Liječ Vjesn 2024;146;suplement 4:30–70
https://doi.org/10.26800/LV-146-supl4-2

ISKUSTVO KLINIČKOG BOLNIČKOG CENTRA ZAGREB S PRIMJENOM SEKVENCIONIRANJA NOVE GENERACIJE U UZNAPREDOVALOM KOLOREKTALNOM KARCINOMU

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Uvod: Kolorektalni karcinom (CRC) predstavlja značajan svjetski javnozdravstveni problem, zauzimajući treće mjesto najčešćeg karcinoma u svijetu. Ukupna petogodišnja stopa preživljenja kod bolesnika s uznapredovalim CRC-om iznosi 5 do 10%. Sekvencioniranje nove generacije (NGS) je metoda ključna za napredak u razumijevanju biologije CRC-a, poboljšanje skrbi bolesnika te razvoj novih terapija.

Metode: Retrospektivno su identificirana 62 bolesnika s uznapredovalim CRC-om kod kojih je proveden NGS u našoj ustanovi u razdoblju od svibnja 2020. do prosinca 2023. Odabir bolesnika kod kojih je proveden NGS je bio prema nahođenju ordinarijusa. NGS analiza je provedena korištenjem FoundationOne®CDx testa koji ispituje četiri primarne klase genomskih promjena u 324 relevantna gena za rak. Također, pruža informacije o opterećenju tumora mutacijama (TMB), mikrostalitskoj nestabilnosti (MSI) i gubitku heterozigotnosti.

Rezultati: Od 62 bolesnika, 28 su bili muškarci, a 34 žene. Lijevostrani CRC je imalo 48 bolesnika, a desnostrani 14. Medijan dobi pri dijagnozi je iznosio 52 godine, a 31 pacijent se inicijalno prezentirao s uznapredovalim CRC-om. 55 bolesnika je bilo ECOG PS 0, dok su ostali imali PS 1. U većine bolesnika su dokazane *RAS* mutacije, 34 bolesnika su imala mutaciju *KRAS*-a, a najčešće se radilo o G13D (9) te G12V (8). Dodatno, uočene su i 2 *NRAS* mutacije. 4 bolesnika je imalo *BRAF* V600E mutaciju, 6 *PIK3CA* mutaciju, 3 *ERBB2* amplifikacije, dok su po 2 imala *BRCA* i *PALB2* mutacije. Što se tiče drugih mutacija, 33 bolesnika je imalo *APC* mutacije, a 39 *TP53* mutacije. Na temelju granice od 10 mut/Mb, 6 bolesnika je imalo visok TMB uz ukupni medijan od 4 mut/Mb, dok je 5 bolesnika imalo MSI tumore.

Zaključak: Iako relativno mala, naša kohorta pokazuje podatke iz stvarnog svijeta koji su u skladu s ostalim studijama. NGS ostaje važna metoda za identifikaciju mutacija i procjenu genomske slike kod CRC-a, individualizaciju terapije te poboljšanje učinkovitosti i ishoda liječenja.

Ključne riječi: sveobuhvatno gensko profiliranje, kolorektalni karcinom, metastatski, ciljana terapija

UNIVERSITY HOSPITAL CENTRE ZAGREB EXPERIENCE WITH NEXT-GENERATION SEQUENCING IN ADVANCED COLORECTAL CANCER

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Introduction: Colorectal cancer (CRC) represents a major global public health issue, ranking as the third most common cancer worldwide, with an overall 5-year survival rate ranging from 5 to 10% in patients with metastatic disease. Next-generation sequencing (NGS) plays a crucial role in advancing the understanding of CRC biology, improving patient care through personalized treatment, and driving the development of innovative therapies.

Methods: Sixty-two patients with advanced CRC who underwent NGS at our institution between May 2020 and December 2023 were retrospectively identified. Patient selection for NGS was at the discretion of the physician. The NGS analysis was conducted using FoundationOne®CDx, which examines four primary classes of genomic alterations in 324 well-known cancer-relevant genes. Additionally, it provides information on tumor mutational burden (TMB), microsatellite instability (MSI), and loss of heterozygosity.

Results: In a cohort of 62 patients, there were 28 males and 34 females. Forty-eight patients had left-sided CRC, while 14 cases were right-sided. The median age at diagnosis was 52 years. Thirty-one patients presented with metastatic disease initially. Most (55) exhibited an ECOG PS of 0, with 7 at PS 1. The majority of patients had *RAS* mutations. Thirty-four patients had *KRAS* mutations, the most common being G13D (9) and G12V (8). Additionally, 2 *NRAS* and 4 *BRAF* V600E mutations were observed. Six patients had PIK3CA mutations, 3 had ERBB2 amplifications, and 2 had *BRCA* and *PALB2* mutations. Regarding currently non-druggable mutations, 33 patients had *APC* mutations, while 39 had *TP53* mutations.

Based on the 10 Mut/Mb cut-off value, 6 patients were TMB-high with a median value of TMB 4 mt/mb. 5 patients had MSI-H tumor

Conclusion: Although relatively small, our cohort shows real-world data which is concordant with other similar studies. NGS is an important method for evaluation of genomic landscape in CRC and improvement of treatment outcomes.

Key words: next-generation sequencing, colorectal cancer, metastatic, cancer therapy

SMANJEN INDEKS MIŠIĆNE MASE KOD BOLESNIKA S METASTATSKIM KOLOREKTALNIM KARCINOMOM – PROSPEKTIVNA STUDIJA

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Uvod: Značajan broj bolesnika s metastatskim kolorektalnim karcinomom (mCRC) suočava se s malnutricijom zbog biologije bolesti i nuspojava povezanih s liječenjem. Malnutricija mijenja ukupni metabolizam i tjelesni sastav, što u konačnici dovodi do smanjenja mišićne mase. Te se promjene mogu mjeriti na različite načine, uključujući bioelektričnu impedancijsku analizu (BIA). Indeks skeletne mišićne mase (SMI) izračunava se dijeljenjem skeletne mišićne mase u kilogramima (mjereno pomoću BIA) s kvadratom visine u metrima. Ova je studija imala za cilj utvrditi je li smanjeni indeks skeletne mišićne mase (SMI) prognostički čimbenik za preživljenje bez progresije bolesti (PFS) kod bolesnika s mCRC.

Metode: U istraživanje je uključeno ukupno 112 bolesnika koji su započeli liječenje mCRC-a u Kliničkom bolničkom centru Zagreb između 1. siječnja 2020. i 31. prosinca 2022. Bolesnici su vagani pomoću BIA vage (Tanita PRO Body Composition Analyzer MC-780MA-N, Tanita Corporation, Tokyo, Japan) prije početka kemoterapije kao dio cjelokupnog fizikalnog pregleda. Ishodi su praćeni do 31. prosinca 2023.

Rezultati: Bolesnici su podijeljeni u dvije skupine, mušku i žensku (po 56 u svakoj skupini). Muška skupina imala je prosječan SMI od 8,86 sa standardnom devijacijom (SD) od 1,02. Muški bolesnici sa SMI manjim od 1 SD prosjeka imali su kraći PFS (7,6 mjeseci naspram 13,4 mjeseca, p=0,010). Ženska skupina imala je prosječan SMI od 6,95 s SD-om od 0,98. Razlika u preživljenju kod žena sa SMI manjim od 1 SD prosjeka nije bila statistički značajna (8,2 naspram 10,8 mjeseci, p=0,09).

Zaključak: Na temelju rezultata našeg istraživanja, SMI se pokazao kao pouzdan prognostički pokazatelj kod muških bolesnika s metastatskim mCRC-om, ali ne i kod žena. Potrebna su daljnja istraživanja kako bi se utvrdila točna granična vrijednost i istražio uzrok te razlike.

Ključne riječi: indeks skeletne mišićne mase, kolorektalni karcinom, preživljenje bez progresije, bioelektrična impedanca

REDUCED MUSCLE MASS INDEX IN PATIENTS WITH METASTATIC COLORECTAL CANCER – PROSPECTIVE SINGLE CENTER STUDY

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Introduction: A significant number of patients with metastatic CRC (mCRC) experience malnutrition due to the disease's biology and treatment-related side effects. Malnutrition alters the overall metabolism and body composition, ultimately leading to a reduction in muscle mass. These changes can be measured in several ways, including bioelectrical impedance analysis (BIA). Skeletal muscle index (SMI) is calculated by dividing the skeletal muscle mass in kilograms (measured using BIA) by the square of height in meters.

This study aimed to determine if reduced skeletal muscle index (SMI) was a prognostic factor for progression-free survival (PFS) in patients with mCRC.

Methods: A total of 112 patients who started treatment for mCRC at University Hospital Center Zagreb between January 1, 2020, and December 31, 2022, were included in the study. Patients were weighed with a BIA scale (Tanita PRO Body Composition Analyzer MC-780MA-N, Tanita Corporation, Tokyo, Japan) before the start of chemotherapy as part of a complete physical examination. Outcomes were monitored until December 31, 2023.

Results: Patients were divided into male and female groups (both 56). The male group had an average SMI of 8.86 with a standard deviation (SD) of 1.02. Male patients with SMI less than 1 SD on average had lower PFS (7.6 months vs 13.4 months, p=0.010). The female group had an average SMI of 6.95 with an SD of 0.98. The difference in survival in the female patients with SMI less than 1 SD on average was not statistically significant (8.2 vs 10.8 months, p=0.09).

Conclusion: Based on the findings of our study, SMI appears to be a reliable prognostic indicator in male patients with metastatic mCRC, but not in females. Further research is required to determine the exact cut-off value and explore the discrepancy's cause.

Keywords: skeletal muscle index, colorectal cancer, progression free survival, bioelectrical impedance

KLINIČKI POTENCIJAL PRIMJENE ONCOTYPE DX TESTA U LIJEČENJU RANOG RAKA DOJKE U HRVATSKOJ – PROSPEKTIVNA MULTICENTRIČNA STUDIJA

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Uvod: Odluka o propisivanju adjuvantne kemoterapije u luminalnim karcinomima dojke predstavlja klinički problem. Tradicionalnim kliničko-patološkim značajkama nedostaje prediktivna vrijednost. Pojava multigenetskih testova, posebice Oncotype DX, olakšala je donošenje odluka. Prethodne studije pokazale su da upotreba Oncotype-a rezultira smanjenjem potrebe za kemoterapijom u 36% pacijenata (49% deeskalirano, 13% eskalirano na kemoterapiju). Nažalost, Hrvatski zavod za zdravstveno osiguranje ne pokriva troškove Oncotype.

Metode: Provedena je prospektivna multicentrična studija u deset od šesnaest zdravstvenih ustanova u Hrvatskoj s organiziranom onkološkom skrbi. Zabilježene su sve bolesnice s novo dijagnosticiranim ranim luminalnim karcinomom dojke. Bolesnice koje su kliničari procijenili kao kandidate za Oncotype, zasebno su zabilježene s odgovarajućim kliničko-patološkim značajkama. Nadalje, upotrijebljeni su podatci radne skupine za karcinom dojke Hrvatskog društva za patologiju i sudsku medicinu o godišnjoj incidenciji karcinoma dojke kako bi se približno odredila potrebu za Oncotype testom, kao i utjecaj upotrebe Oncotype-a u jednoj godini.

Rezultati: Između travnja i lipnja 2023. zabilježena je 241 novodijagnosticirana bolesnica s luminalnim ranim rakom dojke. Među njima, 62 bolesnice (25%) smatralo se podobnim za testiranje na Oncotype. Deset bolesnica (17%) bilo je izvan kriterija kliničkih studija. Prema radnoj skupini patologa za rak dojke, u 2021., bilo je oko 2140 novodijagnosticiranih lokalnih luminalnih karcinoma dojke. Procjena potrebe za Oncotype testom je 535 testova godišnje za Hrvatsku. U našoj studiji bez rezultata Oncotype, 45 bolesnica (72%) preporučena je kemoterapija. Koristeći objavljene podatke, to sugerira da bi u jednoj godini 188 bolesnica moglo biti pošteđeno kemoterapije, dok bi u 18 bolesnica liječenje bilo eskalirano na kemoterapiju, što bi rezultiralo redukcijom propisivanja adjuvantne kemoterapije u 170 bolesnica u jednoj godini.

Zaključak: Multigenetsko testiranje za donošenje odluka o adjuvantnoj kemoterapiji nužno je uvesti u Hrvatsku. Prema procjeni, za hrvatsku populaciju, godišnje bi trebalo napraviti 535 pretraga, što bi rezultiralo sa 170 bolesnica manje na kemoterapiji. Financijski učinak bit će predmet daljnjih istraživanja.

Ključne riječi: Rak dojke, kemoterapija, adjuvantna, prediktivno genetsko testiranje

POSSIBLE CLINICAL IMPACT OF IMPLEMENTING ONCOTYPE DX TEST IN TREATMENT DECISION MAKING FOR EARLY BREAST CANCER IN CROATIA – A PROSPECTIVE MULTICENTER STUDY

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Introduction: The decision to prescribe adjuvant chemotherapy in luminal breast cancers represents a challenging decision. Traditional clinicopathological features lack a predictive value. The widespread use of multigenetic tests, particularly Oncotype DX, has simplified these decisions. Previous studies showed that the use of Oncotype resulted in a decreased need for chemotherapy use in 36% of patients (49% deescalated, 13% escalated to chemotherapy). Unfortunately, Oncotype is not reimbursed by the Croatian Health Insurance Fund.

Methods: Prospective multicentric study was conducted in ten of the sixteen Croatian institutions with established oncology care. All patients with newly diagnosed luminal early breast cancer were recorded. Subgroup of patients who were according to clinicial judgement evaluated as candidates for Oncotype, were separately recorded with corresponding clinicopathological features. Data from a Croatian Pathologist Breast Cancer Working Group was used to approximate the need and clinical impact of Oncotype use in one year.

Results: Between April and June 2023, 241 newly diagnosed luminal early breast cancer patients were recorded. Among them, 62 (25%) were eligible for Oncotype testing. Ten (17%) were outside clinical trial criteria. According to the Breast Cancer Pathologist Working Group, in 2021, there were 2140 newly diagnosed luminal early breast cancers, what, further on, h means approximately 535 multigenetic tests per year is to be prescribed in Croatia. In our study, without Oncoytpe results, 45 (72%) patients were recommended chemotherapy. Using published data, this suggests that in one year, 188 patients could be spared chemotherapy, and in 18 patients, treatment would be escalated to chemotherapy, resulting in less adjuvant chemotherapy prescription in 170 patients.

Conclusion: Multigenetic testing prior to adjuvant chemotherapy decision-making is an unmet need in Croatia. If multigenetic testing was reimbursed, approximately 540 tests would be sufficient to cover the needs of the Croatian population. Testing should result in, per year, 170 patients less receiving chemotherapy. The financial impact is to be further investigated.

Key words: breast cancer, chemotherapy, adjuvant, predictive genomic testing

ULTRA NISKODOZNA RADIOTERAPIJA KOD PACIJENTICE S MYCOSIS FUNGOIDES KOŽE GLAVE I VRATA: PRIKAZ SLUČAJA

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Uvod: Mycosis fungoides (MF) najčešći je oblik kožnog T-staničnog limfoma (CTCL), vrste ne-Hodgkinovog limfoma koji prvenstveno zahvaća kožu. Radioterapija ultra niskim dozama (ULDR) novi je pristup liječenju MF-a, osobito u slučajevima kada tradicionalno liječenje nije indicirano ili u slučajevima kada su iscrpljene druge opcije liječenja.

Prikaz slučaja: 89-godišnja žena javila se na pregled dermatologa radi eritematoznih promjena i plakova na koži lica i vrata. Učinjena je biopsija lezije na licu. Patohistološka analiza verificirala je infiltraciju epidermisa atipičnim limfocitima, imunohistokemijski pozitivnih za CD3, CD4 i CD5, a negativnih za CD79a, CD8 i CD20. Sistemsko liječenje nije indicirano zbog brojnih komorbiditeta. Tim za radioterapiju limfoma naše Ustanove indicirao je palijativnu iradijaciju lokaliziranih lezija na licu. Klinički ciljni volumen (CTV) uključivao je područje od 8 mm od površine kože. Planirani ciljni volumen (PTV) definiran je kao CTV plus margina od 5 mm. PTV je određen rubom od 3 mm od površine kože. Totalna doza od 8 Gy u 2 frakcije, koje su provedene u istom danu, propisana je na srednju dozu PTV-a te je provedena fotonskim snopom 6 MV. Šest mjeseci nakon završetka iradijacije primijećen je potpuni odgovor kožnih lezija bez akutnih nuspojava primijenjenog zračenja.

Zaključak: ULDR predstavlja obećavajuću opciju liječenja MF-a, osobito kod pacijenata kod kojih su konvencionalne mogućnosti liječenja ograničene. Međutim, odluku o primjeni ULDR treba se donijeti individualno na temelju cjelokupnog stanja pacijenta, stadija bolesti i ciljeva liječenja.

Ključne riječi: Radioterapija ultra niskim dozama, Mycosis fungoides, tumori glave i vrata, prikaz slučaja

ULTRA-LOW DOSE RADIOTHERAPY FOR A PATIENT WITH HEAD AND NECK INVOLVEMENT OF MYCOSIS FUNGOIDES: CASE REPORT

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Introduction: Mycosis Fungoides (MF) is the most common form of cutaneous T-cell lymphoma (CTCL), a type of non-Hodgkin lymphoma that primarily affects the skin. Ultra-low dose radiotherapy (ULDR) is an emerging treatment approach for MF, particularly in cases where traditional treatments may not be suitable or for patients who have exhausted other options.

Case Report: An 89-year-old female presented with erythematous patches and plaques on face and neck. A skin biopsy from a cutaneous face lesion was performed and a histological evaluation of the specimen revealed the infiltration of atypical lymphocytes into the epidermis, which was positive for CD3, CD4, and CD5, and negative for CD79a, CD8, and CD20. Systemic treatments were not performed due to comorbid diseases. The oncology board at our radiation therapy department examined the patient and decided to enroll her in a palliative radiation therapy program for the treatment of localized lesions on the face. The clinical target volume

(CTV) included an 8 mm area ranging from the skin surface. The planning target volume (PTV) was defined as the CTV plus a 5 mm margin. The PTV was cropped by a 3 mm margin from the skin surface. A dose of 8Gy in 2 fractions in the same day was prescribed to the mean dose of the PTV using a 6 MV photon beam. Six months after completion of the radiation therapy, complete response was observed for the cutaneous lesions, and there were no observed adverse events resulting from the administered irradiation.

Conclusion: ULDR represents a promising, low-risk option for managing MF, particularly in patients where conventional treatment options are limited or not ideal. However, the decision to use ULDR should be individualized based on the patient's overall condition, disease stage, and treatment goals.

Key words: ultra low dose radiotherapy, Mycosis fungoides, head and neck cancer, case reports

IZBOR LIJEČENJA NAKON PROGRESIJE NA TERAPIJU INHIBITORIMA O CIKLINIMA OVISNIH KINAZA 4/6

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Uvod: Karcinom dojke jedan je od najčešćih karcinoma u svijetu. Najčešći podtip čine $HR^+/HER2^-$ karcinomi dojke za koje standard liječenja predstavlja primjena CDK4/6 inhibitora uz endokrinu terapiju. Međutim, ne postoje prospektivni podaci o idućoj liniji liječenja nakon progresije. Cilj ove studije bio je usporediti učinkovitost liječenja pacijenata s metastatskim $HR^+/HER2^-$ karcinomom dojke nakon progresije na CDK 4/6 inhibitore.

Metode: Provedena je studija u KBC-u Rijeka na pacijenticama s metastatskim $HR^+/HER2^-$ karcinomom dojke liječenim CDK 4/6 inhibitorima tijekom barem jednog mjeseca od listopada 2018. godine. Uspoređivane su vrijednosti ukupnog preživljenja (OS; vrijeme od početka liječenja idućom linijom terapije do smrti ili gubitka kontakta) i preživljenje do progresije bolesti (PFS; vrijeme od početka liječenja idućom linijom terapije do kliničke ili radiološke progresije) nakon progresije na CDK 4/6 inhibitore.

Rezultati: Od 160 pacijentica uključenih u studiju, tijekom terapije CDK4/6 inhibitorima došlo je do progresije bolesti kod 79 pacijenata od kojih je kod 63,3% (N=50) provedena iduća linija liječenja.

Primijećen je duži PFS u pacijenata čija je iduća linija liječenja bila ciljana terapija u odnosu na hormonsku terapiju (HR 0,33 (95% CI 0,15–0,74) i kemoterapiju (HR 0,45 (95% CI 0,44–0,19–1,00)), dok je ukupan OS iznosio 1,4 godine te nije bilo razlike između primijenjene terapije.

Ukupno je 27 pacijenata koji su zatim liječeni drugom linijom terapije uz PFS od 0,3 godine, a OS 0,8 godina, bez razlike u izboru terapije.

Zaključak: U izboru iduće linije terapije, nakon progresije tijekom liječenja CDK4/6 inhibitorima, ciljana terapija povezana je s dužim PFS-om u odnosu na kemoterapiju i hormonsku terapiju. Vrijednosti OS nisu značajnije varirale ovisno o izboru vrste terapije.

Ključne riječi: rak dojke, inhibitori o ciklinima ovisnih kinaza 4/6, ukupno preživljenje, preživljenje bez progresije bolesti

CHOICE OF TREATMENT AFTER PROGRESSION ON CYCLIN DEPENDENT KINASE 4/6 INHIBITORS

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Introduction: Breast cancer is one of the most common cancers in the world. The most common subtype is HR+/HER2- breast cancer, for which the standard treatment consists of CDK4/6 inhibitors along with endocrine therapy. However, there is no prospective data on the next line of treatment after progression. The aim of this study was to compare the effectiveness of treatment in metastatic patients with HR+/HER2- breast cancer after progression on CDK 4/6 inhibitors.

Methods: A study was conducted at KBC Rijeka on female patients with metastatic HR+/HER2- breast cancer treated with CDK 4/6 inhibitors for at least one month from October 2018. Overall survival (OS; time from initiation of next-line therapy to death or loss of contact) and progression-free survival (PFS; time from initiation of next-line therapy to clinical or radiological progression) were compared in patients who underwent subsequent line of therapy after progression on CDK 4/6 inhibitors.

Results: Of the 160 patients included in the study, disease progression occurred in 79 patients on CDK4/6 inhibitors, of which 63.3% (N=50) underwent a subsequent line of treatment.

Longer PFS was observed in patients receiving targeted therapy compared to hormonal therapy (HR 0.33 (95% CI 0.15-0.74) and chemotherapy (HR 0.45 (95% CI 0.44-0.19-1.00)), while OS was 1.4 years regardless of type of therapy.

A total of 27 patients were subsequently treated with second-line therapy, with a PFS of 0.3 years and an OS of 0.8 years, with no difference in the choice of therapy.

Conclusion: In the next line of treatment, after progression on CDK4/6 inhibitors, targeted therapy was associated with longer PFS compared to hormonal therapy and chemotherapy. OS values did not vary significantly in the choice of type of therapy.

Key word:cyclin dependent kinase 4/6 inhibitors,, overall survival, progression free survival, breast cancer

RAZLIKA IZMEĐU NUSPOJAVA INHIBITORA O CIKLINIMA OVISNIH KINAZA 4/6: ISKUSTVA I PREPORUKE ZA SVAKODNEVNU KLINIČKU PRAKSU

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Uvod: Inhibitori o ciklinu ovisnih kinaza 4 i 6 (CDK4/6 inhibitori) su lijekovi koji se koriste u liječenju hormonski ovisnog raka dojke. U Republici Hrvatskoj odobrena su tri različita lijeka sa sličnom efikasnošću, no različitim profilom nuspojava. S obzirom da nema dovoljno podataka iz stvarne kliničke prakse mijenjaju li se nuspojave tijekom vremena, cilj ovog istraživanja bio je analizirati razlike u profilu nuspojava nakon 1, 3 i 6 mjeseci praćenja.

Metode: Istraživanje je provedeno u Klinici za tumore KBC Rijeka na skupini od 163 žena liječenih abemaciklibom, palbociklibom i ribociklibom. Nuspojave su istraživane nakon 1, 3 i 6 mjeseci praćenja. Deskriptivna analiza i hi-kvadrat test je učinjen u programu MedCalc (MedCalc Software bvba, Ostend, Belgija).

Rezultati: Najčešće zabilježene nuspojave su neutropenija (57.0%) i leukopenija (42.9%). Nakon prvog su mjeseca praćenja leukopenija i neutropenija bile najmanje zastupljene u pacijentica liječenih abemaciklibom (33,3%)(p=0,0055; p=0,002). U pacijentica liječenih abemaciklibom prati se i najveća incidencija proljeva (33,3%) u odnosu na palbociklib (1.8%) te ribociklib (0%) (p<0.0001). Nefrotoksičnost nije zabilježena u skupini liječenih palbociklibom, dok kod abemacikliba iznosi 13,9% te 10,9% kod ribocikliba (p=0.02). Nakon tri te šest mjeseci od početka liječenja nema statistički značajne razlike u leukopeniji (p=0.21) te nefrotoksičnosti (p=0,09) među ispitivanim skupinama, dok je ista ponovo zabilježena u incidenciji proljeva skupine liječene abemaciklibom (p<0,0001).

Zaključak: U ranom praćenju, abemaciklib rezultira s najboljim profilom leukograma, no čestim proljevom, radi čega je potreban oprez u pacijenata s ranije poznatim gastrointestinalnim bolestima. Iako se palbociklib povezuje s padom vrijednosti leukograma, rezultira s najmanje nefrotoksičnosti pa bi mogao biti lijek izbora u nefroloških bolesnika. Ribociklib također rezultira padom vrijednosti leukocita i povremenom nefrotoksičnošću, no ne rezultira proljevom. Osim proljeva, razlika u nuspojavama između CDK4/6 inhibitora se smanjila nakon 3 i 6 mjeseci praćenja.

Ključne riječi: inhibitori o ciklinima ovisnih kinaza 4/6, nuspojave; karcinom dojke, metastatski

DIFFERENCE BETWEEN SIDE EFFECTS OF CYCLIN DEPENDENT KINASE 4/6 INHIBITORS: EXPERIENCE AND RECOMMENDATIONS FOR REGULAR CLINICAL USE

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Introduction: Cyclin-dependent kinase inhibitors 4 and 6 (CDK4/6 inhibitors) are hormone-dependent breast cancer treatment drugs. In the Republic of Croatia, three different drugs with similar efficacy but different side effect profiles have been approved. Since there is insufficient data from clinical practice about these side effects over time, this research paper aimed to analyze the incidence of different side effects after 1,3,6-month follow-ups.

Methods: Research was conducted at the Tumor Clinic, University Hospital Center Rijeka, on 163 women treated with abemaciclib, palbociclib, and ribociclib. Side effects were observed after 1, 3, and 6-month follow-ups. Descriptive analysis and Chi-square test were conducted using a computer program called MedCalc (MedCalc Software bvba, Ostend, Belgium).

Results: The most common side effects were neutropenia (57.0%) and leukopenia (42.9%). After the first month, leukopenia and neutropenia were the least present in patients treated with abemaciclib (33.3%)(p=0055; p=0.002). The largest incidence of diarrhea was observed in abemaciclib-treated patients (33.3%) in regard to palbociclib (1.8%) and ribociclib (0%)(p>0,0001). Nephrotoxicity did not occur in the group treated with palbociclib, but it did occur with abemaciclib (13.9%) and ribociclib (10.9%)(p=0.02). After 3 and 6 months of treatment, there is no statistical significance in leukopenia (p=0.21) and nephrotoxicity (p=0.09) between groups. At the same time, the difference in diarrhea incidence is still statistically significant in the abemaciclib group (p<0.0001).

Conclusion: In the early follow-ups, abemaciclib presented with the best leukogram but with frequent diarrhea. Therefore, caution is needed in patients with gastrointestinal diseases. Palbociclib decreases leukocyte count, yet it is the least nephrotoxic drug, so it could be administered to patients with kidney diseases. Ribociclib also presents with decreased leukocyte count and occasional nephrotoxicity but does not cause diarrhea. Except for diarrhea, the difference in side effects among CDK4/6 inhibitors decreased after 3 and 6-month follow-ups.

Key words: cyclin dependent kinase 4/6 inhibitors; side effects; breast cancer, metastatic

TERAPIJSKI PRISTUP KARCINOMU CRIJEVA KOD PACIJENTA S MIASTENIJOM GRAVIS: PRIKAZ SLUČAJA

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Uvod: Ne postoje smjernice koje evaluiraju kemoterapiju karcinoma crijeva uz miasteniju gravis (MG).

Prikaz slučaja: Bolesniku (67 godina) u kliničkoj slici ileusa učinjena je sigmoidektomija s postavljanjem kolostome u hitnoći u ožujku 2024. Patohistološki je dokazan adenokarcinom sigmoidnog kolona pT4aN1b (*KRAS* mutacija G12S; *NRAS* i *BRAF* bez mutacija) s multiplim jetrenim metastazama. Bolesniku je u studenom 2016. dijagnosticirana MG koja se prezentirala disartrijom i disfagijom uz pozitivna protutijela na acetilkolinske receptore. Do sad je imao nekoliko miasteničnih kriza liječenih kortikosteroidima, ponavljanim plazmaferezama i intarvenskim imunoglobulinima. U trenutku planiranja onkološkog liječenja MG je pod kontrolom uz piridostigmin 240 mg i mikofenolat mofetil 200 mg tablete dnevno. Dodatak mikofenolat mofetila je pridonio stabilizaciji MG, te od tada nije zabilježena ni jedna miastenička kriza. Bolesnik je heterozigotni nositelj alela za reduciranu aktivnost dihidropirimidin dehidrogenaze i UDP-glukuroniltransferaze. Multidisciplinarni tim je odlučio započeti liječenje prema FOLFIRI protokolu, ali primjenjujući 75% uobičajene doze uz bevacizumab. Neutropenija, polineuropatija i mogući kolinergički sindrom povezan s irinotekanom su predstavljali poznati prihvatljiv rizik ove terapije. Nakon tri mjeseca na kontrolnom CT-u prsnog koša, trbuha i zdjelice, zabilježena je 35%-tno smanjenje jetrenih metastaza. Postignut je parcijalni odgovor na terapiju prema RECIST kriterijima. Bolesnik je dosad ukupno primio 9 ciklusa FOLFIRI terapije i bevacizumaba. Nije uočena neutropenija i polineuropatija.

Zaključak: Prezentirani bolesnik je starije životne dobi, i liječen imunoglobulinima što predstavlja rizične čimbenike za pojavu ostalih karcinoma u ljudi s MG. Cilj liječenja je kontrola metastatske, neresektabilne bolesti s prvom linijom terapije. Pretpostavljajući da će prva linija liječenja trajati najduže i uz činjenicu o kumulativnoj toksičnosti preparata platine, započeta je kemoterapija bez platine. Uzimamo u obzir mogućnost liječenja preparatima platine u sljedećoj liniji. Odluka o 75% uobičajene doze je temeljena na farmakogenetičkom profilu bolesnika i nedostatku smjernica što se tiče izbora i doze onkoloških lijekova uz neurološku patologiju opisanog slučaja.

Ključne riječi: karcinom kolona, myasthenia gravis, liječenje, kemoterapija

TREATMENT CHALLENGE OF COLON CANCER AND MYASTHENIA GRAVIS: A CASE REPORT

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Introduction: No guidelines related to the treatment of colon cancer and myasthenia gravis (MG) exist.

Case Report: A sigmoidectomy with colostomy placement in March 2024 was performed in a 76-year-old Caucasian presented with ileus. In November 2016, the patient was diagnosed with MG, which presented with dysarthria and dysphagia with positive antibodies to acetylcholine receptors. So far, he experienced several myasthenic crises treated with corticosteroids, repeated plasmapheresis, and intravenous immunoglobulins. Myasthenia is under control with pyridostigmine 240 mg and mycophenolate mofetil 200 mg tablets daily. Mycophenolate mofetil contributed to the stabilization of MG, and since then no myasthenic crisis has been recorded. The patient is a heterozygous carrier of the allele for reduced activity of dihydropyrimidine dehydrogenase and

UDP-glucuronyltransferase. The multidisciplinary team started treatment according to the FOLFIRI protocol, applying 75% of the usual dose with bevacizumab. Neutropenia, polyneuropathy, and possible cholinergic syndrome associated with irinotecan were known acceptable risks of this therapy. After three months, a control CT scan revealed a 35% reduction in liver metastases representing a partial treatment response according to RECIST criteria. So far, the patient has received a total of 9 cycles of FOLFIRI therapy and bevacizumab. Neutropenia and polyneuropathy were not observed.

Conclusion: The presented patient is elderly and treated with immunoglobulins, which represents risk factors for the occurrence of other cancers in people with MG.[1,2] The goal of treatment is to control the metastatic, unresectable disease with first-line therapy. Assuming that the first-line treatment would last the longest and with the fact of the cumulative toxicity of platinum preparations, chemotherapy without platinum was started. We consider the possibility of treatment with platinum preparations in the next line. The decision on 75% of the usual dose is based on the patient's pharmacogenetic profile and the lack of guidelines regarding the choice and dose of antineoplastic drugs in addition to the neurological pathology of the described case.

Key words: colon cancer, myasthenia gravis, treatment, chemotherapy

USPOREDBA TRAJANJA I GODINE ODRŽAVANJA KOLEGIJA ONKOLOGIJE UNUTAR STUDIJA MEDICINE NA MEDICINSKIM FAKULTETIMA U JUGOISTOČNOJ EUROPI

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Uvod: Onkologija je grana medicine koja se bavi dijagnostikom i liječenjem malignih bolesti. Važnost učenja onkologije proizlazi iz činjenice da su prema izvješću Svjetske zdravstvene organizacije iz 2020. godine maligne bolesti drugi uzrok smrti u svijetu. Studenti medicine u jugoistočnoj Europi studiraju šest godina, pri čemu je onkologija dio njihovog nastavnog plana i programa. Cilj ovog istraživanja je osvijestiti razliku u trajanju kolegija iz onkologije različitih studija medicine u jugoistočnoj Europi.

Metode: Podatci o planovima i programima medicinskih fakulteta za period 2023/2024 prikupljeni su s internetskih stranica sveučilišta u jugoistočnoj Europi, uključujući Hrvatsku, Bugarsku, Albaniju, Srbiju, Bosnu i Hercegovinu, Crnu Goru i Sjevernu Makedoniju.

Rezultati: Postoji velika razlika u trajanju i godini održavanja kolegija iz onkologije unutar studija medicine na medicinskim fakultetima diljem jugoistočne Europe, kako unutar pojedinih zemalja, tako i između njih. Od 16 fakulteta čiji su podatci prikupljeni, onkologija nije obavezan kolegij studija medicine na njih dva koji nude onkologiju samo kao izborni predmet. U zemljama gdje je onkologija obavezna, trajanje turnusa može varirati od samo 7 dana do cijelog semestra. Druga razlika između medicinskih studija je godina održavanja kolegija iz onkologije. Kolegij se na četiri fakulteta održava na četvrtoj godini, na sedam fakulteta na petoj te na pet fakulteta na šestoj godini studija.

Zaključak: Ova usporedba programa medicinskih studija fakulteta medicine jugoistočne Europe ukazala je na razlike u trajanju i godini održavanja kolegija iz onkologije. Daljnja istraživanja bila bi korisna kako bi se procijenio učinak različitog trajanja i godine održavanja kolegija iz onkologije na ishode učenja studenata te na njihov budući odabir specijalizacije iz onkologije.

Ključne riječi: onkologija, nastavni plan i program, Jugoistočna Europa, medicinski fakultet

COMPARISON OF THE DURATION AND TIMING OF CLINICAL ROTATION IN ONCOLOGY IN MEDICAL SCHOOLS IN SOUTHEASTERN EUROPE

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Introduction: Oncology is the branch of medicine focused on the diagnosis and treatment of malignant tumors. The importance of learning oncology lies in the fact that cancer is the second cause of death according to a 2020 World Health Organization report. Medical students in Southeastern Europe study for six years with oncology forming part of their curriculum. The purpose of this research is to point out the difference in the duration and timing of clinical rotation in oncology in medical schools in Southeastern Europe.

Methods: Data on medical school curriculums for the year 2023/2024 was collected from websites of universities in the southeastern region including Croatia, Bulgaria, Albania, Serbia, Bosnia and Herzegovina, Montenegro and North Macedonia.

Results: There is a wide variation in duration and timing of clinical rotation in oncology in medical studies in medical schools across Southeastern Europe, both within and between countries. Out of 16 medical schools from which data was collected, oncology is not a compulsory clinical rotation in two of them which only offer oncology as an optional rotation. In other countries where oncology is obligatory the duration of the rotation can range from as short as 7 days to as long as the whole semester. The other difference between medical studies is their timing of the oncology rotation. Medical studies of four medical schools place oncology in the fourth year, seven of them place oncology in the fifth year and five of them in the sixth year of the curriculum.

Conclusion: This report has shown variation in duration and timing of clinical rotation in oncology in medical studies in medical schools in Southeastern Europe. Further research would be useful to evaluate the effect of differing duration and timing of rotation on students' oncology learning outcomes and on their future choice to train in this specialty.

Keywords: oncology, curriculum, Southeastern Europe, medical school

UTJECAJ PORASTA MASE NA DJELOTVORNOST IMUNOTERAPIJE

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Uvod: Veliki broj istraživanja ukazuje kako pretilost može imati značajan utjecaj na učinkovitost imunoterapije. Pretilost se može smatrati kroničnim upalnim stanjem koje proizlazi iz povećane produkcije proupalnih citokina u adipocitima. Može dovesti do smanjene sposobnost imunološkog sustava da prepozna i uništi tumorske stanice. Druge studije sugeriraju kako pretilost može paradoksalno pojačati odgovor na imunoterapiju. Povećana količina leptina i inzulina u pretilih bolesnika može potaknuti imunosne mehanizme.

Metode: U presječnoj studiji smo retrospektivno obradili podatke bolesnika koji su bili na imunoterapiji nivolumabom. Uključeni su bolesnici liječeni u KBCO u razdoblju od 2019. do 2024. godine. Proučavane kategorije su dob, spol, trajanje imunoterapije, tjelesna masa i BMI na početku te na kraju liječenja, uz primarno sijelo (karcinomi glave i vrata, kože, pluća, bubrega i mokraćnog mjehura).

Rezultati: Analizirani su podaci 83 bolesnika, 60 (72,29%) muškaraca i 23 (27,71%) žene. Prosječna masa na početku liječenja bila je 74,76 kg (36; 111) i BMI 25,08 kg/m^2 (13,2; 39,8) dok je prosječna masa na kraju liječenja bila 73,58 kg (33; 110) i BMI 24,65 kg/m^2 (12,1; 37,8). Prosječno trajanje liječenja za sve regije karcinoma liječenim nivolumabom je bilo 171 dan (15; 91; 746), odnosno 24,42 tjedna. 17 bolesnika imalo je porast tjelesne mase, a njih 25 je izgubilo na masi. 41 (49,36%) bolesnik je gubio na masi te primio mali broj ciklusa terapije. S druge strane, 15 (18,07%) bolesnika je tijekom terapije dobilo na masi ili bilo stacionarno te je primilo veći broj ciklusa. Može se zaključiti kako je 56 (67,47%) bolesnika u skupini studija koje sugeriraju da promjene tjelesne mase mogu mijenjati odgovor na imunoterapiju.

Zaključak: Iz rezultata možemo uočiti kako naši podaci prate hipoteze da porast mase pozitivno utječe na trajanje imunoterapije. Bolesnici s dobitkom na masi ili stacionarnom masom tijekom imunoterapije, imaju duže bolest pod kontrolom.

Ključne riječi: tjelesna masa, indeks tjelesne mase, nivolumab, ishodi liječenja

IMPACT OF WEIGHT GAIN ON IMMUNOTHERAPY

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Introduction: A significant number of studies suggests that obesity can have a substantial impact on the effectiveness of immunotherapy. Obesity can be considered a chronic inflammatory condition resulting from increased production of pro-inflammatory cytokines in adipocytes. It may lead to a reduced ability of the immune system to recognize and destroy tumor cells. Other studies suggest that obesity might paradoxically enhance the response to immunotherapy. Increased levels of leptin and insulin in obese patients may stimulate immune mechanisms.

Methods: In a cross-sectional study, we retrospectively analyzed data from patients undergoing nivolumab. The study included patients treated at KBCO between 2019 and 2024. The categories studied included age, sex, duration of immunotherapy, body weight, and BMI at the beginning and end of treatment period, along with cancer regions (head and neck, skin, lung, kidney, and bladder).

Results: Data from 83 patients were analyzed, including 60 (72.29%) men and 23 (27.71%) women. The average weight at the start of treatment was 74.76 kg (range: 36–111) and BMI was 25.08 kg/m^2 (13.2–39.8), while the average weight at the end of treatment was 73.58 kg (33–110) and BMI was 24.65 kg/m^2 (12.1–37.8). The average duration of treatment for all cancer regions treated with nivolumab was 171 days (15-91-746). 17 patients experienced weight gain, while 25 lost weight. 41 (49.36%) patients lost weight and received a small number of therapy cycles. 15 (18.07%) patients gained weight or remained stable and received a greater number of cycles. It can be concluded that 56 (67.47%) patients fall into the study group suggesting that changes in body weight may alter the response to immunotherapy.

Conclusion: The results indicate that our data support the hypothesis that weight gain positively influences the duration of immunotherapy. Patients who gained or maintained weight during immunotherapy had longer disease control.

Keywords: weight, body mass index, nivolumab, treatment outcomes

POJAVNOST NESANIRANIH ZUBA KOD BOLESNIKA KOJI ŽIVE U RURALNOM PODRUČJU, A BOLUJU OD METASTATSKOG KASTRACIJSKI REZISTENTNOG RAKA PROSTATE, U ODNOSU NA ONE KOJI ŽIVE U URBANOM SREDIŠTU – ISKUSTVO JEDNOG CENTRA

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Uvod: Metastatski rak prostate otporan na kastraciju (mKRRP) oblik je uznapredovalog raka prostate koji progredira unatoč androgen deprivacijskoj terapiji. Bolesnicima s metastazama u kostima se zbog rizika od klinički značajnih koštanih neželjenih događaja preporučuju bisfosfonati ili denosumab. Preduvjet za primjenu ovih lijekova je dobro stanje zuba.

Metode: U ovoj retrospektivnoj opservacijskoj studiji, provedenoj na Službi za internu medicinu opće bolnice Šibensko-kninske županije, pretražili smo evidenciju bolesnika s mKRRP-om koristeći lokalno vođeni registar. Pacijenti su liječeni u našoj bolnici od siječnja 2022. do prosinca 2023. godine. Stanje njihovih zuba, kao i cjelokupno oralno zdravlje, ispitivali su onkolog i/ili stomatolozi.

Rezultati: U ovu studiju uključeno je ukupno 26 bolesnika s mKRRP-om, u dobnom rasponu od 49–88 godina. Velika većina njih imala je metastaze u ili također u kostima (88%), dok je manjina (12%) imala isključivo nekoštane metastaze.

Među pacijentima koji su imali metastaze u kostima, njih 19 primilo je medikamentoznu antiresorptivnu terapiju, i to: bisfosfonate (74%), denosumab (16%), a (10%) bolesnika je u početku liječeno bisfosfonatima, ali je zbog razvoja bubrežne insuficijencije antiresorptivna terapija promijenjena u denosumab.

Samo u 3 bolesnika s mKRRP-om i koštanim metastazama nije propisana medikamentozna antiresorptivna terapija, jer je zaključeno kako ih prisutnost metastaza u kostima ne ugrožava.

Zbog nezadovoljavajućeg stanja zuba u 4 bolesnika medikamentozna antiresorptivna terapija nije propisana. Dvoje od ova 4 bolesnika žive u urbanom središtu, a dvoje dolaze iz ruralnih sredina.

Zaključak: Podaci dobiveni u našem istraživanju pokazuju kako u 15% bolesnika, zbog nezadovoljavajućeg stanja zuba, nije propisana medikamentozna antiresorptivna terapija. Nezadovoljavajuće stanje zuba jednakom učestalošću se pojavljivalo neovisno žive li osobe u urbanom središtu ili ruralnim područjima. Potrebne su daljnje studije kako bi se potvrdili rezultati ove studije, koja je provedena u jednom centru.

Ključne riječi: rak prostate; stanje zuba, antiresorptivno liječenje, ruralno, urbano

THE COMPARISON OF FREQUENCY OF POOR DENTAL STATUS IN PATIENTS WITH METASTATIC CASTRATION-RESISTANT PROSTATIC CANCER LIVING IN RURAL AREAS VERSUS THE ONES WHO ARE LIVING IN URBAN CENTER – SINGLE CENTER EXPERIENCE

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Introduction: Metastatic castration-resistant prostate cancer (mCRPC) is advanced prostate cancer that continues to progress despite androgen deprivation therapy. In these patients who are at risk for clinically significant

skeletal-related events (SREs), bisphosphonates or denosumab are recommended. Prerequisite for administration of these agents is good dental status.

Methods: In the present retrospective observational study, conducted at the Department of Internal Medicine at the General Hospital od Šibenik-Knin county, we examined the records of patients with mCRPC using a locally maintained registry. The patients were treated in our hospital from January 2022. to December 2023. Their dental status, as well as overall oral health, was examined by oncologists and/ or dentists.

Results: A total of 26 patients with mCRPC, in the age range of 49–88 years, were included in this study. The vast majority of them had metastases in or also in the bones (88%), while a minority (12%) had exclusively extra osseous metastases.

Among the patients who had bone metastases, 19 of them have received medical antiresorptive therapy: bisphosphonates (74%), denosumab (16%), and (10%) of patients has been treated at the beginning with bisphosphonates, but later with denosumab.

Only in 3 patients with mCRPC, and bone metastases, this therapy was not prescribed because it did not endanger them.

Due to unsatisfactory dental status in 4 of patients with mCRPC, and bone metastases, treatment with antiresorptive therapy was not indicated. Regarding their place of living two of these patients came from urban centers, two are living in rural areas.

Conclusion: The data obtained in our study indicate that there was no difference among 15% of patients with mCRPC and bone metastases, who did not receive bone antiresorptive agents, whether the patients are living in urban centers or rural areas. Further studies are necessary to confirm the results of our single-center study.

Keywords: prostate cancer; dental status, antiresorptive therapy, rural, urban

KALCIFILAKSIJA U BOLESNICE NA TERAPIJI PEMIGATINIBOM – PRIKAZ SLUČAJA

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Uvod: Pemigatinib je inhibitor receptora fibroblastnog faktora rasta (FGFR). Koristi se u liječenju metastatskog kolangiokarcinoma s dokazanom *FGFR2* fuzijom ili preraspodjelom. Dermatotoksičnost je poznata, ali se u literaturi opisuje i kalcifilaksija – ishemija kože uzrokovana kalcifikacijom kapilara. Uzroci i liječenje nisu jasno definirani.

Prikaz slučaja: Bolesnici staroj 41 godinu, bez komorbiditeta, je 2021. dijagnosticiran intrahepatalni kolangiokarcinom. Liječena je transarterijskom kemoembolizacijom (TACE), stereotaksijskom radioterapijom (SBRT) i desnostranom hepatektomijom i metastazektomijom VII segmenta, pa kemoimunoterapijom. U listopadu 2023. započela liječenje pemigatinibom. Nakon 7 mjeseci terapije se na koži ispod desne dojke javila eritematozna promjena s bulom koja je brzo progredirala u dermalnu nekrozu. Patohistološki nalaz je govorio u prilog nekrozi s ovapnjenjima. U srpnju 2024. se javila u našu hitnu službu u kliničkoj slici sepse s multiplim nekrotičnim promjenama kože dubine i do 2 cm s eksponiranim dubokim tkivima. U nalazima je imala visoke upalne parametre, hiperfosfatemiju i hipoalbuminemiju. U mikrobiološkim uzorcima iz rana izolirani su brojne gram pozitivne i gram negativne bakterije. Liječena je antibioticima, analgeticima, parenteralnom hidracijom, 20% albuminima, uz redovite prevoje rana i prekid terapije pemigatinibom. Naknadno su se na natkoljenici javile dvije bulozne promjene koje su bioptirane. Pregledana je od strane dermatologa i imunologa te je postavljena sumnja da se radi o neželjenom učinku lijeka – kalcifilaksija. Ubrzo nakon, unatoč primijenjenim mjerama liječenja bolesnica umire u kliničkoj slici sepse i terminalne maligne bolesti. Nakon smrti pristiže i dermatohistopatološki nalaz koji može odgovarati kalcifilaksiji.

Zaključak: Kalcifilaksija je moguć neželjeni učinak lijeka pemigatiniba premda se opisuje i s drugim lijekovima ili bolestima, poput bubrežnog zatajenja ili hiperparatireoze. Poveznica bi sa terapijom pemigatinibom mogla biti i hiperfosfatemija, koja je poznata nuspojava. Smrtnost je razmjerno visoka, pogotovo kod otvorenih ulceracija. Potrebno je redovito nadzirati bolesnike i pravovremeno prekinuti terapiju. Biti će potrebna dodatna istraživanja kako bi se jasno definiralo zbrinjavanje.

Ključne riječi: pemigatinib, kalcifilaksija, neželjeni učinci, kolangiocelularni karcinom

CALCIPHYLAXIS IN A PATIENT TREATED WITH PEMIGATINIB – A CASE REPORT

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Introduction: Pemigatinib is a fibroblast growth factor receptor (FGFR) inhibitor. It is used in treatment of metastatic cholangiocarcinoma with *FGFR* fusion or rearrangements. Dermatotoxicity is common, but also calciphylaxis – skin necrosis caused by vascular calcification, has been described as a very rare side effect. Mechanism and treatment is not defined.

Case Report: 41-year-old female patient, previously healthy, was diagnosed with intrahepatic cholangiocarcinoma in 2021. She was treated with transarterial chemoembolization (TACE), stereotaxic radiotherapy (SBRT) and right-sided hepatectomy and metastasectomy of the VII segment, and then with chemoimmunotherapy. Treatment with pemigatinib was started in October 2023. After 7 months of therapy, an erythematous skin lesion appeared under the right breast with a bulla that quickly progressed into dermal necrosis. Biopsy reported necrosis with calcifications. In July 2024, she presented to our department with multiple necrotic skin changes, up to 2 cm deep with exposed deep tissue. Laboratory findings showed high CRP, hyperphosphatemia, and hypoalbuminemia. Multiple gram-positive and gram-negative bacteria were isolated from the wounds. Pemigatinib was discontinued. She was treated with antibiotics, analgesics, parenteral hydration, 20% albumin. Wounds were regularly dressed. Later, two new bullous changes appeared on the thigh that were biopsied. She was examined by a dermatologist and an immunologist and calciphylaxis was suspected. Soon after, despite treatment measures, the patient died due to sepsis and terminal malignant disease. Dermatohistopathological exam reported calcium deposits that could correspond with calciphylaxis.

Conclusion: Calciphylaxis could be a side effect of pemigatinib, although it has been described with some other drugs and conditions, such as renal failure or hyperparathyroidism. Hyperphosphatemia, a known side effect of pemigatinib, could be related to calciphylaxis. Mortality is relatively high, especially in advanced stages. Patients must be monitored closely for dermatotoxicity, but further research is needed to better define treatment.

Keywords: pemigatinib, calciphylaxis, side effects, cholangiocarcinoma

KIRURŠKO LIJEČENJE SARKOMA DOJKE U MUŠKARCA

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Uvod: Cilj ovog prikaza slučaja je prikazati rijedak slučaj upalnog nediferenciranog pleomorfnog sarkoma u muškoj dojci.

Prikaz slučaja: 64-godišnji muškarac napipao je bezbolni čvor na lijevoj dojci. Širokoiglena biopsija nije pokazala konačnu dijagnozu jer je klasificirana kao B3 pa je učinjena ekscizijska biopsija tkiva koja je pokazala je nediferencirani pleomorfni sarkom promjera 4,5 cm, infiltriran upalnim stanicama. Nakon što smo potvrdili dijagnozu, indicirana je terapija. Učinjena je Stewartova incizija i mastektomija. Patohistološka analiza potvrdila je negativne rubove kirurške resekcije. Nakon mjesec dana PET CT skeniranje pokazalo je plućne metastaze i pacijent je prošao 6 ciklusa kemoterapije doksorubicinom s dobrim odgovorom i postignutom remisijom plućnih metastaza. Tri godine kasnije, tumor je recidivirao i infiltrirao torakalni zid. Pacijent je ponovno podvrgnut kirurškom zahvatu. Učinili smo ekstirpaciju tumora, resekciju torakalne stijenke s velikim prsnim mišićem te resekciju petog, šestog i sedmog rebra i torakoplastiku uz upotrebu core matriks i biološkom mrežicom za rekonstrukciju defekta. Prema patohistološkom nalazu distalni rub resekcije bio je infiltriran tumorskim stanicama pa je učinjena radioterapija. Veća torakalna resekcija nije bila moguća jer bi utjecala na mehaniku disanja. Postoperativni tijek bio je normalan, bez paradoksalnog disanja. Bolesnik je četiri godine nakon liječenja bio u remisiji prema PET-CT pregledu.

Zaključak: Prikazan je rijedak slučaj nediferenciranog pleomorfnog sarkoma dojke, njegova mogućnost recidiva i udaljenih metastaza, mogućnosti liječenja, važnost i ograničenja operativnog liječenja kao i dobrobit onkoloških zahvata i nepredvidiv klinički tijek bolesti.

Ključne riječi: sarkom dojke; recidiv sarkoma dojke; resekcija toraksa; torakoplastika

SURGICAL TREATMENT OF BREAST SARCOMA IN A MALE PATIENT

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Introduction: The objective of this case report is to present a rare case of inflammatory undifferentiated pleomorphic sarcoma in a male breast.

Case Report: A 64-year-old man palpated a painless nodule on the left breast. Core needle biopsy did not reveal the final diagnosis as it was classified as B3 so an excisional biopsy of the tissue was performed, which revealed an undifferentiated pleomorphic sarcoma with a diameter of 4.5 cm, infiltrated with inflammatory cells. After we confirmed the sarcoma operation therapy was indicated. Stewart incision was performed and mastectomy was done. Pathohistological analysis confirmed negative surgical resection margins. After one month PET CT scan revealed lung metastases and the patient underwent 6 chemotherapy cycles of doxorubicin with good response and contribution of lung metastases remission. Three years later, the tumor recurred and infiltrated the thoracic wall. The patient underwent a surgical procedure again. We did the extirpation of tumor, resection of thoracic wall with large pectoral muscle and within fifth, sixth and seventh ribs resection and thoracoplasty with core matrix and bio-net was performed for reconstruction of the defect. On pathohistology findings distal resection margin was infiltrated by tumor cells so radiotherapy was performed. Larger thoracic resection was not possible as it would affect breathing mechanics. The postoperative course was normal, without paradoxical breathing. The patient has been in remission according to PET-CT examination for four years after the treatment.

Conclusion: We have presented a rare case of undifferentiated pleomorphic sarcoma in the breast, its potential for recurrence and distant metastases, the possibilities of treatment, the importance and limitations of operative treatment as well as the benefit of oncological procedures and unpredictable clinical course of disease.

Keywords: Breast sarcoma, recurrence of breast sarcoma, thoracic wall resection, thoracoplastica

USPJEŠNOST LIJEČENJA INHIBITORIMA O CIKLINIMA OVISNIH KINAZA 4/6 OVISNO O METASTATSKOM SIJELU KARCINOMA DOJKE

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Uvod: Inhibitori kinaza ovisnih o ciklinu 4/6 (CDK 4/6) se koriste u liječenju hormon ovisnih, HER-2 negativnih metastatskih karcinoma dojke. U Republici Hrvatskoj su odobrena tri različita CDK 4/6 inhibitora, no nema dovoljno podataka iz stvarne kliničke prakse ima li određeni lijek prednost pred drugima. U našem smo istraživanju usporedili učinkovitost CDK 4/6 inhibitora ovisno o anatomskoj lokalizaciji metastaza.

Metode: Istraživanje je provedeno na Klinici za tumore Kliničkog bolničkog centra Rijeka na pacijenticama oboljelim od metastatskog karcinoma dojke koje su barem jedan mjesec bile u liječenju CDK 4/6 inhibitorima. Između formiranih skupina su se uspoređivali ukupno preživljenje (OS) te preživljenje bez progresije bolesti (PFS) s obzirom na prisutnost određenih metastaza također uz međusobnu usporedbu i pojedinih CDK 4/6 inhibitora. Za istraživanje se koristila Kaplar-Meier metoda i log-rank test.

Rezultati: Rezultati ukazuju da pacijentice s jetrenim metastazama imaju kraći PFS (1,5 vs 3 godine, p=0.001) i OS (2,8 vs 5,9 godina, p=0,0001) u odnosu na pacijentice bez jetrenih metastaza. Rezultati se nisu razlikovali ovisno o prisutnosti drugih metastatskih sijela. Što se tiče izbora lijeka, pokazali smo da pacijentice s metastazama kosti imaju dulji PFS ako su liječene s ribociklibom nego palbociklibom (3,31 vs 1,46 godina, p=0,03) te pacijentice s metastazama jetre imaju dulji PFS ako su liječene s abemaciklinom nego palbociklibom (2,3 vs 0,72 godine, p=0,02).

Zaključak: Postojanje jetrenih metastaza jedino je metastatsko sijelo koje je utjecalo na preživljenje, a dokazali smo i da je liječenje abemaciklibom povezano s duljim PFS-om od palbocikliba u navedenom settingu. S druge strane, ribociklib je povezan s duljim PFS-om od palbocikliba u pacijentica s koštanim metastazama.

Ključne riječi: inhibitori o ciklinima ovisnih kinaza 4/6, metastaze jetre, rak dojke, ishodi liječenja

EFFECTIVENESS OF CYCLIN DEPENDENT KINASE 4/6 INHIBITOR TREATMENT DEPENDING ON THE BREAST CANCER METASTATIC SITE

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Introduction: Cyclin-dependent kinase 4/6 (CDK 4/6) inhibitors are used in hormone dependent, HER-2 negative metastatic breast cancer treatment. Three different CDK 4/6 inhibitors are approved in the Republic of Croatia but there is not enough data from clinical practice regarding the advance of one CDK 4/6 inhibitor to another. We have compared the effectiveness of CDK 4/6 inhibitors depending on the metastatic site of breast cancer.

Methods: The research has been conducted in The Cancer Clinic of The Clinical Hospital Center Rijeka on breast cancer patients that were on the CDK 4/6 inhibitor therapy for at least a month. Overall survival (OS) and

progression free survival (PFS) were compared between groups that were formed depending on the presence of the specific metastatic site. Same factors were compared between different CDK 4/6 inhibitors, depending on the metastatic site also comparing different CDK 4/6 inhibitors. Kaplar-Meier method and log-rank test were used for the statistical analysis.

Results: Results show that patients with liver metastasis have shorter PFS (1.5 vs 3 years, p=0.001) and OS (2.8 vs 5.9 years, p=0.0001) in comparison to liver metastasis free patients. Results have not differed depending on the presence of other metastatic sites. Regarding the CDK 4/6 inhibitor selection, results show that bone metastasis patients have s longer PFS if treated with ribociclib than palbociclib (3.31 vs 1.46 years, p=0.03) and liver metastasis patients have a longer PFS if treated with abemaciclib than palbociclib (2.3 vs 0.72 years, p=0.02).

Conclusion: Liver metastasis presence is the only metastatic site that influenced the survival, and our research also proved that abemaciclib treatment is correlated with a longer PFS than palbociclib in the mentioned setting. On the other hand, ribociclib is correlated with a longer PFS than palbociclib in skeletal metastasis patients.

Keywords: cyclin dependent kinase 4/6 inhibitors, liver metastasis, breast cancer, treatment outcomes

MIJEŠANI NEUROENDOKRINI I NE-NEUROENDOKRINI TUMOR JEDNJAKA S IZOLIRANIM MOŽDANIM METASTAZAMA

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Uvod: MiNEN (miješani neuroendokrini i ne-neuroendokrini tumor) je rijetka novotvorina koja se najčešće sastoji od neuroendokrinog karcinoma (NEC) i adenokarcinoma, barem 30% svakog histološkog podtipa.

Prikaz slučaja: 53-godišnji pacijent se javio u hitnu službu zbog neuroloških simptoma u svibnju 2022. godine, te su mu na CT-u mozga opisane dvije metastaze. Iste su resecirane, patohistološki se radilo o metastazi velikostaničnog neuroendokrinog karcinoma s Ki67 do 90%. Daljnjom obradom je na PET-CT-u opisana metabolički aktivna lezija jednjaka. Histološki, radilo se o MiNENu koji se sastoji od neuroendokrinog karcinoma i adenokarcinoma, PDL1 CPS je bio 25. Započeta je kemoradioterapija primarnog tumora uz konsolidacijsku kemoterapiju (6 ciklusa cisplatine i 5-fluorouracila) te je provedena radioterapija mozga. Na kontrolnom PET CT-u nije bilo metabolički aktivne bolesti. U srpnju 2023. godine su otkrivene nove moždane metastaze koje su tretirane Gama nožem u srpnju i studenom 2023. godine. Zbog rasta primarnog tumora je u siječnju 2024. započeta kemoterapija po CAPTEM protokolu. U međuvremenu je uzorak primarnog tumora poslan na NGS (Next Generation Sequencing) FMI CDx. Ukupno je primio 6 ciklusa po CAPTEM protokolu. Unatoč tome se vidjela progresija intrakranijski te je liječen ponovno radiokirurgijom u svibnju i lipnju 2024. godine, no uz daljnju progresiju intrakranijski. Budući da je NGS utvrdio visoko mutacijsko opterećenje (TMB 13 mut/Mb) te dvosmislen mikrosatelitski status, započeta je kemoimunoterapija pembrolizumabom i CapOx-om.

Zaključak: Imunoterapija se nije pokazala učinkovitom u liječenju neselektiranih NEC-ova i MiNEN-a. Međutim, visoko tumorsko mutacijsko opterećenje i mikrosatelitska stabilnost su prediktori dobrog odgovora na imunoterapiju, te odobreni prema FDA-u bez obzira na vrstu solidnih tumora. Kod ovog pacijenta smo se odlučili na kemoimunoterapiju koja objedinjuje rezultate molekularne analize te prve linije liječenja metastatskog adenokarcinoma jednjaka.

Budući da su MiNEN-i vrlo rijetki tumori bez puno podataka o liječenju, pogotovo nakon prve linije, smatramo da bi molekularna analiza mogla doprinijeti ishodima bolesnika.

Ključne riječi: miješani neuroendokrini i ne-neuroendokrini tumor; kemoterapija; imunoterapija, metastaze u središnji živčani sustav

ESOPHAGEAL MIXED NEUROENDOCRINE NON-NEUROENDOCRINE NEOPLASMS WITH ISOLATED BRAIN METASTASES TREATED ACCORDING TO COMPREHENSIVE GENOMIC PROFILING

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Introduction: Mixed neuroendocrine non-neuroendocrine neoplasms (MiNENs) are rare tumors composed of two histologically different parts, at least 30% each, usually neuroendocrine carcinoma (NEC) and adenocarcinoma, but different histology types might be present.

Case Report: A 53-year-old patient was referred to the emergency department in May 2022 with neurological symptoms. A brain CT revealed two metastases, which were surgically removed. Pathology reported the tumor as a large cell neuroendocrine carcinoma with a Ki67 index of 90%. Following oncologist consultation, a PET-CT scan detected a metabolically active area in the esophagus, diagnosed from endoscopy samples as MiNEN (neuroendocrine carcinoma and adenocarcinoma), with PDL1 CPS 25. He underwent chemoradiation of the primary tumor with consolidation chemotherapy (cisplatin and 5FU) and whole-brain radiation. A PET-CT reevaluation showed no active disease, but new brain metastases appeared in July 2023, treated with Gamma Knife. Due to primary tumor growth, the CAPTEM protocol was initiated in January 2024, alongside Next Generation Sequencing (NGS) of tumor tissue (FMI CDx). Despite 6 CAPTEM cycles, brain metastases progressed, leading to additional Gamma Knife treatments in May and June 2024, which were ineffective. NGS revealed high tumor mutation burden (TMB) – 13 mut/Mb and equivocal microsatellite status. Considering progressive disease in the brain with possible rapid clinical deterioration it was decided to start CapOx chemotherapy with the addition of check-point inhibitor (CPI) pembrolizumab.

Conclusion: Single-agent CPI has been ineffective in biomarker-unselected NECs or MiNEN. However, tumor MSI-H/dMMR status and high TMB (≥10 mut/Mb) are predictive biomarkers for response to CPI, leading to FDA approval for tissue-agnostic use in progressive solid tumors. Therefore, we have chosen chemoimmunotherapy based both on molecular profiling and as a standard therapeutic option used for metastatic adenocarcinoma. MiNENs are rare neoplasms with scarce data for treatment, especially after the first line, so molecular profiling could improve patient outcomes.

Keywords: Mixed neuroendocrine non-neuroendocrine neoplasms; chemotherapy, immunotherapy, central nervous system metastases

PREDIKTIVNA VRIJEDNOST RADIOLOŠKE OBRADE U PROCJENI STATUSA LIMFNIH ČVOROVA PAZUHA U BOLESNICA S RANIM RAKOM DOJKE

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Uvod: U bolesnica s ranim rakom dojke, odluka o primarnom onkološkom liječenju – operativni zahvat ili neoadjuvantna terapija – ovisi o biologiji bolesti i stadiju definiranom klinički i radiološki koristeći mamografiju (MMG), ultrazvuk (UZV) i magnetsku rezonancu (MR) dojki. Status limfnih čvorova pazuha može promijeniti pristup liječenju. Cilj ovog rada bio je procijeniti pouzdanost radiološke procjene zahvaćenosti pazušnih limfnih čvorova tumorom.

Metode: Provedena je retrospektivna analiza bolesnica s ranim rakom dojke u kojih je, od 1.1.2023. do 31.12.2023., multidisciplinarni tim za tumore dojke KBC Zagreb, na temelju rezultata provedene obrade, indicirao započinjanje onkološkog liječenja operativnim zahvatom. Status limfnih čvorova pazuha procijenjen je radi-

ološki koristeći UZV i MR. Statistički su određene specifičnost i senzitivnost detekcije metastaza u limfnim čvorovima pazuha radiološkim metodama, kao i koeficijent varijacije između radiološkog i patohistološkog stadija tumora.

Rezultati: Prikupljeni su i analizirani podaci ukupno 148 bolesnica s ranim rakom dojke. U 10,8% (16/148) bolesnica radiološki je postavljena sumnja postojanja pozitivnih limfnih čvorova u pazuhu, od toga je konačni patohistološki nalaz iste potvrdio u njih 43,8% (7/16). U 6,8% (10/148) bolesnica opisani su reaktivni limfni čvorovi bez potrebe za dodatnom obradom, od čega su u njih 20% (2/10) patohistološki dokazane metastaze. U preostalih 82,4% (122/148) bolesnica, limfni čvorovi pazuha radiološki su imponirali negativno, no u njih 17,2% (21/122) patohistološki su dokazane metastaze. Osjetljivost radiološke procjene limfnih čvorova pazuha iznosila je 33,3%, dok je specifičnost bila 78,8%. Pozitivna prediktivna vrijednost radiološkog stadija pazuha iznosila je 28,6%, dok je negativna prediktivna vrijednost bila 82,3%. Koeficijent varijacije između radiološkog i konačnog patohistološkog stadija iznosio je 27,2.

Zaključak: Iako je ova analiza pokazala korist radiološke obrade u procjeni statusa limfnih čvorova pazuha, u ispitivanoj skupini nije se pokazala dovoljno osjetljivom za pouzdani dijagnostički alat.

Ključne riječi: rani rak dojke, radiološka obrada, limfni čvorovi pazuha, patohistologija

PREDICTIVE VALUE OF RADIOLOGICAL EVALUATION IN ASSESSING AXILLARY LYMPH NODE STATUS IN PATIENTS WITH EARLY BREAST CANCER

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Introduction: In early breast cancer, decisions on primary oncological treatment–surgery or neoadjuvant therapy – are based on the disease's biology and staging, determined clinically and radiologically using mammography (MMG), ultrasound (US), and magnetic resonance imaging (MRI). Axillary lymph node status can influence treatment approaches. This study aimed to determine the sensitivity and specificity of radiological assessment of axillary involvement.

Methods: A retrospective analysis was conducted on early breast cancer patients for whom the Multidisciplinary Breast Tumor Team at University Hospital Centre Zagreb between January 1, 2023, and December 31, 2023 recommended surgical treatment based on previous evaluations results. Axillary lymph node status was assessed using US and MRI. The study statistically determined the sensitivity, specificity, and coefficient of variation between radiological and pathological tumor staging.

Results: Data from 148 early breast cancer patients were analyzed. Pathological lymph nodes were identified radiologically in 10.8% (16/148) of the patients and confirmed histopathologically in 43.8% (7/16). 6.8% (10/148) of patients had reactive lymph nodes that did not require further assessment, of which 20% (2/10) had histopathological confirmation of metastases. In the remaining 82.4% (122/148) of cases, the axillary lymph nodes were radiologically negative, but in 17.2% (21/122) of them, metastases were proven by pathohistological analysis. The sensitivity of radiological assessment was 33.3%, specificity was 78.8%, with a positive predictive value of 28.6% and a negative predictive value of 82.3%. The coefficient of variation between radiological and pathological staging was 27.2.

Conclusion: While radiological evaluation was useful in assessing axillary lymph node status, it was not sufficiently sensitive as a reliable diagnostic tool in the studied group.

Keywords: early breast cancer, radiological evaluation, axillary lymph nodes, histopathology

ANALIZA ŽIVOTNE DOBI BOLESNIKA S METASTATSKIM RAKOM PROSTATE REZISTENTNIM NA KASTRACIJU I METASTAZAMA U KOSTIMA KOJI SU PRIMALI ANTIRESORPTIVNU TERAPIJU I ONIH KOJI NISU MOGLI ZBOG NESANIRANIH ZUBA – ISKUSTVO JEDNOG CENTRA

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Uvod: Bolesnici s metastatskim rakom prostate rezistentnim na kastraciju (mKRRP), i koštanim metastazama, imaju povećani rizik nastanka neželjenih događaja na kostima. U tih bolesnika preporuča se medikamentozna antiresorptivna terapija, bisfosfonati ili denosumab, ukoliko su zubi sanirani.

Metode: U ovoj retrospektivnoj opservacijskoj studiji, provedenoj na Službi za internu medicinu opće bolnice Šibensko-kninske županije, pretražili smo evidenciju bolesnika s mKRRP-om koristeći lokalno vođeni registar. Pacijenti su liječeni u našoj bolnici od siječnja 2022. do prosinca 2023. godine. Stanje njihovih zuba, kao i cjelokupno oralno zdravlje, ispitivali su onkolog i/ili stomatolozi.

Rezultati: U ovu studiju bilo je uključeno ukupno 26 bolesnika s mKRRP-om. Većina bolesnika imala je metastaze u kostima (88%). Među pacijentima koji su imali metastaze u kostima, njih 19 primilo je medikamentoznu antiresorptivnu terapiju, bisfosfonate ili denosumab. Dobni raspon bolesnika u studiji, koji su primali navedenu terapiju je bio između 49–82 godina (medijan 74 godine). Zbog nezadovoljavajućeg stanja zuba u 4 bolesnika s mKRRP-om, i metastazama u kostima, liječenje medikamentoznom antiresorptivnom terapijom nije bilo indicirano. Dobni raspon bolesnika koji nisu primali istu terapiju bio je između 67–88 godina (medijan 81 godina). Samo u 3 bolesnika s mKRRP-om i koštanim metastazama nije propisana medikamentozna antiresorptivna terapija, jer ih presadnice nisu ugrožavale od pojave neželjenih koštanih događaja.

Zaključak: Podaci dobiveni u našem istraživanju pokazuju kako većina bolesnika s mKRRP-om i metastazama u kostima su bili stariji ljudi, bez obzira jesu li primali medikamentoznu antiresorptivnu terapiju ili ne. Međutim, pacijenti koji zbog nesaniranih zuba nisu mogli primiti navedenu terapiju su bili nešto stariji od onih koji su je primili. Potrebne su daljnje studije kako bi se potvrdili rezultati ove studije provedene u jednom centru.

Ključne riječi: rak prostate, stanje zuba, metastatski, koštane metastaze

AGE ANALYSIS IN PATIENTS WITH METASTATIC CASTRATION-RESISTANT PROSTATIC CANCER AND BONE METASTASES WHO HAVE RECEIVED BONE ANTIRESORPTIVE AGENTS AND THOSE WHO COULD NOT BECAUSE OF POOR DENTAL STATUS – SINGLE CENTER EXPERIENCE

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Introduction: Patients with metastatic castration resistant prostatic cancer (mCRPC), and bone metastases, have a higher risk for clinically significant skeletal-related events. In these patients bone antiresorptive agents are recommended, if their dental status is good.

Methods: In the present retrospective observational study, conducted at the Department of Internal Medicine at the General Hospital of Šibenik-Knin county, we examined the records of patients with mCRPC using a locally maintained registry. The patients were treated in our hospital from January 2022 – December 2023. Their dental status, as well as overall oral health, was examined by oncologists and/or dentists.

Results: A total of 26 patients with mCRPC were included in this study. The majority of patients had metastases in the bones (88%). Among the patients who had bone metastases, 19 of them have received medical antiresorptive therapy, bisphosphonates or denosumab. The age range of patients in the study, who have received it, was between 49–82 years (median 74 years). Due to unsatisfactory dental status in 4 of patients with mCRPC and bone metastases, treatment with antiresorptive therapy was not indicated. The age range of patients in the study, who have not received medical antiresorptive therapy, was between 67–88 years (median 81 years). Only in 3 patients with mCRPC and bone metastases medical antiresorptive therapy was not prescribed because it did not endanger them for possible development of significant unwanted SREs.

Conclusion: The data obtained in our study indicate that the majority of patients with mCRPC and skeletal metastases were older people, whether they have received medical antiresorptive therapy or not. However patients who could not receive antiresorptive therapy, because of poor dental status, were somewhat older then the ones who have received it. Further studies are necessary to confirm the results of this single center study.

Keywords: prostate cancer; dental status, metastatic, bone metastases

WILMSOV TUMOR U ODRASLOJ DOBI: PRIKAZ SLUČAJA

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Uvod: Wilmsov tumor (WT) čini 5% dječjih zloćudnih novotvorina i najčešće se dijagnosticira kod djece mlađe od 5 godina, dok je u odrasloj populaciji zabilježen u samo 3% slučajeva. U 10 do 15% slučajeva javlja se kao dio višestrukih malformacijskih sindroma. Wilmsov tumor kod odraslih obično se dijagnosticira nakon nefrektomije. Liječenje je adjuvantno i temelji se na modificiranom SIOP 2016 UMBRELLA protokolu. Prognoza WT u odrasloj dobi lošija je nego u djece, unatoč identičnoj patohistološkoj prezentaciji.

Prikaz slučaja: Dvadesetčetverogodišnja žena prezentirala se akutnom boli u donjem desnom abdominalnom kvadrantu, a CT-om je opisana Bosniak IV cista promjera 15 cm u donjem polu desnog bubrega. Učinjena je radikalna nefrektomija, a patohistološki se opiše tumor koji se sastoji od 20% blastemske i 80% epitelne komponente, sa žarištima nekroze, ograničen na bubreg, bez znakova invazije perirenalne masti i renalnog sinusa, bez zahvaćanja regionalnih limfnih čvorova i negativnih resekcijskih rubova. Imunohistokemijski tumor je bio pozitivan na CD57, BRAF i WT-1 s Ki67 od 50% te je postavljena dijagnoza Wilmsovog tumora, stadij I, s ne-anaplastičnom histologijom i umjerenim rizikom. Postoperativno učinjenom obradom ne nađe se znakova diseminacije bolesti. Učinjeno je i genetsko testiranje, a nakon krioprezervacije jajnih stanica započeta je adjuvantna kemoterapija. Protokol se sastojao od primjene vinkristina i aktinomicina D uz LHRH agonist. Tijekom liječenja nije bilo potrebe za redukcijom doze obzirom da je bolesnica imala blage nuspojave u vidu mučnine, umora i hemoroidalnog krvarenja. Nakon dva mjeseca od početka terapije učinjena je reevaluacija kojom se ne nađe znakova bolesti.

Zaključak: Wilmsov tumor se rijetko dijagnosticira u odrasloj populaciji i ovo je prvi slučaj u KBC-u Zagreb. Obzirom na rijetkost ovog tumora u odrasloj dobi, važno je prikazati ovakve slučajeve kako bi pridonijeli što većem broju podataka u svrhu boljeg liječenja i praćenja ovih bolesnika.

Ključne riječi: Wilmsov tumor, odrasli, SIOP 2016 UMBRELLA protokol, multipli malformacijski sindromi

ADULT WILMS TUMOR: CASE REPORT

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Introduction: Wilms' tumor (WT) accounts for 5% of childhood cancers, mostly diagnosed in children younger than five years, with only 3% of cases reported in adults. Ten to fifteen percent of cases occur as a part of multiple malformation syndrome. Adult Wilms' tumors are usually diagnosed following nephrectomy for presumed renal cell carcinoma. Modified SIOP 2016 UMBRELLA protocol is used in adjuvant settings. Even though there is no difference in histopathological presentation, prognosis of adult WT is poorer than in the pediatric population.

Case Report: A 24-year-old female has presented with acute pain in the right lower abdominal quadrant. CT-scan showed Bosniak IV cystic lesion of the right kidney lower pole, measuring 15 cm in diameter. After radical nephrectomy, histologically the tumor comprised of 20% blastemal and 80% epithelial elements, with no perirenal fat tissue and renal sinus invasion, clean surgical margins and negative regional lymph nodes. The immunohistochemistry study was positive for CD57, BRAF and WT-1 with Ki67 50%. Wilms tumor, stage I, with non-anaplastic histology and intermediate risk was diagnosed. No distant metastasis were found on initial staging and multiple malformation syndrome genetic testing was performed. The patient underwent oocyte preservation and adjuvant chemotherapy was started. The treatment consisted of vincristine and actinomycin D along with ovarian suppression. During the therapy grade 1 nausea, fatigue, and hemorrhoidal bleeding occurred without the need for dose reduction. After two months of therapy, radiological reevaluation showed no evidence of disease.

Conclusion: Adult Wilms' tumor is a rare disease and this is the first case in UHC Zagreb. Due to its rarity, it is important to register such patients to international databases, in order to assist in research and development of future management guidelines for this tumor.

Keywords: adults, Wilms´ tumor, SIOP 2016 UMBRELLA protocol, multiple malformation syndromes

AVELUMAB KAO TERAPIJA ODRŽAVANJA U UZNAPREDOVALOM UROTELNOM KARCINOMU – AŽURIRANA HRVATSKA ISKUSTVA

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Uvod: Terapija održavanja avelumabom u bolesnika koji nisu progredirali na kemoterapiju baziranu na platini čini standardnu prvu liniju liječenja uznapredovalog urotelnog karcinoma (uUK). Cilj ovog istraživanja bio je opisati kliničke osobine bolesnika i ishode liječenja avelumabom u terapiji održavanja uUK u hrvatskoj onkološkoj praksi.

Metode: Proveli smo retrospektivno kohortno istraživanje u koje smo uključili 10 hrvatskih onkoloških ustanova u kojima se liječe bolesnici s uUK. Anonimizirani podaci su skupno analizirani.

Rezultati: Ukupno 115 bolesnika s uUK liječeno je avelumabom u terapiji održavanja od srpnja 2022. do kolovoza 2024. Medijan dobi bolesnika kod početka terapije bio je 69 godina, 19% bolesnika je imalo tumor gornjeg urotela, 73% bolesnika primilo je cisplatinu (gemcitabin/cisplatin 62%, ddMVAC 11%), 19% je imalo jetrene metastaze. 67% je bilo ECOG PS 0. Za 104 bolesnika (90%) je učinjena analiza učinkovitosti terapije. Stopa ukupnog odgovora na avelumabu bila je 20% (kompletni odgovor 4%, parcijalni odgovor 16%), stabilna bolest 38%, a progresija bolesti kao najbolji odgovor 36%. Nakon medijana praćenja od 13 mjeseci, 50 bolesnika (44%) je doživjelo progresiju na avelumab. 54 bolesnika (47%) je još na tretmanu avelumabom. Medijan do progresije bolesti je 14 mjeseci, dok medijan ukupnog preživljenja nije dosegnut. Ukupna stopa ozbiljnih nuspojava vezanih za imunoterapiju bila je 21% za gr 2, 6% za gr 3 te 2% za gr 4. Osam bolesnika moralo je trajno prekinuti terapiju zbog nuspojava. Šestnaest bolesnika koji su progredirali na terapiju avelumabom dobili su daljnju aktivnu terapiju.

Zaključak: Osvježeni podaci praćenja učinkovitosti avelumaba u hrvatskoj onkološkoj praksi u terapiji održavanja uUK ukazuju na visoku prevalenciju cisplatinskih protokola, visoku stopu odgovora na avelumab te nižu stopu imunoterapijom uvjetovanih nuspojava.

Ključne riječi: urotelni karcinom, avelumab, terapija održavanja, platinski spoj

AVELUMAB AS MAINTENANCE AFTER PLATINUM-BASED CHEMOTHERAPY IN ADVANCED UROTHELIAL CANCER – UPDATED CROATIAN EXPERIENCE

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

Methods: This retrospective cohort study assessed patients from 10 CUOCG-affiliated institutions who received maintenance avelumab. Anonymized data were pooled and centrally analyzed. Herein, updated toxicity, overall response rate, progression-free survival are reported.

Results: Total of 115 patients with aUC who received avelumab maintenance from July 2022 to August 2024 were identified within the CUOCG network. Median age at avelumab initiation was 69 years (range 41–83 years), 19% had upper tract primary tumor, 73% received prior cisplatin-based chemotherapy (gemcitabine/cisplatin 62%, ddMVAC 11%), 19% had liver metastasis and 67% were ECOG PS 0. 104 patients (90%) were available for

response assessment. The overall response rate with avelumab maintenance was 20% (complete response [CR] for 4%, partial response [PR] for 16%), stable disease (SD) 38%; progression as the best response was noted in 36% of patients, respectively. After a median follow-up time of 13 months (95%CI 8–30 months), 50 patients (44%) experienced disease progression. Fifty-four patients (47%) are still on treatment. Median progression-free survival was 14 months (95%CI 8–20), while median overall survival was not reached. The observed rate of immunotherapy-related side-effects was 21% for grade 2, 6% for grade 3, and 2% for grade 4, respectively. Eight patients (7%) required therapy termination due to serious immunotherapy-related side-effects. Sixteen patients (32% of progressing patients) received active treatment post avelumab progression.

Conclusion: Updated real-world outcomes of patients receiving avelumab maintenance in Croatia continue to show high prevalence of cisplatin-based chemotherapy, high overall response rate and lower incidence of immunotherapy-related side-effects compared to registration trial.

Keywords: urothelial cancer, avelumab, maintenance therapy, platinum compound

PREVALENCIJA SARKOPENIČNE PRETILOSTI U BOLESNICA S GINEKOLOŠKIM TUMORIMA

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Uvod: Sarkopenična pretilost kliničko je stanje karakterizirano sarkopenijom odnosno gubitkom mišićne mase i funkcije te pretilošću odnosno povećanjem udjela masnog tkiva. Prevalencija sarkopenije i pretilosti globalno je u značajnom porastu, kako u općoj populaciji tako i među onkološkim bolesnicima. Sarkopenična pretilost povezana je s lošijim ishodima liječenja, dužim boravkom u bolnici i kraćim preživljenjem kod više vrsta raka. Isto tako smatra se da ovo stanje značajno pospješuje karcinogenezu putem poremećaja metaboličke, hormonalne i citokinske ravnoteže odnosno putem oksidativnog stresa, lipotoksičnosti i sistemske kronične upale. Iako zanimanje za sarkopeničnu pretilost postaje sve veće, dosadašnje su studije inkonkluzivne s obzirom na nedostatne definicije ovih stanja i varijabilnosti dijagnostičkih kriterija koji se koriste za procjenu prevalencije sarkopenije i pretilosti.

Metode: Retrospektivna studija koja uključuje 53 bolesnice s ginekološkim tumorima (jajnik, jajovod, endometrij i cerviks) koje su bile hospitalizirane na Klinici za Tumore, KBCSM, tijekom 2024. godine. Pretraživan je Bolnički informatički sustav. Sarkopenija je procijenjena pomoću SARC-F upitnika koje su bolesnice ispunjavale prvi dan hospitalizacije te je izračunat BMI. U obzir su uzete vrijednosti isključivo na prvom ciklusu terapije.

Rezultati: Među 53 bolesnice s ginekološkim tumorima njih 49% bilo je pretilo (BMI ≥ 30) dok je kod 32% prema SARC F upitniku procijenjena sarkopenija (SARC F ≥ 4) prilikom aplikacije prvog ciklusa terapije. Sarkopeničnu pretilost je prema ovim dijagnostičkim kriterijima imalo 17% bolesnica. Prema ovim rezultatima sarkopenična pretilost nije imala značajnijeg utjecaja na karakteristike tumora.

Zaključak: S obzirom na dokazan utjecaj sarkopenične pretilosti na karcinogenezu te na ishode liječenja onkoloških bolesnika kao i na porast prevalencije ovog kliničkog stanja bitno je i u svakodnevnoj kliničkoj praksi mjeriti i evidentirati ove parametre. Ključan korak je definiranje jasnih dijagnostičkih kriterija te izbor najefikasnijih dijagnostičkih metoda koje su prihvatljive u svakodnevnom radu onkologa.

Ključne riječi: sarkopenija, pretilost, ginekološki tumori, prevalencija

PREVALENCE OF SARCOPENIC OBESITY IN PATIENTS WITH GYNECOLOGIC CANCERS

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Introduction: Sarcopenic obesity is a clinical condition characterized by sarcopenia, i.e. loss of muscle mass and function, and obesity, i.e. an increase in the proportion of adipose tissue. The prevalence of sarcopenia and obesity is significantly increasing globally. Sarcopenic obesity is associated with worse treatment outcomes, longer hospital stay and shorter survival in several types of cancer. It is also believed that this condition significantly promotes carcinogenesis through disturbances in metabolic, hormonal and cytokinetic balance.

Although interest in sarcopenic obesity is increasing, studies to date are inconclusive due to insufficient definitions of these conditions and the variability of diagnostic criteria.

Methods: A retrospective study including 53 patients with gynecologic cancers who were hospitalized at the Clinic for Tumors, CHCSM, during the year 2024. The hospital information system was searched. Sarcopenia was assessed using the SARC-F questionnaire, which the patients filled out on the first day of hospitalization, and BMI was calculated. Only values from the first cycle of therapy were taken into account.

Results: Among 53 patients with gynecologic cancer, 49% were obese (BMI ≥ 30), while 32% were assessed for sarcopenia (SARC F ≥ 4) during the first cycle of therapy according to the SARC F questionnaire. According to these diagnostic criteria, 17% of patients had sarcopenic obesity. According to these results, sarcopenic obesity had no significant impact on tumor characteristics.

Conclusion: Considering the proven influence of sarcopenic obesity on carcinogenesis and the outcomes of treatment of oncology patients, as well as the increase in the prevalence of this clinical condition, it is important to measure and record these parameters in everyday clinical practice. The key step is defining clear diagnostic criteria and choosing the most effective diagnostic methods that are acceptable in the everyday work of an oncologist.

Keywords: sarcopenia, obesity, gynecologic cancers,

LIJEČENJE TRIFLURIDIN-TIPERACILOM U TREĆOJ LINIJI METASTATSKOG KOLOREKTALNOG KARCINOMA – ISKUSTVA U KLINIČKOJ PRAKSI

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Uvodi: Trifluridin-tipiracil je odobren i indiciran za liječenje metastatskog kolorektalnog karcinoma (mCRC) u trećoj liniji. Prema rezultatima studije RECOURSE pokazan je jasni benefit u ukupnom preživljenju (engl. *overall survival*) u odnosu na placebo. U studiji SUNLIGHT opisan je jasni benefit dodatka bevacizumaba u ukupnom preživljenju od 3 mjeseca u odnosu na monoterapiju te više nego dvostruko produljenje preživljena bez progresije (engl. *progression-free survival*). U Hrvatskoj je lijek odobren za primjenu od 2021. godine za liječenje mCRC i želučanog karcinoma u trećoj liniji.

Metode: Korištena je deskriptivna analiza podataka iz bolničkog informatičkog sustava (BIS) o pacijentima s dijagnozom metastatskog kolorektalnog karcinoma liječenima u Klinici za tumore trifluridinom-tipiracilom u periodu od početka odobrenja 2021. godine do prosinca 2023. godine.

Rezultati: U analizu je uključeno 29 pacijenata koji su započeli liječenje trifluridinom-tipiracilom zbog proširenog mCRC, od kojih je 12 primalo bevacizumab. Najčešći razlog prekida liječenja je bila progresija bolesti, a nakon nje pogoršanje kliničkog stanja zbog kojega je sustavno liječenje bilo kontraindicirano. Medijan broja ciklusa bez progresije bolesti je bio 3, što označava 12 tjedana. Prosječno trajanje trećelinijskog liječenja kod pacijenata koji su primali bevacizumab je 3,5 mjeseca, dok kod onih bez bevacizumaba je trajanje liječenja bilo

4,1 mjeseca. Kod pacijenata koji su postigli trajanje trećelinijskog liječenja dulje od medijana, prijašnje prvolinijsko i drugolinijsko liječenje je prosječno trajalo 23,2 mjeseca, dok je kod onih ispod medijana prethodno liječenje u prosjeku trajalo 27 mjeseci.

Zaključak: Kod pacijenata liječenih trifluridinom-tipiracilom prema dostupnim podacima u našoj ustanovi trajanje prethodnih linija liječenja povezano je s lošijim ishodima u trećelinijskom liječenju. Dodatak bevacizumaba nije bio povezan s duljim trajanjem trećelinijskog liječenja. Premda je trajanje liječenja trifluridin-tipiracilom relativno kratko u odnosu na prethodne linije liječenja, lijek se pokazuje kao dobra opcija kod pacijenata koji su imali bržu progresiju na liječenju baziranom na fluoropirimidinima, irinotekanu i oksaliplatini.

Ključne riječi: trifluridin-tipiracil, metastatski kolorektalni karcinom, bevacizumab, pretretirani bolesnici

TRIFLURIDINE/TIPERACIL TREATMENT IN THIRD LINE FOR METASTATIC COLORECTAL CANCER – CLINICAL PRACTICE EXPERIENCE

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Introduction: Trifluridine/tipiracil is approved as the third-line treatment for metastatic colorectal cancer (mCRC). RECOURSE study results proved significant benefit in overall survival (OS) when compared to placebo. SUNLIGHT study proved benefit of bevacizumab addition in OS of 3 months compared to trifluridine/tipiracil monotherapy and more than double progression-free survival (PFS) benefit. In 2021 in Croatia the drug was approved for use as a third-line treatment in mCRC and metastatic gastric cancer.

Methods: Descriptive analysis of data from hospital information system (BIS) was used. Data about patients treated with trifluridine/tipiracil from the beginning of 2021 until December of 2023 were analyzed.

Results: 29 patients who started trifluridine/tipiracil treatment in mCRC were analyzed. Bevacizumab was added to the therapy regimen in 12 patients. The most common reason for treatment discontinuation was disease progression, with worsening of clinical state that did not allow systemic treatment the second most common reason. Number of cycles median without disease progression was 3, or 12 weeks. Overall treatment duration in patients who received bevacizumab was 3.5 months, while those who didn't receive bevacizumab had overall treatment duration of 4.1 months. In patients who were treated longer than median number of cycles, prior first and second-line treatment lasted 23.2 months overall, while in those below median number of cycles prior treatment lasted 27 months.

Conclusion: In patients treated with trifluridine/tipiracil longer prior first and second-line treatment was associated with worse outcomes in third-line treatment, according to our data. Bevacizumab addition was not associated with longer treatment duration. Despite its relatively short treatment duration, trifluridine/tipiracil proved a useful treatment option in patients who progressed quickly on treatment based on fluoropyrimidines, irinotecan and oxaliplatin.

Keywords: trifluridine-tipiracil, metastatic colorectal cancer, bevacizumab, heavily pretreated patients

"SENTINEL UMA" – PROJEKT ZA ZAŠTITU MENTALNOG ZDRAVLJA LIJEČNIKA I DRUGIH ZDRAVSTVENIH DJELATNIKA

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Uvod: Projekt "Sentinel Uma," pokrenut je od strane Sekcije mladih onkologa HDIO uz podršku Sekcije mladih psihijatara HPD-a s ciljem destigmatizacije i zaštite mentalnog zdravlja liječnika i svih zdravstvenih djelatnika. Zdravstveni su djelatnici izloženi visokim razinama stresa što često dovodi do sindroma sagorijevanja. Djelatnici koji zbrinjavaju onkološke bolesnike redovito su izloženi traumatičnim situacijama, bilo da se radi o teško bolesnim pacijentima, smrti ili emocionalno zahtjevnom komunikacijom o lošim vijestima. Administrativna opterećenja, manjak resursa i sustavna ograničenja mogu dovesti do bespomoćnosti, moralnog distresa i moralne ozljede. Moralni distres nastaje kada zdravstveni djelatnici znaju što je ispravno, ali su spriječeni djelovati u skladu s moralnim uvjerenjima zbog vanjskih ograničenja, a moralna ozljeda odnosi se na psihološke posljedice koje proizlaze iz osjećaja krivnje zbog izdaje etičkih uvjerenja ili postupaka koje su poduzeli.

Metode i rezultati: U sklopu projekta "Sentinel Uma" provodi se istraživanje o moralnom distresu i moralnoj ozljedi, te njihovoj povezanosti sa stresom, anksioznošću i depresijom. U istraživanju je dosad sudjelovalo 169 zdravstvenih djelatnika, koji su prijavili umjerene razine anksioznosti, depresije i moralne ozljede, te visoke razine stresa i moralnog distresa. Liječnici u neurologiji, kardiologiji, infektologiji i internističkoj onkologiji izloženi su najvišim razinama moralnog distresa i moralne ozljede prvenstveno zbog suočavanja s terminalnim pacijentima, donošenja odluka o prekidu terapije i ograničenja u resursima.

Zaključak: Ovi pilot rezultati ukazuju na potrebu za sustavnim intervencijama koje uključuju psihološku podršku zdravstvenih djelatnika, osobito u visokorizičnim specijalizacijama kao što je internistička onkologija, uz pružanje etičkih savjeta i obuke za suočavanje s izazovima. Uzimajući u obzir dobivene rezultate, u daljnjim koracima ovog projekta, ciljevi će biti podići svijest o važnosti kontinuirane skrbi o mentalnom zdravlju kroz psihoedukaciju zdravstvenih djelatnika i šire javnosti o izazovima mentalnog zdravlja te predložiti konkretne korake za pomoć u izazovima s kojima se zdravstveni djelatnici svakodnevno suočavaju.

Ključne riječi: internistička onkologija, mentalno zdravlje, sindrom sagorijevanja, moralni distres, moralna ozljeda

SENTINEL OF THE MIND: MENTAL HEALTH PROTECTION CAMPAIGN FOR PHYSICIANS AND HEALTH CARE WORKERS

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Introduction: The "Sentinel of the Mind" project was initiated by the Young Oncologist Section of the Croatian Society for Medical Oncology, with the support of the Young Psychiatrists Section of the Croatian Psychiatric Society. Its core mission is to de-stigmatize and protect the mental health of healthcare workers. Healthcare professionals frequently endure intense stress, often leading to burnout. Those who care for cancer patients are particularly vulnerable, facing traumatic situations such as life-threatening illnesses, death, and emotionally

charged conversations on a daily basis. Additional burdens such as administrative overload, resource shortages, and systemic limitations contribute to feelings of helplessness, moral distress, and moral injury. Moral distress arises when healthcare professionals know the right course of action but are obstructed by external factors. Moral injury refers to the psychological impact of ethical violations, particularly when healthcare workers feel guilt from betraying their ethical beliefs.

Methods and results: As part of the "Sentinel of the Mind" initiative, a study was conducted to explore the links between moral distress, moral injury, and levels of stress, anxiety, and depression among healthcare workers. Thus far, 169 healthcare workers have participated in the study, with findings indicating moderate levels of anxiety, depression, and moral injury, but high levels of stress and moral distress. Physicians working in specialties such as neurology, cardiology, infectious diseases, and medical oncology reported the highest levels of moral distress and injury. These elevated levels are likely due to their exposure to terminal illness, the difficult decision-making process around ending treatment, and the general scarcity of resources.

Conclusion: This pilot study underscores the urgent need for systemic interventions that offer psychological support, particularly in fields with the highest risk of burnout, such as medical oncology. It also highlights the importance of providing ethical guidance and training to help healthcare workers navigate the challenges they face. Given these findings, the next steps for the "Sentinel of the Mind" campaign will focus on raising awareness of the importance of continuous mental health care for medical professionals and offering additional educational programs that address the everyday challenges healthcare workers encounter. This will ensure a sustained focus on mental health protection within the healthcare system, promoting resilience and reducing the risk of burnout.

Keywords: oncology, mental health, burnout, moral distress, moral injury

MJERENJE RAZINE PSIHOLOŠKOG DISTRESA U NEOADJUVANTNO LIJEČENIH BOLESNICA S KARCINOMOM DOJKE

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Uvod: Dijagnoza raka dojke može utjecati na žene i fizički i psihički. Zabilježeno je da 50% bolesnica s karcinomom dojke doživi neku vrstu psihološkog distresa zbog svoje bolesti. To može biti osobito izraženo za bolesnice tijekom neoadjuvantnog liječenja. Ovaj pristup nudi višestruke dobro poznate benefite, no postoji i specifična psihološka nelagoda koju mnoge bolesnice doživljavaju, naročito zbog činjenice da im prije operacije slijedi višemjesečno sustavno liječenje.

Cilj našeg istraživanja bio je procijeniti razinu psihološkog distresa kod žena koje prolaze neoadjuvantno liječenje te moguću korelaciju između demografskih i socioekonomskih karakteristike i razine distresa.

Metode: U istraživanje su bile uključene 53 bolesnice s rakom dojke u različitim ciklusima neoadjuvantnog liječenja. Koristili smo upitnik DASS-21 – validirani i otvoreni alat za probir stresa, anksioznosti i depresije. Demografske i socioekonomske karakteristike uključivale su dob, razinu obrazovanja, status zaposlenja, prihode te bračni status.

Rezultati: Prosječna dob bolesnica bila je 53,34 godine i sve su bile žene. 28,3% od svih uključenih bile su mlađe od 45 godina. Većina bolesnica imala je blagu depresiju (11,3%), anksioznost (15,1%) i stres (11,3%). Tešku depresiju imalo je 5,6 % žena, dok je 3,7 % imalo tešku anksioznost. Izrazito tešku depresiju prijavilo je 3,7% žena, dok je izrazito tešku anksioznost i stres imalo 5,6% odnosno 1,9%. Pokazalo se da je mlađa dob (<45 godina) povezana sa sve tri podskupine tegoba.

Zaključak: Važno je napomenuti da je više od polovice bolesnica u našem istraživanju prijavilo određenu razinu psihološkog distresa, dok je 13,2% ocijenjeno kao teški ili izrazito teški distres. Korištenjem ovakvih instrumenata u našoj praksi možemo identificirati bolesnike koji su u većem riziku od razvoja značajnih psiholoških poteškoća te im na vrijeme pružiti psihološku pomoć koja im je potrebna kako bi uspješno završili liječenje.

Ključne riječi: karcinom dojke, distres, neoadjuvantno liječenje, probir

SCREENING FOR PSYCHOLOGICAL DISTRESS IN NEOADJUVANTLY TREATED BREAST CANCER PATIENTS

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Introduction: Breast cancer diagnosis can affect women both physically and psychologically. It has been reported that 50% of BC patients experience some psychological distress because of their disease. This can be especially true for patients during neoadjuvant treatment. While this approach offers multiple well-known benefits, there is also a specific psychological distress and discomfort that many patients experience, specifically because they will have to endure several months of therapy before surgery.

Our research aimed to evaluate the levels of psychological distress in women receiving neoadjuvant treatment and possible correlation between demographic and socioeconomic characteristics and stress levels.

Methods: 53 breast cancer patients were included in this research at various cycles of their neoadjuvant treatment. We used the DASS-21 questionnaire – a validated and open-access tool used for screening of stress, anxiety, and depression. Demographic and socioeconomic characteristics included age, education level, employment status, income, and marital status.

Results: The mean age was 53.34 years and all of them were women. 28.3% of them were younger than 45 years. Most of the patients had mild depression (11.3%), anxiety (15.1%) and stress (11.3%). Severe depression was found in 5.6 % of women while 3.7% had severe anxiety. Extremely severe depression was reported by 3.7% of women while extremely severe anxiety and stress had 5.6% and 1.9% respectively. Younger age (<45 years) has been shown to correlate with all three distress subgroups.

Conclusion: It is important to note that more than half the patients in our research reported at least mild distress while 13.2% scored for severe or extremely severe distress. Using these instruments in our practice can help identify patients that are at a higher risk of developing significant psychological difficulties and provide them in time with the psychological help they need in order to successfully complete their treatment.

Keywords: breast cancer, psychological distress, neoadjuvant therapy, screening

ANGIOSARKOM DOJKE UZROKOVAN RADIOTERAPIJOM

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Uvod: Poštedni kirurški zahvat potom radioterapija dojke je standard u liječenju ranog karcinoma dojke. Angiosarkom nastao nakon provedene radioterapije je iznimno rijetka maligna bolest koja ima agresivan tijek i loš ishod. Čini svega 0.05%–0.3% svih malignih tumora dojke. Javlja se više godina nakon zračenja, najčešće 5–7.

Prikaz slučaja: Bolesnica u dobi od 82 godine dolazi na kontrolu. Prije 6 godina učinjena joj je kvadrantektomija s biopsijom limfnog čvora „čuvara". Patohistološki nalaz potvrdio je da se radi o invanzivnom karcinomu, pT1N0, tumor 1,3x1,1 cm, l.č. 0/2, ER 100%, PR neg., HER 2 neg., Ki67 7%, imunofenotip: luminal B. Provedena je adjuvantna radioterapija i hormonska terapija (TD 4256cGy/16 frakcija te „boost" 12Gy/4 frakcije te je kroz 5 godina uzimala letrozol). Klinički dojka zadebljane kože, modra, kvrgava – posumnja se na angiosarkom. Ultrazvuk dojke opiše desno zadebljalu kožu sa supkutanim hematomom, BI-RADS 3. Magnetska rezonanca- nema suspektnih tvorbi niti zona patološkog nakupljanja. MSCT toraksa, abdomena i zdjelice ne opiše diseminacije bolesti. Učini se biopsija dojke koja potvrdi da se radi o angiosarkomu nakon provedene radioterapije. Imunohi-

stokemijski više od 80% stanica je jako c-MYC pozitivno. FISH analizom je nađen povećan broj crvenih signala (prosječno 10,6 signala po stanici) što upućuje na amplifikaciju MYC gena. Učini se mastektomija desne dojke te je definitivni patohistološki nalaz u izradi.

Zaključak: Angiosarkom uzrokovan radioterapijom ima lošu prognozu te stopu 5-godišnjeg preživljenja od 10–54%. Iako ne postoje jasne smjernice za liječenje, radikalan kirurški zahvat je terapija izbora. Stope povrata bolesti su visoke i kod bolesnika s R0 resekcijom, 54–92%, ali bolesnici s R1 i R2 resekcijom imaju još lošiju prognozu. Uloga adjuvantne kemoterapije također je dvojbena. Kod žena koje su zračene prije više godina s odgovarajućom kliničkom slikom svakako treba razmišljati i o ovom entitetu.

Ključne riječi: angiosarkom, postradioterapijski, rak dojke, patologija

RADIATION INDUCED ANGIOSARCOMA OF THE BREAST

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Introduction: Breast-conserving surgery followed by radiotherapy is the standard treatment for early breast cancer. Radiation induced angiosarcoma is an extremely rare malignancy with a poor prognosis. It represents only 0.05% to 0.3% of all malignant breast tumors. It usually appears several years after radiation (most commonly 5–7 years).

Case Report: An 82-year-old female patient presented for follow-up. Six years ago, she underwent a quadrantectomy with sentinel lymph node biopsy. The pathohistological examination confirmed invasive carcinoma, pT1N0, tumor size 1.3x1.1 cm, lymph nodes 0/2, ER 100%, PR negative, HER2 negative, Ki67 7%, with a luminal B immunophenotype. The patient received adjuvant radiotherapy (TD 4256 cGy/16 fractions with a boost of 12 Gy/4 fractions) and hormonal therapy (letrozole) for five years. On clinical examination, the breast appeared with thickened skin, a bluish discoloration, and nodularity, raising suspicion of angiosarcoma. Breast ultrasound revealed thickened skin with a subcutaneous hematoma, BI-RADS 3. Magnetic resonance imaging (MRI) showed no suspicious masses or areas of pathological enhancement. Thoracic, abdominal, and pelvic MSCT scans showed no evidence of disease dissemination. A biopsy confirmed radiation induced angiosarcoma. Immunohistochemical analysis demonstrated that over 80% of the cells were strongly positive for c-MYC. FISH analysis revealed an increased number of red signals (an average of 10.6 per cell), indicating MYC gene amplification. A mastectomy of the right breast was performed, and the final pathological report is awaited.

Conclusion: Angiosarcoma has a poor prognosis, with a 5-year survival rate between 10% and 54%. Although there are no clear guidelines, surgery is the treatment of choice. Recurrence rates remain high, even in patients who achieve R0 resection, ranging from 54% to 92%. Patients with R1 or R2 resections have an even worse prognosis. For women with a history of radiotherapy and appropriate clinical symptoms, angiosarcoma should be considered as a potential diagnosis.

Keywords: radiation, angiosarcoma, breast cancer, pathology

KAKO SE PONAŠA ADENOKARCINOM KOLONA S KOMPONENTOM SVIJETLIH STANICA?

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Uvod: Karcinom svijetlih stanica debelog crijeva (CCACC) je podtip kolorektalnog karcinoma kojeg su prvi opisali Hellstrom i Fisher 1964.godine. Tumor je iznimno rijedak i prema PubMed database do sada je opisano 25 slučajeva.

Prikaz slučaja: 65-godišnji pacijent javio se u hitnu službu KB „Sveti Duh zbog mase u lijevom hemiabdomenu, povraćanja i nadutosti unazad mjesec dana. U laboratorijskim nalazima bio je snižen hemoglobin (115 g/l) i povišen CRP (49 mg/l). Učinjeni MSCT abdomena je ukazao na infiltrativni proces sigmoidnoig debelog crijeva s metastazama u jetri. Tijekom pripreme za kolonoskopiju pacijent je razvio kliničke i radiološke znakove za intestinalnu opstrukciju te je premješten na Kirurški odjel. Učinjena je medijalna laparotomija na kojoj je nađen dilatiran transverzalni kolon i cekum te u području sigmoidnog dijela tumor u dužini do 10 cm. Učinjena je subtotalna kolektomija s apendektomijom te terminalna ileostomija. Histološki nalaz pokazao je da se radi o mucinoznom adenokarcinomu s komponentom svijetlih stanica koji infiltrira okolno subserozno masno tkivo bez znakova limfovaskularne i neuralne invazije. Metastaze su nađene u 8 od 9 izoliranih limfnih čvorova. Imunohistokemijska analiza pokazala je da su tumorske stanice svijetle komponente imaju slijedeće karakteristike: CK20+, CD10–, CDX2+, CK7–, CEA+, MUC2–, AFP– i PAS–.

Zaključak: Etiologija svijetlih stanica u clear cell adenokarcinomu debelog crijeva je još uvijek nejasna, ali može biti povezana s akumulacijom glikogena, mucina i lipida. U kliničkoj praksi teško je teško razlikovati metastatski karcinom, na primjer, metastatski karcinom svijetlih stanica i primarni CCACC ako je komponenta svijetlih stanica dominantna. Iz tog razloga neophodna je potvrda kolorektalnog podrijetla tumorskih stanica imunohistokemijskom analizom. Dodatno, potrebno je osvijestiti patologe o važnosti CCACC-a jer se ovaj podtip vjerojatno ponaša zloćudnije od drugih podtipova kolorektalnog karcinoma.

Ključne riječi: Karcinom svijetlih stanica debelog crijeva, kolorektalni karcinom, imunohistokemijska analiza, diferencijalna dijagnoza

HOW DOES ADENOCARCINOMA OF THE COLON WITH A COMPONENT OF CLEAR CELLS BEHAVE?

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Introduction: Colon clear cell carcinoma (CCACC) is a subtype of colorectal cancer (CCA) first described by Hellstrom and Fisher in 1964. The tumor is extremely rare and according to the PubMed database, 25 cases have been described so far.

Case Report: A 65-year-old patient reported to the Emergency Department Clinical Hospital Sveti Duh because of a mass in the left hemiabdomen, vomiting and bloating for the past month. In laboratory findings, hemoglobin was decreased (115 g/l) and CRP was elevated (49 mg/l). The performed MSCT of the abdomen showed the infiltrative process of the sigmoid colon with metastases in the liver. During the preparation for the colonoscopy, the patient developed clinical and radiological signs of intestinal obstruction and was transferred to the Surgical Department. A medial laparotomy was performed, where a dilated transverse colon and cecum with a tumor up to 10 cm in length were found in the sigmoid region. Subtotal colectomy with appendectomy and terminal ileostomy were performed. The histological findings showed that it was a mucinous adenocarcinoma with a clear cell component infiltrating the surrounding subserosal fatty tissue without signs of lymphovascular and neural invasion. Immunohistochemical analysis showed that the tumor clear cell components have the following characteristics: CK20+, CD10–, CDX2+, CK7–, CEA+, MUC2–, AFP– and PAS–.

Conclusion: In clinical practice it is difficult to differentiate between metastatic carcinoma, for example, metastatic clear cell carcinoma and primary CCACC if the clear cell component is dominant. For this reason, it is necessary to confirm the colorectal origin of tumor cells by immunohistochemical analysis. Additionally, pathologists need to be made aware of the importance of CCACC as this subtype is likely to behave more malignantly than other CCA subtypes.

Keywords: colorectal clear cell carcinoma, colorectal carcinoma, immunohistochemical analysis, differential diagnosis

SVEOBUHVATNO GENSKO PROFILIRANJE U BOLESNIKA S UZNAPREDOVALIM UROTELNIM KARCINOMOM: PRVI REZULTATI HRVATSKE URO-ONKOLOŠKE MREŽE

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Uvod: Mnogi bolesnici s uznapredovalim urotelnim karcinomom imaju somatske patogene genske alteracije. S ciljem poboljšanja ishoda liječenja postoji potreba za uključivanjem novih kliničkih genskih testova u rutinsku upotrebu u bolesnika s uznapredovalim urotelnim karcinomom. Cilj ovog istraživanja bio je ustanoviti prihvaćanje i primjenu sveobuhvatnog genskog profiliranja (SGP) u svakodnevnoj kliničkoj praksi u bolesnika s uznapredovalim urotelnim karcinomom.

Metode: Podaci iz šest centara, članova hrvatske uro-onkološke mreže, retrospektivno su analizirani vezano za korištenje SGP-a tijekom standardnog liječenja bolesnika s uznapredovalim urotelnim karcinomom. Primarni cilj bilo je utvrditi izvedivost SGP-a u svakodnevnoj kliničkoj praksi za ovu izazovnu skupinu bolesnika, korištenjem testa FoundationOne.

Rezultati: Od 2020. do 2024. za 81 bolesnika učinjeno je SGP. Bolesnici su primili imunoterapiju (N=71; 87%) kao prvu liniju (68%) ili drugu liniju liječenja (32%). Srednja dob bila je 68 godina, 67% muškaraca, 79% s primarnim tumorom mokraćnog mjehura, 18% s metastazama u jetri, 74% ECOG PS 1. Uzorak za SGP bio je primarno tumorsko tkivo, metastaze i krv u 84%, 13% i 2% bolesnika. U 11 bolesnika (13%) analiza nije uspjela zbog nedovoljne količine tumorskog tkiva. Prosječno vrijeme do pristizanja izvješća bilo je 1 mjesec. Ukupno 229 genomskih promjena identificirano je u 61 genu, medijan od 3 po bolesniku. 8 najčešćih mutacija su: TERT (25, 30%), TP53 (20, 24%), MTAP (15, 18%), FGFR3 (14, 16%), PIK3CA (9, 10%), ERBB2/ HER2 (8,9%), CDKN2A (7,8%) i ARID1A (7,8%). Potencijalno targetabilna promjena pronađena je u 39 (47%) bolesnika. Sedam bolesnika (8%) primilo je ciljanu terapiju što je rezultiralo u 3 slučaja parcijalnim odgovorom, 3 stabilna bolest i 1 progresija bolesti. Bolesnici s TMB>10 mut/Mb (N=24) imali su numerički veće stope odgovora i ukupnog preživljenja na imunoterapiju.

Zaključak: Integracija SGP-a u liječenju bolesnika s uznapredovalim karcinomom urotela izvediva je i donosi nove terapijske mogućnosti dijelu bolesnika s inače ograničenim mogućnostima liječenja.

Ključne riječi: molekularno profiliranje, urotelni karcinom, ciljana terapija, sveobuhvatno gensko profiliranje

COMPREHENSIVE GENOMIC PROFILING IN PATIENTS WITH ADVANCED UROTHELIAL CANCER: FIRST RESULTS FROM CROATIAN URO-ONCOLOGY NETWORK

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Introduction: Many patients with advanced urothelial cancer (aUC) harbor somatic pathogenic genomic alterations. There is an unmet need to incorporate novel clinical genomic assays into routine care of patients with aUC to improve the benefit of cancer therapy. The aim of this study was to assess uptake and implementation of comprehensive genomic profiling (CGP) in everyday clinical practice of patients with aUC.

Methods: Data from six Croatian Uro-Oncology Network-associated centers were retrospectively analyzed for utilization of CGP during the standard-of-care treatment of patients with aUC. The primary endpoint was feasibility of CGP in real-world settings for this challenging patient population, using FoundationOne platform.

Results: From 2020 to 2024, 81 patients underwent CGP. Patients received ICI (N=71; 87%) as the first line (68%) or second line (32%). Median age was 68 years, 67% male, 79% with bladder primary, 18% with liver metastasis, 74% ECOG PS 1. Specimen for CGP was primary tumor tissue, metastasis and blood in 84%, 13%, and 2% of cases, respectively. In 11 patients (13%) analysis failed due to insufficient amount of tumor tissue. The median turnover time was 1 month. A total of 229 genomic alterations were identified in 61 genes, median of 3 per patient. The 8 most often altered genes were: TERT (25, 30%), TP53 (20, 24%), MTAP (15, 18%), FGFR3 (14, 16%), PIK3CA (9, 10%), ERBB2/HER2 (8, 9%), CDKN2A (7, 8%), and ARID1A (7, 8%). Potentially actionable alteration was found in 39 (47%) patients. Seven patients (8%) received targeted therapy resulting in 3 cases of partial response, 3 stable disease, and 1 progressive disease. Patients with TMB>10 mut/Mb (N=24) had numerically higher response rates and overall survival on ICI.

Conclusion: Integration of CGP in management of patients with aUC is feasible and yields new therapeutic options in a discernible proportion of patients with otherwise limited treatment options.

Keywords: molecular profiling, urothelial cancer, targeted therapy, comprehensive genomic profiling

LJEKARNIČKA SKRB ZA PACIJENTICE S RAKOM DOJKE U FARMAKOTERAPIJSKOM SAVJETOVALIŠTU DOMA ZDRAVLJA ZAGREB CENTAR

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Uvod: Zdravstvena skrb žena s rakom dojke zahtjeva integrirani pristup koji uključuje i pružanje ljekarničke skrbi od strane farmaceuta što potencijalno može doprinijeti smanjenju simptoma nuspojava terapije te poboljšati kvalitetu života i adherenciju. Svrha ovog istraživanja bila je odrediti vrstu i učestalost provedenih intervencija za rješavanje identificiranih terapijskih problema (TP) te njihovu prihvaćenosti kod pacijentica s dijagnosticiranim rakom dojke kojima je u Farmakoterapijskom savjetovalištu Doma zdravlja Zagreb Centar (DZZC) pružena usluga upravljanja farmakoterapijom.

Metode: Provedeno je prospektivno intervencijsko istraživanje u Farmakoterapijskom savjetovalištu DZZC-a u razdoblju od studenog 2022. do svibnja 2024. godine u koje su bile uključene pacijentice starije od 18 godina s postavljenom dijagnozom raka dojke te s najmanje jednom konzultacijom. Na inicijalnoj konzultaciji, uz prikupljanje podataka, određeni su TP i predložene su intervencije za njihovo rješavanje, dok je na kontrolnim konzultacijama utvrđen stupanj njihove prihvaćenosti.

Rezultati: U provedeno istraživanje bila je uključena 81 pacijentica prosječne dobi 58 (33–100) godina koje su u prosjeku bolovale od 10 (1–5) komorbiditeta te koristile 7 (1–20) lijekova i 4 (1–22) dodatka prehrani. Na prve dvije konzultacije identificirano je ukupno 416 TP (5,0 ± 3,7), dok su najčešće intervencije za njihovo rješavanje uključivale „Uvođenje dodatka prehrani/dermatokozmetike/biljnog pripravka“ (24,5 %), „Uvođenje nove terapije“ (16,1 %), i „Edukacija pacijenta“ (12,9 %). Najčešći dodaci prehrani koji su bili predloženi za uvođenje bili su vitamini B kompleksa (9,29%), beta glukani (6,56%), vaginalete za vlaženje rodnice (6,01%), magnezij (4,92%) i vitamin C (4,92%). Od ukupno 243 intervencije predložene pacijenticama, njih 90,0 % je bilo prihvaćeno, dok je od strane liječnika prihvaćena 71 intervencija (87,1 %).

Zaključak: Visok stupanj prihvaćenosti intervencija od strane pacijentica i liječnika ukazuje na spremnost prihvaćanja suradnje i uključivanja farmaceuta u skrb onkoloških pacijentica s ciljem prevencije terapijskih problema.

Ključne riječi: rak dojke, upravljanje farmakoterapijom, ljekarnička skrb, dodaci prehrani

PHARMACEUTICAL CARE FOR BREAST CANCER PATIENTS AT THE PHARMACOTHERAPY COUNSELING CENTER OF THE HEALTH CARE CENTER ZAGREB-CENTER

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Introduction: Health care for women with breast cancer requires an integrated approach, including pharmaceutical care provided by pharmacists that can potentially reduce the symptoms of side effects, improve quality of life, and enhance adherence. This study aimed to determine the type and frequency of proposed interventions for the resolution of identified drug therapy problems (DTPs), as well as their acceptance in patients with breast cancer who were provided with Comprehensive Medication Management services at the Pharmacotherapy Counseling Center of the Health Care Center Zagreb-Centar (HCCZC).

Methods: A prospective interventional study was conducted at the Pharmacotherapy Counseling Center of HCCZC from November 2022 to May 2024, involving patients over 18 years old diagnosed with breast cancer who attended at least one consultation. During the initial consultation, data was collected, DTPs were identified,

and interventions to address them were proposed. During follow-up consultations, the acceptance of proposed interventions was assessed.

Results: The study included 81 patients with an average age of 58 (33–100) years, who had an average of 10 (1–5) comorbidities, used 7 (1–20) medications, and 4 (1–22) dietary supplements. A total of 416 TPs were identified (5.0 ± 3.7) during the initial consultation. At the same time, the most common interventions for their resolution were "Introduction of dietary supplement/dermocosmetics/herbal product" (24.5%), "Introduction of new therapy" (16.1%), and "Patient education" (12.9%). The most recommended dietary supplements were vitamin B complex (9.29%), beta-glucans (6.56%), vaginal moisturizing tablets (6.01%), magnesium (4.92%), and vitamin C (4.92%). Out of 243 interventions proposed to the patients, 90.0% were accepted by them, while physicians accepted 71 interventions (87.1%).

Conclusion: The high acceptance rate of interventions by patients and physicians indicates the readiness to collaborate with and include pharmacists in the care of oncology patients to prevent DTPs.

Keywords: breast cancer, Comprehensive Medication Management services, pharmaceutical care, food supplement

LINIJE LIJEČENJA I ISHODI METASTATSKIH BILIJARNIH KARCINOMA NA KLINICI ZA ONKOLOGIJU I RADIOTERAPIJU KLINIČKOG BOLNIČKOG CENTRA SPLIT U PERIOD OD 2019. DO 2022. GODINE

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Uvod: Bilijarni karcinomi se većinom dijagnosticiraju u uznapredovalom ili metastatskom stadiju (M1) kada su terapijske opcije skromne.

Metode: Proveli smo retrospektivnu analizu medicinskih povijesti pacijenata s dijagnosticiranim bilijarnim karcinomima prezentiranih na multidisciplinarnom timu (MDT) Klinike za onkologiju i radioterapiju KBC Split, u periodu 2019–2022. Podaci su analizirani deskriptivnim statističkim metodama, uz korištenje Microsoft Excela.

Rezultati: Identificirali smo ukupno 58 pacijenata s M1 karcinomima bilijarnog sustava. Od ukupne kohorte, samo 75,4% (n=43)je liječeno prvom linijom sistemske terapije, sa srednjim PFS 93 dana. Preostalih 24,9% je zbog lošeg općeg stanja primalo simptomatsko suportivnu terapiju. Drugu liniju je primilo ukupno 23 pacijenta (55,8%) sa srednjim PFS 60 dana. Treću liniju je primilo 9 pacijenata (20,9%) sa srednjim PFS 67 dana. Ukupno 4 pacijenta (9,5%) je primilo četvrtu liniju terapije sa srednjim PFS 26,5 dana. Samo 1 pacijent je primio petu liniju (medijan PFS 12 dana) i šestu liniju (medijan PFS 40 dana). Gensko profiliranje je provedeno kod 8 pacijenata, od kojih je kod 3 pacijenta dokazana neka od mutacija za koju postoji terapijska opcija, te su liječeni ciljanom terapijom u nekoj od linija sistemskog liječenja. Srednje preživljenje M1 pacijenata u našoj analizi je iznosilo 22 mjeseca.

Zaključak: Rezultati naše retrospektivne analize su pokazali značajan pad u broju pacijenata u kasnijim linijama sistemskog liječenja. Srednje preživljenje pacijenata s M1 stadijem bilijarnih malignih tumora iznosi 22 mjeseca, a oko trećina pacijenata koja zbog općeg stanja nisu mogla primiti nijednu liniju sistemske terapije ukazuju na potrebu za unaprjeđenjem strategija liječenja malignoma bilijarnog sustava. Vrijednost upotrebe ciljane terapije bazirane na preciznoj onkologiji bi se trebala dalje istraživati, te biti potencijalno dostupna svim pacijentima s M1 stadijem.

Ključne riječi: bilijarni karcinomi, metastatski, liječenje, sveobuhvatno gensko profiliranje

TREATMENT PATTERNS AND THE OUTCOMES OF METASTATIC BILIARY TRACT CANCERS (BTC) AT THE DEPARTMENT OF ONCOLOGY AND RADIOTHERAPY, UNIVERSITY HOSPITAL SPLIT DURING 2019–2022

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Introduction: BTC are a group of tumors that are in most cases diagnosed in the advanced and metastatic phase of the disease when therapeutic options and results are modest.

Methods: A retrospective analysis of patients presented on our MDT over 4 years (1/19 – 12/22) was conducted. The data were analyzed using descriptive statistics methods, with the use of Microsoft Excel tools.

Results: We identified a total of 58 patients with metastatic (M1) BTC. Among those, only 75.4% of patients (n=43) received the first line of systemic therapy, with a median PFS of 93 days. The remaining 24.9% had only the best supportive care (BSC), due to their poor performance status. A total of 23 patients (55.8%) received second-line treatment, with median PFS of 60 days. A total of 9 patients (20.9%) received third line of therapy, with median PFS of 67 days. 4 patients (9.5%) received the fourth line of therapy, with median PFS of 26.5 days. Only 1 patient received fifth line (5L) with median PFS of 12 days and sixth line of therapy with median PFS of 40 days. Comprehensive Genomic Profiling (CGP) was performed in 8 patients, out of whom 3 patients had actionable mutations and were treated with targeted therapy. The median OS in our subset of patients with M1 BTC was 22 months.

Conclusion: The results of our retrospective analysis showed a significant decrease in the number of patients in later lines of treatment. The median overall survival of 22 months and about a third of patients not receiving anticancer therapy define the unmet need in this patient population. The value of the use of targeted therapy based on precision medicine should be further investigated and potentially available to all patients with actionable mutations.

Keywords: biliary tract cancer, metastatic, comprehensive genetic profiling, cancer tretatment

KARCINOM BILIJARNOG SUSTAVA – RETROSPEKTIVNA ANALIZA KLINIKE ZA ONKOLOGIJU I RADIOTERAPIJU KLINIČKOG BOLNIČKOG CENTRA SPLIT U PERIOD OD SIJEČNJA 2019. DO PROSINCA 2022. GODINE, USPOREDBA EPIDEMIOLOŠKIH PODATAKA

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Uvod: Karcinomi bilijarnog sustava su grupa rijetkih malignoma koja se razvija iz žučnog mjehura i/ili žučnih vodova. Zbog inicijalno asimptomatskog razvoja, te agresivne prirode bolesti se tipično dijagnosticiraju u lokalno uznapredovalom ili metastatskom stadiju.

Metode: retrospektivna analiza povijesti bolesti pacijenata s malignim tumorima bilijarnog sustava prezentiranih na multidisciplinarnom timu Klinike za Onkologiju i radioterapiju, u periodu od 101.19–12.22. Korištene su deskriptivne statističke metode i Microsoft Excel.

Rezultati: identificirano je ukupno 85 pacijenata s malignim tumorima bilijarnog sustava. Srednja dob u vrijeme dijagnoze je bila 70 godina (31–90), te je najčešći patohistološki podtip bio adenokarcinom (94,1%). Distribucija po spolu je bila 60% muškaraca i 40 % žena. 47,1% pacijenata je imalo inicijalno metastatsku bolest (M1). Operacija s kurativnom namjerom je učinjena kod 34 pacijenta koji nisu imali dokaza metastatske bolesti (M0), od kojih je 50% primalo adjuvantnu kemoterapiju, a kod ostalih je provedeno kliničko praćenje. Dio pacijenata je razvio M1 bolest tijekom naše analize, pa smo finalno imali 58 pacijenata s M1 stadijem. Gotovo trećina M1 (24,9%) nije primila nijednu liniju sistemske terapije zbog lošeg općeg stanja, a prvu liniju sistemske terapije je primilo 75,1% pacijenata.

Zaključak: Analizom smo potvrdili da je većina malignih tumora bilijarnog sustava na Klinici za onkologiju i radioterapiju KBC Split u promatranom periodu dijagnosticirana u uznapredovalom stadiju, kod pacijenata starije životne dobi i često su lošeg općeg stanja.

Ključne riječi: bilijarni karcinomi, epidemiologija, kemoterapija, adenokarcinom

BILIARY TRACT CANCERS – SINGLE INSTITUTION RETROSPECTIVE ANALYSIS (2019–2022), THE CROSS-SECTION OF EPIDEMIOLOGICAL DATA

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Introduction: BTC comprises a rare group of malignancies that involve the gallbladder and biliary tree. Due to their aggressive nature and initially asymptomatic course, they are typically diagnosed in the locally advanced and metastatic phase.

Methods: A retrospective analysis of patients presented on our multidisciplinary team (MDT) over the course of 4 years (1/19 – 12/22) was conducted. The data were analyzed using descriptive statistics methods, with the use of Microsoft Excel tools.

Results: We identified a total of 85 patients with diagnosed BTC. The median age at the time of diagnosis was 70 years (range 31–90) and the most common pathohistological subtype was adenocarcinoma (94.1%). The distribution by gender was 60% male and 40% female. 47.1% of patients were initially metastatic (M1). Curative intent surgery was performed in 34 patients, out of whom 50% were treated with adjuvant chemotherapy and the remaining 50% were in close follow up. Some of those patients developed metastatic disease in later stages of our analysis so we had a total of 58 patients with M1 disease. Among those, 75.1% were treated with systemic therapy and 24.9% had only the best supportive care (BSC), due to their poor performance status.

Conclusion: It is confirmed that in our institution the tumors of the biliary system are diagnosed in an advanced stage, in people of older age and often with low performance status.

Keywords: biliary tract cancer, epidemiology, chemotherapy, adenocarcinoma