četiri (22,4%) bolesnika umrlo je od recidiva raka usne šupljine. Najčešći kompetitivni uzroci smrti bili su: kardiovaskularne bolesti (n = 18; 42,9%), te drugi primarni tumori (n = 11; 26,2%). Rak pluća činio je 54,5% (6 od 11) smrtnih slučajeva povezanih s drugim primarnim tumorima. Pacijenti s intraoralnim karcinomom liječeni kirurškim zahvatom potencijalno su visoko izlječivi za prvi (indeks) karcinom, ali se suočavaju sa značajnim rizikom smrti od kompetitivnih uzroka. Gotovo trećina ovih pacijenata umrla je od kompetitivnih uzroka smrti koji su glavni uzrok smrtnosti nakon četvrte godine praćenja.

Ova studija naglašava važnost prilagođenih strategija praćenja koje uključuju specifične rizike ove populacije.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

COMPARISON OF TUMOR INDICES AND OTHER COMPETING RISK FACTORS AS CAUSES OF DEATH IN PATIENTS WITH ORAL CANCER

Asst. prof. Petar Suton, MD, PhD [1]
[1] *University Hospital Dubrava, Zagreb*

O-4

Survivors of head and neck squamous cell carcinoma face excess mortality from multiple causes. However, impact and patterns of all-cause mortality remains unknown in oral cancer patients.

The aim of this study was to analyse these patterns in long-term survivors. We retrospectively studied clinically node-negative (cN0) oral cancer patients primarily surgically treated at tertiary cancer center.

A total of 152 patients were identified. Median follow-up of our cohort was 59 months. A total of 76 patients died. Thirty-four (22.4%) patients died from primary tumor recurrence and 42 (27.6%) patients died from competing causes. The most common competing causes of death were: cardiovascular disease (n = 18; 42.9%), followed by second primary cancer (SPC) (n = 11; 26.2%). Lung cancer accounted for 54.5% (6 of 11) of SPC associated deaths. Patients with cN0 oral cancer treated with up-front surgery are potentially highly curable for index cancer but face significant risks of mortality from causes other than disease recurrence. Nearly one-third of these patients died from competing causes of death which are major cause of mortality after the fourth year of follow-up period.

This study highlights the importance of adjusted follow-up strategies addressing this population specific risks.

DEVELOPED THROUGH COLLABORATION - TOOL AND RESOURCES TO ENHANCE PATIENT CARE

Michael Reff RPh, MBA [1,2]
[1] *National Community Oncology Dispensing Association (NCODA)*
[2] *American Society of Clinical Oncology (ASCO)*

O-5

Advancing high-quality cancer care requires collaboration across the global oncology community. While healthcare delivery occurs locally, the sharing of knowledge, best practices, and innovation extends beyond geographic borders.

The Network for Collaborative Oncology Development and Advancement (NCODA) is a global oncology nonprofit organization dedicated to improving patient-centered cancer care by connecting oncology professionals and advancing the role of medically integrated oncology care teams through collaboration, education, and innovation. NCODA works to strengthen international partnerships and facilitate knowledge exchange across the oncology ecosystem.

Central to NCODA's approach is the medically integrated pharmacy (MIP) model, which promotes coordinated, team-based oncology care to improve treatment access, adherence, and patient outcomes. Through partnerships with healthcare professionals, academic institutions, advocacy organizations, and industry collaborators, NCODA facilitates the development and dissemination of best practices and practical clinical resources that support treatment adherence, patient education, and coordinated care.

Examples include Positive Quality Interventions (PQIs), which are precise and concise peer-reviewed clinical guidance resources that provide quality standards and effective practices to support multidisciplinary oncology teams caring for patients receiving oral or IV oncolytics, and Treatment Support Kits (TSKs), which provide patients with supportive care tools designed to help manage common treatment-related toxicities and improve tolerance to therapy.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

O-5

Additional initiatives include educational programming, patient education sheets, patient satisfaction surveys, publications such as Oncolytics Today, and international and global engagement opportunities that allow oncology professionals to share best practices and advance quality cancer care. NCODA also promotes excellence in oncology practice through its Center of Excellence (COE) Accreditation program, which recognizes practices that demonstrate a commitment to high-quality, patient-centered care and the advancement of medically integrated oncology services.
Since its founding in 2015, NCODA has grown into a global network of thousands of oncology professionals and practice sites across multiple countries, with expanding international collaborations and professional pharmacy student organizations in regions such as Croatia, Canada, Ireland, Austria, Greece, and Turkey.

Strengthening relationships and sharing expertise across the oncology community are essential to advancing patient-centered cancer care. NCODA's continued global engagement demonstrates the value of collaboration in building a unified oncology ecosystem dedicated to improving outcomes and supporting patients throughout their cancer journey.

Continued international collaboration and knowledge exchange will be critical to advancing innovation and improving cancer care for patients worldwide.

REGULACIJA IMUNOSNOG ODGOVORA U KONTEKSTU UPALNIH BOLESTI CRIJEVA

Doc. dr. sc. Marina Babić Čač, dipl. ing. mol. biologije [1]
[1] *Medicinski fakultet, Sveučilište u Rijeci, Rijeka*

O-6

Upalne bolesti crijeva (IBD, od eng. inflammatory bowel disease), poput Crohnove bolesti i ulceroznog kolitisa, karakterizira kronična upala i oštećenje tkiva u gastrointestinalnom traktu. Patogeneza IBD-a je složena te uključuje genetske i okolišne čimbenike, kao i disregulirani imunološki odgovor.

Više od dvije trećine imunoloških stanica tijela nalazi se u crijevima, gdje u zajedno sa crijevnim mikrobiomom, stanicama crijevnog epitela te komponentama sluznice čine lokalni imunološki sustav. Njihov je zadatak složen jer su potrebne za održavanje ravnoteže između tolerancije na bezopasne simbionte i antigene iz hrane te štetnih patogena i oštećenja barijere. Kod IBD-a, ova je ravnoteža narušena i rezultira nekontroliranom imunološkom reakcijom na vlastito tkivo. Imunološke reakcije u kontekstu IBD-a posredovane su putem limfocita T i urođenih limfoidnih stanica, u dinamičkoj komunikaciji s drugim stanicama u mukoznoj barijeri, kao i s enteričkim živčanim sustavom i mikrobiotom. Oštećenje tkiva, proinflamatorni milje, kao i stanični stres uzrokovan mikrobnim produktima, citokinima i reaktivnim kisikovim vrstama, mogu dovesti do pojačane regulacije molekula stresa, poput liganada za aktivirajući receptor NKG2D. NKG2D+ limfociti T, kao i stanice koje eksprimiraju povišene razine NKG2D liganada, identificirane su kod pacijenata s Crohnovom bolešću. Iako je uloga NKG2D u regulaciji limfocitnog odgovora od interesa za razvoj novih terapijskih pristupa, doprinos NKG2D-NKG2DL osi u oblikovanju crijevnog imunološkog odgovora još uvijek nije u potpunosti razjašnjen.

Rezultati koji pokazuju doprinos NKG2D, kao detektora staničnog stresa, crijevnom imunološkom odgovoru, posebice u oblikovanju urođenog limfoidnog staničnog odjeljka, će biti diskutirani.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

IMMUNE RESPONSE REGULATION IN INFLAMMATORY BOWEL DISEASE

Asst. prof. Marina Babić Čač, PhD, Molecular Biology [1]
[1] *The Faculty of Medicine of the University of Rijeka, Rijeka*

O-6

Inflammatory bowel disease (IBD), such as Crohn's disease and ulcerative colitis, is characterized by chronic inflammation and tissue damage in the gastrointestinal tract. Pathogenesis of IBD is complicated and includes genetic and environmental factors as well as dysregulated immune response. More than two thirds of the body's immune cells reside in the gut, where they interact with the gut microbiome, intestinal epithelial cells and local immune system of the lining mucosa. Their task is complex as they are required for maintaining balance between tolerance to harmless symbionts and food-derived antigens and harmful pathogens and barrier insults. In IBD, this balance is ticked and results in uncontrolled immune reaction to own tissue.

Immune reactions in the context of IBD are mediated through T lymphocytes and innate lymphoid cells, in a dynamic communication with other cells in the mucosal barrier as well as enteric nervous system and microbiota. Tissue damage, proinflammatory milieu as well as cellular stress caused by microbial products, cytokines and reactive oxygen species can lead to upregulation of stress molecules, such as ligands for the activating receptor NKG2D. NKG2D+ Th cells as well as cells expressing elevated levels of NKG2D ligands have been identified in patients with Crohn's disease. Although the role of NKG2D in the regulation of the lymphocyte response has been a topic of therapeutic interest, contribution of NKG2D-NKG2DL axis in the shaping of intestinal immune response is still not fully elucidated.

Our data, showing the contribution of NKG2D, as cellular stress sensor, to the intestinal immune response, particularly in shaping innate lymphoid cell compartment, will be discussed.

NOVOSTI U LIJEČENJU CROHNOVE BOLESTI; DOSTUPNE TERAPIJE I ONE U RAZVOJU

Dominik Kralj, dr. med [1]
[1] *KBC Sestre milosrdnice, Zagreb*

O-7

Liječenje Crohnove bolesti (CB) prolazi kroz značajnu promjenu paradigme u kojoj cilj više nije samo kontrola simptoma, već postizanje dubokog zacjeljivanja sluznice i prevencija trajnog oštećenja crijeva. Unatoč brojnim dostupnim opcijama, značajan broj bolesnika i dalje doseže tzv. „terapijski strop" s trenutnim monoterapijama. U predavanju je napravljen pregled suvremenih terapijskih opcija dostupnih u 2026. godini, uključujući biološke lijekove i male molekule. Uz etablirane anti-TNF lijekove i anti-integrine, analizira se primjena novih selektivnih IL-23 inhibitora (risankizumab, mirikizumab, guselkumab) te JAK inhibitora poput upadacitiniba. Poseban naglasak stavljen je na koncept napredne kombinacijske terapije (ACT), koja koristi sinergiju različitih mehanizama djelovanja (npr. dualni biološki lijekovi ili kombinacija biološkog lijeka i male molekule) kako bi se probio terapijski strop kod najtežih bolesnika. Također, razmatraju se novi pristupi u liječenju fistulirajuće Crohnove bolesti. U narednim godinama je fokus na prevenciju fibroze putem anti-TL1A antitijela.

Zaključno, rana intervencija unutar „terapijskog prozora" i personalizirani „treat-to-target" pristup ključni su za promjenu prirodnog tijeka bolesti. Napredne kombinacijske terapije i novi molekularni ciljevi predstavljaju budućnost koja obećava nadilaženje trenutnih ograničenja u farmakoterapiji Crohnove bolesti.

Ključne riječi: Crohnova bolest, biološka terapija, kombinacijska terapija.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

NEW DEVELOPMENTS IN CROHN'S DISEASE TREATMENT: APPROVED THERAPIES AND THOSE IN DEVELOPMENT

Dominik Kralj, MD [1]
[1] *University Hospital Centre Sestre milosrdnice, Zagreb*

O-7

The treatment of Crohn's disease (CD) is undergoing a significant paradigm shift in which the goal is no longer just symptom control, but achieving deep mucosal healing and preventing permanent bowel damage. Despite numerous available options, a significant number of patients still reach a so-called "therapeutic ceiling" with current monotherapies. The lecture provides an overview of modern therapeutic options available in 2026, including biological drugs and small molecules. In addition to established anti-TNF drugs and anti-integrins, the application of new selective IL-23 inhibitors (risankizumab, mirikizumab, guselkumab) and JAK inhibitors such as upadacitinib is analyzed. Special emphasis is placed on the concept of Advanced Combination Therapy (ACT), which utilizes the synergy of different mechanisms of action (e.g., dual biologics or a combination of a biological drug and a small molecule) to break the therapeutic ceiling in the most refractory patients. Furthermore, new approaches in the treatment of fistulizing Crohn's disease are considered. In the coming years, the focus is on fibrosis prevention via anti-TL1A antibodies.

In conclusion, early intervention within the "window of opportunity" and a personalized "treat-to-target" approach are key to altering the natural course of the disease. Advanced combination therapies and new molecular targets represent a future that promises to overcome current limitations in the pharmacotherapy of Crohn's disease.

Keywords: Crohn's disease, biological therapy, combination therapy.

NOVOSTI U LIJEČENJU ULCEROZNOG KOLITISA; DOSTUPNE TERAPIJE I ONE U RAZVOJU

Boris Brozović, dr. med. [1]
[1] *KBC Rijeka, Rijeka*

O-8

Ulcerozni kolitis i dalje predstavlja značajan terapijski izazov unatoč velikom napretku posljednjih desetljeća.

Današnje standardne terapije – anti-TNF lijekovi, anti-integrini, inhibitori IL-12/23, JAK inhibitori i S1P modulatori – omogućile su bolju kontrolu bolesti, ali klinički odgovori ostaju ograničeni, a terapijski "strop" jasno vidljiv.

Upravo zato je razvoj novih terapija eksplodirao: više od stotinu lijekova nalazi se u fazama II i III. Najperspektivniji uključuju selektivne JAK1/TYK2 inhibitore nove generacije, inovativne anti-trafficking terapije, selektivne blokatore IL-23 puta te posebno TL1A inhibitore, koji pokazuju iznimno obećavajuću ranu učinkovitost.

Paralelno, kombinirane terapije, uključujući dualne biološke lijekove, pokazuju obećavajuće rezultate i mogućnost probijanja terapijskog "stropa".

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

NEW DEVELOPMENTS IN ULCERATIVE COLITIS TREATMENT: APPROVED THERAPIES AND THOSE IN DEVELOPMENT

Boris Brozović, MD [1]
[1] *University Hospital Centre Rijeka, Rijeka*

O-8

Ulcerative colitis continues to represent a major therapeutic challenge despite substantial progress over recent decades.

Current standard treatments—including anti-TNF agents, anti-integrins, IL-12/23 inhibitors, JAK inhibitors, and S1P modulators—have improved disease control, yet clinical responses remain limited and a clear therapeutic "ceiling" persists. This has driven an unprecedented expansion of new therapies, with more than one hundred investigational agents now in Phase II and III development.

The most promising among them include next-generation selective JAK1/TYK2 inhibitors, innovative anti-trafficking therapies, selective IL-23 pathway blockers, and especially TL1A inhibitors, which show remarkably encouraging early efficacy.

In parallel, combination strategies, including dual biologic therapy, are yielding promising results and may offer a realistic path to overcoming the long-standing therapeutic "ceiling".

ULOGA KIRURGA U LIJEČENJU UPALNIH BOLESTI CRIJEVA

Damir Karlović, dr. med. [1]
[1] *KBC Rijeka, Rijeka*

O-9

Upalne bolesti crijeva (UBC), uključujući Crohnovu bolest i ulcerozni kolitis, kronična su stanja obilježena relapsno-remitirajućim tijekom i značajnim utjecajem na kvalitetu života bolesnika. Iako je liječenje UBC-a primarno utemeljeno na farmakoterapiji sukladno aktualnim ECCO smjernicama, sve je jasnije da kirurško liječenje nije isključivo krajnja terapijska opcija, već sastavni dio suvremenog, racionalnog i individualiziranog pristupa bolesniku.

Kirurg ima ključnu ulogu u zbrinjavanju komplikacija bolesti, refraktorne aktivnosti unatoč optimalnoj farmakoterapiji te u hitnim stanjima. Nova saznanja i stavovi, potvrđeni ECCO smjernicama, ukazuju da kod bolesnika s izoliranom Crohnovom bolešću terminalnog ileuma laparoskopska ileokakalna resekcija predstavlja ravnopravnu, a u odabranih bolesnika i preferiranu terapijsku opciju, u usporedbi s eskalacijom biološke terapije, uz usporedive kratkoročne i dugoročne kliničke ishode te kvalitetu života.

Kirurško liječenje UBC-a obuhvaća širok spektar zahvata, uključujući strikturoplastike, segmentalne resekcije crijeva, totalnu proktokolektomiju s formiranjem ileoanalnog rezervoara (POUCH), kao i kompleksno kirurško liječenje perianalne Crohnove bolesti. U ovom radu prikazuje se pregled suvremene uloge kirurga u liječenju UBC-a uz osvrt na iskustva Kliničkog bolničkog centra Rijeka, s posebnim naglaskom na pravovremeno donošenje kirurških odluka te perioperativno upravljanje bolesnicima liječenima imunosupresivnom i biološkom terapijom.

Zaključno, kirurg je neizostavan i ravnopravan član multidisciplinarnog tima koji uključuje gastroenterologe, farmaceute, radiologe i ostale specijaliste. Integrirani multidisciplinarni pristup ključan je za postizanje racionalnog, sigurnog i učinkovitog liječenja bolesnika s upalnim bolestima crijeva.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

THE ROLE OF THE SURGEON IN THE MANAGEMENT OF INFLAMMATORY BOWEL DISEASE

Damir Karlović, MD [1]
[1] *University Hospital Centre Rijeka, Rijeka*

O-9

Inflammatory bowel disease (IBD), including Crohn's disease and ulcerative colitis, comprises chronic conditions characterized by a relapsing–remitting course and a substantial impact on patients' quality of life. Although IBD management is primarily based on pharmacological therapy in accordance with current ECCO guidelines, it is increasingly recognized that surgery should not be regarded solely as a last-resort option, but rather as an integral component of a contemporary, rational, and individualized treatment strategy.

Surgeons play a pivotal role in the management of disease-related complications, medically refractory disease despite optimal pharmacotherapy, and emergency situations. Emerging evidence and current ECCO recommendations indicate that in patients with isolated terminal ileal Crohn's disease, laparoscopic ileocaecal resection represents an equivalent—and in selected patients, a preferred—therapeutic option compared with escalation of biologic therapy, providing comparable short- and long-term clinical outcomes as well as quality of life.

Surgical management of IBD encompasses a broad spectrum of procedures, including strictureplasties, segmental bowel resections, total proctocolectomy with ileal pouch–anal anastomosis (IPAA), and complex surgical treatment of perianal Crohn's disease. This review presents the contemporary role of surgery in IBD management, with an overview of clinical experience from the University Hospital Centre Rijeka, emphasizing timely surgical decision-making and perioperative management of patients receiving immunosuppressive and biologic therapies.

In conclusion, the surgeon is an indispensable and equal member of the multidisciplinary team, working in close collaboration with gastroenterologists, pharmacists, radiologists, and other specialists. An integrated multidisciplinary approach is essential to achieve rational, safe, and effective management of patients with inflammatory bowel disease.

IZAZOVI U CIJEPLJENJU ODRASLIH BOLESNIKA

Doc. prim. dr. sc. Diana Nonković, dr. med. [1]
[1] *Nastavni zavod za javno zdravstvo Splitsko dalmatinske županije*

O - 10

Predavanje ističe važnost cijepljenja odraslih kao jedne od učinkovitih mjera prevencije zaraznih bolesti i očuvanja javnog zdravlja.

Poseban naglasak stavljen je na rizične skupine, uključujući imunokompromitirane bolesnike, starije osobe i osobe s kroničnim bolestima, kod kojih je rizik od teških ishoda respiratornih infekcija značajno veći.

Unatoč dostupnosti cjepiva za prevenciju određenih respiratornih infekcija, procijepljenost odraslih ostaje nezadovoljavajuća, često zbog nedostatne informiranosti i cjepne neodlučnosti. Cijepljenje ne samo da smanjuje hospitalizacije i smrtnost, već doprinosi i smanjenju uporabe antibiotika te borbi protiv antimikrobne rezistencije.

Zaključno, zdravstveni djelatnici imaju ključnu ulogu u edukaciji i motiviranju bolesnika kako bi se poboljšala procijepljenost i zaštitilo zdravlje rizičnih populacija.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

CHALLENGES IN THE IMMUNIZATION OF ADULT PATIENTS

Asst. prof. prim. Diana Nonković, MD, PhD [1]
[1] *Teaching Institute of Public Health of Split-Dalmatia County*

O - 10

The presentation emphasizes the importance of adult vaccination as one of the effective measures for preventing infectious diseases and preserving public health.

Special attention is given to high-risk groups, including immunocompromised patients, older adults, and individuals with chronic diseases, in whom the risk of severe outcomes from respiratory infections is significantly higher.

Despite the availability of vaccines for the prevention of certain respiratory infections, adult vaccination coverage remains unsatisfactory, often due to insufficient awareness and vaccine hesitancy. Vaccination not only reduces hospitalizations and mortality but also contributes to decreased antibiotic use and the fight against antimicrobial resistance.

In conclusion, healthcare professionals play a key role in educating and motivating patients to improve vaccination coverage and protect the health of at-risk populations.

STARI I NOVI PRIMARNI ISHODI U KLINIČKIM ISPITIVANJIMA U HEMATOLOGIJI, ZAŠTO SU RELEVANTNI?

Dr. sc. Marko Lucijanić, dr. med. [1]
[1] *KB Dubrava, Zagreb*

O – 11

Predavanje će pružiti pregled primarnih ishoda u kliničkim ispitivanjima u hematologiji iz perspektive kroničnih mijeloproliferativnih neoplazmi i aktualnih kliničkih ispitivanja.

Raspravit će se tradicionalni i ishodi prijavljeni od pacijenata te trebamo li nove primarne ishode za nove lijekove.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

PRIMARY ENDPOINTS IN HEMATOLOGY CLINICAL TRIALS - OLD AND NEW? ARE THEY RELEVANT?

Marko Lucijanić, MD, PhD [1]
[1] *University Hospital Dubrava, Zagreb*

O – 11

The lecture will provide an overview of primary outcomes in clinical trials in hematology from the perspective of chronic myeloproliferative neoplasms and current clinical trials.

Traditional and patient-reported outcomes will be discussed, and whether we need novel primary outcomes for new drugs

PRIKRIVENA ŠEĆERNA BOLEST U BOLESNIKA S KRONIČNIM MIJELOPROLIFERATIVNIM NEOPLAZMAMA

Doc. dr. sc. Ivan Krečak, dr. med.[1-3], Josipa Budimir, dr. med.[1],
Izv. prof. dr. sc. Zinaida Perić, dr. med.[3,4], Dr. sc. Marko Lucijanić, dr. med.[5,6],
Doc. dr. sc. Marko Skelin, mag. pharm[2,3,7], Prof.dr.sc. Sanja Klobučar, dr. med.[3,4]

[1] *Služba interne medicine, Opća bolnica Šibensko-kninske županije, Šibenik*
[2] *Veleučilište u Šibeniku, Šibenik*
[3] *Medicinski fakultet Rijeka, Rijeka*
[4] *Klinika za unutarnje bolesti, Klinički bolnički centar Rijeka, Rijeka*
[5] *Klinika za unutarnje bolesti, Klinička bolnica Dubrava*
[6] *Medicinski fakultet Zagreb, Zagreb*
[7] *Odjel bolničke ljekarne, Opća bolnica Šibensko-kninske županije, Šibenik*

O – 12

Uvod: Bolesnike s BCR::ABL1-negativnim mijeloproliferativnim neoplazmama (MPN), esencijalnom trombocitemijom (ET), policitemijom verom (PV) i mijelofibrozom (MF) karakterizira snažna mijeloproliferacija i visok kardiovaskularni rizik. Stroga kontrola klasičnih kardiovaskularnih komorbiditeta poput intermedijarne hiperglikemije (IH) i šećerne bolesti (ŠB) u ovih bolesnika je imperativ. Zanimljivo, prema literaturnim podacima, prevalencija ŠB u MPN jest neuobičajeno niska (<15%). Mogući razlozi su hipoglikemija uzrokovana tumorom i kraći život eritrocita što potencijalno može uzrokovati lažno niže vrijednosti glukoze u plazmi natašte (GUP) i HbA1c kao i utjecaj citoreduktivnog liječenja. Primarni cilj ovog istraživanja jest utvrditi stvarnu pojavnost IH i ŠB u bolesnika s MPN koristeći uređaje za kontinuirano mjerenje glukoze (engl. continuous glucosae monitoring, CGM) koji mjere intersticijsku koncentraciju glukoze i nisu ovisno o parametrima krvne slike.

Ispitanici i metode: Ova aktivna prospektivna multicentrična studija trenutno se provodi u tri hematološka centra u Republici Hrvatskoj (Opća bolnica Šibensko-kninske županije, Klinički bolnički centar Rijeka i Klinička bolnica Dubrava) tijekom 2025. i uključuje bolesnike s MPN dijagnosticirane prema trenutno važećim kriterijima Svjetske zdravstvene organizacije iz 2022. Svim bolesnicima se na dan istraživanja uzorkuje krv, napravi klasična obrada za detekciju IH i ŠB (GUP natašte, HbA1c te test oralnog opterećenja glukozom) i postavi uređaj za CGM. Dijagnoza IH i ŠB se prema klasičnim kriterijima postavlja prema kriterijima Američke Asocijacije za Dijabetes; definicija ovih stanja prema očitanju CGM definirana je kao vrijeme u uskom rasponu (eng. time in tight range, TITR; ref. interval 3,9-7,8mmol/L) od 70-89% za IH te <70% za ŠB.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

O – 12

Rezultati: Trenutno je uključeno 33 ispitanika (ET=10, PV=17, MF=5, MPN-u=1); medijan dobi je 71 godina (36-85), 14 (42,4%) njih su žene, raniju dijagnozu IH ima jedan (3%) bolesnik, a ŠB njih 8 (24,2%). Vrijednost HbA1c ne korelira s hemoglobinom, hematokritom, brojem eritrocita kao ni s prosječnom vrijednosti glukoze mjerenom s CGM (p>0,050 za sve analize). Kod bolesnika bez ranije dijagnoze IH i ŠB (n=21) je klasičnom dijagnostikom dijagnosticirana IH u njih 9 (40,9%) bolesnika, a ŠB u jednog (4,5%) bolesnika. Nakon postavljanja CGM, IH je dijagnosticirana u 7 (31,8%) bolesnika, kao i ŠB u 7 bolesnika (31,8%). Kod jedinog bolesnika s ranijom dijagnozom IH dijagnosticirana je ŠB.

Zaključak: Prevalencija IH (n=7, 31,8%) i ŠB (n=15, 45,5%) već u ovom preliminarnom uzorku čini se zapravo vrlo visokom u bolesnika s MPN. Tradicionalne dijagnostičke metode za detekciju MPN čine se suboptimalnima u ovoj populaciji bolesnika što ukazuje na potencijalnu korist CGM u postavljanju dijagnoze, praćenju i liječenju MPN bolesnika s IH i ŠB. Daljnje uključivanje ispitanika i praćenje je u tijeku.

Ključne riječi: Mijeloproliferativne neoplazme; šećerna

UNMASKING DIJABETES MELLITUS IN PATIENTS WITH CHRONIC MYELOPROLIFERATIVE NEOPLASMS

Asst. prof. Ivan Krečak, MD, PhD[1-3], Josipa Budimir, MD[1],
Assoc. prof. Zinaida Perić, MD, PhD[3,4], Dr. sc. Marko Lucijanić, MD, PhD[5,6],
Asst. prof. Marko Skelin, MPharm, PhD[2,3,7], Prof. Sanja Klobučar, MD, PhD[3,4]

[1] *General Hospital of Šibenik-Knin County, Šibenik*
[2] *University of Applied Sciences, Sibenik*
[3] *Faculty of Medicine, University of Rijeka, Rijeka*
[4] *University Hospital Center Rijeka, Rijeka*
[5] *University Hospital Dubrava, Zagreb*
[6] *University of Zagreb, Zagreb*
[7] *Pharmacy Department, General Hospital of Sibenik-Knin County, Sibenik*

O – 12

Introduction: Patients with BCR::ABL1-negative myeloproliferative neoplasms (MPN), essential thrombocythemia (ET), polycythemia vera (PV), and myelofibrosis (MF) are characterized by strong myeloproliferation and high cardiovascular risk. Strict control of classical cardiovascular comorbidities such as intermediate hyperglycemia (IH) and diabetes mellitus (DM) in these patients is imperative. Interestingly, according to literature data, the prevalence of DM in MPN is unusually low (<15%). Possible reasons are tumor-induced hypoglycemia and shorter erythrocyte half-life, which can potentially cause falsely lower fasting plasma glucose (FPG) and HbA1c values, as well as the potential effect of cytoreductive treatment. The primary goal of this study was to determine the actual incidence of IH and D in patients with MPN using continuous glucose monitoring (CGM) devices that measure interstitial glucose concentration and are not dependent on blood count parameters.

Subjects and methods: This active prospective multicenter study is currently being conducted in three hematology centers in the Republic of Croatia (Šibenik-Knin County General Hospital, Rijeka Clinical Hospital Center and Dubrava Clinical Hospital) during 2025 and includes patients with MPN diagnosed according to 2022 World Health Organization criteria. All patients have blood samples taken on the day of the study, classic work-up for the detection of IH and DM (FPG, HbA1c and oral glucose tolerance test) is performed, and a CGM device is installed. The diagnosis of IH and DM is made according to criteria of the American Diabetes Association; the definition of these conditions according to CGM readings is defined as time in tight range (TITR; ref. 3.9-7.8mmol/L) of 70-89% for IH and <70% for DM.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

Results: Currently, 33 subjects are included (ET=10, PV=17, MF=5, MPN-u=1); median age is 71 years (36-85), 14 (42.4%) are women, 1 (3%) patient has a previous diagnosis of IH, and 8 (24.2%) have DM. HbA1c values were not shown to correlate with hemoglobin, hematocrit, erythrocyte count, or average glucose value measured with CGM (p>0.050 for all analyses). In patients without a previous diagnosis of IH and DM (n=21), IH was diagnosed in 9 (40.9%) patients and DM in one (4.5%) patient by classical diagnostics. After CGM placement, IH was diagnosed in 7 (31.8%) patients, as well as DM in 7 patients (31.8%). One patient with a previous diagnosis of IH was diagnosed with DM.

Conclusion: The prevalence of IH (n=7, 31,8%) and DM (n=15, 45,5%) in this preliminary sample appears to be actually very high in patients with MPN. Traditional diagnostic methods for the detection of MPN seem to be suboptimal in this patient population, which indicates the potential benefit of CGM in the diagnosis, monitoring and treatment of MPN in patients with IH and DM. The accrual is ongoing.

Keywords: Myeloproliferative neoplasms; diabetes mellitus: hyperglycemia; diagnosis; HbA1c

KRONIČNA MIJELOIČNA LEUKEMIJA: EVOLUCIJA TERAPIJE I PERSPEKTIVE NOVIH GENERACIJA INHIBITORA TIROZIN KINAZA (TKI)

Dr. sc. Aron Grubešić, dr. med. [1]
[1] *Specijalna bolnica Medico, Rijeka*

O – 13

Uvod: Kronična mijeloična leukemija (KML) klonalna je mijeloproliferativna neoplazma BCR::ABL1 fuzijskog onkogena i konstitutivno aktivne tirozin-kinaze. Uvođenje imatiniba 2001. godine označilo je paradigmatski pomak u onkologiji: transformacijom KML iz fatalne u kroničnu bolest desetogodišnje preživljenje poraslo je s ispod 20 % na više od 85–90 %. Rezistencija, toksičnosti i pitanje doživotne terapije ostaju ključni klinički izazovi.

Cilj: Prikazati evoluciju terapijskih ciljeva u KML, mehanizme djelovanja generacija inhibitora tirozin kinaza (TKI), klinički značaj alosteričke STAMP inhibicije te suvremene spoznaje o prekidu terapije (Treatment-Free Remission, TFR).
Metode. Pregled recentne literature i kliničkih smjernica (ELN 2020), s analizom pivotalnih studija: IRIS, ENESTnd, DASISION, OPTIC, ASC4FIRST te TFR studija STIM, EURO-SKI, ENESTfreedom i DASFREE.

Rezultati: ATP-kompetitivni TKI (imatinib, dasatinib, nilotinib, bosutinib, ponatinib) razlikuju se po konformacijskoj selektivnosti (DFG-in/Tip I vs. DFG-out/Tip II), što izravno određuje spektar mutacijske rezistencije. T315I gatekeeper mutacija bila je dugo terapijska prepreka, prevladana ponatinibom, a potom asciminibom u dozi 200 mg BID. Asciminib, prvi STAMP inhibitor (Specifically Targeting the ABL Myristoyl Pocket), stabilizira neaktivnu kinaznu konformaciju allosteričkim mehanizmom, omogućuje dual targeting kombinacijom s ATP-TKI te pokazuje MMR od 67,7 % pri 48 tjedana u studiji ASC4FIRST. TFR je ostvariv u 40–52 % bolesnika koji postignu stabilnu duboku molekularnu remisiju (MR4/MR4.5) ≥ 2 godine; dubina i trajanje remisije važniji su prediktori uspjeha od generacije TKI.

Zaključak: Razvoj TKI u KML paradigmatski je primjer precizne onkologije: razumijevanje strukturne osnove rezistencije dovelo je do terapija koje prevazilaze gotovo sve kliničke prepreke. STAMP inhibicija otvara put kombinacijskim strategijama i potencijalnom trajnom izlječenju bez doživotne farmakoterapije.

Ključne riječi: kronična mijeloična leukemija, TKI, STAMP, asciminib, T315I, TFR, BCR::ABL1

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

CHRONIC MYELOID LEUKEMIA: EVOLUTION OF THERAPY AND PERSPECTIVES ON NEW GENERATIONS OF TYROSINE KINASE INHIBITORS (TKIS)

Aron Grubešić MD, PhD [1]
[1] *Special Hospital Medico, Rijeka*

O – 13

Introduction: Chronic myeloid leukaemia (CML) is a clonal myeloproliferative neoplasm driven by the Philadelphia chromosome – translocation t(9;22) generating the BCR::ABL1 fusion oncogene and a constitutively active tyrosine kinase. The introduction of imatinib in 2001 marked a paradigm shift in oncology, transforming CML from a fatal disease into a chronic condition and raising the ten-year overall survival from below 20 % to more than 85–90 %. Despite this success, resistance, toxicity, and the question of lifelong therapy remain key clinical challenges.

Aim: To review the evolution of therapeutic targets in CML, the mechanisms of action across TKI generations, the clinical relevance of allosteric STAMP inhibition, and current evidence on Treatment-Free Remission (TFR).
Methods. Narrative review of current literature and clinical guidelines (ELN 2020), with analysis of pivotal trials: IRIS, ENESTnd, DASISION, OPTIC, ASC4FIRST, and TFR studies STIM, EURO-SKI, ENESTfreedom and DASFREE.

Results: ATP-competitive TKIs (imatinib, dasatinib, nilotinib, bosutinib, ponatinib) differ in conformational selectivity (DFG-in/Type I vs. DFG-out/Type II), which directly defines the mutational resistance profile. The T315I gatekeeper mutation was a major therapeutic obstacle, addressed by ponatinib and subsequently by asciminib at 200 mg BID. Asciminib, the first STAMP inhibitor (Specifically Targeting the ABL Myristoyl Pocket), stabilises the inactive kinase conformation through an allosteric mechanism, enables dual targeting in combination with ATP-TKIs, and demonstrated MMR of 67.7 % at 48 weeks in the ASC4FIRST trial. TFR is achievable in 40–52 % of patients who attain stable deep molecular remission (MR4/MR4.5) for ≥ 2 years; depth and duration of remission are stronger predictors of TFR success than the TKI generation used.

Conclusion: The development of TKIs in CML exemplifies precision oncology: understanding the structural basis of resistance has yielded therapies that overcome virtually all clinical obstacles. STAMP inhibition opens the path to combination strategies and potentially durable treatment-free cure without lifelong pharmacotherapy.

Keywords: chronic myeloid leukaemia, TKI, STAMP, asciminib, T315I, TFR, BCR::ABL1

SUBDOZIRANJE I SUBKUTANE PRIMJENE TERAPIJE KOD LIJEČENJA SOLIDNIH TUMORA

Prof. dr. sc. Dragan Trivanović, dr. med.[1]
[1] *OB Pula*

O-14

Danas se administracija lijekova u onkologiji prilagođuje želji pacijenata i kvaliteti života uz zadržavanje učinkovitosti i smanjenje nuspojava i financijske toksičnosti. Tako se primjerice subdoziranje modernih lijekova u nižim dozama od preporučenih od strane regulatornih agencija pokazalo opravdano temeljeno na dokazima iz farmakoekonomskih, farmakokinetskih i klasičnih kliničkih studija. Istovremeno se želi smanjiti boravak pacijenata u dnevnim bolnicama onkologije i aplicirati lijekove na najlakši način izbjegavajući intravensku primjenu. Subkutane aplikacije pokazale su značajni iskorak u liječenju prema pacijentima uz zadržavanje učinkovitosti.

Personaliziranje liječenja danas osim ciljanih mutacija i/ili prediktivnih biomarkera mora uključiti i prilagodbu spolu, životnim navikama i želji pacijenata.

U predavanju prikazuju se primjeri na najčešćim modernim lijekovima u liječenju solidnih tumora.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

SUBTHERAPEUTIC DOSING AND SUBCUTANEOUS ADMINISTRATION IN SOLID TUMOR TREATMENT

Prof. Dragan Trivanović, MD, PhD[1]
[1] *General Hospital Pula, Pula*

O-14

Drug administration in oncology is being adapted to patients' wishes and quality of life while maintaining efficacy and reducing side effects and financial toxicity. For example, subdosing modern drugs in lower doses than those recommended by regulatory agencies has proven to be justified based on evidence from pharmacoeconomic, pharmacokinetic and classical clinical studies. The aim is to reduce the length of stay of patients in oncology outpatient clinics and administer drugs in the easiest way possible, avoiding intravenous administration. Subcutaneous applications have shown a significant step forward in treating patients while maintaining efficacy.

Personalizing treatment today, in addition to targeted mutations and/or predictive biomarkers, must also include adaptation to gender, lifestyle and patient wishes.

The lecture will present examples of the most common modern drugs in the treatment of solid tumors.

GERIJATRIJSKA ONKOLOGIJA: POMICANJE GRANICA PREMA PRECIZNOJ ONKOLOGIJI ZA STARIJE OSOBE OBOLJELE OD RAKA

Nicolò Matteo Luca Battisti, MD, MRCP, MD(Res)[1]
[1] *Breast Unit of The Royal Marsden NHS Foundation Trust, London, UK*

O – 15

Starenje stanovništva preoblikuje globalni onkološki krajolik. Do 2040. godine gotovo tri četvrtine osoba koje su preživjele rak bit će u dobi od 65 godina ili starije, no starije osobe i dalje su nedovoljno zastupljene u kliničkim ispitivanjima i nedovoljno obuhvaćene tradicionalnim onkološkim modelima skrbi. Ovaj nesrazmjer između demografske stvarnosti i stvaranja znanstvenih dokaza pridonosi trajnoj nesigurnosti, terapijskoj heterogenosti te riziku i od nedovoljnog i od pretjeranog liječenja u svakodnevnoj kliničkoj praksi.

Liječenje raka u starijih osoba inherentno je složeno. Sama kronološka dob ne predstavlja adekvatan pokazatelj fiziološke rezerve, ranjivosti i podnošljivosti liječenja. Multimorbiditet, polifarmacija, kognitivna oštećenja, funkcionalni pad i socijalne odrednice zdravlja međusobno djeluju i utječu na ishode liječenja, toksičnost i kvalitetu života. Novija prospektivna istraživanja pokazuju da uključivanje sveobuhvatne gerijatrijske procjene (CGA) u onkološku skrb smanjuje toksičnost povezanu s liječenjem, poboljšava ishode usmjerene na pacijenta i podupire primjerenije terapijsko odlučivanje. Međunarodne konsenzusne smjernice danas preporučuju rutinski gerijatrijski probir i prilagođene multidisciplinarne intervencije kao standard skrbi.

Ovo izlaganje razmatra kako gerijatrijska onkologija unapređuje širi koncept precizne onkologije – onaj koji integrira biologiju tumora s biologijom pacijenta. Ključne teme uključuju strategije gerijatrijskog probira, intervencije temeljene na CGA-i, alate za predviđanje toksičnosti kemoterapije, modele zajedničke i sveobuhvatne skrbi te „gerijatrijizaciju" kliničkih ispitivanja. Oslanjajući se na međunarodne inicijative i konsenzusne prioritete, izlaganje će istaknuti praktične pristupe integriranju gerijatrijskih načela u farmakoterapijske putove.

Pomicanje granica prema preciznoj onkologiji za starije osobe zahtijeva strukturnu integraciju gerijatrije u onkološku skrb, redizajn istraživačkih okvira i globalnu suradnju. Usklađivanje intenziteta liječenja s biološkom dobi i individualnom ranjivošću ključno je za pružanje sigurnije, učinkovitije i pravednije skrbi za oboljele od raka u svijetu koji stari.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

GERIATRIC ONCOLOGY: MOVING THE NEEDLE TOWARDS PRECISION ONCOLOGY FOR OLDER ADULTS WITH CANCER

Nicolò Matteo Luca Battisti, MD, MRCP, MD(Res)[1]
[1] *Breast Unit of The Royal Marsden NHS Foundation Trust, London, UK*

O – 15

Population ageing is reshaping the global cancer landscape. By 2040, nearly three quarters of cancer survivors will be aged 65 years or older, yet older adults remain underrepresented in clinical trials and underserved by traditional oncology models. This mismatch between demographic reality and evidence generation contributes to persistent uncertainty, therapeutic heterogeneity, and the risks of both under- and over-treatment in routine practice.

Managing cancer in older adults is intrinsically complex. Chronological age alone is an inadequate surrogate for physiological reserve, vulnerability, and treatment tolerance. Multimorbidity, polypharmacy, cognitive impairment, functional decline, and social determinants of health interact to influence outcomes, toxicity, and quality of life. Recent prospective studies demonstrate that incorporating comprehensive geriatric assessment (CGA) into oncology care reduces treatment-related toxicity, improves patient-centred outcomes, and supports more appropriate therapeutic decision-making. International consensus guidelines now recommend routine geriatric screening and tailored multidisciplinary interventions as standards of care.

This presentation explores how geriatric oncology is advancing a broader concept of precision oncology - one that integrates tumour biology with patient biology. Key themes include geriatric screening strategies, CGA-driven interventions, chemotherapy toxicity prediction tools, shared-care and comprehensive care models, and the "geriatricising" of clinical trials. Drawing on international initiatives and consensus priorities, the session will highlight practical approaches to embedding geriatric principles within pharmacotherapy pathways.

Moving the needle towards precision oncology for older adults requires structural integration of geriatrics into cancer care, redesign of research frameworks, and global collaboration. Aligning treatment intensity with biological age and individual vulnerability is essential to deliver safer, more effective, and more equitable cancer care in an ageing world.

LIJEČENJE METASTATSKOG HORMONSKI OSJETLJIVOG RAKA PROSTATE

Prof. dr. sc. Tomislav Omrčen, dr. med.[1]
[1] *KBC Split, Split*

O - 16

Metastatski hormonski osjetljiv rak prostate (mHSPC) predstavlja heterogenu bolest s promjenjivom prognozom. Tradicionalno se liječio isključivo androgenom deprivacijskom terapijom (ADT), no recentni terapijski pomaci značajno su promijenili standard liječenja.

Zadnjih godina rezultati ključnih randomiziranih kliničkih ispitivanja koja su ispitivala učinkovitost kombinirane terapije: ADT s kemoterapijom (docetaksel) ili novim hormonskim lijekovima (inhibitori signalnog puta androgenog receptora, ARPI) u bolesnika s mHSPC-om doveli su do značajnog napretka u ishodima bolesnika s mHSPC.

Dodavanje docetaksela ili jednog od ARPI (abirateron, enzalutamid, apalutamid) ADT-u rezultiralo je značajnim produljenjem ukupnog preživljenja (OS) i vremena do progresije bolesti, neovisno o volumenu metastatske bolesti i vremenu njenog nastanka. Trojna terapija (ADT plus docetaksel plus ARPI) pokazuje dodatnu korist u odabranih bolesnika s visokim rizikom. Radioterapija primarnog tumora ima važnu ulogu u liječenju odabranih bolesnika s mHSPC, osobito onih s niskim volumenom metastatske bolesti. Randomizirana klinička ispitivanja pokazala su da dodavanje radioterapije prostate uz sustavno liječenje može poboljšati OS i lokalnu kontrolu bolesti u ovoj skupini bolesnika. Stoga se radioterapija primarnog tumora danas smatra dijelom multimodalnog pristupa u liječenju mHSPC kod pažljivo odabranih bolesnika.

Zaključno, liječenje mHSPC zahtijeva individualizirani pristup temeljen na kliničkim značajkama bolesnika i opterećenju bolešću. Rano intenziviranje liječenja postalo je novi standard skrbi, s ciljem poboljšanja dugoročnih ishoda i kvalitete života bolesnika.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

MANAGEMENT OF METASTATIC HORMONE-SENSITIVE PROSTATE CANCER

Prof. Tomislav Omrčen, MD, PhD[1]
[1] *University Hospital Centre Split, Split*

O - 16

Metastatic hormone-sensitive prostate cancer (mHSPC) is a heterogeneous disease with a variable prognosis. Traditionally, it was treated exclusively with androgen deprivation therapy (ADT); however, recent therapeutic advances have significantly changed the standard of care.

In recent years, the results of key randomized clinical trials evaluating the efficacy of combination therapy—ADT with chemotherapy (docetaxel) or with novel hormonal agents (androgen receptor pathway inhibitors, ARPIs)—in patients with mHSPC have led to substantial improvements in clinical outcomes. The addition of docetaxel or one of the ARPIs (abiraterone, enzalutamide, apalutamide) to ADT resulted in significant prolongation of overall survival and time to disease progression, regardless of metastatic disease volume and timing of metastatic onset. Triplet therapy (ADT plus docetaxel plus an ARPI) has demonstrated additional benefit in selected high-risk patients.

Radiotherapy to the primary tumor plays an important role in the management of selected patients with metastatic hormone-sensitive prostate cancer, particularly those with low-volume metastatic disease. Randomized clinical trials have demonstrated that the addition of prostate radiotherapy to systemic therapy can improve overall survival and local disease control in this patient population. Consequently, radiotherapy of the primary tumor is now considered an integral part of a multimodal treatment approach for carefully selected patients with mHSPC.

In conclusion, the management of mHSPC requires an individualized approach based on patients' clinical characteristics and disease burden. Early treatment intensification has become the new standard of care, with the aim of improving long-term outcomes and patients' quality of life.

ONKOLOŠKO LIJEČENJE MELANOMA

Prof. dr. sc. Antonio Juretić, dr. med.[1]
[1] *KB Dubrava, Zagreb*

O-17

Melanom je zloćudni tumor stanica melanocita koje stvaraju melanin (crni pigment). Zbog velike sklonosti ranom metastaziranju ubraja se među najagresivnije tumore kože. Po incidenciji spada među razmjerno rjeđe tumore ali incidencija mu je u porastu. Po podacima Hrvatskog zavoda za javno zdravstvo za 2022. g., po učestalosti je na 10. mjestu u popisu ukupnog zloćudnih bolesti (994/26105 = 4%).
Boja kože, svijetla put i izloženost ultraljubičastom zračenju te česte opekline od sunca u mladosti rizični su faktori za razvoj melanoma kože iako se melanom javlja i u regijama tijela koja su neizložena sunčevim zrakama.

Prognostički, nalaz razmjerno većeg primarnog tumora u smislu njegove debljine u mm i nalaza ulceracije, zatim nalaz lokoregionalno proširene bolesti ili metastatske bolesti ukazuje na prognostički loš ishod za bolesnika. Strategija liječenja melanoma ovisi, uz suglasnost bolesnika, o općem stanju i dobi bolesnika, patohistološkim karakteristikama melanoma, procjeni proširenosti bolesti i dostupnosti pojedinih terapijskih opcija.

Uz uobičajene standardne terapijske modalitete kojima se smatraju kirurško liječenje, zračenje i kemoterapija, unatrag zadnjih desetak godina terapijske opcije i ishodi lijećenja u bolesnika s melanomom su poboljšani uvađanjem lijekova iz grupe „molekularno-ciljana terapije“ i imunoterapije. Molekularno-ciljana se terapija temelji na blokadi molekula u tumorskim stanicama koje se u vezi prijenosa signala rasta ili proliferacije a kako su te molekule najčešće određene mutacijama gena skupine onkogena i tumor supresorskih gena, u tumorskim stanicama dolazi do njihovog nekontroliranog rasta i stjecanja drugih karakteristika zlućudnih stanica (sklonost metastatiranju, rast u uvjetima hipoksije).

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

O-17

U liječenju melanoma u tom smislu ako se ima nalazi „mutirane“ molekule BRAF (BRAFV600) primjenjuju se oralni lijekovi koji blokiraju „mutiranu“ molekulu BRAF i molekulu MEK (BRAFV600 i MEK inhibitori). Pretpostavka je tumorske imunologije da se tumorske stanice antigeno mogu razlikovati od normalnih zdravih stanica i da imunološki sustav može prepoznati tu antigensku razliku, odnosno reagirati protiv tumorskih stanica i izazvati njihovo uništenje.

U liječenju melanoma primjenju se monoklonskih antitijela koja blokiraju tzv. inhibitorne receptore u anergičnih limfocita, tako da dolazi do njihove reaktivacije. Ta su antitijela usmjerena protiv membranskih molekula CTLA-4, PD-1, PD-L1 i LAG-3, a terapija je naziva „blokada molekula kontrolnih točaka“. Ta antitijela ne djeluju protiv tumorskih stanica. Postoji i opcija primjene i limfokina i limfocita s antigen kimeričnim receptorima (CARs, prema enl. Chimeric Antigen Receptors).

Uvađanjem navedene ciljane terapije i imunoterapije očekivalo se je kroz razmjerno veću specifičnost tih modaliteta da se neće imati izraženih nuspojava liječenja, ali nuspojave postoje i kod tih terapija. Ti se razni terapijski modaliteti i pristupi mogu primijeniti kao primarni modaliteti liječenja s radikalnom namjerom, zatim u bolesnika u riziku od povrata bolesti u adjuvantnoj primjeni ali i neoadjuvantno prije operacije ili kod nalaza metastatske bolesti.

U predavanju dat će se kratak prikaz mjesta i uloge navedenih terapijskih modaliteta

MALIGNANT MELANOMA TREATMENT AND MANAGEMENT

Prof. Antonio Juretić, MD, PhD[1]
[1] *University hospital Dubrava, Zagreb*

O-17

Melanoma is a malignant tumor of melanocyte cells that produce melanin (black pigment). Due to its high tendency to metastasize early, it is one of the most aggressive skin tumors. In terms of incidence, it is a relatively rare tumor, but its incidence is increasing. According to data from the Croatian Institute of Public Health for 2022, it is 10th in frequency in the list of total malignant diseases (994/26105 = 4%).
Skin color, fair complexion and exposure to ultraviolet radiation, as well as frequent sunburns in youth are risk factors for the development of skin melanoma, although melanoma also occurs in regions of the body that are not exposed to sunlight.

Prognostically, the finding of a relatively larger primary tumor in terms of its thickness in mm and the finding of ulceration, then the finding of locoregionally extended disease or metastatic disease indicates a poor prognostic outcome for the patient. The treatment strategy for melanoma depends, with the patient's consent, on the general condition and age of the patient, the pathohistological characteristics of the melanoma, the assessment of the extent of the disease and the availability of individual therapeutic options.

In addition to the usual standard therapeutic modalities, which are considered surgery, radiation and chemotherapy, over the past ten years, therapeutic options and treatment outcomes in patients with melanoma have been improved by the introduction of drugs from the group of "molecular-targeted therapy" and immunotherapy.

Molecular-targeted therapy is based on the blockade of molecules in tumor cells that are involved in the transmission of growth or proliferation signals, and since these molecules are most often determined by mutations in genes from the oncogene and tumor suppressor gene groups what causes in tumor cells their uncontrolled growth occurs and the acquisition of other characteristics of malignant cells (tendency to metastasize, growth in hypoxia).

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

O-17

Oral drugs that block the "mutated" BRAF molecule and the MEK molecule (BRAFV600 and MEK inhibitors) are used in the treatment of melanoma having BRAFV600 mutation. The assumption of tumor immunology is that tumor cells can be antigenically distinct from normal healthy cells and that the immune system can recognize this antigenic difference, i.e. react against tumor cells and cause their destruction.

In the treatment of melanoma, monoclonal antibodies are used that block the so-called inhibitory receptors in anergic lymphocytes, so that they are reactivated. These antibodies are directed against the membrane molecules CTLA-4, PD-1, PD-L1 and LAG-3, and the therapy is called "checkpoint immunotherapy (checkpoint inhibitors)". These antibodies do not act against tumor cells.

There is also the option of using lymphokines and lymphocytes with chimeric antigen receptors (CARs, Chimeric Antigen Receptors). With the introduction of the aforementioned targeted therapy and immunotherapy, it was expected that there would be no pronounced side effects of treatment through the greater specificity of these modalities, but side effects also exist with these therapies.

These various therapeutic modalities and approaches can be applied as primary treatment modalities with radical intent, then in patients at risk of disease recurrence in adjuvant application but also neoadjuvant before surgery or when metastatic disease is found.

The lecture will give a brief description of the place and role of the mentioned therapeutic modalities.

IMUNOTERAPIJA U SOLIDNIM TUMORIMA – RACIONALNI PRISTUP TERAPIJI I LIJEČENJE NUSPOJAVA

Dr. sc. Marin Golčić, dr. med.[1]
[1] *KBC Rijeka, Rijeka*

O – 18

Imunoterapija je u posljednjem desetljeću značajno promijenila paradigmu liječenja solidnih tumora, omogućujući višestruko produljenje preživljenja, osobito u metastatskoj bolesti. Na primjer, za metastatski melanom je 2015. medijan preživljenja iznosio manje od 12 mjeseci, dok 2025. doseže i do 72 mjeseca, što predstavlja gotovo sedmerostruko produljenje, a u preko trećine pacijenata dugoročno nema uopće povrata bolesti. Uz melanom, posebno se ističu tumori poput raka pluća, urotela, kolona, a posebno je zanimljivo i odobrenje za bilo kakve solidne tumore s MSI-H statusom, što je do tada bilo nezamislivo.

Imunoterapija se danas sve više koristi i u adjuvantnom i neoadjuvantnom okruženju, primjerice kod melanoma stadija IIB i IIC, gdje je zabilježeno smanjenje rizika povrata bolesti. Međutim, u nekim indikacijama nema jasnog dokaza o produljenju ukupnog preživljenja, već samo dužem vremenu bez povrata bolesti, što otvara pitanja financijske opravdanosti i kliničke koristi.

Značajan problem predstavljaju nuspojave. Barem 16 % bolesnika ima značajnu, često i po život opasnu nuspojavu koje su prvenstveno autoimunog podrijetla, a mogu zahvatiti bilo koji organ (npr., kolitis, tireoiditis, miokarditis, neurološki poremećaji). Liječenje često zahtijeva kortikosteroide, biološku terapiju, a kod refraktornog kolitisa i fekalnu mikrobiotu transplantaciju.

Zaključno, imunoterapija je revolucionarna u liječenju značajnog broja tumora, ali zahtijeva individualni i racionalni pristup uz aktivno uključivanje pacijenta u odluke.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

IMMUNOTHERAPY IN SOLID TUMORS – A RATIONAL THERAPEUTIC APPROACH AND MANAGEMENT OF ADVERSE EFFECTS

Marin Golčić, MD, PhD[1]
[1] *University Hospital Centre Rijeka, Rijeka*

O – 18

Immunotherapy has significantly changed the treatment paradigm of solid tumors over the past decade, enabling multiple-fold improvements in survival, particularly in metastatic disease. For example, in metastatic melanoma, the median overall survival in 2015 was less than 12 months, whereas by 2025 it has reached up to 72 months, representing an almost sevenfold increase. Moreover, in more than one third of patients, there is no disease recurrence at all in the long term. In addition to melanoma, tumors such as lung cancer, urothelial carcinoma, and colorectal cancer have particularly benefited, and the approval of immunotherapy for any solid tumor with MSI-H status is especially noteworthy, as this was previously unimaginable.

Today, immunotherapy is increasingly used in both the adjuvant and neoadjuvant settings, for example in stage IIB and IIC melanoma, where a reduction in the risk of disease recurrence has been demonstrated. However, in some indications there is no clear evidence of improved overall survival, but rather only prolonged recurrence-free survival, which raises questions regarding financial justification and true clinical benefit.

Adverse events represent a significant challenge. At least 16% of patients experience severe, often life-threatening side effects, primarily of autoimmune origin, which can affect virtually any organ system (e.g., colitis, thyroiditis, myocarditis, neurological disorders). Management often requires corticosteroids, biologic therapy, and in cases of refractory colitis, fecal microbiota transplantation.

In conclusion, immunotherapy is revolutionary in the treatment of a significant number of cancers, but it requires an individualized and rational approach, with active patient involvement in decision-making.

LJEČENJE DEBLJINE I MIKRONUTRITIVNA PODRŠKA U ONKOLOŠKIH PACIJENATA

Doc. dr. sc. Ana-Marija Liberati Pršo, dr. med[1]
[1] *KB Sveti Duh*

O – 20

Uvod:
Prevalencija pretilosti i prekomjerne težine u Hrvatskoj izuzetno je visoka: oko 59% odraslih ima BMI ≥25 kg/m², a približno 30% ispunjava kriterije za pretilost, pri čemu je prevalencija viša u žena te je u skladu s uzlaznim trendom srednje i istočne Europe. Prekomjerna tjelesna masa prepoznata je kao rizični čimbenik za niz sijela karcinoma (dojka, endometrij, jajnikj, kolorektum, gušterača, jednjak, bubrezi, jetra, žučni mjehur, multipli mijelom, štitnjača) te je povezana s većom smrtnošću i lošijom prognozom.

Cilj:
Prikazati ključne mehanizme kojima pretilost utječe na karcinogenezu i ishode liječenja, razmotriti načela nefarmakološkog i farmakološkog liječenja pretilosti u onkoloških bolesnika te naglasiti ulogu procjene i ciljanog liječenja mikronutritivnih deficita, uz posebnu važnost racionalne suplementacije u kliničkoj praksi liječnika i magistara farmacije.

Metode:
Sažetak se temelji na recentnim smjernicama i pregledima (ASCO, ESMO, ESPEN) te novijim epidemiološkim, kliničkim i farmakološkim podacima o povezanosti pretilosti, ishoda liječenja raka i nutritivnih intervencija, uključujući primjenu agonista GLP-1/GLP-1/GIP receptora i mikronutritivnu podršku.

Rezultati:
Mehanizmi koji povezuju pretilost i karcinome uključuju hiperinzulinemiju i porast bioraspoloživog IGF-1, promjene spolnih hormona, disbalans adipokina, kroničnu metainflamaciju, metaboličko remodeliranje i oksidativni stres, što pridonosi karcinogenezi i progresiji bolesti. Pretilost je povezana s rekurencijom bolesti i kraćim preživljenjem te može utjecati na doziranje i toksičnost sistemske terapije i kompleksnost kirurškog liječenja. U aktivnoj fazi onkološkog liječenja jedan od prioriteta je očuvanje mišićne mase i sprječavanje malnutricije; strukturirani gubitak težine preporučuje se primarno u fazi remisije, dok se tijekom liječenja razmatra samo blagi, strogo nadzirani gubitak uz fokus na redukciju masnog tkiva.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

Nefarmakološke intervencije uključuju umjeren kalorijski deficit (15–20%), visokoproteinsku prehranu po obrascu Mediteranske dijete, uz redovito nutricionističko savjetovanje te ciljanu tjelovježbu u granicama podnošljivosti. Podaci o sigurnosti i učinkovitosti agonista GLP-1 te GLP-1/GIP receptora tijekom aktivne onkološke terapije još su ograničeni; rutinska primjena nije preporučena bez multidisciplinarne procjene, uz osobit oprez u sarkopeničnoj debljini i kod GLP-1R-pozitivnih neuroendokrinih tumora.

Pretilost je često praćena mikronutritivnim deficitima (vitamin D, vitamini B skupine, željezo, cink i dr.), koji se mogu dodatno pogoršati smanjenim unosom hrane i nuspojavama lijekova za mršavljenje, pa se preporučuje sustavna procjena statusa, ciljano laboratorijsko praćenje (posebno 25(OH)D, željezo/B12/folat) i individualizirana nadoknada. Rutinska, neselektivna suplementacija vitaminima i mineralima nije preporučena; mikronutrijenti se indiciraju isključivo kod dokumentiranih deficita ili specifičnih kliničkih stanja, u dozama bliskim preporučenom dnevnom unosu, uz oprez zbog mogućih interakcija s onkološkom terapijom i signala o mogućem nepovoljnom utjecaju visokodoznih antioksidansa tijekom kemoterapije

Zaključak:
Liječenje pretilosti u onkoloških bolesnika zahtijeva individualizirani, multimodalni pristup koji uravnotežuje potencijalne onkološke koristi i gubitak težine s rizikom sarkopenije i malnutricije. Za liječnike i farmaceute ključno je sustavno prepoznavanje i korekcija mikronutritivnih deficita, racionalna uporaba lijekova za liječenje debljine i dodataka prehrani te aktivna komunikacija s bolesnicima o sigurnosti i stvarnim koristima suplementacije, u sklopu multidisciplinarne nutritivne skrbi.

OBESITY TREATMENT AND MICRONUTRIENT SUPPORT IN ONCOLOGY PATIENTS

Asst. prof. Ana-Marija Liberati Pršo, MD, PhD [1]
[1] *University Hospital Sveti Duh*

O – 20

Background:
Obesity is highly prevalent in Croatia, where approximately 59% of adults have a BMI ≥25 kg/m² and around 30% meet criteria for obesity, with a higher prevalence in women and an upward trend comparable to other Central and Eastern European countries. Excess body weight is a recognized risk factor for cancer (postmenopausal breast cancer, endometrium, ovary, colorectum, pancreas, oesophagus, kidney, liver, gallbladder and thyroid cancer, multiple myeloma) and is associated with poorer prognosis and higher mortality rates.

Objective:
To present key mechanisms linking obesity with carcinogenesis and cancer treatment outcomes, to outline principles of non-pharmacological and pharmacological obesity treatment in cancer patients, and to highlight the role of evaluation and targeted management of micronutrient deficiencies, with particular emphasis on rational supplementation in the daily practice of physicians and pharmacists.

Methods:
This summary is based on recent guidelines and reviews (ASCO, ESMO, ESPEN) and updated epidemiological, clinical, and pharmacological data on the relationship between obesity, cancer outcomes, and nutritional interventions, including the use of GLP-1 and GLP-1/GIP receptor agonists and micronutritional support.

Results:
Mechanisms linking obesity and cancer include hyperinsulinaemia with increased bioavailable IGF-1, alterations in sex hormones, adipokine imbalance, chronic low-grade inflammation, metabolic remodelling, and oxidative stress, all of which promote carcinogenesis and disease progression. Obesity is associated with higher recurrence rates and shorter survival in several cancer types and can influence systemic therapy dosing and toxicity, as well as the complexity of surgical treatment. During active systemic therapy, the priority is to preserve muscle mass and prevent malnutrition; structured weight loss is primarily recommended in remission/survivorship, whereas during treatment only modest, closely supervised weight reduction focused on fat mass is considered.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

Non-pharmacological interventions include a moderate caloric deficit (15–20% below estimated needs), high-protein intake within a Mediterranean dietary pattern, regular dietitian follow-up, and tailored exercise - as clinically tolerated. Evidence on the safety and efficacy of GLP-1 and GLP-1/GIP receptor agonists during active cancer therapy remains limited; routine use is not recommended without multidisciplinary evaluation, with particular caution in sarcopenic obesity, and GLP-1 receptor–positive neuroendocrine tumours.
Obesity is frequently accompanied by micronutrient deficiencies (vitamin D, B vitamins iron, zinc and others), which may be exacerbated by reduced food intake and adverse effects of anti-obesity drugs; systematic assessment, targeted laboratory monitoring (especially 25(OH)D, iron/B12/folate), and individualized replacement are therefore recommended. Routine, non-selective vitamin and mineral supplementation is not advised; micronutrients should be used only in documented deficiencies or specific clinical situations, at doses close to recommended daily intake, with caution regarding potential interactions with anticancer therapies and signals of possible detrimental effects of high-dose antioxidants during chemotherapy.

Conclusion:
Management of obesity in cancer patients requires an individualized, multimodal approach that balances potential oncological benefits of weight loss against the risk of sarcopenia and malnutrition. For physicians and pharmacists, systematic identification and correction of micronutrient deficiencies, rational use of anti-obesity medications and dietary supplements, and proactive communication with patients about the safety and true benefits of supplementation are essential components of multidisciplinary nutritional care

REFEEDING SINDROM – PREVENCIJA I LIJEČENJE

Dr. sc. Dina Ljubas Kelečić, mag. pharm. [1]
[1] *KBC Zagreb, Zagreb*

O – 22

Refeeding sindrom je ozbiljna metabolička komplikacija kod pothranjenih bolesnika nakon ponovnog uvođenja nutritivne potpore.

Unatoč poznatoj patofiziologiji i brojnim prikazima slučajeva u literaturi, RFS ostaje značajan klinički problem s incidencijom do 34% u određenim bolničkim populacijama. Patofiziologija temelji se na prijelazu iz katabolizma u anabolizam s posljedičnim elektrolitskim disbalansom, gdje je hipofosfatemija glavno obilježje.

Tiamin ima ključnu koenzimsku ulogu u metabolizmu ugljikohidrata, a tjelesne zalihe su ograničene i iscrpljuju se nakon 2-3 tjedna gladovanja. Deficit tiamina manifestira se neurološkim komplikacijama, ponajprije Wernickeovom encefalopatijom i Wernicke-Korsakoffovim sindromom.

Kliničke manifestacije zahvaćaju kardiovaskularni sustav i živčani sustav. Rizične skupine uključuju bolesnike s teškom malnutricijom, značajnim gubitkom tjelesne mase i prolongiranim gladovanjem. Prevencija zahtijeva pravovremenu identifikaciju rizičnih bolesnika, postupno uvođenje prehrane i profilaktičku primjenu tiamina uz praćenje elektrolita.

Implementacija preventivnih strategija od strane multidisciplinarnih nutritivnih timova ključna je za smanjenje morbiditeta i mortaliteta.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

REFEEDING SYNDROME – PREVENTION AND TREATMENT

Dina Ljubas Kelečić, MPharm, PhD [1]
[1] *University Hospital Centre Zagreb, Zagreb*

O – 22

Refeeding syndrome is a serious metabolic complication in malnourished patients following the reintroduction of nutritional support.

Despite well-established pathophysiology and numerous case reports in the literature, RFS remains a significant clinical problem with an incidence of up to 34% in certain hospital populations. The pathophysiology is based on the transition from catabolism to anabolism with consequent electrolyte imbalance, with hypophosphatemia being the main feature. Thiamine has a crucial coenzyme role in carbohydrate metabolism, and body stores are limited and depleted after 2-3 weeks of starvation.

Thiamine deficiency manifests as neurological complications, primarily Wernicke's encephalopathy and Wernicke-Korsakoff syndrome. Clinical manifestations affect the cardiovascular system and the nervous system.

Risk groups include patients with severe malnutrition, significant weight loss, and prolonged starvation.

Prevention requires timely identification of at-risk patients, gradual introduction of nutrition, and prophylactic thiamine administration with electrolyte monitoring. Implementation of preventive strategies by multidisciplinary nutrition teams is crucial for reducing morbidity and mortality.

PRIPREMA NOVIH GENERACIJA LJEKARNIKA ZA PRAKSU USMJERENU NA PACIJENTA

Izv. prof. dr. sc. Iva Mucalo, mag. pharm. [1]
[1] *Farmaceutsko - biokemijski fakultet Sveučilišta u Zagrebu, Zagreb*

O – 23

Obrazovanje ljekarnika posljednjih se desetljeća postupno udaljava od dominantno laboratorijski usmjerenog modela prema modelu koji u središte stavlja pacijenta i njegove terapijske potrebe. Razvoj studijskog programa sve više odražava promjene u ulozi ljekarnika te stavlja naglasak na jačanje kliničkih kompetencija i rada s pacijentima.

Od bolonjske reforme 2005. godine postupno se uvode i proširuju kolegiji Klinička farmacija s farmakoterapijom, Ljekarnička skrb, Socijalna farmacija i Konzultacijske vještine, uz primjenu metoda poput učenja temeljenog na rješavanju problema, rada u malim skupinama, simuliranih i stvarnih konzultacija te izrade individualnih planova ljekarničke skrbi.

Nastava uključuje intervjue sa stvarnim pacijentima, analizu njihova iskustva bolesti i terapije te strukturiranu procjenu terapijskih potreba. Sadržaji usmjereni na pacijenta integrirani su i u stručne prakse te Stručno osposobljavanje za ljekarnike, kao i u rad Farmakoterapijskog savjetovališta u suradnji s Domom zdravlja Zagreb Centar.

Cilj ovakvog kurikuluma jest obrazovati ljekarnika koji, uz temeljito farmakološko znanje, razumije terapijsko iskustvo pacijenta, prepoznaje i rješava terapijske probleme te aktivno pridonosi boljim zdravstvenim ishodima.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

TRAINING THE NEW GENERATION OF PHARMACISTS FOR PATIENT-CENTERED PRACTICE

Assoc. prof. Iva Mucalo, MPharm, PhD[1]
[1] *Faculty of Pharmacy and Biochemistry, University of Zagreb, Zagreb*

O – 23

Education of pharmacists over the past decades has gradually shifted away from a predominantly laboratory-oriented model toward one that places the patient and their therapeutic needs at the center. The development of study programs increasingly reflects changes in the role of the pharmacist, emphasizing the strengthening of clinical competencies and patient-centered practice.

Since the Bologna reform in 2005, courses such as Clinical Pharmacy with Pharmacotherapy, Pharmaceutical Care, Social Pharmacy, and Consultation Skills have been progressively introduced and expanded.
These courses apply teaching methods including problem-based learning, small-group work, simulated and real consultations, and the development of individualized pharmaceutical care plans.

Teaching activities include interviews with real patients, analysis of their experiences of illness and therapy, and structured assessment of therapeutic needs. Patient-centered content is also integrated into professional placements and the Professional Training for Pharmacists, as well as into the work of the Pharmacotherapy Counseling Service in cooperation with the Dom zdravlja Zagreb Centar.

The aim of such a curriculum is to educate pharmacists who, in addition to thorough pharmacological knowledge, understand the patient's therapeutic experience, identify and resolve therapy-related problems, and actively contribute to improved health outcomes.

PROJEKT NCODA HRVATSKA

Ana Vrkić[1]
[1] *CPSA*

O-24

Network for Collaborative Oncology Development & Advancement (NCODA) međunarodna je, neprofitna profesionalna organizacija usmjerena na unapređenje medicinski integrirane i pacijentu usmjerene onkološke skrbi.

Kroz povezivanje kliničke prakse, farmacije, edukacije i industrije, NCODA sustavno doprinosi razvoju sigurnije i kvalitetnije onkološke farmakoterapije.

Poseban naglasak stavlja se na razvoj i implementaciju Positive Quality Interventions (PQI), standardiziranih, stručno utemeljenih alata koji omogućuju ujednačenu i optimalnu primjenu onkološke terapije u kliničkoj praksi. PQI-jevi definiraju kliničke probleme, ciljeve intervencija, uloge članova tima te mjerljive pokazatelje kvalitete skrbi.

Unutar NCODA-e djeluje Professional Student Organization (PSO), međunarodna studentska organizacija koja okuplja studente farmacije i drugih zdravstvenih usmjerenja te ih aktivno uključuje u edukacijske, istraživačke i stručne aktivnosti u području onkologije.

Osnivanjem NCODA Hrvatska omogućeno je povezivanje studenata s međunarodnom NCODA mrežom, razvoj edukacijskih aktivnosti, upoznavanje s PQI-jevim i jačanje suradnje s kliničkom praksom. Time se potiče rani profesionalni razvoj studenata i njihova aktivna uloga u unapređenju racionalne i sigurne onkološke farmakoterapije.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

PROJECT NCODA CROATIA

Ana Vrkić[1]
[1] *CPSA*

O-24

The Network for Collaborative Oncology Development & Advancement (NCODA) is an international, non-profit professional organization focused on advancing medically integrated, patient-centered oncology care. By connecting clinical practice, pharmacy, education, and industry, NCODA contributes to the continuous improvement of quality and safety in oncology pharmacotherapy.

A key component of NCODA's activities is the development and implementation of Positive Quality Interventions (PQIs), standardized, evidence-based tools designed to support consistent and optimal application of oncology therapies in clinical practice. PQIs address specific clinical challenges, define intervention goals, clarify team member roles, and include measurable quality indicators.

Within NCODA, the Professional Student Organization (PSO) serves as an international platform for pharmacy and other healthcare students, actively involving them in educational, research, and professional activities in oncology.

The establishment of NCODA Croatia enables students to engage with the international NCODA network, participate in educational initiatives, become familiar with PQIs, and strengthen collaboration with clinical practice. This approach supports early professional development and encourages students to take an active role in promoting rational and safe oncology pharmacotherapy.

CPSA PROJEKTI CPSA-E U 2026. GODINI - MULTIPROFESIONALNA SURADNJA

Filip Simić[1]
[1] *CPSA*

O - 25

Udruga studenata farmacije i medicinske biokemije Hrvatske (CPSA) jedina je udruga u Republici Hrvatskoj koja zastupa interese studenata farmacije i medicinske biokemije.

Ciljevi udruge su unaprjeđivanje suradnje između studenata u Hrvatskoj i inozemstvu, kao i širenje svijesti o javnom zdravlju među djecom, adolescentima, studentima i odraslima. Sve navedeno Udruga postiže organizacijom mnogih javnozdravstvenih projekata, edukativnih aktivnosti i skupova, natjecanja, redovitim vođenjem društvenih mreža i organizacijom društveno-humanitarnih aktivnosti te studentskih razmjena.

Osim suradnje na razini studenata farmacije i medicinske biokemije, Udruga sudjeluje u brojnim multidisciplinarnim projektima u suradnji sa studentima medicine, nutricionizma, ekonomije i dr.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

CPSA PROJECTS IN 2026 – MULTIPROFESSIONAL COLLABORATION

Filip Simić[1]
[1] *CPSA*

O - 25

The Croatian Pharmaceutical and Medical Biochemistry Students' Association (CPSA) is the only organization in the Republic of Croatia that represents the interests of students of pharmacy and medical biochemistry.

The Association's goals include improving cooperation among students in Croatia and abroad, as well as raising awareness of public health among children, adolescents, students, and adults. The Association achieves these goals by organizing numerous public health projects, educational activities and events, competitions, maintaining an active presence on social media, and organizing social and humanitarian activities as well as student exchange programs.

In addition to collaboration at the level of pharmacy and medical biochemistry students, the Association participates in numerous multidisciplinary projects in cooperation with students of medicine, nutrition, economics, and other related fields.

PREDNOSTI CENTRALNE PRIPREME ANTINEOPLASTIKA

Anamarija Husnjak, mag. pharm. [1]
[1] *OB Varaždin, Varaždin*

O - 26

Antineoplastici pripadaju skupini visokorizičnih lijekova zbog svoje toksičnosti, uskog terapijskog raspona i potencijalno ozbiljnih posljedica pogrešaka u pripremi i primjeni. U praksi bolničkih ustanova još uvijek je prisutna varijabilnost u načinu pripreme, često uz decentralizirani model, što povećava rizik za pacijente, izloženost zdravstvenih djelatnika te dovodi do neracionalne potrošnje skupih lijekova. Centralna priprema u bolničkoj ljekarni predstavlja odgovor na navedene izazove te usklađivanje s važećim regulatornim zahtjevima.

Rad prikazuje prednosti centralne pripreme antineoplastika i ostalih sterilnih visokorizičnih lijekova u kontekstu EU GMP regulative, s posebnim naglaskom na Annex 1. Centralizirani model omogućuje aseptičku pripremu u validiranim prostorima, standardizirane postupke, farmaceutsku validaciju terapije, dokumentiranu sljedivost te kontinuirani mikrobiološki monitoring, čime se osigurava kontrolirani i dokazivi proces.

Cilj ovog rada je prikazati prednosti centralne pripreme antineoplastika s aspekta sigurnosti pacijenta i zaštite osoblja, kvalitete i standardizacije procesa, farmakoekonomskih učinaka te organizacijske uloge bolničkog farmaceuta. Poseban naglasak stavljen je na smanjenje rizika kontaminacije, pogrešaka u doziranju i izloženosti citotoksičnim lijekovima, kao i na racionalnije korištenje terapija kroz grupnu pripremu i bolje iskorištenje pakiranja.

Zaključno, centralna priprema antineoplastika predstavlja nužan i održiv model moderne bolničke prakse, koji istodobno osigurava sigurnost pacijenata, štiti zdravstvene djelatnike i jača ulogu bolničkog farmaceuta kao jamca kvalitete i sigurnosti terapije.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

BENEFITS OF CENTRALIZED PREPARATION OF ANTINEOPLASTIC AGENTS

Anamarija Husnjak, MPharm[1]
[1] *General Hospital Varaždin, Varaždin*

O - 26

Antineoplastic drugs belong to the group of high-risk medications due to their toxicity, narrow therapeutic range, and the potentially serious consequences of errors in preparation and administration. In hospital practice, there is still variability in preparation methods, often following a decentralized model, which increases risk for patients, exposure of healthcare workers, and leads to irrational use of expensive drugs. Centralized preparation in the hospital pharmacy addresses these challenges and ensures compliance with current regulatory requirements.

This paper presents the advantages of centralized preparation of antineoplastics and other sterile high-risk drugs in the context of EU GMP regulations, with particular emphasis on Annex 1. The centralized model allows aseptic preparation in validated facilities, standardized procedures, pharmaceutical validation of therapy, documented traceability, and continuous microbiological monitoring, ensuring a controlled and verifiable process.

The aim of this paper is to demonstrate the benefits of centralized preparation of antineoplastics from the perspective of patient and staff safety, quality and process standardization, pharmacoeconomic effects, and the organizational role of the hospital pharmacist. Special emphasis is placed on reducing the risk of contamination, dosing errors, and exposure to cytotoxic drugs, as well as on more rational use of therapies through batch preparation and better utilization of packaging.

In conclusion, centralized preparation of antineoplastics represents a necessary and sustainable model of modern hospital practice, simultaneously ensuring patient safety, protecting healthcare workers, and strengthening the role of the hospital pharmacist as a guarantor of therapy quality and safety.

SIGURNA PRIPRAVA CITOTOKSIČNIH LIJEKOVA – ISKUSTVA IZ KBC-A OSIJEK

Aurora Antolović - Amidžić, mag. pharm[1]
[1] *KBC Osijek, Osijek*

O – 27

Priprema citotoksičnih lijekova u KBC-u Osijek, organizirana je davne 2007. godine.
Tada smo pripremali četrdeset priprema dnevno, dok je danas ta brojka uvećana 8 puta.
Priprema je uključivala volumetriju, ručno vođenje tijeka izrade, naziva lijeka, serije, roka valjanosti, izračuna.

Danas, gravimetrijska priprema uz korištenje gravimetrijskog sustava konfiguriranog preko precizne vage. Bar kod čitak nam osigurava sigurnost.
Izrada je organizirana kroz sustav bioloških kabineta, izolatora i robota.

U izolatorima izrađujemo biološku terapiju volumetrijskom metodom.
Najizazovniji dio je robot s kojim smo nakon nekoliko mjeseci „prepiranja“ napokon pronašli zajednički jezik. Maksimalno izrađujemo 65 pripravaka po danu.
Robot je velika pomoć pri izradi isključivo citotoksičnih lijekova. Izrada pripravaka elastomernih pumpi i bolus terapija je ostala farmaceutskim tehničarima.

Problem nam predstavlja unos lijekova u bazu te se nadamo brojci od 80-tak izrada kada nam se ista poveća za dodatnih 6 lijekova.

Uvođenjem novih tehnika rada u radni proces osigurava se kvalitetnija skrb za pacijente, a za djelatnike sigurnost.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

ENSURING SAFETY IN CYTOTOXIC DRUG PREPARATION: INSIGHTS FROM CLINICAL HOSPITAL CENTRE OSIJEK

Aurora Antolović - Amidžić, MPharm[1]
[1] *University Hospital Centre Osijek, Osijek*

O – 27

The preparation of cytotoxic drugs at KBC Osijek was organized back in 2007.
At that time, we prepared forty preparations per day, while today that number has increased 8 times.
The preparation included volumetry, manual recording of the production process, drug names, batch numbers, expiry dates, and calculations.

Today, gravimetric preparation is used with a gravimetric system configured via a precision scale. A barcode reader ensures our safety.
Production is organized through a system of biological cabinets, isolators, and robots.

In isolators, we produce biological therapy using the volumetric method.
The most challenging part is the robot, with which we finally found a common language after several months of “arguing.” We produce a maximum of 65 preparations per day.
The robot is a great help in producing exclusively cytotoxic drugs. The production of elastomeric pump preparations and bolus therapies has been left to pharmaceutical technicians.

Our challenge is the entry of drugs into the database, and we hope for a figure of around 80 preparations when it increases by an additional 6 drugs.

By introducing new work techniques into the workflow, better care for patients is ensured, and safety for the staff.

PRIPREMA CITOTOKSIČNIH LIJEKOVA U KBC RIJEKA

Marina Paladin, mag. pharm. [1]
[1] *KBC Rijeka, Rijeka*

O - 28

Centralizirana priprema citotoksičnih lijekova u bolničkoj ljekarni KBC-a Rijeka započela je 2025. godine.

Proteklih 6 mjeseci suočili smo se s mnogim izazovima i inovacijama. Posebnu pažnju posvetili smo sigurnosti i zaštiti zdravstvenog osoblja koje priprema citotoksične lijekove. Koristeći suvremenu medicinsku opremu i robotizaciju procesa, osigurali smo precizno doziranje lijekova za bolesnike. Primjenom zatvorenih sustava smanjili smo izloženost osoblja citotoksičnim lijekovima te poboljšali kvalitetu izrade gotovih pripravaka. Izazovi s kojima se susrećemo su najviše vezani za nedostatak programskog rješenja koji bi osigurao još veću sigurnost za bolesnike i minimizirao medikacijske pogreške.

Uz parenteralne pripravke, laboratorij za centraliziranu pripremu citotoksičnih lijekova priprema i suspenzije koje sadrže citotoksične lijekove koristeći automatiziran uređaj za magistralnu pripremu lijekova, WetMill. WetMill uređaj ima inovativni pristup pripremanja suspenzija iz cijelih tableta ili kapsula, smanjujući izloženost osoblja djelatnim tvarima.

Ovom prezentacijom istaknuti ćemo i važnost kreiranja i primjene desenzibilizacijskih protokola za bolesnike koji su imali reakcije preosjetljivosti na citotoksične lijekove.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

PREPARATION OF CYTOTOXIC DRUGS AT CLINICAL HOSPITAL CENTRE RIJEKA

Marina Paladin, MPharm. [1]
[1] *University Hospital Centre Rijeka Rijeka*

O - 28

The centralized preparation of cytotoxic drugs in the hospital pharmacy of University Hospital Centre Rijeka began in 2025.

Over the past six months, we have faced numerous challenges and introduced several innovations. We placed special emphasis on the safety and protection of healthcare personnel involved in the preparation of cytotoxic drugs. By using modern medical equipment and process automation, we ensured precise drug dosing for patients. Through the implementation of closed-system drug transfer devices, we reduced staff exposure to cytotoxic agents and improved the quality of the final compounded preparations. The challenges we are currently facing are mainly related to the lack of a comprehensive software solution that would further enhance patient safety and minimize medication errors.

In addition to parenteral preparations, the centralized cytotoxic drug compounding laboratory also prepares suspensions containing cytotoxic agents using an automated compounding device, WetMill. The WetMill device offers an innovative approach to preparing suspensions from whole tablets or capsules, thereby reducing staff exposure to active pharmaceutical ingredients.

In this presentation, we will also highlight the importance of developing and implementing desensitization protocols for patients who have experienced hypersensitivity reactions to cytotoxic drugs

EKG PROMJENE KOJE NE DOPUŠTAJU PRIMJENU KEMOTERAPIJE I ŠTO PRATITI KOD ONKOLOŠKIH BOLESNIKA

Izv. prof. dr. sc. Mislav Puljević, dr. med.[1]
[1] *KBC Zagreb, Zagreb*

O – 29

EKG promjene koje ne dopuštaju primjenu kemoterapije i što pratiti kod onkoloških bolesnika / Preventing Cardiac Events During Chemotherapy: ECG Patterns That Change Management and How to Monitor

Predavanje prikazuje ulogu EKG-a kao brzog i praktičnog sigurnosnog alata u kardio-onkologiji, s ciljem da se onkološko liječenje provede učinkovito, ali uz minimalan rizik ozbiljnih kardiovaskularnih komplikacija. Naglasak je na situacijama u kojima EKG nalaz neposredno utječe na odluku o primjeni terapije: nastavak uz definirani plan praćenja, kratkotrajna odgoda radi ciljane obrade ili privremena obustava do stabilizacije i korekcije reverzibilnih čimbenika.

U fokusu su četiri skupine nalaza koje EKG najčešće rano detektira: produljenje QTc intervala i proaritmijski rizik, ishemijske promjene odnosno koronarni vazospazam (ST–T promjene), poremećaji intraventrikularnog i AV provođenja te klinički značajne aritmije. Posebno se naglašava važnost usporedbe s prethodnim EKG-om i prepoznavanja dinamičkih promjena, jer trend često ima veću prognostičku vrijednost od izolirane vrijednosti u jednom mjerenju.

Kao ključni "alarmi" navode se QTc ≥ 500 ms ili porast QTc-a ≥ 60 ms u odnosu na početni nalaz, što u pravilu zahtijeva privremenu obustavu terapije, korekciju elektrolita (K, Mg, Ca), reviziju popratne terapije s QT-produljujućim potencijalom te ponavljanje EKG-a nakon intervencija. Novonastale ST–T promjene zahtijevaju potvrdu nalaza i ciljanu procjenu (vitalni znakovi, elektroliti te selektivno serijsko određivanje hs-troponina), uz napomenu da uredan troponin ne isključuje koronarni vazospazam, osobito u bolesnika na fluoropirimidinima. Jasne situacije za "ne primijeniti terapiju danas" uključuju torsade de pointes/sustavne ventrikulske aritmije te visokostupanjske AV blokove (Mobitz II ili kompletni AV blok), pri čemu hemodinamska nestabilnost ima apsolutni prioritet.

Zaključno, standardizirani algoritmi i checkliste smanjuju varijabilnost kliničkih odluka, povećavaju sigurnost bolesnika i olakšavaju očuvanje kontinuiteta onkološkog liječenja.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

ECG CHANGES THAT PRECLUDE CHEMOTHERAPY ADMINISTRATION AND MONITORING IN ONCOLOGY PATIENTS

Assoc. prof. Mislav Puljević, MD, PhD[1]
[1] *University Hospital Centre Zagreb*

O – 29

The lecture explains how the ECG can be used as a fast, practical safety checkpoint in cardio-oncology—helping teams deliver cancer therapy safely without creating avoidable cardiac harm or unnecessary treatment delays. The emphasis is on real-world decisions made at the point of care: when it is reasonable to proceed with treatment with a clear monitoring plan, when a short postponement is safer to allow focused evaluation, and when therapy should be held until the situation is clarified and stabilized.

The talk centers on four ECG patterns that most often change immediate management: QTc prolongation with an increased risk of malignant ventricular arrhythmias, ST–T abnormalities suggesting myocardial ischemia or coronary vasospasm, atrioventricular or intraventricular conduction disease, and clinically important arrhythmias. A key message is that an ECG only becomes truly useful when it is interpreted in context—especially by comparing it with prior tracings—because the direction and speed of change often matter more than a single number measured once.

Specific high-risk signals are highlighted. A QTc of 500 ms or more, or a rise in QTc of 60 ms or more from baseline, usually justifies pausing therapy long enough to correct reversible drivers (particularly potassium, magnesium, and calcium abnormalities), review interacting medications that prolong QT, and then repeat the ECG after corrective steps. New, contiguous ST–T changes should be confirmed and followed by a targeted same-day assessment, including vital signs, electrolytes, and—when appropriate—serial high-sensitivity troponin testing. Importantly, a normal troponin does not rule out coronary vasospasm, which is especially relevant in patients treated with fluoropyrimidines. Finally, certain findings are treated as "not today" situations: torsades de pointes or sustained ventricular arrhythmias, and high-grade AV block (Mobitz II or complete AV block), with hemodynamic instability always taking priority over infusion plans.

Overall, the lecture argues that simple, standardized algorithms and checklists reduce variability, improve safety, and help patients stay on their cancer treatment pathway with fewer preventable interruptions.

NOVA PRIMJENA POSTOJEĆIH LIJEKOVA U HEMATOLOGIJI

Darko Krnić, dr. med.[1]
[1] *pharma& , Austria*

O - 30

Prenamjena lijekova je postupak istraživanja novih terapijskih indikacija za već odobrene tvari ili one u fazi ispitivanja.

Glavne prednosti ovog pristupa su veća brzina dolaska do pacijenta, znatno niži troškovi razvoja i već poznat profil sigurnosti.

Prenamjena lijekova izravno smanjuje financijsku toksičnost (visokih troškova liječenja koji opterećuju pacijente i zdravstvene sustave) jer značajno snižava troškove razvoja, štedeći u nekim slučajevima stotine milijuna dolara po novoj indikaciji.

Globalni regulatori poput FDA, EMA-e i WHO-a aktivno podržavaju ove inicijative kroz brojne olakšice i pilot-projekte.

Prenamjena lijekova nije samo znanstveni trend, već nužnost koja koristi postojeće resurse za rješavanje nezadovoljenih medicinskih potreba. Ovakvi inovativni pristupi ubrzavaju dostupnost liječenja i značajno poboljšavaju ishode za hematološke bolesnike.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

NEW APPLICATIONS OF EXISTING DRUGS IN HEMATOLOGY

Darko Krnić, MD[1]
[1] *pharma& , Austria*

O - 30

Drug repurposing is the process of researching new therapeutic indications for already approved substances or those in the clinical trial phases.

The main advantages of this approach are faster access for patients, significantly lower development costs, and a well-known safety profile.

Drug repurposing directly reduces financial toxicity (the high costs of treatment that burden patients and healthcare systems) because it significantly lowers development costs, saving sometimes hundreds of millions of dollars per new indication.

Global regulators such as the FDA, EMA, and WHO actively support these initiatives through numerous incentives and pilot projects. Drug repurposing is not just a scientific trend, but a necessity that uses existing resources to address unmet medical needs. Such innovative approaches accelerate availability and clinical outcomes for hematology patients.

CIRKADIJALNA REGULACIJA I FARMAKOGENOMSKI PRISTUPI U PRECIZNOJ ONKOLOGIJI

Prof. dr. sc. Elitza Markova-Car [1]
[1] *Medicinski fakultet Sveučilišta u Rijeci, Rijeka*

O – 31

Precizna onkologija sve se više oslanja na integraciju molekularne genetike i kronobiologije kako bi se individualiziralo liječenje raka i poboljšali klinički ishodi.

Dvije komplementarne strategije, farmakogenomika i kronoterapija, postupno se prenose iz istraživačkog okruženja u rutinsku onkološku praksu. Farmakogenomska varijabilnost ima ključnu ulogu u sigurnosti kemoterapije, osobito u režimima temeljenima na fluoropirimidinima. Genetski polimorfizmi u genu DPYD, uključujući c.1905+1G>A, c.1679T>G, c.2846A>T i c.1129-5923C>G, smanjuju aktivnost dihidropirimidinske dehidrogenaze (DPD) i značajno povećavaju rizik od teške, potencijalno životno ugrožavajuće toksičnosti. Međunarodne kliničke smjernice (CPIC, DPWG, EMA) danas preporučuju predterapijsko DPYD genotipiziranje radi prilagodbe doze i sprječavanja nuspojava.

U skladu s tim preporukama, u Kliničkom bolničkom centru Rijeka uvedeno je rutinsko testiranje na DPD-deficijenciju, uz proširenje standardnog panela varijanti novim klinički relevantnim polimorfizmima, poput c.496A>G i c.2194G>A. Ovakav farmakogenomski pristup omogućuje sigurniju primjenu fluoropirimidina uz očuvanje terapijske učinkovitosti. Paralelno s time, cirkadijalni ritmovi reguliraju temeljne fiziološke procese važne za biologiju raka, uključujući metabolizam lijekova, popravak DNA, napredovanje staničnog ciklusa i imunološke odgovore.

Poremećaj cirkadijalnog sata povezan je s tumorigenezom, kemorezistencijom i ishodima preživljenja. Kronoterapija, vremenski usklađena primjena kemoterapije prema cirkadijalnom ritmu, pokazala je poboljšanu podnošljivost i učinkovitost u kliničkim ispitivanjima, osobito pri vremenski moduliranoj primjeni 5-fluorouracila, oksaliplatina i irinotekana.

Posebno je važno da novi dokazi upućuju na spolno specifične kronoterapijske rasporede te ističu ulogu satnih gena u odgovoru na terapiju i razvoju rezistencije. Integracija farmakogenomskog testiranja s vremenski prilagođenom kemoterapijom predstavlja pragmatičan i klinički primjenjiv okvir za preciznu onkologiju. Kombiniranjem genetskog profiliranja s kronobiološkom optimizacijom terapije, ovaj dvostruki pristup nudi put prema sigurnijem, učinkovitijem i uistinu na pacijenta usmjerenom liječenju raka.

Ključne riječi: farmakogenomika, kronoterapija, DPYD

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

CIRCADIAN REGULATION AND PHARMACOGENOMIC APPROACHES IN PRECISION ONCOLOGY

Prof. Elitza Markova-Car, PhD [1]
[1] *The Faculty of Medicine of the University of Rijeka*

O – 31

Precision oncology increasingly relies on integrating molecular genetics and chronobiology to individualize cancer therapy and improve clinical outcomes.

Two complementary strategies, pharmacogenomics and chronotherapy, are now translating from research into routine oncology practice. Pharmacogenomic variability plays a critical role in chemotherapy safety, particularly in fluoropyrimidine-based regimens. Genetic polymorphisms in the DPYD gene, including c.1905+1G>A, c.1679T>G, c.2846A>T, and c.1129-5923C>G, reduce dihydropyrimidine dehydrogenase (DPD) activity and markedly increase the risk of severe, potentially life-threatening toxicity. International clinical guidelines (CPIC, DPWG, EMA) now recommend pre-treatment DPYD genotyping to guide dose adjustments and prevent adverse outcomes.

In line with these recommendations, routine DPD deficiency screening has been implemented at the University Hospital Centre Rijeka, expanding the standard variant panel to include emerging clinically relevant polymorphisms such as c.496A>G and c.2194G>A. This pharmacogenomic approach enables safer fluoropyrimidine therapy while preserving therapeutic efficacy. In parallel, circadian rhythms regulate fundamental physiological processes relevant to cancer biology, including drug metabolism, DNA repair, cell cycle progression, and immune responses.

Disruption of the circadian clock has been implicated in tumorigenesis, chemoresistance, and survival outcomes. Chronotherapy, administering chemotherapy according to circadian timing, has demonstrated improved tolerability and efficacy in clinical trials, particularly with circadian-modulated delivery of 5-fluorouracil, oxaliplatin, and irinotecan.

Notably, emerging evidence supports sex-specific chronotherapeutic schedules and highlights the role of clock genes in therapy response and resistance. The integration of pharmacogenomic testing with circadian-guided chemotherapy represents a pragmatic and clinically actionable framework for precision oncology. By combining genetic profiling with chronobiological optimization, this dual strategy offers a pathway to safer, more effective, and truly patient-centered cancer treatment.

Keywords: pharmacogenomics, chronotherapy, DPYD

KAD BRZO RJEŠENJE OSTAVI TRAG: PANDORINA KUTIJA OFF-LABEL PRIMJENE LIJEKOVA ZA MRŠAVLJENJE

Andrej Belančić, dr. med.[1]
[1] *KBC Rijeka, Rijeka*

O – 32

Agonisti receptora glukagonu sličnog peptida-1 (GLP-1 RA) i dualni agonisti transformirali su liječenje šećerne bolesti tipa 2 i pretilosti, omogućujući održiv gubitak tjelesne mase te značajne kardiometaboličke koristi. Međutim, njihova brza primjena izvan odobrenih indikacija otvorila je novu „zonu rizika".

Potaknuti utjecajem slavnih osoba, društvenim mrežama i potrošačkom potražnjom za brzim mršavljenjem, ovi se lijekovi sve češće koriste kod osoba bez medicinske potrebe. Takva praksa narušava načela medicine utemeljene na dokazima, doprinosi nestašicama lijekova i izlaže korisnike izbježnim rizicima. Nuspojave nadilaze prolazne gastrointestinalne smetnje te uključuju metaboličke, nutritivne, mišićno-koštane i psihološke komplikacije, uključujući pogoršanje problema s tjelesnom slikom i poremećaje hranjenja. Primjena u nedovoljno istraženim populacijama iskrivljuje stvarnu sliku djelotvornosti i sigurnosti u svakodnevnoj praksi, potencijalno precjenjujući koristi i podcjenjujući rizike.

Na društvenoj razini, fokus na kozmetičke ishode odvraća pozornost od pretilosti kao kronične, recidivirajuće bolesti koja zahtijeva promjene životnog stila i multidisciplinarni pristup, te narušava javno razumijevanje realnih očekivanja, dostižnih ishoda i stvarnog sigurnosnog profila ovih lijekova.

Središnja poruka je jasna: u rukama imamo jedan od najsnažnijih farmakoloških alata u borbi protiv pretilosti i njezinih komplikacija. Otključavanje njihova transformativnog potencijala zahtijeva strukturiranu i na dokazima utemeljenu primjenu. GLP-1 RA i dualni agonisti trebaju nadopunjavati, a ne zamjenjivati intervencije usmjerene na promjenu životnog stila, izbjegavajući „sindrom kauča". Izvanindikacijska estetska primjena, poput „sindroma crvenog tepiha", nosi etičke, sigurnosne i dugoročne psihološke rizike te ju treba izbjegavati.

U konačnici, uspjeh ovih terapija neće se mjeriti isključivo rezultatima kliničkih ispitivanja, nego i odgovornošću njihove primjene u svakodnevnoj kliničkoj praksi. Stoga rješavanje ovog izazova zahtijeva edukaciju propisivača, stroži regulatorni nadzor te racionalnu, na dokazima utemeljenu uporabu.

Ključne riječi: Tjelesna slika; Kozmetičko mršavljenje; Zlouporaba lijekova; Agonisti receptora glukagonu sličnog peptida-1; Izvanindikacijska primjena

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

THE CONSEQUENCES OF OFF-LABEL WEIGHT LOSS DRUG USE: OPENING PANDORA'S BOX

Andrej Belančić, MD[1]
[1] *University Hospital Centre Rijeka, Rijeka*

O – 32

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and dual agonists have transformed type 2 diabetes and obesity management, achieving durable weight loss and cardiometabolic benefits. Yet their rapid adoption beyond approved indications has opened a new "danger zone".

Fueled by celebrity influence, social media, and consumer demand for rapid weight reduction, these agents are increasingly used by individuals without medical need. This diversion undermines evidence-based care, contributes to drug shortages, and exposes users to preventable harms. Adverse effects extend beyond transient gastrointestinal intolerance to metabolic, nutritional, musculoskeletal, and psychological complications, including exacerbation of body image concerns and disordered eating. Use in unstudied populations distorts the real-world picture of both efficacy and safety, exaggerating benefits and obscuring risks.

At a societal level, the focus on cosmetic outcomes diverts attention from obesity as a chronic, relapsing disease requiring lifestyle and multidisciplinary management, skewing public understanding of realistic expectations, achievable outcomes, and the true safety profile of these agents.

The central message is clear: we hold in our hands one of the most potent pharmacological tools against obesity and its complications. Unlocking their transformative potential requires structured, evidence-based implementation. GLP-1 RAs and dual agonists should complement—not replace—lifestyle interventions, avoiding "couch potato syndrome." Off-label aesthetic use, such as "red carpet syndrome," carries ethical, safety, and long-term psychological risks, and should be avoided.

The success of these therapies will ultimately be measured not solely by clinical trial outcomes, but by how responsibly they are applied in real-world practice. Thus, addressing this challenge requires prescriber education, stricter regulatory oversight, and rational, evidence-based use.

Keywords: Body Image; Cosmetic Weight Loss; Drug Misuse; Glucagon-Like Peptide-1 Receptor Agonists; Off-Label Use

POSTER IZLAGANJA

EKONOMSKI DOKAZI KOJI USPOREĐUJU EMPAGLIFLOZIN I DAPAGLIFLOZIN U DIJABETESU, ZATAJIVANJU SRCA I KRONIČNOJ BUBREŽNOJ BOLESTI: SUSTAVNI PREGLED ANALIZA TROŠKOVNE UČINKOVITOSTI I TROŠKOVNE KORISNOSTI

Ana Galić [1] , Ida Štimac [2] , Andrej Belančić, dr.med. [3]

[1] Farmaceutsko-biokemijski fakultet, Sveučilište u Zagrebu
[2] Sveučilište u Rijeci, Medicinski fakultet, Rijeka
[3] Odjel za temeljnu i kliničku farmakologiju i toksikologiju, Sveučilište u Rijeci, Medicinski fakultet, Rijeka

PS – 1

Inhibitori natrij–glukoza kotransportera 2 (SGLT2) postali su temelj liječenja šećerne bolesti tipa 2 (T2DM), kronične bubrežne bolesti (KBB) i zatajivanja srca, uz snažne dokaze o kliničkim koristima koje nadilaze samu glikemijsku kontrolu. Kako se indikacije za primjenu šire, a terapija zahtijeva dugotrajnu primjenu, razumijevanje relativne ekonomske vrijednosti pojedinih SGLT2 inhibitora postaje sve važnije za donošenje odluka u zdravstvenom sustavu. Stoga je ovaj sustavni pregled literature imao za cilj procijeniti i usporediti dokaze o troškovnoj učinkovitosti i troškovnoj korisnosti empagliflozina i dapagliflozina u ove tri indikacije.

Sustavni pregled literature proveden je u skladu sa smjernicama Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Pretraživanje baze PubMed/MEDLINE provedeno je 27. studenoga 2025. kako bi se identificirale studije koje su izvještavale o analizama troškovne učinkovitosti (CEA) ili troškovne korisnosti (CUA) uspoređujući empagliflozin i dapagliflozin u dijabetesu (T2DM), zatajivanju srca (HF) i/ili kroničnoj bubrežnoj bolesti (KBB). Uključene su studije objavljene od 1. siječnja 2020. nadalje. Primijenjene su sljedeće strategije pretraživanja: (1) empagliflozin AND dapagliflozin AND cost*; i (2) empagliflozin AND dapagliflozin AND econom*. Metodološka kvaliteta uključenih ekonomskih evaluacija procijenjena je pomoću BMJ kontrolne liste, dok je kvaliteta izvještavanja ocijenjena prema smjernicama Consolidated Health Economic Evaluation Reporting Standards (CHEERS).

Podaci su ručno izdvojeni u obrasce za ekstrakciju u programu Microsoft Excel 360. Izdvojene varijable uključivale su prvog autora, godinu objave, državu, perspektivu analize, vrstu ekonomske evaluacije, godinu i valutu troškova, vremenski horizont, vrstu modela, karakteristike populacije/primarnu dijagnozu, detalje intervencije, ekonomske ishode, zaključke i dodatne napomene.

PS – 1

Početno pretraživanje identificiralo je 55 i 37 studija iz dviju strategija pretraživanja. Nakon primjene kriterija uključenja, u pregled je uključeno ukupno 13 studija: sedam o zatajivanju srca, četiri o T2DM-u i dvije o dijabetičkoj bubrežnoj bolesti (DKB). Uočen je značajan stupanj heterogenosti među studijama u pogledu perspektiva, ekonomskih modela (pretežito Markovljevi modeli) i vremenskih horizonta (uglavnom doživotni). Među studijama o T2DM-u, tri su bile CEAs, a jedna CUA, provedene u Sjedinjenim Američkim Državama, Iranu, Grčkoj i Kini. Većina tih studija pokazala je da je empagliflozin troškovno učinkovitiji od dapagliflozina. Studije o zatajivanju srca uključivale su tri studije o HFrEF-u, dvije o HFpEF-u, jednu o miješanoj populaciji HFpEF/HFmrEF te jednu s neprecizirano definiranim tipom HF-a. Pet studija bile su CEAs, a dvije CUAs, provedene u Sjedinjenim Američkim Državama (n=4), Kini (n=2) i Tajlandu (n=1). Većina tih studija upućivala je na to da je dapagliflozin troškovno učinkovitiji od empagliflozina. Nisu identificirane studije koje bi uspoređivale troškovnu učinkovitost empagliflozina i dapagliflozina u KBB-u kod bolesnika bez dijabetesa. U području DKB-a, jedna CEA iz Kine i jedna CUA iz Tajlanda pokazale su troškovnu učinkovitost oba lijeka; međutim, nije bilo moguće donijeti jasan zaključak o nadmoći jednog lijeka nad drugim.

Ovaj sustavni pregled literature pokazuje da su i empagliflozin i dapagliflozin troškovno učinkovite terapijske opcije u liječenju T2DM-a, zatajivanja srca i dijabetičke bubrežne bolesti, pri čemu njihova relativna ekonomska vrijednost varira ovisno o indikaciji.

Empagliflozin se češće pokazuje troškovno učinkovitijim u T2DM-u, vjerojatno zbog dokazanog učinka na smanjenje velikih nepovoljnih kardiovaskularnih događaja. Suprotno tome, dapagliflozin pokazuje veću troškovnu učinkovitost u populacijama sa zatajivanjem srca. Analize troškovne učinkovitosti i troškovne korisnosti u indikaciji kronične bubrežne bolesti i dalje su prijeko potrebne. Za dijabetičku bubrežnu bolest trenutačni dokazi ne daju jasnu prednost niti jednom od ova dva lijeka.

Ovi nalazi naglašavaju potrebu za indikacijski specifičnim ekonomskim evaluacijama kako bi se poduprlo donošenje odluka u zdravstvenom sustavu u kontekstu sve šire kliničke primjene SGLT2 inhibitora.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

ECONOMIC EVIDENCE COMPARING EMPAGLIFLOZIN AND DAPAGLIFLOZIN IN DIABETES, HEART FAILURE, AND CHRONIC KIDNEY DISEASE: A SYSTEMATIC REVIEW OF COST-EFFECTIVENESS AND COST-UTILITY ANALYSES

Ana Galić [1] , Ida Štimac [2] , Andrej Belančić, MD [3]

[1] Faculty of Pharmacy and Medicinal Biochemistry, University of Zagreb
[2] Faculty of Medicine, University of Rijeka
[3] Department of Basic and Clinical Pharmacology and Toxicology, University of Rijeka, Faculty of Medicine, Rijeka, Croatia

PS – 1

Sodium–glucose cotransporter 2 (SGLT2) inhibitors have become a cornerstone of care across type 2 diabetes mellitus (T2DM), chronic kidney disease, and heart failure, with robust evidence supporting their clinical benefits beyond glycaemic control. As indications expand and long-term treatment is required, understanding the relative economic value of individual SGLT2 inhibitors is increasingly important for healthcare decision-making.

Thus, this systematic literature review evaluated and compared the cost-effectiveness and cost-utility evidence for empagliflozin and dapagliflozin across these three indications. We conducted a systematic literature review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. PubMed/MEDLINE was searched on 27 November 2025 to identify studies reporting cost-effectiveness (CEAs) or cost-utility analyses (CUAs) comparing empagliflozin and dapagliflozin in diabetes (T2DM), heart failure (HF), and/or chronic kidney disease (CKD). Eligible studies were published from 1 January 2020 onwards. The following search strategies were applied: (1) empagliflozin AND dapagliflozin AND cost*; and (2) empagliflozin AND dapagliflozin AND econom*. Methodological quality of included economic evaluations was assessed using the BMJ checklist, while reporting quality was evaluated using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist.

Data were extracted manually into Microsoft Excel 360 extraction forms. Extracted variables included first author, publication year, country, perspective, type of economic evaluation, costing year and currency, time horizon, model type, population characteristics/primary diagnosis, intervention details, economic outcomes, conclusions, and additional comments.

PS – 1

The initial search identified 55 and 37 studies from the two search strategies, respectively. After applying inclusion criteria, 13 studies were included in the review: seven on HF, four on T2DM, and two on diabetic kidney disease (DKD). There was substantial heterogeneity across studies regarding perspectives, economic models (predominantly Markov models), and time horizons (mostly lifetime). Among the T2DM studies, three were CEAs, and one was a CUA, conducted in the United States, Iran, Greece, and China, respectively. These predominantly indicated that empagliflozin was more cost-effective than dapagliflozin. The HF studies included three on HFrEF, two on HFpEF, one on mixed HFpEF/HFmrEF, and one on unspecified. Five were CEAs and two CUAs, conducted in the United States (n=4), China (n=2), and Thailand (n=1).

These studies mostly suggested that dapagliflozin was more cost-effective than empagliflozin. No studies were identified comparing the cost-effectiveness of empagliflozin versus dapagliflozin in CKD in patients without diabetes. In DKD, one CEA from China and one CUA from Thailand reported cost-effectiveness for both agents; however, no clear conclusion regarding superiority could be drawn.

This systematic literature review highlights that both empagliflozin and dapagliflozin are cost-effective treatment options across T2DM, HF, and DKD, with their relative economic value varying by indication. Empagliflozin tends to be more cost-effective in T2DM, likely driven by its demonstrated benefit in reducing major adverse cardiovascular events. Conversely, dapagliflozin shows greater cost-effectiveness in HF populations. CEAs and CUAs in the CKD indication are highly needed. For DKD, the current evidence does not clearly favour one agent over the other.

These findings emphasize the need for indication-specific economic evaluations to inform healthcare decision-making as the clinical use of SGLT2 inhibitors continues to expand.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

AUTOIMUNA BOLEST I POLIFARMACIJA U SVAKODNEVNOJ PRAKSI: ULOGA FARMAKOTERAPIJSKOG SAVJETOVALIŠTA U OPTIMIZACIJI TERAPIJE – PRIKAZ SLUČAJA

Ana Močić, mag. pharm.[1] , Antun Roca, mag. pharm.[1] , Lucia Bačelić, mag. pharm.[1]

[1] ZU Ljekarna Šibenik

PS – 2

Uvod:

Bolesnici s kroničnim autoimunim bolestima često zahtijevaju dugotrajnu imunosupresivnu terapiju i sistemske glukokortikoide, što povećava rizik polifarmacije, nuspojava i metaboličkih komplikacija, uključujući dislipidemiju i povišen kardiovaskularni rizik. U takvim kompleksnim kliničkim situacijama nerijetko se uočava nesklad između preporuka smjernica i njihove primjene. Farmakoterapijsko savjetovalište u javnoj ljekarni može imati važnu ulogu u identifikaciji farmakoterapijskih problema i optimizaciji terapije.

Prikaz slučaja:

Prikazana je 63-godišnja pacijentica s dijagnozom gigantocelularnog arteritisa, reumatske polimijalgije i reumatoidnog vaskulitisa, liječena dugotrajnom terapijom glukokortikoidima i metotreksatom. Kronološkom analizom laboratorijskih nalaza utvrđena je perzistentna dislipidemija (LDL 3,84–4,67 mmol/L) uz dodatne čimbenike kardiovaskularnog rizika povezane s kroničnom upalom i kortikosteroidnom terapijom. U farmakoterapijskom savjetovalištu identificirani su ključni problemi, uključujući smanjenu podnošljivost metotreksata i neliječenu dislipidemiju. Provedena je intervencija koja je uključivala preporuku uvođenja statinske terapije, optimizaciju suplementacije folnom kiselinom, strukturirano praćenje krvnog tlaka te plan sigurnosnog laboratorijskog praćenja. Nakon ponovljenih savjetovanja i dokumentirane procjene rizika pacijentica je upućena kardiologu, nakon čega je započeta statinska terapija, uz planiranu kontrolu lipidnog profila.

Zaključak:

Ovaj prikaz slučaja pokazuje da farmakoterapijsko savjetovalište u javnoj ljekarni može imati važnu ulogu u racionalizaciji terapije, smanjenju nesklada između smjernica i kliničke primjene te unapređenju sigurnosti liječenja kod bolesnika s autoimunim bolestima i polifarmacijom.

Ključne riječi: autoimuna bolest; polifarmacija; farmakoterapijsko savjetovalište

AUTOIMMUNE DISEASE AND POLYPHARMACY IN EVERYDAY PRACTICE: THE ROLE OF A PHARMACOTHERAPY COUNSELING SERVICE IN THERAPY OPTIMIZATION – A CASE REPORT

Ana Močić, MPharm.[1] , Antun Roca, MPharm.[1], Lucia Bačelić, MPharm.[1]

[1] Primary Health Care Pharmacy Šibenik

PS – 2

Introduction:

Patients with chronic autoimmune diseases often require long-term immunosuppressive therapy and systemic glucocorticoids, which increases the risk of polypharmacy, adverse drug reactions, and metabolic complications, including dyslipidemia and elevated cardiovascular risk. In such complex clinical settings, a discrepancy between guideline recommendations and their implementation is frequently observed. Pharmacotherapy counseling services in community pharmacies can play an important role in identifying pharmacotherapy-related problems and optimizing treatment.

Case Presentation:

A 63-year-old female patient diagnosed with giant cell arteritis, polymyalgia rheumatica, and rheumatoid vasculitis was treated with long-term glucocorticoid and methotrexate therapy. Chronological analysis of laboratory findings revealed persistent dyslipidemia (LDL 3.84–4.67 mmol/L) in the presence of additional cardiovascular risk factors related to chronic inflammation and corticosteroid therapy. In the pharmacotherapy counseling service, key therapeutic issues were identified, including reduced methotrexate tolerability and untreated dyslipidemia. The intervention included a recommendation to initiate statin therapy, optimization of folic acid supplementation, structured blood pressure monitoring, and a safety laboratory monitoring plan. Following repeated counseling sessions and documented risk assessment, the patient was referred to a cardiologist, after which statin therapy was initiated, with follow-up lipid profile assessment planned.

Conclusion:

This case report demonstrates that pharmacotherapy counseling services in community pharmacies can play a significant role in rationalizing therapy, reducing the discrepancy between clinical guidelines and real-world practice, and improving treatment safety in patients with autoimmune diseases and polypharmacy.

Keywords: autoimmune disease; polypharmacy; pharmacotherapy counseling service

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

PORAST SREDNJEG VOLUMENA ERITROCITA (MCV) TIJEKOM LIJEČENJA HIDROKSIUREJOM U BOLESNIKA S ESENCIJALNOM TROMBOCITEMIJOM I POLICITEMIJOM VEROM NE PREDVIĐA KLINIČKE ISHODE

Antonija Dužaić[1], Doc. dr. sc. Marko Skelin, mag. pharm[1-3] , Doc. dr. sc. Ivan Krečak, dr. med.[1,3,4]

[1] Medicinski fakultet u Rijeci
[2] Odjel bolnička ljekarna, Opća bolnica Šibensko-kninske županije
[3] Sveučilište primijenjenih znanosti u Šibeniku
[4] Odjel interne medicine
[5] Opća bolnica Šibensko-kninske županije

PS – 3

Uvod:
Hidroksiureja je standardna citoreduktivna terapija u bolesnika s esencijalnom trombocitemijom (ET) i policitemijom verom (PT). Tijekom liječenja često dolazi do porasta srednjeg volumena eritrocita (MCV), no klinički značaj ove pojave nije u potpunosti razjašnjen. Cilj ovog istraživanja bio je analizirati ima li porast MCV-a tijekom liječenja hidroksiurejom utjecaj na važne kliničke ishode u bolesnika s ET i PT.

Metode:
Provedeno je retrospektivno, unicentrično istraživanje u Općoj bolnici Šibensko-kninske županije. Uključeni su bolesnici s dijagnozom ET i PV liječeni hidroksiurejom u razdoblju od 2009. do 2022. godine. Vrijednosti MCV-a analizirane su u trenutku postavljanja dijagnoze i nakon tri mjeseca liječenja. Omjer MCV-a nakon tri mjeseca i početne vrijednosti > 1 definiran je kao porast MCV-a. Analizirana je povezanost porasta MCV-a s kliničkim ishodima: trombozom, krvarenjem, transformacijom bolesti i smrću.

Rezultati:
Ukupno je uključeno 80 bolesnika (ET=46, PV=34), medijan dobi bio je 71 godina, a 65% bolesnika bile su žene. Medijan dnevne doze hidroksiureje iznosio je 1000 mg. Nije bilo značajnih razlika u početnim vrijednostima MCV-a između ET i PV bolesnika. U ukupnoj populaciji zabilježen je statistički značajan porast MCV-a nakon tri mjeseca liječenja. Taj je porast bio izražen u bolesnika s ET, dok u bolesnika s PV nije bio statistički značajan. Porast MCV-a zabilježen je u 60% bolesnika. Nije pronađena povezanost porasta MCV-a s analiziranim kliničkim ishodima.

Zaključak:
Porast MCV-a tijekom liječenja hidroksiurejom u bolesnika s ET i PV nema značajne kliničke implikacije te se može smatrati benignom pojavom. Ovi rezultati mogu doprinijeti boljem razumijevanju laboratorijskih promjena tijekom terapije i smanjenju nepotrebne zabrinutosti bolesnika. Ograničenja istraživanja uključuju retrospektivni dizajn i mali broj ispitanika.

Ključne riječi: hidroksiureja, MCV, mijeloproliferativne neoplazme

INCREASE IN MEAN CORPUSCULAR VOLUME (MCV) DURING TREATMENT WITH HYDROXYUREA IN PATIENTS WITH ESSENTIAL THROMBOCYTHEMIA AND POLYCYTHEMIA VERA DOES NOT PREDICT CLINICAL OUTCOMES

Antonija Dužaić[1], Asst. prof. Marko Skelin, MPharm, PhD[1-3], Asst. prof. Ivan Krečak, MD, PhD[1,3,4]

[1] Faculty of Medicine Rijeka
[2] Pharmacy department, General Hospital of Sibenik-Knin Country
[3] University of Applied Sciences 4) Department of Internal Medicine
[4] General Hospital of Sibenik-Knin Country

PS – 3

Introduction:
Hydroxyurea is a standard cytoreductive therapy in patients with essential thrombocythemia (ET) and polycythemia vera (PV). An increase in mean corpuscular volume (MCV) is frequently observed during treatment; however, its clinical relevance remains unclear. The aim of this study was to evaluate whether an increase in MCV during hydroxyurea therapy is associated with major clinical outcomes in patients with ET and PV.

Methods:
This retrospective single-center study was conducted at the General Hospital of Sibenik-Knin Country, Croatia. Patients diagnosed with ET or PV and treated with hydroxyurea between 2009 and 2022 were included. MCV values were assessed at diagnosis and after three months of treatment. An MCV ratio greater than 1 (three-month value divided by baseline value) was defined as an increase in MCV. Associations between MCV increase and major clinical outcomes, including thrombosis, bleeding, disease transformation, and death, were analyzed.

Results:
A total od 80 patients (ET=46, PV=34) were included. The median age was 71 years, and 65% of patients were female. The median daily dose of hydroxyurea was 1000 mg. No significant differences in baseline MCV values were observed after three months of treatment. This increase was statistically significant in ET patients but not in PV patients. An increase in MCV was observed in 60% of patients. No association was found between MCV increase and any of the evaluated clinical outcomes.

Conclusion:
An increase in MCV during hydroxyurea treatment in patients with ET and PV does not predict adverse clinical outcomes and appears to be a benign laboratory finding. These results my help clinicians reassure patients regarding MCV changes during therapy. Study limitations include its retrospective design and the relativly small sample size.

Keywords: hydroxyurea, MCV, myeloproliferative neoplasms

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

KARDIOVASKULARNI ISHODI INKRETINSKIH MIMETIKA: META - ANALIZA

Bruna Perkov-Stipičin, mag pharm.[1], Doc. dr. sc. Marko Skelin, mag. pharm[1,2,3], Doc. dr. sc. Ivan Krečak, dr. med.[2,3,4]

[1]Odjel farmacije, Opća bolnica Šibensko-kninske županije, Šibenik
[2] Medicinski fakultet, Sveučilište u Rijeci, Rijeka
[3] Veleučilište u Šibeniku, Hrvatska
[4] Služba interne medicine, Opća bolnica Šibensko-kninske županije, Šibenik

PS – 4

UVOD
Studije kardiovaskularnih ishoda (CVOT) s inkretinskim mimeticima pokazale su da pojedini agonisti receptora za glukagonu sličan peptid-1 (GLP-1) te dualni agonisti GLP-1 i inzulinotropnog polipeptida ovisnog o glukozi (GIP) receptora mogu značajno smanjiti rizik od velikih štetnih kardiovaskularnih (KV) događaja (MACE) u bolesnika sa ili bez šećerne bolesti tipa 2 (ŠBT2). MACE je kompozitni ishod koji obuhvaća 3 (3P-MACE: KV smrtnost, nefatalni infarkt miokarda, nefatalni moždani udar) ili 4 (4P-MACE: 3P+hospitalizacija zbog nestabilne angine) ključna KV događaja. Cilj meta-analize je ispitati učinak inkretinskih mimetika na rizik od 3P-MACE-a, pojedinačnih KV ishoda, hospitalizacije zbog srčanog zatajenja te smrtnosti od bilo kojeg uzroka.

METODE
Proveden je sustavni pregled literature te je uključeno 16 randomiziranih, placebom kontroliranih studija koje su ispitivale KV učinke inkretinskih mimetika, objavljenih od 2015. do 2025. godine, s ukupno 98,859 ispitanika. Rezultati analize su iskazani kumulativnim omjerom hazarda (HR). Obrada i vizualizacija podataka provedena je uporabom mrežnog alata (MetaAnalysisOnline.com).

REZULTATI
Kumulativno, inkretinski mimetici smanjili su rizik od 3P-MACE-a za 15 % (HR=0.85, P<0.0001) u usporedbi s placebom. KV smrtnost smanjena je za 13 % (HR=0.87, P<0.0001), a ukupna za 12 % (HR=0.88, P<0.0001). Rizik od infarkta miokarda smanjen je za 14 % (HR=0.86, P=0.0021), dok je rizik od moždanog udara smanjen za 13 % (HR=0.87, P=0.0011). Najmanje smanjenje rizika zabilježeno je kod hospitalizacija zbog srčanog zatajenja (10 %; HR=0.90, P=0.0035).

ZAKLJUČAK
Inkretinski mimetici imaju povoljan učinak na smanjenje rizika od KV ishoda u usporedbi s placebom. Najveće smanjenje zabilježeno je kod ukupnog MACE ishoda, dok je sličan rezultat uočen kod ostalih ishoda, s najmanjim smanjenjem rizika od hospitalizacija zbog stčanog zatajenja. Ova novija meta-analiza dokazuje povoljan utjecaj inkretinskih mimetika na KV ishode i smrtnost kod pacijenata sa ili bez ŠBT2.

Ključne riječi: GIP/GLP-1 agonisti, kardiovaskularni ishodi, CVOT

CARDIOVASCULAR OUTCOMES OF INCRETIN MIMETICS: A META-ANALYSIS

Bruna Perkov-Stipičin, MPharm[1], Asst. prof. Marko Skelin, MPharm, PhD[1-3], Asst. prof. Ivan Krečak, MD, PhD[2,3,4]

[1] Pharmacy Department, General Hospital of Šibenik-Knin County, Šibenik
[2] Faculty of Medicine, University of Rijeka, Rijeka
[3] University of Applied Sciences, Šibenik, Croatia
[4] Internal Medicine Department, General Hospital of Šibenik-Knin County, Šibenik

PS – 4

INTRODUCTION

Cardiovascular outcome trials (CVOTs) with incretin-based therapies have demonstrated that certain agonists of the glucagon-like peptide-1 (GLP-1) receptor, as well as dual agonists of the GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) receptors, can significantly reduce the risk of major adverse cardiovascular events (MACE) in patients with or without type 2 diabetes mellitus (T2DM). MACE is a composite endpoint comprising three (3-point MACE: cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke) or four components (4P-MACE: 3P-MACE plus hospitalization for unstable angina). The aim of this meta-analysis is to evaluate the effect of incretin-based therapies on the risk of 3P- MACE, its components, heart failure hospitalization, and all-cause mortality.

METHODS

A systematic literature review was conducted, including 16 randomized, placebo-controlled trials investigating the cardiovascular effects of incretin mimetics, published between 2015 and 2025, with a total of 98,859 participants. Results were expressed as pooled hazard ratios (HR). Data processing and visualization were performed using a web-based tool (MetaAnalysisOnline.com).

RESULTS

Overall, incretin mimetics reduced the risk of 3P-MACE by 15% compared with placebo (HR = 0.85, P < 0.0001). Cardiovascular mortality was reduced by 13% (HR = 0.87, P < 0.0001), and all-cause mortality by 12% (HR = 0.88, P < 0.0001). The risk of myocardial infarction was reduced by 14% (HR = 0.86, P = 0.0021), while the risk of stroke was reduced by 13% (HR = 0.87, P = 0.0011). The smallest risk reduction was observed for heart failure hospitalization (10%; HR = 0.90, P = 0.0035).

CONCLUSION

Incretin mimetics reduced the risk of cardiovascular outcomes compared with placebo. The greatest risk reduction was observed for composite MACE, with similar effects across other endpoints, while the smallest reduction was seen for heart failure hospitalization. This updated meta-analysis demonstrates a favorable impact of incretin mimetics on cardiovascular outcomes and mortality in patients with and without T2DM.

Keywords: GIP/GLP-1 agonists, cardiovascular outcomes, CVOTs

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

ANALIZA FARMAKOTERAPIJE PACIJENATA NA TERAPIJI VARFARINOM NA ODJELU ORALNE KIRURGIJE

Dr. sc. Dijana Grgurević, univ. mag. pharm.[1], Viktorija Grgurević[2], Marija Mikulčić, mag. pharm.[3], Vedrana Vidić, univ. mag. pharm., spec. kliničke farm.[4], Maria Levanić, mag. pharm.[1] , Dr. sc. Joško Grgurević, dr. med. dent.[5]

[1] Bolnička ljekarna, Klinička farmacija, KB Dubrava
[2] Fakultet za dentalnu medicinu i zdravstvo Osijek, Osijek
[3] Specijalna bolnica za medicinsku rehabilitaciju Varaždinske Toplice,
[4] Opća bolnica Zabok i bolnica hrvatskih veterana, Zabok
[5] Stomatološka poliklinika Zagreb, Oralna kirurgija, Zagreb

PS – 5

UVOD: Pacijenti na terapiji varfarinom predstavljaju najveći rizik za razvoj komplikacija tijekom oralnokirurških zahvata. Zahtijevaju kontrolu terapije, te prilagodbu doze kako bi se postigao željeni terapijski učinak i istodobno minimizirao rizik od štetnih učinaka povezanih sa suviškom antikoagulacije (krvarenje) i nedovoljnom antikoagulacijom (tromboza). Većinom su to pacijenti sa većim brojem komorbiditeta te se nerijetko viđa polipragmazija koja pak povećava mogućnost interakcija lijekova, medikacijskih pogrešaka i neželjenih nuspojava.

CILJ: Cilj istraživanja je po prvi puta analizirati cjelokupnu farmakoterapiju pacijenata na terapiji varfarinom na Odjelu oralne kirurgije, te ukazati na važnost poznavanja i upravljanja farmakoterapijom radi smanjenja neželjenih nuspojava lijekova i neželjenih ishoda liječenja, posebice u oralnokirurškim zahvatima.

ISPITANICI I METODE: Provedeno je retrospektivno istraživanje u trajanju 3 mjeseca na Odjelu oralne kirurgije. U istraživanju je sudjelovalo 60 pacijenata na terapiji varfarinom. Prosječna dob pacijenata u studiji bila je 68 godina Za utvrđivanje potencijalnih klinički značajnih interakcija lijekova (X, D, C kategorije) korištena je baza podataka Lexi-Comp®Online. Za utvrđivanje PNL-ova (potencijalno neprikladnih lijekova) korištena je EU(7)-PIM lista.

REZULTATI: U istraživanje je uključeno 60 pacijenata prosječne starosti 67,7 godina, od čega 68,3 % muškaraca. Pacijenti su u prosijeku imali 9 propisanih lijekova. 53,6% pacijenata koristilo je 10 ili više lijekova. Pacijenti u studiji imaju prosječno 12 značajnih interakcija lijekova. U 5% pacijenata uočena je X interakcija (0% sa varfarinom). 71% pacijenata ima D interakcije (od toga 63,3% s varfarinom, najčešće sa alopurinolom), a 100% ima C interakcije (od toga 19,4% s varfarinom, najčešće sa nesteroidnim antireumatskim lijekovima). 98% interakcija s varfarinom povećalo je rizik od produljenog krvarenja. PIM-ovi temeljeni na EU(7)-PIM kriterijima pojavili su se u 63% sudionika (86% pacijenata je dugotrajno liječeno benzodiazepinima koji povećavaju mogućnost pada i ozljeda).

ZAKLJUČAK: Utvrđen je visoki udio pacijenata s klinički značajnim interakcijama. Prema rezultatima ove studije, rizik od ozbiljnih nuspojava lijekova mogao bi se značajno smanjiti ukoliko bi se ispravno pristupilo upravljanju interakcijama lijekova i pažljivijem propisivanju novih skupina lijekova koje mogu dovesti do novih neželjenih klinički značajnih interakcija, a time i neželjenih nuspojava poput produženog krvarenja.

PHARMACOTHERAPY ANALYSIS IN PATIENTS RECEIVING WARFARIN THERAPY AT THE DEPARTMENT OF ORAL SURGERY

Dijana Grgurević, PhD, MPharm[1], Viktorija Grgurević[2], Marija Mikulčić, MPharm[3], Vedrana Vidić, MPharm, Clinical Pharmacy Specialist[4], Maria Levanić, MPharm[1] , Joško Grgurević, PhD, DMD[5]

[1] *Department of clinical pharmacy, University Hospital Dubrava, Zagreb*
[2] *Faculty of Dental Medicine and Health Osijek, Osijek*
[3] *Hospital pharmacy, Special hospital for medical rehabilitation Varazdinske Toplice, Varaždinske Toplice*
[4] *Hospital pharmacy, Zabok general hospital and croatian veterans' hospital, Zabok*
[5] *Department of Oral surgery, Zagreb dental clinic, Zagreb*

PS – 5

INTRODUCTION: Patients receiving warfarin therapy represent a high-risk group for the development of complications during oral surgical procedures. They require careful monitoring and dose adjustment to achieve the desired therapeutic effect while minimizing the bleeding risk associated with excessive anticoagulation and thrombosis due to insufficient anticoagulation. These patients often have multiple comorbidities and are frequently exposed to polypharmacy, which further increases the risk of drug–drug interactions, medication errors, and adverse drug reactions.

AIM: The aim of this study was, for the first time, to comprehensively analyze the pharmacotherapy of patients receiving warfarin at the Department of Oral Surgery and to emphasize the importance of understanding and managing pharmacotherapy in order to reduce adverse drug reactions and unfavorable treatment outcomes, particularly in oral surgical procedures.

PATIENTS AND METHODS: A three-month retrospective study was conducted at the Department of Oral Surgery. The study included 60 patients receiving warfarin therapy. The mean age of the participants was 68 years. The Lexi-Comp® Online database was used to identify potentially clinically significant drug–drug interactions (categories X, D, and C). Potentially inappropriate medications (PIMs) were identified using the EU(7)-PIM list.

RESULTS: The study included 60 patients with a mean age of 67.7 years, of whom 68.3% were male. Patients were prescribed an average of 9 medications. A total of 53.6% of patients were taking 10 or more medications. On average, patients had 12 clinically significant drug–drug interactions. X-category interactions were observed in 5% of patients, none involving warfarin. D-category interactions were present in 71% of patients, 63.3% involving warfarin, most commonly with allopurinol. C-category interactions were identified in 100% of patients, 19.4% involving warfarin, most frequently with nonsteroidal anti-inflammatory drugs. In 98% of cases, interactions involving warfarin increased the risk of prolonged bleeding. PIMs based on the EU(7)-PIM criteria were identified in 63% of participants; 86% of patients were receiving long-term benzodiazepine therapy, which is associated with an increased risk of falls and injuries.

CONCLUSION: A high prevalence of clinically significant drug–drug interactions was identified. According to the results of this study, the risk of serious adverse drug reactions could be significantly reduced through appropriate management of drug-drug interactions and more cautious prescribing of new drug classes that may lead to additional clinically significant interactions and adverse outcomes, such as prolonged bleeding.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

UČESTALOST KRONIČNE OPSTRUKTIVNE PLUĆNE BOLESTI I ASTME U BOLESNIKA S POLICITEMIJOM VEROM I ESENCIJALNOM TROMBOCITEMIJOM TE NJIHOV PROGNOSTIČKI ZNAČAJ

Iva Ivanković[1], Doc. dr. sc. Marko Skelin, mag. pharm[1-3] , Doc. dr. sc. Ivan Krečak, dr. med[1,3,4]

[1] *Medicinski fakultet, Sveučilište u Rijeci, Rijeka*
[2] *Opća bolnica Šibensko-kninske županije, Služba za bolničku ljekarnu, Šibenik*
[3] *Sveučilište primijenjenih znanosti u Šibeniku, 22000 Šibenik*
[4] *Opća bolnica Šibensko-kninske županije, Odjel za unutarnje bolesti, Šibenik*

PS – 6

Učestalost kronične opstruktivne plućne bolesti (KOPB) i astme kod bolesnika s mijeloproliferativnim neoplazmama (MPN), i kao njihov prognostički značaj, nisu dovoljno istražene. Ciljevi ovog istraživanja bili su: (1) analizirati učestalost KOPB-a i astme kod bolesnika s policitemijom verom (PV) i esencijalnom trombocitemijom (ET), (2) ispitati povezanost ovih respiratornih bolesti s MPN-om, (3) procijeniti njihov rizik na prombotski rizik i preživljenje.

Provedeno je retrospektivno multicentrično kohortno istraživanje u Hrvatskoj i Srbiji koje je uključivalo 246 bolesnika s PV-om i ET-om dijagnosticiranih u razdoblju od 1997. do 2003. godine. Vrijeme do trombotskog događaja (venski ili arterijski) i ukupno preživljavanje mjerili su se od postavljanja dijagnoze.

REZULTATI:
KOPB je zabilježen u 6,5 % , a astma u 1,6 % bolesnika, bez značajnih razlika u fenotipu bolesti. Prisutnost KOPB-a/astme je bila učestalija kod bolesnika s aktivnim ili ranijim pušenjem (p=0,021) i konstitucijskim simptomima (p=0,001). Nakon medijana praćenja od 47,5 mjeseci, KOPB/astma su bili povezani s kraćim vremenom do tromboze (135 vs. 180 mjeseci; HR 7,75; p=0,005), prvenstveno zbog povećanog rizika od venskih tromboza. Negativan učinak na vrijeme do tromboze se zadržao i u multivarijantnoj analizi (HR 6,54; p=0,010), neovisno o dobi > 60 godina, utjecaj na ukupno preživljavanje nije utvrđen.

ZAKLJUČAK:
Prisutnost KOPB-a/astme u bolesnika s PV-om ili ET-om povezana je s povećanim trombotskim rizikom, osobito venskim. Ovi rezultati upućuju na moguću povezanost čestih respiratornih bolesti i mogu pridonijeti daljnjoj personalizaciji liječenja.

Ključne riječi: mijeloproliferativna neoplazma, KOPB, tromboza/ myeloproliferative neoplasms, COPD, thrombosis

PREVALENCE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND ASTHMA IN POLYCYTHEMIA VERA AND ESSENTIAL THROMBOCYTHEMIA AND ITS PROGNOSTIC IMPLICATIONS

Iva Ivanković[1], Asst. prof. Marko Skelin, MPharm[1-3] ,
Asst. prof. Ivan Krečak, MD, PhD[1,3,4]

[1] Faculty of Medicine, University of Rijeka, Rijeka
[2] General Hospital of Šibenik-Knin County, Hospital Pharmacy Department, Šibenik
[3] University of Applied Sciences in Šibenik, 22000 Šibenik
[4] General Hospital of Šibenik-Knin County, Department of Internal Medicine, Šibenik

PS – 6

The prevalence of chronic obstructive pulmonary disease (COPD) and asthma in patients with myeloproliferative neoplasms (MPNs), as well as their prognostic significance, has not been sufficiently investigated. The aims of this study were: (1) to analyze the prevalence of COPD and asthma in patients with polycythemia vera (PV) and essential thrombocythemia (ET), (2) to examine the association of these respiratory diseases with MPNs, and (3) to assess their impact on thrombotic risk and survival.

A retrospective multicenter cohort study was conducted in Croatia and Serbia and included 246 patients with PV and ET diagnosed between 1997 and 2003. Time to thrombotic event (venous or arterial) and overall survival were measured from the time of diagnosis.

RESULTS:

COPD was observed in 6.5% and asthma in 1.6% of patients, with no significant differences in disease phenotype. The presence of COPD/asthma was more frequent in patients with current or prior smoking history (p=0.021) and constitutional symptoms (p=0.001). After a median follow-up of 47.5 months, COPD/asthma was associated with a shorter time to thrombosis (135 vs. 180 months; HR 7.75; p=0.005), primarily due to an increased risk of venous thrombotic events. The negative effect on time to thrombosis persisted in multivariable analysis (HR 6.54; p=0.010), independently of age >60 years. No impact on overall survival was observed.

CONCLUSION:

The presence of COPD or asthma in patients with PV or ET is associated with an increased thrombotic risk, particularly venous thrombosis. These findings suggest a potential link between common respiratory diseases and adverse outcomes and may contribute to further personalization of treatment.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

RAZLIKOVANJEPOLICITEMIJE VERE OD POLICITEMIJE POVEZANE S INHIBITOROM NATRIJ-GLUKOZNOG KOTRANSPORTERA 2

Ivana Sirovec[1], Doc. dr. sc. Marko Skelin, mag. pharm[1-3] ,
Doc. dr. sc. Ivan Krečak, dr. med[1,3,4]

[1] Medicinski fakultet u Rijeci
[2] Odjel bolnička ljekarna, Opća bolnica Šibenik - Knin
[3] Sveučilište primijenjenih znanosti u Šibeniku
[4] Odjel interne medicine, Opća bolnica Šibenik - Knin

PS – 7

Uvod
Policitemija povezana s uporabom inhibitora natrij glukoza kotransportera 2 (SGLT2i) prepoznata je kao česta pojava te rezultira s povoljnim kliničkim ishodima. Unatoč tome, bolesnici s povišenim vrijednostima hematokrita i hemoglobina često se upućuju hematolozima radi isključenja policitemije vere (PV), mijeloproliferativne neoplazme povezane s povećanim kardiovaskularnim i i trombotskim rizikom. Cilj ovog istraživanja bio je utvrditi postoje li i koje su to laboratorijske i kliničke razlike između SGLT2i-povezane policitemije i policitemije vere koje bi pomogle u donošenju odluke za potrebnim JAK2 testiranjem ili hematološkom obradom.

Metode i rezultati
Provedeno je retrospektivno multicentrično istraživanje u tri bolnice u Hrvatskoj. U razdoblju od ožujka 2018. do svibnja 2025. istraživanje je uključilo 22 bolesnika liječena SGLT2 inhibitorima (empagliflozin n=16, dapagliflozin n=6) i 23 bolesnika s PV-om. Indikacije za primjenu SGLT2i bile su kronično zatajenje srca, šećerna bolest, njihova kombinacija ili kronična bubrežna bolest. U usporedbi s bolesnicima liječenima SGLT2i, skoro svi bolesnici s PV-om su imali prisutnu JAK2 mutaciju, niže koncentracije eritropoetina te više vrijednosti krnog tlaka i palpabilnu splenomegaliju. Također su imali više vrijednosti ukupnog broja leukocita, apsolutnog broja neutrofila i trombocita, laktat-dehidrogenaze (LDH), širinu raspodjele volumena eritrocita (RDW), omjera neutrofila i limfocita (NLR) te omjera trombocita i limfocita (PLR), uz niže vrijednosti apsolutnog broja limfocita i monocita ($p < 0,05$). Analiza ROC krivulja pokazala je da su povišen broj trombocita (>272×10⁹/L) i povišen PLR (>123) imali najbolju kombinaciju osjetljivosti i specifičnosti (>90%) u razlikovanju PV-a od SGLT2i-povezane policitemije.

Zaključak
Iako je SGLT2i- policitemija uglavnom povezana s povoljnim kliničkim ishodima, bitno je razlikovati je od policitemije vere zbog različitih terapijskih i prognostičkih ishod. Povećan broj trombocita, povećani omjer trombocita i leukocita (PLR), leukocitoza, povišeni LDH te prisutnost splenomegalije predstavljaju ključne kliničke i laboratorijske pokazatelje koji mogu pridonijeti i pomoći u odabiru bolesnika za JAK2 testiranje i hematološko upućivanje.

Ključne riječi: policitemija vera, SGLT2 inhibitori, JAK2 mutacija.

DIFFERENTIATING POLYCYTHEMIA VERA FROM SODIUM–GLUCOSE COTRANSPORTER 2 INHIBITOR–ASSOCIATED POLYCYTHEMIA

Ivana Sirovec[1], Asst. prof. Marko Skelin, MPharm[1-3] ,
Asst. prof. Ivan Krečak, MD, PhD[1,3,4]

[1] *School of Medicine, University of Rijeka*
[2] *Pharmacy department, General Hospital of Šibenik-Knin County*
[3] *University of Applied Sciences, Šibenik*
[4] *Department of Internal Medicine, General Hospital of Šibenik-Knin County, Šibenik*

PS – 7

Introduction

Polycythemia associated with the use of sodium–glucose cotransporter 2 inhibitors (SGLT2i) has been recognized as a common phenomenon and is associated with favorable clinical outcomes. Nevertheless, patients with elevated hematocrit and hemoglobin values are frequently referred to hematologists in order to exclude polycythemia vera (PV), a myeloproliferative neoplasm associated with increased cardiovascular and thrombotic risk. The aim of this study was to determine whether laboratory and clinical differences exist between SGLT2i-associated polycythemia and polycythemia vera that could assist in decision-making regarding the need for JAK2 mutation testing or further hematologic evaluation.

Methods and Results

A retrospective multicenter study was conducted in three hospitals in Croatia. Between March 2018 and May 2025, the study included 22 patients treated with SGLT2 inhibitors (empagliflozin n=16, dapagliflozin n=6) and 23 patients diagnosed with polycythemia vera. Indications for SGLT2i therapy included chronic heart failure, diabetes mellitus, their combination, or chronic kidney disease. Compared with patients treated with SGLT2 inhibitors, almost all patients with polycythemia vera harbored a JAK2 mutation, had lower erythropoietin concentrations, higher blood pressure values, and palpable splenomegaly. In addition, they exhibited higher total leukocyte counts, absolute neutrophil and platelet counts, lactate dehydrogenase (LDH) levels, red blood cell distribution width (RDW), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR), along with lower absolute lymphocyte and monocyte counts ($p < 0.05$). Receiver operating characteristic (ROC) curve analysis demonstrated that an elevated platelet count (>272×10⁹/L) and an increased PLR (>123) showed the best combination of sensitivity and specificity (>90%) for distinguishing polycythemia vera from SGLT2i-associated polycythemia.

Conclusion

Although SGLT2i-associated polycythemia is generally linked to favorable clinical outcomes, it is essential to differentiate it from polycythemia vera due to differences in therapeutic approaches and prognostic implications. Thrombocytosis, an increased platelet-to-lymphocyte ratio, leukocytosis, elevated LDH levels, and the presence of splenomegaly represent key clinical and laboratory indicators that may assist in identifying patients who require JAK2 mutation testing and referral for hematologic evaluation.

Keywords: polycythemia vera; SGLT2 inhibitors; JAK2 mutation

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

PREGLED FARMAKOTERAPIJE U OSOBA STARIJE ŽIVOTNE DOBI: RETROSPEKTIVNO PRESJEČNO ISTRAŽIVANJE U JAVNOJ LJEKARNI

Klaudija Bralić, mag. pharm.[1], Doc. dr. sc. Marko Skelin, mag. pharm[2-4] ,
Vesna Šunjić, dr. med.[5]

[1] *Zdravstvena ustanova Ljekarna Šibenik*
[2] *Opća bolnica Šibensko-kninske županije, Služba za bolničku ljekarnu, Šibenik, Hrvatska*
[3] *Medicinski fakultet Sveučilišta u Rijeci, Rijeka, Hrvatska*
[4] *Sveučilište primijenjenih znanosti u Šibeniku, Hrvatska*
[5] *Specijalistička ordinacija obiteljske medicine Vesna Šunjić*

PS – 8

UVOD

S porastom životne dobi dolazi do povećanja broja kroničnih bolesti i lijekova u terapiji, pri čemu je politerapija čest uzrok primjene potencijalno neprikladnih lijekova (eng. potentially inappropriate medications, PIM). Istraživanje obuhvaća starije osobe s politerapijom i barem jednom od dijagnoza: esencijalna hipertenzija (I10), šećerna bolest neovisna o inzulinu (E11), kronična bubrežna bolest (N18) ili anksiozni poremećaji (F41). Cilj je pružiti uvid u pojavnost PIM-ova i interakcija kod starijih osoba te istaknuti ulogu javnog ljekarnika u optimizaciji farmakoterapije.

METODE

Provedeno je retrospektivno presječno istraživanje na uzorku od 50 pacijenata. Iz informacijskog sustava Eskulap prikupljeni su demografski podatci, povijest preuzimanja lijekova na recept, dijagnoze te doziranje lijekova. Iz eKartona obiteljskog liječnika prikupljeni su podatci o procijenjenoj bubrežnoj funkciji (eGFR), a uvidom u medicinsku dokumentaciju provjereno je postojanje dijagnoza i lijekova koji nisu evidentirani u sustavu Eskulap. Za identifikaciju PIM – ova korišteni su STOPP/START kriteriji, za interakcije lijek–lijek Lexidrug™ (Lexi-Interact™) baza podataka, a za procjenu interakcija lijek–bolest i doziranja prema bubrežnoj funkciji korišteni su podatci iz SmPC – a. Ishodi uključuju udio ispitanika s barem jednim PIM, učestalost interakcija lijek – lijek i lijek – bolest te prikladnost doziranja lijekova prema stadiju KBB.

REZULTATI

Barem jedan PIM zabilježen je u 34 pacijenta (68%). Barem jedna interakcija kategorije C identificirana je u 49 pacijenata (98%), kategorije D u 19 pacijenata (38%), a kategorije X u 4 pacijenta (8%). Najčešći PIM – ovi bili su benzodiazepini, inhibitori protonske pumpe, nesteroidni protuupalni lijekovi i centralno djelujući antihipertenzivi.
Interakcije lijek – bolest identificirane su u 38 pacijenata (76%). Najčešće su zabilježene interakcije kortikosteroida s dijagnozom šećerne bolesti, nesteroidnih protuupalnih lijekova s arterijskom hipertenzijom te tiazidskih diuretika s gihtom. U 5 pacijenata (10%) bila je potrebna prilagodba doze prema eGFR, dok je u 8 pacijenata (16%) identificirana kontraindikacija za primjenu lijeka.

PS – 8

ZAKLJUČAK

PIM – ovi su češće prisutni kod pacijenata s većom razinom politerapije. Klinički značajne interakcije lijek–lijek i lijek–bolest prisutne su kod značajnog broja starijih pacijenata s politerapijom. Identificirane potrebe za prilagodbom doze prema bubrežnoj funkciji i kontraindikacije naglašavaju važnost sustavne procjene terapije i ulogu ljekarnika u optimizaciji farmakoterapije.

Ključne riječi: politerapija, potencijalno neprikladni lijekovi, interakcije

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

REVIEW OF PHARMACOTHERAPY IN OLDER ADULTS: A RETROSPECTIVE CROSS – SECTIONAL STUDY IN A COMMUNITY PHARMACY

Klaudija Bralić, MPharm[1], Doc. dr. sc. Marko Skelin, MPharm[2-4] , Vesna Šunjić, MD[5]

[1] *Healthcare Institution Pharmacy Šibenik*
[2] *Pharmacy department, General Hospital of Šibenik-Knin County, Šibenik, Croatia*
[3] *Faculty of Medicine, University of Rijeka, Rijeka, Croatia*
[4] *University of Applied Sciences, Šibenik, Croatia*
[5] *Specialist Family Medicine Practice Vesna Šunjić*

PS – 8

INTRODUCTION

With advancing age, the prevalence of chronic diseases and polypharmacy increases, which is a common cause of potentially inappropriate medication (PIM) use. This study includes older adults with polypharmacy and at least one of the following diagnoses: essential hypertension (I10), type 2 diabetes mellitus (E11), chronic kidney disease (N18), or anxiety disorders (F41). The aim of the study was to assess the occurrence of PIMs and drug-related interactions in this population and to emphasize the role of the community pharmacist in optimizing pharmacotherapy.

METHODS

A retrospective cross-sectional study was conducted on a sample of 50 patients. Data were collected from the Eskulap information system, including demographics, prescription history, diagnoses, and medication dosages. Additional data on estimated glomerular filtration rate (eGFR) were obtained from the primary care electronic health record, and medical documentation was reviewed to identify unrecorded diagnoses and medications. PIMs were identified using STOPP/START criteria, drug–drug interactions with the Lexidrug™ (Lexi-Interact™) database, and drug–disease interactions and dosage appropriateness according to kidney function were assessed using SmPC information. Outcomes included the proportion of patients with at least one PIM, frequency of drug–drug and drug–disease interactions, and dosage appropriateness according to CKD stage.

RESULTS

At least one PIM was recorded in 34 patients (68%). At least one category C drug–drug interaction was identified in 49 patients (98%), category D in 19 patients (38%), and category X in 4 patients (8%). The most frequent PIMs were benzodiazepines, proton pump inhibitors, nonsteroidal anti-inflammatory drugs, and centrally acting antihypertensives. Drug–disease interactions were identified in 38 patients (76%), most commonly corticosteroids in patients with diabetes, NSAIDs in patients with hypertension, and thiazide diuretics in patients with gout. Dose adjustment according to eGFR was required in 5 patients (10%), and contraindications were identified in 8 patients (16%).

PS – 8

CONCLUSION

PIMs are more frequent in patients with higher levels of polypharmacy. Clinically significant drug–drug and drug–disease interactions are common among older adults with polypharmacy. Identified needs for dose adjustments according to kidney function and contraindications highlight the need for systematic pharmacotherapy review and the role of the pharmacist in optimizing pharmacotherapy.

Keywords: polypharmacy, potentially inappropriate medications, interactions

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

LIZOZIM: OD ANTIMIKROBNOG ENZIBIOTIKA DO INOVATIVNE ONKOLOŠKE TERAPIJE

Doc. dr. Sanita Maleškić Kapo, dr. med,[1], Prof. dr. sc. Svjetlana Loga - Zec, dr. med, [1], Dr. med. Aziz Šukalo[2], Prof. dr. sc. Una Glamočlija [2], Meliha Mehić, dr. med.,[2], Elmedin Zubetljak[2]

[1] Univerzitet u Sarajevu – Medicinski fakultet, Sarajevo, Bosna i Hercegovina
[2] Bosnalijek d.d., Sarajevo, Bosna i Hercegovina

PS – 9

Otkriće lizozima 1922. godine, šest godina prije revolucionarnog otkrića penicilina, postalo je temelj za razumijevanje prirodnih antimikrobnih mehanizama. Termin "enzibiotik", upotrijebljen 2001. godine, opisuje enzime bakteriofaga koji degradiraju bakterijsku staničnu stijenku, djelujući kao prirodni antibakterijski agensi.

Lizozim predstavlja paradigmatski primjer enzibiotika s detaljno karakteriziranim mehanizmom djelovanja koji uključuje hidrolizu peptidoglikana bakterijske stanične stijenke. Značajna prednost lizozima u antimikrobnoj terapiji je izuzetno nizak rizik razvoja rezistencije, koja se uglavnom ograničava na neenzimske mehanizme djelovanja ovog enzima.

U posljednjem desetljeću, znanstveni interes za lizozim značajno se proširio izvan njegove tradicionalne uloge u antimikrobnoj obrani, s posebnim fokusom na njegovo antitumorsko djelovanje. Rastući broj istraživanja ukazuje na potencijal lizozima kao biomarkera za ranu dijagnozu, precizno određivanje stadija i prognozu različitih malignih oboljenja.

Cilj ovog rada je istražiti antitumorsku aktivnost lizozima koja se manifestira kroz dva komplementarna mehanizma: indirektno djelovanje kroz modulaciju imunološkog odgovora i direktno citotoksično djelovanje na tumorske stanice.

Imunološki mehanizmi uključuju interakciju lizozima s različitim populacijama limfocita, potičući njihovu aktivaciju i proliferaciju, što rezultira pojačanim imunološkim nadzorom nad tumorskim stanicama. Direktno antitumorsko djelovanje obuhvaća inhibiciju angiogeneze, ključnog procesa u rastu i metastaziranju tumora, te specifične interakcije s membranom malignih stanica koje mogu inducirati apoptozu. Posebno obećavajuća je sposobnost lizozima da sinergistički pojačava djelovanje konvencionalnih antineoplastičnih lijekova, što otvara mogućnost razvoja kombiniranih terapijskih protokola s poboljšanom učinkovitošću i smanjenom toksičnošću.

PS – 9

U kontekstu onkološke potporne terapije, lizozim pokazuje značajan potencijal u liječenju oralnog mukozitisa, česte i ozbiljne komplikacije radioterapije glave i vrata. Klinička istraživanja demonstriraju da topikalni preparati na bazi lizozima učinkovito smanjuju upalu, ulceracije i bol oralnih sluznica kod pacijenata podvrgnutih radioterapiji. Randomizirana klinička ispitivanja pokazala su da pacijenti tretirani lizozimskim sprejom doživljavaju značajno smanjenje intenziteta boli prilikom konzumacije hrane u usporedbi s konvencionalnim terapijskim pristupima, što direktno poboljšava kvalitetu života i nutritivni status onkoloških pacijenata.

Smanjena ekspresija ili aktivnost lizozima u organizmu može služiti kao indikator neadekvatnog imunološkog odgovora na tumorsko tkivo, naglašavajući potencijalnu dijagnostičku vrijednost ovog enzima. Daljnja istraživanja mehanizama antitumorskog djelovanja lizozima i razvoj novih formulacija mogla bi značajno unaprijediti terapijske mogućnosti u onkologiji, bilo kao monoterapija u ranim stadijima bolesti ili kao adjuvantna terapija uz standardne protokole liječenja uznapredovalih malignih oboljenja.

Ključne riječi: lizozim, enzibiotik, tumor

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

LYSOZYME: FROM AN ANTIMICROBIAL ENZYBIOTIC TO AN INNOVATIVE ONCOLOGICAL THERAPY

Sanita Maleškić Kapo, MD, PhD[1], Prof. Svjetlana Loga-Zec, MD, PhD[1], Aziz Šukalo, MD[2], Prof. Una Glamočlija, PhD[2], Meliha Mehić, MD[2], Elmedin Zubetljak[2]

[1] University of Sarajevo – Faculty of Medicine, Sarajevo, Bosnia and Herzegovina
[2] Bosnalijek d.d., Sarajevo, Bosnia and Herzegovina

PS – 9

The discovery of lysozyme in 1922, six years prior to the revolutionary discovery of penicillin, laid the foundation for understanding natural antimicrobial defense mechanisms. The term “enzybiotic”, introduced in 2001, describes bacteriophage-derived enzymes that degrade the bacterial cell wall and act as natural antibacterial agents.

Lysozyme represents a paradigmatic example of an enzybiotic with a well-characterized mechanism of action involving the hydrolysis of peptidoglycan in the bacterial cell wall. A major advantage of lysozyme in antimicrobial therapy is the exceptionally low risk of resistance development, which is largely limited to non-enzymatic resistance mechanisms. Over the past decade, scientific interest in lysozyme has expanded significantly beyond its traditional role in antimicrobial defense, with particular focus on its antitumor activity. A growing body of evidence suggests the potential of lysozyme as a biomarker for early diagnosis, accurate staging, and prognosis of various malignancies.

The aim of this paper is to explore the antitumor activity of lysozyme, which is manifested through two complementary mechanisms: indirect effects via modulation of the immune response and direct cytotoxic effects on tumor cells.

Immunological mechanisms include interactions between lysozyme and various lymphocyte populations, promoting their activation and proliferation, which results in enhanced immune surveillance of tumor cells. Direct antitumor activity involves inhibition of angiogenesis—a key process in tumor growth and metastasis—as well as specific interactions with malignant cell membranes that may induce apoptosis. Particularly promising is lysozyme’s ability to synergistically enhance the effects of conventional antineoplastic drugs, opening the possibility for the development of combination therapeutic protocols with improved efficacy and reduced toxicity.

PS – 9

In the context of supportive oncological therapy, lysozyme demonstrates significant potential in the treatment of oral mucositis, a common and severe complication of head and neck radiotherapy. Clinical studies have shown that topical lysozyme-based preparations effectively reduce inflammation, ulceration, and pain of the oral mucosa in patients undergoing radiotherapy. Randomized clinical trials have demonstrated that patients treated with lysozyme spray experience a significant reduction in pain intensity during food intake compared with conventional therapeutic approaches, thereby directly improving quality of life and nutritional status in oncology patients.

Reduced expression or activity of lysozyme in the body may serve as an indicator of an inadequate immune response to tumor tissue, highlighting the potential diagnostic value of this enzyme. Further investigation into the mechanisms underlying the antitumor activity of lysozyme, as well as the development of novel formulations, could significantly enhance therapeutic options in oncology—either as monotherapy in early-stage disease or as an adjuvant therapy alongside standard treatment protocols for advanced malignancies.

Keywords: lysozyme, enzybiotic, tumor

PRIPREMLJENOST PACIJENTA NA UZORKOVANJE KRVI KOD LABORATORIJSKE OBRADE BOLESTI ŠTITNJAČE

Trifunović Jasenka, mag. med. biokem,[1], Marija Mikulčić, mag. pharm.[1], Vedrana Međeši, mag. pharm. [2]

[1] Specijalna bolnica za medicinsku rehabilitaciju Varaždinske Toplice, Varaždinske Toplice
[2] Opća bolnica Zabok i bolnica hrvatskih veterana, Bračak

PS – 10

Uvod:
Hrvatsko društvo za medicinsku biokemiju i laboratorijsku medicinu (HDMBLM) 2025. godine donijelo je Nacionalne preporuke vezane uz laboratorijsku obradu bolesti štitnjače. U preporukama se navodi da se lijekovi koji se koriste za liječenje bolesti štitnjače trebaju uzeti nakon uzorkovanja krvi jer mogu utjecati na izmjerene koncentracije slobodnog tiroksina (fT4) i ukupnog trijodtironina (TT3), a što za posljedicu može imati daljnju pogrešno doziranu farmakoterapiju.

Metode:
U razdoblju studeni - prosinac 2025. godine provedena je anketa u Odjelu laboratorijske dijagnostike među pacijentima koji su došli na uzorkovanje krvi, a imali su ordinirane pretrage vezane uz laboratorijsku obradu bolesti štitnjače. Ispitanici su upitani koriste li lijekove za liječenje bolesti štitnjače i jesu li uzeli lijekove za liječenje bolesti štitnjače prije uzorkovanja krvi. Rezultati: Anketu je ispunilo 203 pacijenta koji su imali ordinirane pretrage vezane uz laboratorijsku obradu bolesti štitnjače. Terapiju koristi 62 % (N = 125) ispitanika od kojih njih 54 % (N = 67) je uzelo terapiju prije uzorkovanja krvi.

Zaključak:
Veliki broj pacijenata koji dolazi u laboratorij na pretrage vezane uz bolesti štitnjače uzima lijekove za liječenje bolesti štitnjače prije uzorkovanja krvi što može dovesti do lažno povišene koncentracije fT4 kod pacijenata koji koriste nadomjesnu terapiju i lažno snižene vrijednosti TT3 kod pacijenata koji koriste supresivnu terapiju. Liječnici, farmaceuti i laboratorijski djelatnici bi trebali informirati pacijente oko pravilne pripreme za uzorkovanje krvi.

Ključne riječi: bolesti štitnjače, uzorkovanje krvi, farmakoterapija

PATIENT PREPAREDNESS FOR BLOOD SAMPLING IN THE LABORATORY EVALUATION OF THYROID DISEASES

Jasenka Trifunović, MSc[1], Marija Mikulčić, MPharm[1], Vedrana Međeši, MPharm[2]

[1] Special hospital for medical rehabilitation Varazdinske Toplice, Varazdinske Toplice
[2] General Hospital Zabok and Hospital of Croatian Veterans, Bracak

PS – 10

Introduction:
In 2025, the Croatian Society of Medical Biochemistry and Laboratory Medicine (CSMBLM) issued National Recommendations related to the laboratory evaluation of thyroid diseases. The recommendations state that medications used in the treatment of thyroid disorders should be taken after blood sampling, as they may affect the measured concentrations of free thyroxine (fT4) and total triiodothyronine (TT3). Failure to follow this recommendation may result in misleading laboratory results and consequently inappropriate dosing of pharmacotherapy.

Methods:
During the period from November to December 2025, a survey was conducted in the Department of Laboratory Diagnostics among patients who presented for blood sampling and had laboratory tests ordered for the evaluation of thyroid diseases. Participants were asked whether they were using medications for the treatment of thyroid disorders and whether they had taken their medication prior to blood sampling.

Results:
The survey was completed by 203 patients who had laboratory tests ordered for the evaluation of thyroid diseases. Thyroid medication was used by 62% (N = 125) of respondents, of whom 54% (N = 67) reported taking their medication before blood sampling.

Conclusion:
A large proportion of patients undergoing laboratory testing for thyroid diseases take thyroid medication prior to blood sampling, which may lead to falsely elevated fT4 concentrations in patients receiving replacement therapy and falsely decreased TT3 values in patients receiving suppressive therapy. Physicians, pharmacists, and laboratory professionals should actively inform patients about proper preparation for blood sampling.

Keywords: thyroid diseases, blood sampling, pharmacotherapy

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

KARDIOTORAKALNI OMJER POVEZAN JE S LOŠIJIM PREŽIVLJAVANJEM KOD BOLESNIKA S ESENCIJALNOM TROMBOCITEMIJOM I POLICITEMIJOM VEROM

Nina Dabcevic[1], Doc. dr. sc. Marko Skelin, mag. pharm[1,2,3]
Ivana Sirovec[1], Doc. dr. sc. Ivan Krečak, dr. med.[1,3,4]

[1] Medicinski fakultet u Rijeci
[2] Odjel bolnička ljekarna, Opća bolnica Šibenik-Knin
[3] Sveučilište primijenjenih znanosti u Šibeniku
[4] Odjel interne medicine, Opća bolnica Šibenik-Knin

PS – 11

Uvod

BCR::ABL1-negativne mijeloproliferativne neoplazme, uključujući esencijalnu trombocitemiju (ET) i policitemiju veru (PV), karakteriziraju se konstitutivno aktivnim JAK-STAT signalnim putem koji rezultira prekomjernom mijeloproliferacijom i povišenim kardiovaskularnim rizikom. Kardiotorakalni omjer (CTR), izračunat pomoću radiografije kao omjer kardijalnog i torakalnog promjera, jednostavan je pokazatelj povećanja srca gdje vrijednosti >0,50 ukazuju na kardiomegaliju koja je povezana s lošijim preživljavanjem u različitim kliničkim stanjima. S obzirom na povišenu mijeloproliferaciju, povećani volumen krvi i visok kardiovaskularni rizik u ET i PV, cilj ove studije bio je ispitati može li CTR na postavljanju dijagnoze pružiti dodatne prognostičke informacije.

Metode i rezultati

Retrospektivna unicentrična studija provedena je u Općoj bolnici Šibenik-Knin te je uključila pacijente s ET i PV dijagnosticirane između 2009. i 2022. prema kriterijima Svjetske zdravstvene organizacije 2022., koji su imali dostupne rentgenografske snimke prsa. Primarni ishodi bili su vrijeme do trombotičkog događaja i ukupno preživljavanje. Uključen je 91 pacijent (ET=52, PV=39) s medijanom CTR od 0,50 (raspon 0,34-0,74); visoki CTR (>0,50) imalo je 45 (49,5%) pacijenata. Pacijenti sa visokim CTR su stariji, pretežno visokorizični, učestaliji s kroničnim zatajenjem srca, imaju povišene leukocite i trombocite, nižeg torakalnog, a višeg kardijalnog promjera te povišeni NT-proBNP (p<0,05 za sve analize). Medijan duljine praćenja od 90 mjeseci (raspon 10-314), zabilježio je 19 trombotičkih događaja (13 arterijskih, 6 venskih) i 28 smrtnih slučajeva. Visoki CTR nije povezan s vremenom do tromboze, ali je bio neovisno povezan s lošijim ukupnim preživljavanjem. U multivarijantnoj Cox regresijskoj analizi, visoki CTR (HR 4,94, p=0,026), kronično zatajenje srca (HR3,24, p=0,070), PV fenotip (HR4,39, p=0,036) i visokorizična bolest (HR 3,24, p=0,070) bili su neovisno povezani s lošijim ukupnim preživljavanjem nakon dodatne prilagodbe za spol, citoreduktivnu terapiju i prisutnost najmanje jednog kardiovaskularnog čimbenika rizika.

PS – 11

Zaključak

CTR izmjeren na postavljanu dijagnoze može pružiti dodatne prognostičke informacije, jer visoki CTR u PV i ET može predstavljati integrativnu mjeru tereta bolesti kroničnog opterećenja srca. Nedostatak povezanosti visokog CTR-a s trombotičkim događajima sugerira da nije idealan prediktor bolesti specifične za MPN komplikacije. S obzirom da su kronično zatajenje srca i nepoznati uzroci bili glavni uzroci smrtnosti, čini se da visoki CTR može primarno identificirati bolesnike s lošijim preživljenjem vezanih uz zatajenje srca. Rezultati sugeriraju da bi CTR mogao biti jeftin, jednostavan te široko primjenjivan alat koji može poboljšati prognozu kod ET i PV.

Ključne riječi: kardiotorakalni omjer; esencijalna trombocitemija; policitemija vera

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

CARDIOTHORACIC RATIO ASSOCIATED WITH WORSE OVERALL SURVIVAL IN PATIENTS WITH ESSENTIAL THROMBOCYTHEMIA AND POLYCYTHEMIA VERA

Nina Dabcevic[1], Asst. prof. Marko Skelin, MPharm, PhD[1,2,3]
Ivana Sirovec[1], Asst. prof. Ivan Krečak, MD, PhD[1,3,4]

[1] *Faculty of Medicine Rijeka*
[2] *Pharmacy department, General Hospital of Sibenik-Knin County*
[3] *University of Applied Sciences*
[4] *Department of Internal Medicine, General Hospital of Sibenik- Knin County*

PS – 11

Introduction

BCR::ABL1-negative myeloproliferative neoplasms, including essential thrombocythemia (ET) and polycythemia vera (PV), are characterized by constitutively active JAK-STAT signaling, resulting in excessive myeloproliferation and elevated cardiovascular risk. The cardiothoracic ratio (CTR), calculated from chest radiography as the ratio od cardiac to thoracic diameter, is a simple indicator of cardiac enlargement. Values exceeding 0.50 indicate cardiomegaly, which is associated with worse overall survival in various clinical conditions. Given the increased myeloproliferation, elevated blood volume, and high cardiovascular risk in ET and PV, this study aimed to investigate whether CTR at diagnosis provides additional prognostic information.

Methods and Results

A retrospective single-center study was conducted at General Hospital Sibenik-Knin, including ET and PV patients diagnosed between 2009-2022 according to WHO 2022 criteria with available chest radiographs. Primary outcomes were time to thrombotic event and overall survival. Ninety-one patients were included (ET=52, PV=39) with median CTR of 0.50 (range 0.34-0.74); high CTR (>0.50) occurred in 45 patients (49.5%). Patients with high CTR were older, predominantly high-risk, more frequently had chronic heart failure, elevated leukocytes and platelets, lower thoracic diameter, higher cardiac diameter, and elevated NT-proBNP ($p<0.05$). During median 90-month follow-up (range 10-314 months), 19 thrombotic events (13 arterial, 6 venous) and 28 deaths were recorded. High CTR was not associated with time to thrombosis but was independently associated with worse overall survival. In multivariate Cox regression, high CTR (HR4.94, p=0.026), chronic heart failure (HR 3.24, p=0.074), PV phenotype (HR 4.39, p=0.036), and high-risk disease (HR 3.24, p=0.070) were independently associated with worse overall survival after adjustment for sex, cytoreductive therapy, and cardiovascular risk factors.

Conclusion

CTR measured at diagnosis provides additional prognostic information, as elevated CTR may represent an integrative measure of chronic cardiac burden in ET and PV. The lack of association between high CTR and thrombotic events suggests it is not an ideal predictor of MPN-specific complications. Since chronic heart failure and unknown causes were principal mortal causes, elevated CTR primarily identifies patients with worse overall survival related to heart failure, suggesting CTR could be a cost-effective, simple and widely applicable tool for improving prognosis in ET and PV.

Keywords: cardiothoracic ratio; essential thrombocythemia; polycythemia vera

PRIMJENA FARMAKOGENETIČKOG TESTIRANJA U INDIVIDUALIZACIJI LIJEČENJA – PRIKAZ SLUČAJA

Vedrana Međeši, mag. pharm.[1] , Mia Jurinjak, mag. pharm.[1] , Siniša Roginić, dr. med.[1], Domagoj Futivić, dr. med.[1], Alen Friščić, mag. pharm[1], Livija Šimičević, mag. med. biochem[2,3], Doc. dr. sc. Lana Ganoci mag. med. biochem[2,3]

[1] Opća bolnica Zabok i bolnica hrvatskih veterana, Zabok
[2] Medicinski fakultet Sveučilišta u Zagrebu, Zagreb
[3] Klinički bolnički centar Zagreb, Zagreb

PS – 12

Uvod

Prepoznavanje farmakogenetičkih čimbenika u pacijenata koji ne reagiraju na standardnu terapiju ili razvijaju ozbiljne nuspojave ključno je za optimizaciju liječenja, smanjenje rizika i poboljšanje ishoda liječenja. Ovaj prikaz slučaja naglašava kliničku važnost farmakogenetičke analize, pri čemu je upravo genetički profil pacijentice omogućio razumijevanje mehanizma nastanka nuspojave.

Prikaz slučaja:

Pacijentica (76 godina) zaprimljena je u bolnicu zbog akutnog bubrežnog zatajenja nastalog uslijed rabdomiolize. Navodila je grčeve u trbuhu, mučninu i povraćanje, a tegobe su započele nakon uvođenja amiodarona 200 mg dnevno. Pacijentica je još u terapiji uzimala bisoprolol 2,5 mg, edoksaban 30 mg, duloksetin 60 mg, metformin 500 mg, metoklopramid 10 mg, pantoprazol 20 mg, perindopril 2 mg i rosuvastatin 20 mg. Zbog sumnje na individualnu nepodnošljivost terapije provedeno je farmakogenetičko testiranje.

Utvrđeno je da je pacijentica brzi metabolizator lijekova-supstrata CYP2C19, što može rezultirati smanjenom učinkovitošću inhibitora protonske pumpe (IPP). U slučaju perzistiranja simptoma GERB-a preporučuje se povećanje doze IPP za 50-100%. Nadalje, utvrđena je smanjena transportna funkcija proteina ABCG2 i SLCO1B1 što može dovesti do povećane sistemske izloženosti rosuvastatinu i posljedično povećanog rizika od miotoksičnosti, osobito pri dozama > 20 mg. Amiodaron je poznati inhibitor nekoliko membranskih prijenosnika, uključujući SLCO1B1 i ABCG2. Inhibicija ovih prijenosnika dovodi do smanjenog unosa rosuvastatina u jetru i smanjene bilijarne ekskrecije, čime se dodatno povećava sistemska izloženost lijeku.

Farmakokinetička interakcija amiodarona i rosuvastatina, u kombinaciji s genetički smanjenom funkcijom prijenosnika, rezultirala je sinergističkim povećanjem izloženosti rosuvastatinu i značajno povećanim rizikom od rabdomiolize. Amiodaron je ukinut, te je preporučena alternativna nestatinska terapija za snižavanje lipida.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

Zaključak:

Primjena farmakogenetičkog testiranja u individualizaciji liječenja je ključna za razumijevanje interindividualnih razlika u odgovoru na terapiju i riziku od nuspojava. Varijante enzima CYP450 mogu promijeniti brzinu metabolizma lijekova, povećavajući rizik od terapijskog neuspjeha ili pojave nuspojava, dok su varijante gena za prijenosnike SLCO1B1 i ABCG2 povezane s povećanom sistemskom izloženošću statinima i većim rizikom od miotoksičnosti.

Implementacija farmakogenetičkog testiranja u kliničku praksu može poboljšati ishode liječenja uz individualizirani odabir terapije i prilagodbu doziranja, čime se povećava sigurnost i učinkovitost liječenja, osobito u starijih i politerapijom opterećenih bolesnika.

Ključne riječi: farmakogenetika, rabdomioliza, interakcije lijek-lijek-gen

APPLICATION OF PHARMACOGENETIC TESTING IN TREATMENT INDIVIDUALIZATION – A CASE REPORT

Vedrana Međeši, MPharm[1] , Mia Jurinjak, MPharm[1] , Siniša Roginić, MD[1], Domagoj Futivić, MD[1], Alen Friščić, MPharm[1], Livija Šimičević, MSc[2,3], Assist. Prof. Lana Ganoci, PhD, MSc[2,3]

[1] General Hospital Zabok and Hospital of Croatian Veterans, Zabok, Croatia
[2] Faculty of Medicine, University of Zagreb, Zagreb, Croatia
[3] University Hospital Centre Zagreb, Zagreb, Croatia

PS – 12

Introduction:

Identification of pharmacogenetic factors in patients who do not respond to standard therapy or develop serious adverse drug reactions is essential for treatment optimization, risk reduction, and improvement of therapeutic outcomes. This case report highlights the clinical relevance of pharmacogenetic analysis, as the patient's genetic profile enabled a clear understanding of the mechanism underlying the observed adverse drug reaction.

Case Report:

A 76-year-old female patient was admitted to hospital due to acute renal failure caused by rhabdomyolysis. She reported abdominal cramps, nausea, and vomiting, with symptoms occurring after the initiation of amiodarone at a dose of 200 mg daily. Her concomitant therapy included bisoprolol 2.5 mg, edoxaban 30 mg, duloxetine 60 mg, metformin 500 mg, metoclopramide 10 mg, pantoprazole 20 mg, perindopril 2 mg, and rosuvastatin 20 mg. Due to suspected individual intolerance to therapy, pharmacogenetic testing was performed. The patient was identified as a rapid metabolizer of CYP2C19 substrate drugs, which may result in reduced efficacy of proton pump inhibitors (PPIs). In cases of persistent gastroesophageal reflux disease (GERD) symptoms, an increase in the PPI dose by 50–100% is recommended.

Furthermore, reduced transport function of the ABCG2 and SLCO1B1 proteins was identified, which may lead to increased systemic exposure to rosuvastatin and consequently an elevated risk of myotoxicity, particularly at doses exceeding 20 mg. Amiodarone is a known inhibitor of several membrane transporters, including SLCO1B1 and ABCG2. Inhibition of these transporters results in reduced hepatic uptake of rosuvastatin and decreased biliary excretion, further increasing systemic drug exposure.

The pharmacokinetic interaction between amiodarone and rosuvastatin, combined with genetically reduced transporter function, resulted in a synergistic increase in rosuvastatin exposure and a significantly increased risk of rhabdomyolysis. Amiodarone was discontinued, and alternative non-statin lipid-lowering therapy was recommended.

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

PS – 12

Conclusion:

The application of pharmacogenetic testing in treatment individualization is crucial for understanding interindividual differences in therapeutic response and the risk of adverse drug reactions. Variants of CYP450 enzymes may alter drug metabolism rates, increasing the risk of therapeutic failure or adverse effects, while variants in the SLCO1B1 and ABCG2 transporter genes are associated with increased systemic exposure to statins and a higher risk of myotoxicity.

Implementation of pharmacogenetic testing in clinical practice can improve treatment outcomes through individualized therapy selection and dose adjustment, thereby enhancing treatment safety and efficacy, particularly in elderly patients and those receiving multiple concomitant medications.

Keywords: pharmacogenetics, rhabdomyolysis, drug–drug–gene interactions

PROBIR RAKA DOJKE: UTJEČE LI NA UKUPNU SMRTNOST? SUSTAVNI PREGLED I META-ANALIZA

Vlatka Bračić, mag. pharm.,[1], Doc. dr. sc. Marko Skelin, mag. pharm[1,2,3], Bruna Perkov-Stipičin, mag pharm.[1], Lorena Kostrić, mag. pharm.[4]

[1] Odjel za farmaciju, Opća bolnica Šibensko-kninske županije, Šibenik, Hrvatska
[2] Medicinski fakultet, Sveučilište u Rijeci, Rijeka, Hrvatska
[3] Veleučilište u Šibeniku, Šibenik, Hrvatska
[4] Zdravstvena ustanova Prima Pharme Ljekarne

PS – 13

Uvod: Rak dojke najčešća je zloćudna bolest i vodeći uzrok smrtnosti od raka među ženama u svijetu. Probir predstavlja ključan alat u kontroli raka u mnogim zemljama jer omogućuje otkrivanje karcinoma u ranim stadijima. Međutim, iako probir smanjuje smrtnost specifičnu za rak dojke, njegov utjecaj na ukupno očekivano trajanje života i dalje je predmet rasprave.

Cilj: Cilj ovog sustavnog pregleda i meta-analize bio je procijeniti utjecaj probira raka dojke na ukupnu smrtnost u usporedbi s kontrolnom skupinom bez probira.

Materijali i metode: Pretražene su različite baze podataka i onkološke mrežne stranice te su identificirana 353 zapisa. Uključena su randomizirana kontrolirana ispitivanja (RCT) koja su uspoređivala probir s izostankom probira, pri čemu je prijava ukupne smrtnosti bila obvezan kriterij uključivanja. Nakon procjene 58 cjelovitih radova, za meta-analizu je odabrano 10 RCT-ova. Rezultati su analizirani kao omjeri stopa incidencije (IRR) s 95 % intervalima pouzdanosti korištenjem programa RevMan 5.3.

Rezultati: Ova meta-analiza pokazala je da probir značajno smanjuje smrtnost specifičnu za rak dojke. Prilagođeni omjer stopa incidencije (IRR) iznosio je 0,85 (95 % CI: 0,77–0,94; p = 0,002), dok je sirovi IRR iznosio 0,86 (95 % CI: 0,75–0,98; p = 0,02), čime se potvrđuje visoka učinkovitost u smanjenju smrtnosti specifične za bolest. Nasuprot tome, utjecaj na ukupnu smrtnost bio je znatno manji. Prilagođeni IRR za ukupnu smrtnost iznosio je 0,97 (95 % CI: 0,94–1,00; p = 0,03), dok je sirovi IRR iznosio 0,96 (95 % CI: 0,93–0,98; p = 0,002). Uočena je umjerena do visoka heterogenost (I^2: 57–75 %), vjerojatno zbog različitih razdoblja praćenja, metoda probira i populacija uključenih u istraživanja.

Zaključak: Ova meta-analiza potvrđuje da probir raka dojke značajno smanjuje smrtnost specifičnu za bolest, potvrđujući visoku učinkovitost programa probira u ranom otkrivanju i uspješnom liječenju. Međutim, minimalno smanjenje ukupne smrtnosti upućuje na to da ovi programi ne dovode do značajnih promjena u ukupnom očekivanom trajanju života.

Ključne riječi: probir raka dojke, ukupna smrtnost, meta-analiza

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

BREAST CANCER SCREENING: DOES IT AFFECT ALL-CAUSE MORTALITY? A SYSTEMATIC REVIEW AND META-ANALYSIS

Vlatka Bračić, MPharm[1], Asst. prof. Marko Skelin, MPharm, PhD[1,2,3], Bruna Perkov-Stipičin, MPharm[1], Lorena Kostrić, MPharm[4]

[1] Pharmacy Department, General Hospital of Šibenik-Knin County, Šibenik, Croatia
[2] Faculty of Medicine, University of Rijeka, Rijeka, Croatia
[3] University of Applied Sciences, Šibenik, Croatia
[4] Healthcare Institution Prima Pharme Pharmacies

PS – 13

Introduction: Breast cancer is the most common malignancy and the leading cause of cancer-related mortality among women worldwide. Screening is a critical tool for cancer control in many countries, enabling the detection of carcinomas in their early stages. However, while screening reduces cancer-specific deaths, its impact on overall life expectancy remains a subject of debate.

Objective: The aim of this systematic review and meta-analysis was to evaluate the impact of breast cancer screening on all-cause mortality compared to a non-screening control group.

Materials and methods: Different databases and oncology websites were searched, identifying 353 records. We included randomized controlled trials (RCTs) comparing screening to no screening, with reporting of all-cause mortality as a mandatory inclusion criterion. After evaluating 58 full-text articles, 10 RCTs were selected for meta-analysis. Results were analyzed as Incidence Rate Ratios (IRR) with 95% confidence intervals using RevMan 5.3

Results: This meta-analysis demonstrated that screening significantly reduces breast cancer-specific mortality. Specifically, the adjusted incidence rate ratio (IRR) was 0.85 (95% CI: 0.77- 0.94, p = 0.002), and the crude IRR was 0.86 (95% CI: 0.75-0.98, p = 0.02), confirming high disease-specific efficacy. In contrast, the impact on all-cause mortality was substantially smaller. The adjusted IRR for all-cause mortality was 0.97 (95% CI: 0.94-1.00, p = 0.03), while the crude IRR was 0.96 (95% CI: 0.93-0.98, p = 0.002). Moderate to high heterogeneity (I^2: 57-75%) was observed, likely due to varying follow-up periods, screening methods, and study populations.

Conclusion: This meta-analysis confirms that breast cancer screening significantly reduces disease-specific mortality, demonstrating the high efficacy of screening programs in early detection and successful treatment. However, the minimal decrease in all-cause mortality suggests that these programs do not lead to substantial changes in overall life expectancy.

Key words: Breast cancer screening, all-cause mortality, meta-analysis

PANCITOPENIJA U BOLESNIKA S ANAMNEZOM TETRALOGIJE FALLOT I AGENEZE PLUĆNOG ZALISKA TIJEKOM PRODULJENE TERAPIJE BETA-LAKTAMSKIM ANTIBIOTICIMA ZBOG ENDOKARDITISA PROTETSKOG ZALISKA: PRIKAZ SLUČAJA

Paula Stepanić[1], Ana Vrkić[2] , Tajana Grenko-Malnar, dr. med.[1,3], Andrej Belančić, dr. med.[3]

[1] Medicinski fakultet Sveučilišta u Rijeci, Rijeka, Hrvatska
[2] CPSA
[3] Klinički bolnički centar Rijeka, Rijeka, Hrvatska

PS – 14

Bolesnici s prirođenim srčanim greškama koji zahtijevaju ponavljane kirurške i transkateterske zahvate imaju povećan rizik od infektivnog endokarditisa te produljene izloženosti antimikrobnoj terapiji. Lijekom inducirane citopenije, iako rijetke, predstavljaju potencijalno po život opasnu komplikaciju, osobito tijekom dugotrajne terapije β-laktamskim antibioticima. Prikazujemo slučaj reverzibilne pancitopenije povezane s produljenim antibiotskim liječenjem u mlađeg odraslog bolesnika sa složenom prirođenom srčanom greškom, uz naglasak na dijagnostičke izazove i terapijske odluke.

Muškarac u dobi od 25 godina s anamnezom tetralogije Fallot i ageneze plućnog zaliska podvrgnut je kardiokirurškom zahvatu zbog infektivnog endokarditisa koji je zahvatio transkateterski plućni zalistak Melody. Postoperativno je nastavljena parenteralna antimikrobna terapija gentamicinom (120 mg i.v. dvaput dnevno), ceftriaksonom (2 g i.v. jednom dnevno) i flukloksacilinom (2 g i.v. četiri puta dnevno). Nakon približno tri tjedna liječenja uočen je postupni pad broja leukocita i trombocita. Nakon 40 dana terapije dokumentirana je pancitopenija (hemoglobin 102 g/L, leukociti 0,8 ×10⁹/L, trombociti 87 ×10⁹/L), uz blagi porast upalnih parametara (CRP 54 mg/L, prokalcitonin 0,32 ng/mL), dok su ponovljene mikrobiološke kulture ostale sterilne. Nakon multidisciplinarne konzultacije s kliničkim farmakologom, infektologom i hematologom, posumnjalo se na supresiju koštane srži induciranu antibioticima, prvenstveno povezanu s ceftriaksonom, a moguće i s flukloksacilinom. Navedeni lijekovi su ukinuti te su zamijenjeni meropenemom i vankomicinom radi dovršetka potrebne parenteralne terapije. Budući da je 4Ts bodovni sustav iznosio 5, što upućuje na moguću heparinom induciranu trombocitopeniju, enoksaparin je zamijenjen fondaparinuksom, dok je primjena čimbenika stimulacije kolonija granulocita dodatno pridonijela potpunoj normalizaciji krvne slike.

Daljnji tijek bio je uredan, osim reakcije preosjetljivosti na vankomicin koja je zahtijevala zamjenu teikoplaninom, nakon čega je bolesnik otpušten u dobrom kliničkom stanju.
Ovaj slučaj naglašava važnost opreza i praćenja hematološke toksičnosti tijekom produljene terapije β-laktamskim antibioticima, osobito u bolesnika sa složenim srčanim bolestima. Rano prepoznavanje, interdisciplinarna suradnja i pravodobna prilagodba antimikrobne terapije ključni su za povoljan ishod.

Ključne riječi: beta-laktamski antibiotici, endokarditis, pancitopenija

3. ŠKOLA RACIONALNE I SIGURNE FARMAKOTERAPIJE S MEĐUNARODNIM SUDJELOVANJEM
3rd SCHOOL OF RATIONAL AND SAFE PHARMACOTHERAPY WITH INTERNATIONAL PARTICIPATION

PANCYTOPENIA IN A PATIENT WITH A HISTORY OF TETRALOGY OF FALLOT AND PULMONARY VALVE AGENESIS RECEIVING PROLONGED BETA-LACTAM THERAPY FOR PROSTHETIC VALVE ENDOCARDITIS: A CASE REPORT

Paula Stepanić[1], Ana Vrkić[2] , Tajana Grenko-Malnar, MD[1,3] , Andrej Belančić, MD[3]

[1] Medicinski fakultet Sveučilišta u Rijeci, Rijeka, Hrvatska
[2] CPSA
[3] Klinički bolnički centar Rijeka, Rijeka, Hrvatska

PS – 14

Congenital heart disease patients requiring repeated surgical and transcatheter interventions are at increased risk of infective endocarditis and prolonged antimicrobial exposure. Drug-induced cytopenias, although uncommon, represent a potentially life-threatening complication, particularly during long-term β-lactam therapy. We present a case of reversible pancytopenia associated with prolonged antibiotic treatment in a young adult with complex congenital heart disease, highlighting diagnostic challenges and management considerations.

A 25-year-old man with a history of tetralogy of Fallot and pulmonary valve agenesis underwent cardiac surgery for infective endocarditis involving a Melody transcatheter pulmonary valve. Postoperatively, parenteral antimicrobial therapy was continued with gentamicin (120 mg i.v. twice daily), ceftriaxone (2 g i.v. once daily), and flucloxacillin (2 g i.v. four times daily). After approximately three weeks of treatment, a gradual decline in leukocyte and platelet counts was observed. Following 40 days of therapy, pancytopenia was documented (haemoglobin 102 g/L, leukocytes 0.8 ×10⁹/L, platelets 87 ×10⁹/L), accompanied by a mild rise in inflammatory markers (CRP 54 mg/L, procalcitonin 0.32 ng/mL), while repeated microbiological cultures remained sterile. After multidisciplinary consultation with clinical pharmacology, infectious diseases, and haematology specialists, antibiotic-induced bone marrow suppression was suspected, primarily related to ceftriaxone and possibly flucloxacillin. These agents were discontinued and replaced with meropenem and vancomycin to complete the required parenteral therapy. Given a 4Ts score of 5 suggesting possible heparin-induced thrombocytopenia, enoxaparin was replaced with fondaparinux, while granulocyte colony-stimulating factor further facilitated complete normalization of blood counts. The subsequent course was uneventful, apart from a hypersensitivity reaction to vancomycin necessitating substitution with teicoplanin, and the patient was discharged in good clinical condition.

This case underscores the importance of vigilance for haematological toxicity during prolonged β-lactam therapy, especially in complex cardiac patients. Early recognition, interdisciplinary collaboration, and timely modification of antimicrobial regimens are crucial for favourable outcomes.

Ključne riječi: Beta-Lactam Antibiotics, Endocarditis, Pancytopenia

SPONZORI

Organizacijski odbor Škole najljepše zahvaljuje sponzorima na pruženoj potpori.

ZLATNI SPONZOR - GOLDEN SPONSOR

MSD

SREBRNI SPONZOR - SILVER SPONSOR

AstraZeneca

BRONČANI SPONZORI - BRONZE SPONSORS

novo nordisk®

OKTAL PHARMA

jgl Osjeti život

PLIVA | teva

PharmaS

NOVARTIS

Abbott

B BRAUN SHARING EXPERTISE

astellas

PHOENIX Farmacija d.o.o. a PHOENIX company

SPONZORI - SPONSORS

abbvie

Swixx BioPharma

Lilly A MEDICINE COMPANY

MiP

ZENTIVA

Pfizer

Johnson&Johnson

ALPHA MEDICAL

SONIMED

Biocon Biologics®

SALVUS

MACOPLAST

FRESENIUS KABI

altamedics

VIVITPHARMA

MERCK

AGMAR

Roche

BERLIN-CHEMIE MENARINI

STADA

MEDIJSKI POKROVITELJ

DANAS Medicina

ALYMSYS

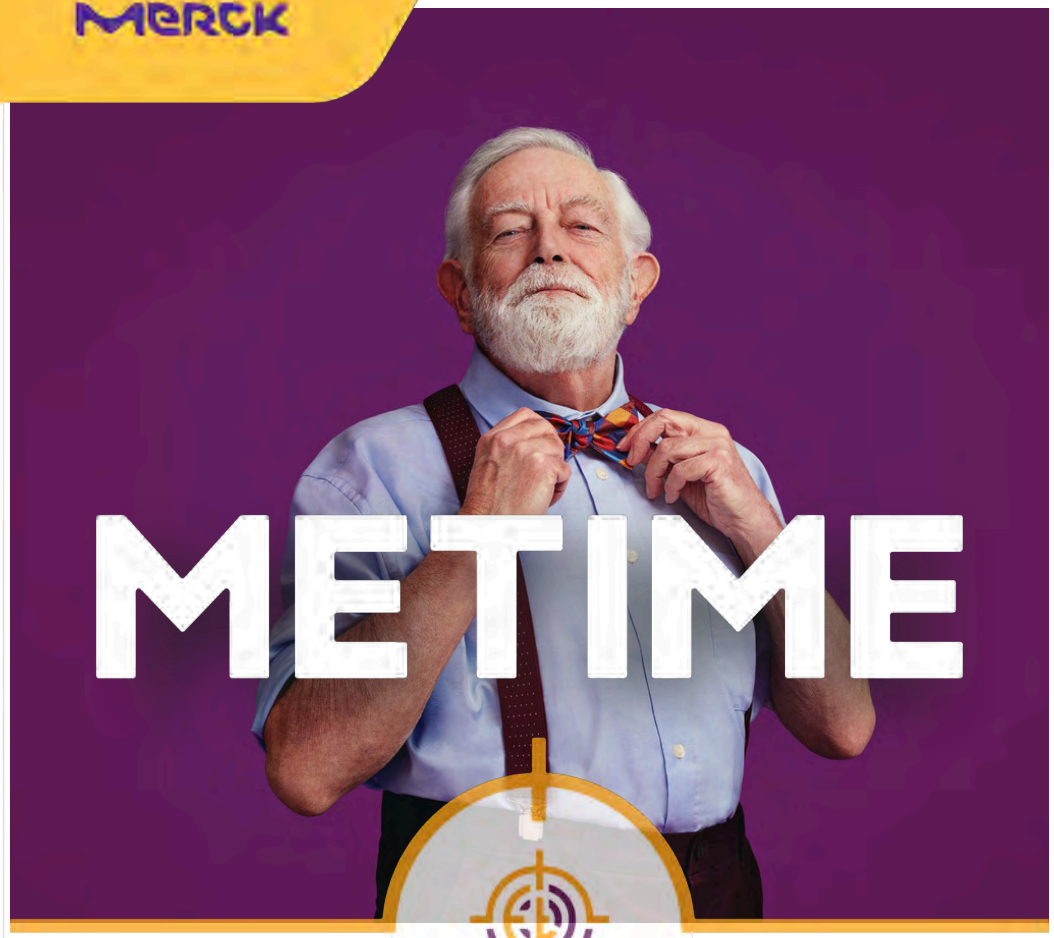
Bevacizumab

There's a place where
similarity and quality
find each other

ZENTIVA

ALY-HR-RU-292021

MERCK



TEPMETKO®

tepotinib

▼ Ovaj je lijek pod dodatnim praćenjem. Time se omogućuje brzo otkrivanje novih sigurnosnih informacija. Od zdravstvenih radnika se traži da prijave svaku sumnju na nuspojavu za ovaj lijek. Samo za zdravstvene radnike.
Posljednji odobreni Sažetak opisa svojstava lijeka Tepmetko dostupan je na internetskoj stranici Europske agencije za lijekove https://www.ema.europa.eu. HR-TEP-00043; 10/2025

LEPEZA HER2 EKSPRESIJE OTVARA NOVE MOGUĆNOSTI

Razine ekspresije HER2 unutar kategorije HER2-negativne bolesti zaslužuju više pažnje[1]

% bolesnika s HR+ / HER2-negativnim metastatskim rakom dojke[1]

~15% ima HER2 status 0 (IHC 0 bez membranskog bojenja)[1,2]

Među HER2-negativnim tumorima,

~85% ima niske razine ekspresije HER2 (HER2-low ili HER2-ultralow status: IHC 2+/ISH− ili IHC 1+ ili IHC 0 s membranskim bojenjem u < 10% tumorskih stanica) .[1,2]

Nakon što se iscrpe standardne mogućnosti liječenja metastatskog HER2-negativnog raka dojke, potrebne su dodatne terapijske opcije kako bi se promijenili ishodi liječenja.[1]

HER2- receptor humanog epidermalnog faktora rasta 2; IHC-imunohistokemija; ISH- in situ hibridizacija

Referenca: 1. Tarantino P, Hamilton E, Tolaney SM, et al. HER2-low breast cancer: pathological and clinical landscape. J Clin Oncol. 2020;38(17):1951-1962
2. Curigliano G et al. Presented at ASCO Annual Meeting; May 31 – June 4, 2024; Chicago, IL. Presentation LBA1000

Daiichi-Sankyo AstraZeneca

AstraZeneca d.o.o., Ulica Vjekoslava Heinzela 70, 10000 Zagreb, Tel: +385 1 4628 000, www.astrazeneca.com

SAMO ZA ZDRAVSTVENE RADNIKE

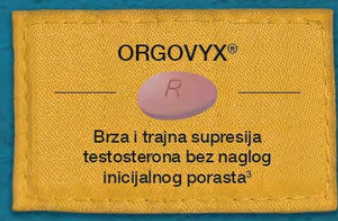
Veeva ID: HR-8987, siječanj 2026.

ORGOVYX® (relugolix) 120 mg tableta

accord PharmaS®

Prvi & jedini oralni ADT*

Predstavljamo ORGOVYX®, jedini oralni ADT za uznapredovali hormonski osjetljivi rak prostate.[1,2]



*Ovaj materijal izradilo je društvo Accord Healthcare Ltd i namijenjen je samo zdravstvenim djelatnicima

ADT - androgen deprivacijska terapija

▼Ovaj je lijek pod dodatnim praćenjem. Svaku sumnju na nuspojavu prijavite na pharmacovigilance@pharmas.hr

Vegzelma™
bevacizumab

CELL- VEGZ-2/2026-oglas

CELLTRION

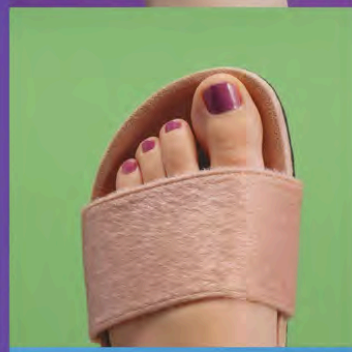
Samo za zdravstvene radnike

Ovaj je lijek pod dodatnim praćenjem. Time se omogućuje brzo otkrivanje novih sigurnosnih informacija.
Od zdravstvenih radnika se traži da prijave svaku sumnju na nuspojavu za ovaj lijek.

OKTAL PHARMA
Vaš najbolji izbor

FungilacSET
AMOROLFIN
50 mg/ml ljekoviti lak za nokte

Samo jednom tjedno, za lijepe nokte i dok se liječe.



samo 1X tjedno

Prije upotrebe pažljivo pročitajte uputu o lijeku, a o rizicima i nuspojavama upitajte svog liječnika ili ljekarnika.
Uputa o lijeku FungilacSET 50 mg/ml ljekoviti lak za nokte, kolovoz 2022, broj odobrenja HR-H-392860249
Datum sastavljanja: veljača 2025. | FLS-LDU-0425-003

jgl

3. ŠKOLA RACIONALNE I SIGURNE
FARMAKOTERAPIJE
S MEĐUNARODNIM SUDJELOVANJEM

3rd SCHOOL OF RATIONAL AND SAFE
PHARMACOTHERAPY
WITH INTERNATIONAL PARTICIPATION

Young experts; a new era of medicine!

TEHNIČKI ORGANIZATOR

Travel TILAGO d.o.o.
Luka 98, Luka - Sali