POSTER PRESENTATIONS

P1 – TREATMENT PATTERNS AND OUTCOMES OF EGFR POSITIVE NSCLC PATIENTS TREATED WITH OSIMERTINIB IN FIRST LINE SETTING

ANA GELTAR[1], Urška Janžič[1,2]

[1]*Department of Oncology, University Clinic Golnik, Golnik, Slovenia*
[2]*Medical Faculty, University of Ljubljana, Ljubljana, Slovenia*

Introduction: Targeted therapy has significantly transformed the treatment landscape of metastatic lung adenocarcinoma with EGFR mutations, improving survival outcomes compared to traditional chemotherapy. Osimertinib, a third-generation EGFR tyrosine kinase inhibitor (TKI), is now a standard first-line treatment due to its superior efficacy and low rate of serious adverse events.

Methods: We prospectively collected and analyzed data of 45 patients with metastatic EGFR-mutated lung adenocarcinoma through our Hospital based registry, who received osimertinib as first-line treatment from February 2022 onwards. Among them, 27 patients harbored exon 19 deletion,16 patients had the L858R (one of each with concurrent T790M mutation), one had only T790M, and two had the L861Q mutation. Additionally, 10 patients had concurrent TP53 mutations, and 23 exhibited at least one other genetic alteration, including six with additional EGFR mutations.

Results: As of the latest follow-up, 23 patients remain on osimertinib, while 19 experienced disease progression, and two patients were lost to follow up. Rebiopsy was performed in 9/19 progression cases, revealing that EGFR mutations persistance in seven patients (with additional EGFR mutations identified), one patient no longer had an EGFR mutation, and one result was inconclusive. Other detected mutations included BRAF fusion, CDKN2A amplification, CDKN2A loss, TP53 mutation, CTNNB1 mutation, PIK3CA mutation, RET fusion, and KRAS p.G12V mutation. Eight patients received second line treatment: two patients carboplatin/paclitaxel/atezolizumab/bevacizumab, one carboplatin/pemetrexed, three afatinib, one carboplatin/pemetrexed/amivantamab, and one osimertinib plus selpercatinib. Two patients continued osimertinib beyond progression.

Conclusions: Our findings emphasize the genetic heterogeneity of EGFR-mutated lung cancer and the complexity of resistance mechanisms emerging during osimertinib treatment. Further studies are needed to optimize sequential treatment strategies for patients with disease progression.

Keywords: EGFR mutation, osimertinib, lung adenocarcinoma, targeted therapy, resistance mechanisms

P2 – CLINICAL OUTCOMES OF MELANOMA BRAIN METASTASES IN THE ERA OF IMMUNOTHERAPY AND TARGETED THERAPY: A RETROSPECTIVE SINGLE CENTER STUDY

DORA ANTUNOVIĆ[1], Marin Šunjić[1], Kristina Urch[1], Jure Murgić[1,2], Nina Dabelić[1], Jasmina Marić Brozić[1,3]

[1]*Department of Oncology and Nuclear medicine, Sestre milosrdnice University Hospital Center, Zagreb, Croatia*
[2]*School of Medicine, Catholic University of Croatia, Zagreb, Croatia*
[3]*School of Medicine, University of Zagreb, Zagreb, Croatia*

Introduction: Brain metastases (BM) are present in up to 30% of patients at the time of initial melanoma diagnosis, with an additional 20-30% developing BM during the course of the disease. Despite recent progress in systemic treatments, patients with BM continue to have poor outcomes. Contemporary treatment options for melanoma BM include surgery, stereotactic radiosurgery (SRS), gamma knife, and whole brain radiotherapy (WBRT) as local modalities. Systemic options include immunotherapy (anti-CTLA4 and anti-PD-1) and targeted therapy (BRAF V600 and MEK inhibitors). However, the optimal management of patients with BM remains controversial. This study aims to assess the mature outcomes of melanoma patients with BM treated with immunotherapy and targeted therapy at a single tertiary center.

Methods: A single-institution retrospective chart review was conducted, covering the period from 2015 to 2024. All patients with melanoma brain metastases (BM) were eligible for inclusion in this study. Descriptive statistics were utilized to summarize the data, and overall survival (OS) was calculated using the log-rank method. Variables associated with OS were identified using the Cox hazard regression model, with a p-value of < 0.05 considered significant.

Results: Eighty-three patients with BM were identified, comprising 58 males and 25 females. BRAF mutation was detected in 51 patients (61.4%). The median age at melanoma diagnosis was 61 years (range 21-84 years), and the median time from primary melanoma diagnosis to BM was 23 months (range 0-211 months). Seventeen patients (20%) were diagnosed with synchronous BM, and symptomatic BM were present in 51 patients (61.4%). Regarding local therapy, 45 patients were treated with radiotherapy: WBRT (n=24), gamma knife (n=16), and SRS (n=5). Regarding systemic treatment, 55 patients received immunotherapy: 37 patients received BRAF/MEK inhibitors, and 24 patients received both systemic modalities following progression on another agent. In addition to immunotherapy, 33 patients received radiotherapy. After a median follow-up of 56 months (95% CI 35-109 months), the median overall survival (OS) was 8 months (95% CI 6-150 months). Age, sex, initial neurologic symptoms, serum LDH level, BRAF status, and therapy with BRAF/MEK inhibitors were not significantly associated with overall survival on univariate analysis. Patients who received radiotherapy lived significantly longer (HR 0.56, 95% CI 0.34-0.91, p=0.01), with no difference regarding the radiation treatment modality. Patients treated with immunotherapy also lived significantly longer (HR 0.25, 95% CI 0.14-0.44, p<0.0001). There was no significant difference in OS when comparing the combination of immunotherapy and radiotherapy to immunotherapy alone.

Conclusions: Patients with melanoma brain metastases (BM) show significant treatment benefits when treated with immunotherapy and radiotherapy. These single-center retrospective results align with findings from published clinical trials. However, the overall prognosis for this patient population remains poor. Further studies are necessary to determine the optimal treatment approaches.

Keywords: melanoma brain metastases, immunotherapy, radiotherapy, BRAF/MEK inhibitors, stereotactic radiosurgery

REFERENCES

1. Phillips WJ, Baghai T, Ong M, Lo B, Ibrahim A, Smith T, et al. A contemporary report of clinical outcomes in patients with melanoma brain metastases. Current Oncology. 2021;28(1):428-439. Doi: 10.3390/curroncol28010045.
2. Glitza Oliva IC, Palaia J, Sakkal LA, Patel D, Moshyk A, Han N, et al. Real-world outcomes in patients with melanoma brain metastasis: a US multisite retrospective chart review study of systemic treatments. BMJ Open. 2025 Jan 30;15(1):e091098. doi: 10.1136/bmjopen-2024-091098.
3. Vosoughi E, Lee JM, Miller JR, Nosrati M, Minor DR, Abendroth R, et al. Survival and clinical outcomes of patients with melanoma brain metastasis in the era of checkpoint inhibitors and targeted therapies. BMC Cancer. 2018 Apr 27;18(1):490. doi: 10.1186/s12885-018-4374-x.

P3 – TOXICITY OF BRIGATINIB IN THE TREATMENT OF METASTATIC ALK-POSITIVE NON-SMALL CELL LUNG CANCER – A CASE REPORT

ANDRIJANA KOJIĆ[1], Feđa Đorđević[1], Katarina Ljujić[1], Dimitrije Kolović[1], Jelena Spasić[1]

[1]*Institute of Oncology and Radiology of Serbia, Belgrade, Serbia*

Introduction: Non-small cell lung cancer (NSCLC) with ALK gene rearrangement (ALK-positive NSCLC) occurs with a frequency of 3-5%. Brigatinib is a second-generation ALK tyrosine kinase inhibitor (TKI) approved in Serbia for the first-line treatment of metastatic ALK-positive NSCLC. Photosensitivity as a side effect of brigatinib is reported in less than 4% of patients.

Aim: We present a case of rare toxicity of brigatinib manifesting as photosensitivity.

Case presentation: A 59-year-old female was diagnosed with metastatic ALK-positive lung adenocarcinoma in February 2024. Treatment with brigatinib was initiated in March 2024 at a standard dose of 180 mg daily. During the fourth month of treatment, the patient developed pronounced erythema with signs of dry desquamation on sun-exposed areas and periorbital edema, indicating grade 3 photosensitivity toxicity. Brigatinib therapy was suspended for two weeks, and topical and systemic corticosteroids along with antihistamines were administered, leading to complete resolution of skin changes. Treatment with brigatinib reinitiated at the same dosage. Shortly after resuming therapy, within the first week, skin changes reappeared in the same areas, clinically more pronounced but still at grade 3. The skin changes were treated again, with a pause in brigatinib administration, resulting again in complete recovery. Treatment continued at a reduced dose of 90 mg daily due to recurrent grade 3 toxicity, as recommended. At the last follow-up at IORS in October 2024, the patient tolerates therapy well, with no skin changes. Best therapy response is partial remission.

Conclusion: Although rare, photosensitivity as a result of brigatinib administration poses a significant clinical challenge. Effective preventive measures, including patient education on sun protection and local skin care, are essential for mitigating this side effect and maintaining treatment continuity.

Keywords: ALK, NSCLC, brigatinib, photosensitivity

P4 – USE OF THE TEMOZOLOMIDE AND IRINOTECAN (TEMIRI) CHEMOTHERAPY PROTOCOL IN THE TREATMENT OF RELAPSED / REFRACTORY EWING SARCOMA IN ADULTS: A SINGLE-CENTER EXPERIENCE

DIMITRIJE ĐURĐEVIĆ[1], Slobodan Kutić[1], Sofija Pantelić[1], Dušan Ristić[1], Branka Živković[1]

[1]*Institute of Oncology and Radiology of Serbia, Belgrade, Srbija*

Introduction: The chemotherapy protocol based on temozolomide and irinotecan (TemIri) is the standard of care for relapsed/refractory (R/R) Ewing sarcoma. However, experiences with the application of this protocol remain limited, primarily due insufficient application in clinical practice.

Aim: To investigate the effectiveness of the TemIri HT protocol in the treatment of R/R Ewing sarcoma.

Methods: This retrospective study included 12 patients diagnosed with Ewing sarcoma between 2019 and 2024, who were treated at the Institute of Oncology and Radiology of Serbia (IORS). Therapy response was assessed based on the RECIST 1.1 criteria and expressed through the objective response rate (ORR) and clinical benefit ratio (CBR). Data were obtained from medical records.

Results: The median age of the patients was 29.5 years (range: 18-38), with a male predominance (8/12). In 41.6% of the patients, the protocol was applied as the second line of treatment, while in the rest, it was used in subsequent lines. Extraosseous disease was present in 2 patients. Partial remission (PR) was observed in 41.6% (5/12) of patients, disease progression (PD) occurred in 33.3% (4/12), and disease stabilization (SD) was seen in the remaining patients. This resulted in an ORR of 41.7% and a CBR of 66.7%. The line of treatment did not statistically correlate with the response to therapy. Pre-treatment serum lactate dehydrogenase (LDH) levels showed a negative correlation with the CBR ($p = 0.004$, $r = -0.768$), and the highest recorded LDH levels during chemotherapy negatively correlated with both the CBR ($p = 0.018$, $r = -0.667$) and the ORR ($p = 0.004$, $r = -0.589$).

Conclusions: The use of the TemIri HT protocol in the treatment of R/R Ewing sarcoma significantly contributes to the overall response to therapy, which was observed in 40% of patients. The response was not influenced by the line of treatment in which the protocol was applied, while LDH levels were identified as a predictive factor.

Keywords: Ewing sarcoma, irinotecan, TemIri, temozolomide

REFERENCES

1. Kurucu N, Sari N, Ilhan IE. Irinotecan and temozolamide treatment for relapsed Ewing Sarcoma: A single-center experience and review of the literature. Pediatric Hematology and Oncology. 2014;32(1):50–59. doi:10.3109/08880018.2014.954070.
2. Blanchette PS. et al. (no date) Irinotecan and temozolomide in adults with recurrent sarcoma, Journal of Solid Tumors. Available at: https://doi.org/10.5430/jst.v5n2p105.
3. Casey DA, Wexler LH, Merchant MS, Chou AJ, Merola PR, Price AP, Meyers PA. Irinotecan and temozolomide for Ewing sarcoma: the Memorial Sloan-Kettering experience. Pediatr Blood Cancer. 2009 Dec;53(6):1029-34. doi: 10.1002/pbc.22206. PMID: 19637327.

P5 – PROGNOSTIC SIGNIFICANCE OF THE KELIM SCORE AS A PREDICTOR OF RESPONSE TO CHEMOTHERAPY IN PATIENTS WITH EPITHELIAL OVARIAN CANCER

ANA PARIC[1], Maja Pezer Naletilic[1], Kresimir Tomic[1], Monika Glibic[1], Sanda Cale[1], Ana Puljic Cuk[1], Semir Vranic[2,3]

[1]*Department of Oncology, University Hospital Center Mostar, Mostar, Bosnia and Herzegovina*
[2]*College of Medicine, QU Health, Qatar University, Doha, Qatar*
[3]*Department of Medical Sciences, Academy of Sciences and Arts of Bosnia and Herzegovina, Sarajevo, Bosnia and Herzegovina*

Introduction: Ovarian cancer is the leading cause of death among gynecological malignancies in Europe and remains a significant public health challenge(1). Despite therapeutic advances, there is still a critical need for better prognostic and predictive markers for individualized treatment strategies. The KELIM score (Kinetics of Elimination of CA-125), which reflects the early kinetics of the tumor marker CA-125 during chemotherapy, has emerged in previous studies as a potentially valuable prognostic tool. Notably, patients with low KELIM scores, indicating poor chemosensitivity, and demonstrated a significant improvement in overall survival with the addition of anti-vascular endothelial growth factor (anti-VEGF) bevacizumab(2,3). We assessed the utility of the KELIM score in the patients with epithelial ovarian cancer treated with chemotherapy at our institution.

Methods: We conducted a retrospective analysis of medical records of patients with epithelial ovarian cancer who received neoadjuvant, adjuvant, or primary chemotherapy at the University Clinical Hospital Mostar between 2013 and 2023. The KELIM score was calculated using an online tool, based on a minimum of three CA-125 measurements obtained during the first 100 days of chemotherapy. Scores were classified as favorable (≥1) or unfavorable (<1) following calculation.

Results: Ninety-two patients with epithelial ovarian cancer were included in this retrospective analysis. The median age at diagnosis was 61 years (range 23–80). High-grade serous ovarian carcinoma was the most common subtype (85%). 78% of patients presented with a good ECOG performance status. 64% of patients were diagnosed at the FIGO stage III, most of which were in the stage IIIc (76%). BRCA1/2 status was available for 26% of patients, of whom 37.5% were BRCA1– positive. The most frequently used regimens were dose-dense paclitaxel and carboplatin (55%) and the standard 3-weekly schedule (43%). 54% underwent primary debulking surgery followed by adjuvant chemotherapy, 30% received neoadjuvant chemotherapy followed by interval debulking surgery, and 15% were treated with chemotherapy alone. The median progression-free survival (PFS) for first-line chemotherapy was 16 months. 44% of patients had a platinum-free interval (PFI) >12 months, 25% had a PFI of 6-12 months, while 32% < six months. Among patients with available data, 39% had a favorable KELIM score (≥1), while 61% had an unfavorable score (<1).

Conclusions: Given the cost constraints and limited access to targeted therapies in low– to middle-income countries such as Bosnia and Herzegovina, the KELIM model could offer a cost-effective and accessible tool to guide treatment decisions. Using early CA-125 kinetics, clinicians can identify patients who are less likely to respond adequately to standard chemotherapy and who may benefit most from the addition of bevacizumab. This stratified approach allows for optimized use of limited resources, directing bevacizumab to those with the highest potential benefit while sparing others from unnecessary toxicity and cost.

Keywords: ovarian cancer, KELIM score, prognostic biomarker, chemotherapy response

REFERENCES

1. International Agency for Research on Cancer. Europe Fact Sheet. GLOBOCAN 2020; Lyon, France: IARC; 2021. Available from: https://gco.iarc.who.int/media/globocan/factsheets/populations/908-europe-fact-sheet.pdf
2. Colomban O, Tod M, Peron J, Perren TJ, Leary A, Cook AD, et al. Bevacizumab for newly diagnosed ovarian cancers: best candidates among high-risk disease patients (ICON-7). JNCI Cancer Spectr. 2020 Apr 4;4(3):pkaa026.
3. You B, Purdy C, Copeland LJ, Swisher EM, Bookman MA, Fleming G, et al. Identification of patients with ovarian cancer experiencing the highest benefit from bevacizumab in the first– line setting on the basis of their tumor-intrinsic chemosensitivity (KELIM): The GOG-0218 Validation Study. Journal of Clinical Oncology. 2022 Dec 1;40(34):3965–74.

P6 – ACTIVITY OF PEMBROLIZUMAB IN CERVICAL CANCER– CASE REPORT

IRENA CONIĆ[1,2], Slavica Stojnev[3,4], Ivan Petković[1,2], Ana Cvetanović[1,2], Dane Krtinić[1,5]

[1]*Department for Oncology, Faculty of Medicine, University of Niš, Niš, Serbia*
[2]*Clinic for Oncology, University Clinical Center Niš, Niš, Serbia*
[3]*Department for Pathology, Faculty of Medicine, University of Niš, Niš, Serbia*
[4]*Center for Pathology, Univerity Clinical Center Niš, Niš, Serbia*
[5]*Department for Pharmacology, Faculty of Medicine, University of Niš, Niš, Serbia*

Introduction: Pembrolizumab has shown efficacy in persistent, recurrent, or metastatic cervical cancer. The effect of chemotherapy might be enhanced by immunotherapy. This is a case report of the first patient at the Clinic for Oncology in Niš who started treatment with immunotherapy for cervical cancer in January 2025. in addition to standard chemotherapy paclitaxel/carboplatin.

Case presentation: The patient was treated with chemoradiotherapy for cervical cancer in FIGO stage IIB two years ago. She tolerated the treatment well. Two years after the treatment radical chemoradiotherapy, progression of the disease occurred with enlargement of the retroperitoneal and para-aortic lymph nodes, confirmed by MRI of the abdomen and pelvis and PET/CT. On the PET/CT, a retroperitoneal para-aortic left in the infrarenal segment, from the height of L4, a conglomerate of lymph nodes extending caudally along the left common iliac artery measuring 35x31 mm with intense FDG accumulation (SUVmax up to 20.2) was seen. Above the described conglomerate, smaller para-aortic left lymph nodes of shorter diameter 6mm with increased FDG accumulation were seen. Programmed cell death ligand 1 (PD-L1) status were assessed from tumor samples. The treatment was carried out immunochemotherapy. Irrespective of PD-L1 expression status, pembrolizumab was administered at fixed dose of 200 mg intravenously every 3 weeks. Paclitaxel was administered 175mg/m2 and carboplatin AUC 5. Treatment response was evaluated by MRI, using iRECIST criteria. MRI showed a retroperitoneal paraaortic left enlarged lymph node measuring 20x17mm. After the 4th cycle of immunochemotherapy, a partial remission was confirmed. Then the immunochemotherapy treatment was continued for another 4 cycles. Treatment with pembrolizumab immunotherapy is ongoing. The patient subjectively tolerates the therapy well, and the laboratory analyzes are within the wider limits of References values.

Conclusions: Immunochemotherapy pembrolizumab with paclitaxel/carboplatin has a favorable effect on the treatment of recurrent and metastatic cervical cancer.

Keywords: cervical cancer, chemotherapy, imunotherapy

P7 – EPITHELIOID HEMANGIOENDOTHELIOMA IN BOSNIA AND HERZEGOVINA: A CASE SERIES ANALYSIS OF DIFFERENT TREATMENT STRATEGIES IN AN ULTRA-RARE CANCER

EMIR SOKOLOVIĆ[1], Amina Hadžibeganović[2], Ema Čampara[1], Amil Družić[1], Elma Kapisazović[1], Timur Cerić[1], Berisa Hasanbegović[1], Semir Bešlija[1]

[1]*Clinic of Oncology, Clinical Center University of Sarajevo, Sarajevo, Bosnia and Herzegovina*
[2]*Clinic for Oncology and Radiotherapy, University Clinical Center Tuzla, Tuzla, Bosnia and Herzegovina*

Introduction: Epithelioid hemangioendothelioma (EHE) is an ultra-rare vascular sarcoma with an incidence of 0.379 per million person-years in Europe. It is genetically defined by WWTR1-CAMTA1 or YAP1-TFE3 translocations. No specific therapeutic agent is currently approved for EHE, though several are being tested in early-phase basket trials. In the absence of prospective data, management is based on expert consensus. A notable development is the ongoing EUROCAN prospective registry, expected to provide real-world insights.

Methods: We present a retrospective case series of four histologically confirmed EHE patients treated at the Clinical Center University of Sarajevo between January 2020 and December 2024. Patients originated from two administrative regions with a combined population of 664,834, resulting in a crude incidence of approximately 1.2 cases per million person-years—noticeably higher than reported European averages. Patient ages ranged from 33 to 68 years (median: 47). Primary sites were visceral in three patients and bone in one. Two patients had localized disease at diagnosis and underwent surgery (one with adjuvant radiotherapy), while the other two were metastatic at presentation and managed with systemic therapy. Only two patients were correctly diagnosed and treated as EHE from the start, while the others were initially misclassified and treated as carcinoma or undifferentiated sarcoma.

Results: All systemic agents mentioned in literature were employed across the cohort, including pazopanib, gemcitabine/docetaxel, everolimus, and paclitaxel/carboplatin. Progression-free survival (PFS) with first– line therapy ranged from 2 to 8 months in patients receiving chemotherapy. One patient achieved prolonged disease stability for 48+ months on first-line pazopanib and remains alive after 50 months, highlighting its potential efficacy in symptomatic patients. Another patient with localized visceral disease is currently on close follow-up without systemic therapy or radiotherapy. Overall survival (OS) ranged from 12 to 50 months.

Conclusions: These findings demonstrate the diversity of diagnostic and therapeutic approaches used for EHE and underscore the importance of accurate and timely diagnosis. The notably higher local incidence, variability in treatment responses, and favorable outcome in the pazopanib-treated case warrant further collaborative data analysis.

Keywords: epithelioid hemangioendothelioma, sarcoma, ultra-rare tumors, pazopanib, retrospective study

REFERENCES

1. Paulson KG, Ravi V, Rubin BP, Park M, Loggers ET, Cranmer LD, et al. Incidence, demographics, and survival of malignant hemangioendothelioma in the United States. Cancer Med. 2023 Jun 1;12(14):15101–6.
2. Epithelioid hemangioendothelioma [Internet]. [cited 2025 Apr 3]. Available from: https://www.pathologyoutlines.com/topic/softtissuehemangioendotheliomaepithelioid.html

3. The EHE Foundation [Internet]. [cited 2025 Apr 3]. EHE Clinical Trials. Available from: https://fightehe.org/ehe-clinical-trials/
4. Frezza AM, Leonard H, Aggerholm-Pedersen N, Badalamenti G, Baili P, Baldi GG, et al. The observational EURACAN prospective clinical registry dedicated to epithelioid hemangioendothelioma: The protocol of an international and collaborative effort on an ultra-rare entity. PLOS ONE. 2024 Aug 12;19(8):e0308387.
5. Stacchiotti S, Miah AB, Frezza AM, Messiou C, Morosi C, Caraceni A, et al. Epithelioid hemangioendothelioma, an ultra-rare cancer: a consensus paper from the community of experts. ESMO Open [Internet]. 2021 Jun 1 [cited 2025 Apr 3];6(3). Available from: https://www.esmoopen.com/article/S2059-7029(21)00130-7/fulltext

P8 – EPITHELIOID HEMANGIOENDOTHELIOMA IN BOSNIA AND HERZEGOVINA: A CASE SERIES ANALYSIS OF DIFFERENT TREATMENT STRATEGIES IN AN ULTRA-RARE CANCER

IVANA VUKOVIC, Bojana Golubovic, Nada Cicmil Sarić

[1]*Institute of Oncology, Clinical Center of Montenegro, Podgorica, Montenegro*

Introduction: Alpelisib is an alpha-specific inhibitor of class I phosphoinositide 3-kinase (PI3K alpha). Alpelisib is used as a second-line treatment for metastatic hormone receptor-positive breast cancer. According to study results and clinical practice guidelines, the progression-free survival (PFS) for alpelisib in second-line treatment of metastatic breast cancer (MBC) ranges from 7 to 11 months. Alpelisib was approved in Montenegro in February 2023; however, its clinical use began later in July 2023, as this period was necessary to obtain the first analyses of PIK3CA gene mutations. In Montenegro, at the Pathology Center of the Clinical Center of Montenegro, PIK3CA mutation testing was performed on 98 patients from June 2023 to November 2024. The most frequently detected mutation was in exon 21 of this gene. Out of the 98 samples analyzed during this period, analysis could not be performed in 7 cases due to insufficient or poor-quality samples or due to the duration of biopsy storage.

Aim: The objective of this study was to assess, through our clinical experience, the efficacy and safety of alpelisib in second-line treatment of HR-positive MBC and to determine whether our experience aligns with the results from global literature.

Methods: Data for the study were obtained from our medical reports. From November 2023 to November 2024, 14 patients with HR positive MBC were treated with alpelisib (Piqray) as second-line therapy at the Institute of Oncology of Montenegro. In the first line of treatment, 13 patients received CDK 4/6 inhibitors, while only one patient had previously been treated with capecitabine. The patients included in the study had a median age of approximately 60 years. Of the 14 patients included in the study, approximately 36% (5) had multiple metastases in different organs, while 64% (9) had metastases in a single organ system. The most common metastatic site was the bone system, affecting 50% of the patients, followed by the liver (31.4%) and lungs (29%).

Conclusions: During the period of approximately one year, 14 patients were treated with alpelisib at our Institute of Oncology. In the follow-up of one year, our results show that the most common adverse effect, as expected, was hyperglycemia. It developed in 5 patients (in 4, it was successfully managed with oral antidiabetic medications, while in 1 patient, therapy had to be discontinued). Of the 14 patients, 1 had an intense maculopapular rash, which required discontinuation of therapy. The duration of alpelisib therapy ranged from 1 to 11 months (median 5.5 months). In two patients, a fatal outcome occurred after 2

months of therapy, while in 2 others, therapy was discontinued due to the mentioned side effects (for two patients, we do not have data). Currently, of the 14 patients treated with alpelisib during this period, 8 patients remain on active treatment with alpelisib + Faslodex.

Keywords: alpelisib, PIK3CA mutation, experience

REFERENCES

1. Alexander Valerievich Sultanbaev et al; Results of a retrospective study on the efficacy and safety of alpelisib in patients with HR+/HER2– metastatic breast cancer in real-world clinical practice. Journal of Clinical Oncology, 2024;42(16_ suppl.):e13058
2. Fabrice André, M.D et al: SOLAR-1 Study Group, Alpelisib for PIK3CA-mutated, hormone receptor–positive advanced breast cancer.N Engl J Med 2019;380:1929-1940, DOI: 10.1056/NEJMoa1813904
3. Turner S, et al. Effectiveness of alpelisib + fulvestrant compared with real-world standard treatment among patients with HR+, HER2-, PIK3CA-mutated breast cancer. Oncologist. 2021 Jul;26(7):e1133-e1142.doi: 10.1002/onco.13804.

P9 – DESCRIPTIVE ANALYSIS: CHARACTERISTICS OF PATIENTS WITH HIGH-GRADE OVARIAN CANCER ON MAINTENANCE OLAPARIB THERAPY WITH BEVACIZUMAB IN MONTENEGRO VS THE PAOLA-1 STUDY

IVANA VUKOVIC, Sanja Lekic, Bojana Scekic, Bojana Golubovic

[1]*Institute of Oncology, Clinical Center of Montenegro, Podgorica, Montenegro*

Introduction: In Montenegro, the drug olaparib for the PAOLA-1 indication has been on the positive list of medicines since February 2022. The PAOLA-1 study investigates the addition of olaparib to standard therapy with bevacizumab in maintenance therapy for patients with initial high-grade serous or endometrioid ovarian cancer, focusing on those who are HRD positive.

Aims: To analyze the characteristics of ovarian cancer patients at FIGO stage III/IV who are HRD mutation positive in Montenegro and compare them with the characteristics of patients from the PAOLA-1 study. We analyzed age, ECOG PS, histological subtype, FIGO stage, surgical interventions and outcomes, and HRD/BRCA status.

Methods: Data for this descriptive analysis were obtained from medical reports from the Institute of Oncology in Montenegro from November 2022 to April 2025, since the start of HRD/BRCA testing in Montenegro.

Results: During this period, genetic testing for HRD mutations was conducted for 28 patients in Montenegro, with 14 patients found positive for HRD mutation with initially high-grade ovarian cancer. Of the 14 HRD – positive patients, 11 began maintenance therapy with olaparib combined with bevacizumab as per PAOLA-1 study indications (two are still undergoing chemotherapy, and one discontinued specific oncological treatment due to EF dropping to 25%). The average disease onset age was 62 years (PAOLA-1 study: 61), and all patients were initially in relatively good general health status, ECOG 0-2 (100% of patients). In terms of disease stage, in Montenegro, 8 patients had FIGO stage III (5 with FIGO IIIA and 3

with FIGO IIIC – 73.73%), and 3 had FIGO stage IV – 27.27% (PAOLA-1 study: 70% FIGO stage III and 30% FIGO stage IV). Most patients initially received cytoreductive surgery – 8 (72.72% – one was treated initially with the HIPEC procedure); in 2 patients no surgical treatment was conducted (18.18%) and in 1 patient (9.09%) interval debulking surgery was performed (PAOLA-1 study: 85% underwent initial cytoreduction, 5% with no surgical treatment, and 10% with interval debulking surgery). The median follow-up was 9.3 months, with 36% having a BRCA mutation and 64% being BRCA non-mutated (PAOLA-1 study: 30% BRCA mutation, 70% non-BRCA mutation).

Conclusions: Comparing the characteristics of ovarian cancer patients at FIGO III/IV stage who are HRD positive from our study with patients from the PAOLA-1 study, significant similarities are observed. Both groups have a similar age structure (mainly over 50 years) and similar disease stage patterns (primarily at stage III, with most of ours at FIGO IIIA stage). Most patients, both in our study and in the PAOLA-1 study, underwent cytoreductive surgery, either primary or interval, to optimize treatment outcomes. Additionally, the genetic profile focusing on HRD and BRCA mutations was quite similar, enhancing the understanding of the specific treatments impact and the potential for olaparib combined with bevacizumab in these high-risk groups. These findings support the personalization of therapeutic strategies and highlight the importance of genetic testing in shaping treatment approaches for ovarian cancer patients.

Keywords: lynparza, characteristics of patients

REFERENCES

1. Ray-Coquard I et al. Olaparib plus bevacizumab as first-line maintenance in ovarian cancer. N Engl J Med. 2019;381:2416–28
2. Moore K et al. Maintenance olaparib in patients with newly diagnosed advanced ovarian cancer. N Engl J Med. 2018;379(26):2495–2505.
3. Colombo N et al. ESMO-ESGO consensus conference recommendations on ovarian cancer: pathology and molecular biology, early and advanced stages, borderline tumors, and recurrent disease. Annals Oncol. 2019;30:672–705. doi:10.1093/annonc/mdz062.
4. Summary of Product Characteristics (SmPC), Lynparza, July 2023 Available from: chromeextension://efaidnbmnnnibpcajpcglclefindmkaj/https://www.ema.europa.eu/en/documents/variation-report/lynparza-h-c-ws2463-epar-assessment-report-variation_en.pdf

P10 – DEVELOPMENT OF MEDICATION RELATED OSTEONECROSIS OF THE JAW IN PATIENTS WITH HR-POSITIVE HER2-NEGATIVE METASTATIC BREAST CANCER TREATED WITH CYCLE-DEPENDENT KINASE 4/6 INHIBITORS AND ANTIRESORPTIVE THERAPY

IVO TODORIĆ[1], Luka Trkmić[1], Tomislav Tokić[1], Marija Križić[2], Katarina Čular[2], Natalija Dedić Plavetić[1,2], Marko Granić[3], Tajana Silovski[1,2]

[1]*Medical School, University of Zagreb, Zagreb, Crioatia*
[2]*Department of Medical Oncology, University Hospital Centre Zagreb, Zagreb, Croatia*
[3]*Department of Pathology and Cytology, Sestre milosrdnice University Hospital Centre, Zagreb, Croatia*
[4]*Department of Oncology, University Hospital Centre Zagreb, Zagreb, Croatia*

Introduction: Antiresorptive therapy (ART) is used for the treatment of patients with advanced cancer and bone metastases. Medication Related Osteonecrosis of the Jaw (MRONJ) is known side effect of all ART agents like denosumab and bisphosphonate – more often of those given intravenously like zoledronate, rather than those taken orally like ibandronate. According to the literature, with every passing year of ART, the risk of developing MRONJ doubles. The aim of the conducted study was to determine the correlation of MRONJ development in patients with hormone receptor positive, HER2 negative (HR+/HER2-) metastatic breast carcinoma (mBC) treated with cycle-dependent kinase 4/6 inhibitors (CDK4/6i) and ART.

Methods: The conducted retrospective study analyzed patients with HR+/HER– mBC who were treated with CDK4/6i in first or subsequent lines of therapy and ART at University Hospital Centre Zagreb, with prior Ethics Committee approval. Characteristics of treatment pattern (antitumor drugs, type and duration of ART) in patients who developed MRONJ, were thoroughly examined and analyzed.

Results: Among 388 patients with HR+/HER– mBC treated with CDK4/6 inhibitors, 275 had bone metastasis and were treated with ART. Of those, 15 developed MRONJ – in 10 patients MRONJ occurred during and in 5 patients after stopping of CDK4/6i treatment. Among 164 patients who were taking ribociclib, 73.8% (121/164) had bone metastasis and 7.4% (9/121) developed MRONJ. Of overall 65 patients on abemaciclib, 61.5% (40/65) had bone metastases and were treated by ART, and 7.5% (3/40) developed MRONJ. Finally, among 160 patients treated with palbociclib, 71.3% (114/160) had bone metastasis, and 2.6% (3/114) developed MRONJ. Considering ART, at the time of MRONJ diagnosis, 7 patients were receiving zoledronate, 4 denosumab, and 4 peroral ibandronate. The median duration of ART that led to the development of MRONJ was 26.5 months.

Conclusions: According to the obtained results, although this study encompassed a small number of patients, it seems that development of MRONJ is less likely to develop in patients with HR+/HER2– mBC with bone metastases treated with CDK4/6i palbociclib and ART in comparison to those treated with ribociclib and abemaciclib. MRONJ could also more commonly occur in patients treated with zoledronate especially in those receiving ART for longer than 2 years. Further studies with larger cohorts are needed to confirm this preliminary observations.

Keywords: MRONJ, metastatic breast cancer, CDK4/6 inhibitors, ART

REFERENCES

1. Bedogni A, Mauceri R, Fusco V, Bertoldo F, Bettini G, Di Fede O, et al. Italian position paper (SIPMO-SICMF) oncmedication-related osteonecrosis of the jaw (MRONJ). Oral Dis. 2024 Sep;30(6):3679-3709.
2. Marcianò A, Guzzo GM, Peditto M, Picone A, Oteri G. Medication-related osteonecrosis of the jaws and CDK4/6 inhibitors: A recent association. Int J Environ Res Public Health. 2020 Decc18;17(24):9509.
3. Senín LD, Pancorbo DM, Garcés MYR, Santos-Rubio MD, Calero JB. Relationship between medication-related osteonecrosis of the jaw and CDK4/6 inhibitors in breast cancer. CurrcOncol. 2024 Jan 1;31(1):250-259.

P11 – APLASTIC ANEMIA CAUSED BY CHEMOIMMUNOTHERAPY IN PATIENT WITH LUNG CANCER: A CASE REPORT

IVO DILBER[1], Ivan Zekanović[2], Mirisa Tokić[1], Katarina Horvat Pavlov[3], Kata Međugorac[4]

[1]*Department of Oncology and Nuclear Medicine, Zadar General Hospital, Zadar, Croatia*
[2]*Department of Hematology, Zadar General Hospital, Zadar, Croatia*
[3]*School of Dental Medicine, University of Zagreb, Zagreb, Croatia*

Case report: Hematologic side effects caused by immunotherapy (ICI) are rare but often pose a challenge in the differential diagnosis of cytopenia (1, 2, 3). We present a 66-year-old male caucasian, being treated for heart failure, arterial hypertension and diabetes, who was diagnosed with lung adenocarcinoma with metastases in both lungs and the pleura. PD-L1 expression was 1%, while predictive biomarkers (EGFR, ALK, ROS1, MET, RET) were negative. The patient had no prior history of known hematological diseases, either personally or in the family. Ten days after the second cycle of chemoimmunotherapy, the patient was admitted to the hospital with febrile neutropenia accompanied by high inflammatory markers. He also presented with skin rash on his chest and back. Total leukocytes were 0.4 (3.4–9.7×10 9 /L), erythrocytes 3.65×10 12 /L, hemoglobin 120 (128-175 g/L), RDW-CV 10.7%, platelets 102 (158-424×10 9 /L), along with acute kidney failure. In follow-up lab tests after multiple administrations of filgrastim, there was no recovery in leukocyte count, with hemoglobin dropping to 108g/L and platelets to 49×10 9 /L. There were no signs of hemolysis. Given the poor bone marrow response to G-CSF stimulation, a cytological bone marrow puncture was performed, indicating suspected bone marrow aplasia, and treatment with corticosteroids (metilprednisolone 1 mg/kg) was initiated along with platelet and red blood cell transfusions. A subsequent bone biopsy supported a diagnosis of aplastic anemia. The bone trabeculae

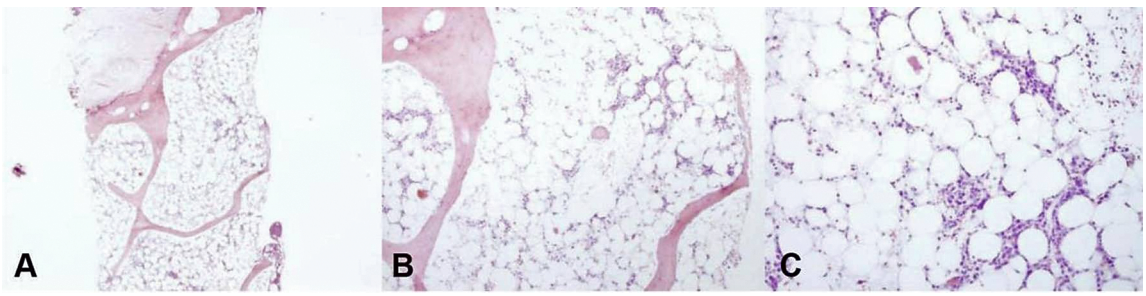

Figure 1. *Hypocellular bone marrow, consisting of only 10% of haematopoetic cells. A. HE (×4). B. HE (×10). C. Only few megakaryocytes, reduced maturation of granulocytes, reduced erythropoesis morphologically without changes, HE (×40).*

were described as normal, while the bone marrow was described as severely hypocellular, with about 10% hematopoietic cells. Only a few megakaryocytes, morphologically normal, were observed. Granulopoiesis maturation was reduced, with only rare erythroblasts (Figure 1). The patient experienced gradual but slow recovery of granulopoiesis, with prolonged anemia and thrombocytopenia (lowest hemoglobin 54 g/L, platelets 22×10 9 /L). Leukocytes and granulocytes recovered during period of three weeks, thrombocytes in two months and erythrocytes in eighteen months. After the start of corticosteroide administration skin rash disappeared. Given the treatment side effects and worsening clinical condition, active oncological treatment was discontinued. Clinicians should be aware that any of the medications used to treat lung adenocarcinoma can potentially cause severe pancytopenia, including aplastic anemia.

Keywords: aplastic anemia, lung cancer, chemotherapy, immunotherapy, pancytopenia, side effects

REFERENCES

1. Wright JJ, Powers AC, Johnson DB. Endocrine toxicities of immune checkpoint inhibitors. Nat Rev Endocrinol. 2021 Jul;17(7):389-399. doi: 10.1038/s41574-021– 00484-3.
2. Jessel S, Weiss SA, Austin M, et al. Immune checkpoint inhibitor-induced hypophysitis and patterns of loss of pituitary function. Front Oncol. 2022 Mar 8;12:836859. doi: 10.3389/fonc.2022.836859.
3. Guo Q, Zhao JN, Liu T, et al. Immune checkpoint inhibitor-induced aplastic anaemia: Case series and large-scale pharmacovigilance analysis. Front Pharmacol. 2023 Jan 26;14:1057134. doi: 10.3389/fphar.2023.1057134.

P12 – RARE BUT REAL: TREATING METASTATIC MAMMARY-LIKE ADENOCARCINOMA OF THE VULVA AS TRIPLE-NEGATIVE BREAST CANCER

JOVANA TRIFUNOVIĆ[1], Nemanja Trifunović[2], Sara Filipović[1], Nemanja Stevanović[1], Miroslav Kreačić[1]

[1]*Oncology Hospital, Clinical Hospital Center Zemun, Belgrade, Serbia*
[2]*Department of General Surgery, Clinical Hospital Center Zemun, Belgrade, Serbia*

Introduction: Mammary-like adenocarcinoma of the vulva (MLAV) is an extremely rare malignant neoplasm arising from anogenital mammary-like glands, structures first described as part of normal vulvar histology. Adenocarcinomas constitute less than 0.1% of all vulvar malignancies, with MLAV representing an even rarer subtype. Since its initial description in 1936, only around 40 cases have been documented by 2022. Histologically and molecularly, MLAV closely resembles breast carcinoma, and all four intrinsic breast cancer subtypes—luminal A, luminal B, HER2-enriched, and basal-like—have been identified in MLAV. Despite this, no specific treatment guidelines exist in the ESMO, NCCN, or St. Gallen recommendations. Management is therefore modeled on breast cancer protocols, tailored to the tumor's immunohistochemical profile and stage.

Case report: A 65-year-old woman presented with a solitary lesion on the right labia majora. Excisional biopsy was initially interpreted within the differential of Paget's disease. Six months later, she developed right-sided inguinal lymphadenopathy, and lymphadenectomy was performed. Histopathological analysis revealed infiltrating adenocarcinoma with transition from mammary– like glands, confirming MLAV. Immunohistochemistry showed expression of GATA3, GCDFP– 15, CK7 (CK20–), and patchy presence of myoepithelial markers (SMA, p63), while ER and HER2 were negative or low-positive.

Paget-like epidermotropism was also observed. Staging CT revealed metastatic disease in the liver and bones, with a pathological fracture at L1. Given the triple-negative profile, therapy was initiated according to the triple-negative breast cancer (TNBC) paradigm. Palliative radiotherapy was applied to the spine, followed by systemic chemotherapy with paclitaxel and carboplatin. After five cycles, hepatic lesions showed regression, but bone disease progressed. Due to an allergic reaction to paclitaxel, characterized by hypotension, flushing, and laryngospasm, treatment was switched to capecitabine. The patient is currently on the third cycle, with preserved general condition (ECOG PS 1).

Conclusions: This case illustrates the clinical variability of MLAV—from indolent, skin-localized forms amenable to conservative surgery, to aggressive metastatic disease requiring systemic therapy. Although some authors propose a predominantly local growth pattern with rare metastasis, our case underscores the need to recognize the full biological spectrum of this tumor type. The application of breast cancer molecular profiling and treatment algorithms appears rational and may inform clinical decision-making, especially for advanced or triple-negative tumors. Given+ the extreme rarity and heterogeneity of MLAV, a multidisciplinary and individualized approach remains essential. Further research and case aggregation are needed to better define diagnostic criteria, molecular subtypes, and optimal therapeutic strategies.

Keywords: mammary-like adenocarcinoma, MLAV, adenocarcinoma, triple-negative breast cancer

REFERENCES

1. Tessier-Cloutier B, Asleh-Aburaya K, Shah V, McCluggage WG, Tinker A, Gilks CB. Molecular subtyping of mammary-like adenocarcinoma of the vulva shows molecular similarity to breast carcinomas. Histopathology. 2017 Jun;70(7):1144–50. doi: 10.1111/his.13159.
2. Senkus E, Kyriakides S, Ohno S, Penault-Llorca F, Poortmans P, Rutgers E, et al. Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2015 Sep;26(Suppl 5):v8–v30. doi: 10.1093/annonc/mdv298
3. Abbott JJ, Ahmed I. Adenocarcinoma of mammary-like glands of the vulva: Report of a case and review of the literature. Am J Dermatopathol. 2006 Apr;28(2):127-33. doi: 10.1097/01.dad.0000171601.25315.2b.
4. Baykal C, Dünder I, Turkmen IC, Ozyar E. An unusual case of mammary gland-like carcinoma of vulva: Case report and review of literature. Eur J Gynaecol Oncol. 2015;36(3): 333-4.

P13 – LIVER TRANSPLANTATION IN A PATIENT WITH HEPATOCELLULAR CARCINOMA AND CHRONIC HEPATITIS C: THE ROLE OF DOWNSTAGING WITH IMMUNOTHERAPY

JOSIP BASIĆ[1], Ivan Romić[2], Hrvoje Silovski[2]

[1]*School of Medicine, University of Zagreb, Zagreb, Croatia*
[2]*Department of Surgery, University Hospital Center Zagreb, Zagreb, Croatia*

Introduction: Hepatocellular carcinoma (HCC) is the most common primary liver malignancy, typically developing in the context of chronic liver disease. Major risk factors include cirrhosis due to chronic hepatitis B or C infection, alcohol abuse, and metabolic dysfunction-associated steatohepatitis. HCC is the fourth leading cause of cancer-related mortality worldwide, with a five-year survival rate of approximately 18%. Late diagnosis remains a major challenge, often due to asymptomatic early disease and inad-

equate surveillance of at-risk populations. Recently, immunotherapy has emerged as a significant advancement in the treatment of unresectable or advanced-stage HCC, particularly the combination of atezolizumab (anti–PD– L1) and bevacizumab (anti–VEGF), which has demonstrated improved survival outcomes compared to sorafenib in first-line therapy. We present a case of hepatocellular carcinoma treated with immunotherapy that resulted in downstaging which allowed a successful liver transplant.

Case report: A 69-year-old male was initially evaluated in 2018 for elevated liver enzymes. Serology confirmed chronic HCV infection (genotype 3a, HCV RNA 6.34 IU/mL), but antiviral therapy was not initiated. Contributing factors included the absence of symptoms and limited DAA availability. In 2019, the patient was diagnosed with cryoglobulinemia, a known extrahepatic manifestation of HCV. In September 2021, a rise in alpha-fetoprotein (AFP) and hepatic nodules on imaging raised suspicion for HCC. A contrast-enhanced multislice CT in December 2021 revealed multifocal liver lesions. Fine-needle aspiration in February 2022 confirmed well-differentiated HCC. Transarterial chemoembolization (TACE) was performed in April 2022. Antiviral therapy with glecaprevir/pibrentasvir (May–August 2022) led to sustained virologic response. In December 2022, systemic therapy with atezolizumab and bevacizumab was started. Follow– up imaging in February 2024 showed partial regression, with one lesion showing progression. In March 2024, staging confirmed the disease remained confined to the liver. A successful liver transplantation was performed in April 2024. The postoperative course was uneventful, with only minor ischemic changes noted.

Conclusions: This case underscores the risk of HCC in patients with undiagnosed or untreated chronic hepatitis C, even in the absence of symptoms. Early screening and prompt initiation of antiviral therapy are essential to prevent malignant progression. The introduction of immune checkpoint inhibitors, such as atezolizumab combined with bevacizumab, offers new therapeutic options for patients with advanced disease. In select cases, timely intervention can enable curative approaches like liver transplantation.

Keywords: hepatocellular carcinoma, hepatitis C, immunotherapy, liver transplantation

REFERENCES

1. El-Serag HB, Kanwal F. Epidemiology, risk factors, and diagnosis of hepatocellular carcinoma. UpToDate. Available at: https://www.uptodate.com/contents/epidemiology-risk-factors-and-diagnosis-of– hepatocellular-carcinoma
2. Singal AG, Lampertico P, Nahon P. Epidemiology and surveillance for hepatocellular carcinoma: New trends. J Hepatol. 2020;72(2):250–261. doi:10.1016/j.jhep.2019.08.025
3. Kanwal F, Kramer JR, Asch SM, Cao Y, El-Serag HB. Risk of hepatocellular cancer in HCV patients treated with direct-acting antiviral agents. Gastroenterology. 2017;152(3):640–653.e1. doi:10.1053/j.gastro.2016.11.006
4. Finn RS, Qin S, Ikeda M, et al. Atezolizumab plus bevacizumab in unresectable hepatocellular carcinoma. N Engl J Med. 2020;382(20):1894–1905. doi:10.1056/NEJMoa1915745

P14 – REAL-WORLD DATA OF PEMBROLIZUMAB MONOTHERAPY IN THE TREATMENT OF METASTATIC NON-SMALL CELL LUNG CANCER (NSCLC) – EXPERIENCE FROM THE INSTITUTE FOR ONCOLOGY AND RADIOLOGY OF SERBIA (IORS)

KATARINA LJUJIĆ, Feđa Đorđević, Dimitrije Kolović, Andrijana Kojić, Nemanja Stanić, Neda Nikolić, Jelena Spasić

Institute for Oncology and Radiology of Serbia, Belgrade, Serbia

Introduction: Pembrolizumab is a standard therapeutic option for the treatment of patients with advanced NSCLC with programmed cell death-ligand 1 (PD-L1) expression ≥ 50%, either as monotherapy or in combination with platinum-based chemotherapy. 1 Real-world data regarding the efficacy and safety of drugs have become a valuable source of information for patients, clinicians and regulators, since real-world settings may greatly differ from clinical trials.

Aim: The aim of this analysis is to present real-world data of pembrolizumab monotherapy in patients with metastatic NSCLC and PD-L1≥50% treated at IORS.

Results: Data from 100 consecutive patients were obtained from hospital medical records. The median age of patients was 64 years, with a range from 20 to 87 years, 59 were male and 41 female. In the group, 56% of patients had never smoked, 33% had formerly smoked, and 11% were actively smoking at the start of treatment. Most patients had ECOG PS 1 (60%), while 15% had ECOG PS 0 and 25% had ECOG PS 2. Adenocarcinoma was the most common histological subtype, present in 70% of patients, followed by squamous cell carcinoma in 25%, and not otherwise specified (NOS), in 5%. At the start of treatment, 89% of patients had two or more metastatic sites. The most common metastatic sites were lungs, pleura, brain, bones, and adrenal glands respectively. Expression levels of PD-L1 were between 50-60% in 32 patients, 61-70% in 19, 71-80% in 23, 81-90% in 16, and 91-100% in 10 patients. The best response of partial regression was registered in 36% of patients, stable disease in 41%, and disease progression in 19%. Following progression, 16% of patients received chemotherapy, 7% were treated with radiotherapy, and 5% were treated with both modalities. Immune-related adverse events were registered in 26% of patients. The most commonly observed toxicities were skin changes (8%) and arthritis (7%). Pembrolizumab was permanently discontinued in 3 patients due to grade 3 or 4 toxicity including pneumonitis, mucositis and skin toxicity. At the time of analysis, 33 patients remained on pembrolizumab, while 59 patients had died. The median time to progression was 13.86 months (95% CI, 7.25-20.48), and overall survival was 19.25 months (95% CI, 12.93– 25.57).

Conclusions: The experience of pembrolizumab monotherapy as first-line treatment of patients with NSCLC and PD-L1 expression of ≥ 50% at IORS aligns with literature data regarding efficacy and safety. Investigations are continuing on a larger group of our patients treated with pembrolizumab, also evaluating potential predictive markers of response and toxicity.

Keywords: pembrolizumab, NSCLC, PD-L1

REFERENCES

1. Hendriks LE, Kerr K, Menis J, et al. Non-oncogene-addicted metastatic non-small-cell lung cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up Annals of Oncology. 2023;34(4):358 – 376.

P15 – CLINICAL CHARACTERISTICS AND OUTCOMES OF SHORT-TERM RESPONDERS TO CDK4/6 INHIBITORS IN HR+/HER2– mBC

KATARINA ČULAR[1], Kristina Kanceljak[1], Marija Križić[1], Marina Popović[1,2], Natalija Dedić Plavetić[1,2], Tajana Silovski[1,2]

[1]*Department of Oncology, University Hospital Center Zagreb, Zagreb, Croatia*
[2]*School of Medicine, University of Zagreb, Zagreb, Croatia*

Introduction: The standard first-line treatment of hormone receptor (HR) positive/ HER2 negative metastatic breast cancer (mBC) is the combination of CDK 4/6 inhibitors (CDK4/6i) and endocrine therapy (ET), which has been proven to prolong overall survival (OS) in multiple studies. Despite the widespread use of CDK4/6i, there are no markers in clinical practice that could predict tumor response.

Methods: This retrospective study included 411 patients with HR+, HER2– mBC treated with ET and CDK4/6i between August 2018 and August 2024 at the University Hospital Centre Zagreb, with prior Ethics committee approval. A cohort of patients with treatment durations shorter than 6 months was identified, and patient demographics, clinical presentation, tumor characteristics, and treatment data were collected. OS analysis was done with the final data cut– off date of December 31, 2023, using type 1 right censoring.

Results: A cohort of 21.4% (88/411) of patients with CDK4/6i treatment duration less than 6 months was identified, 45.45% (N=40) of whom stopped due to disease progression. Only 15% (N=6) were endocrine sensitive, while primary endocrine resistance was noted in 32.5% (N=13) and secondary in 52.5% (N=21) of patients. CDK4/6i were first-line treatment for 23 patients, second-line for 2, and third or higher line for 16. Most patients, 70% (N=32), had visceral metastases, 25 of whom had liver metastases. Bone marrow infiltration was present in 5 patients, and brain metastases in 8. Of the short-term responders, 38 died in the follow-up period. Median OS for these patients was 14 months (95% CI 10-18), significantly shorter than the median OS for the overall patient group, which was 32 months (95% CI 29-35). Furthermore, 27.27% (N=24) of patients exhibited poor baseline performance status at treatment initiation, with therapy subsequently discontinued due to further deterioration in functional status or death due to malignancy or comorbidities. Treatment was stopped in 15.91% (N=14) of patients due to side effects. It is important to note that all side effects were grade 3 or lower, but dose reduction and reinduction were attempted in only 3 patients. In 5 patients, treatment was started based on the pathohistological diagnosis of the primary tumor, however, further diagnostic work-up found a change in tumor biology, and treatment was continued accordingly. Lastly, 4 patients stopped treatment of their own accord.

Conclusions: Patients who experienced rapid disease progression on CDK4/6i demonstrated significantly shorter overall survival (OS). This cohort had predominantly endocrine-resistant and biologically aggressive disease, underscoring the critical need to optimize first-line therapeutic strategies. Further investigation is warranted to identify predictive biomarkers that can more accurately predict therapeutic response.

Keywords: breast cancer, CDK 4/6 inhibitors, endocrine resistance

REFERENCES

1. Bui NQ, Wang Y, Chen K, Wang P. (2021). Biomarkers predictive of resistance to CDK4/6 inhibitors in metastatic breast cancer: A systematic review. JCO Precision Oncology. 2021; 5:403–417. Doi: 10.1200/PO.21.00002
2. Gyawali B, Nishikawa T, Shimokata T. (2022). Real-world outcomes of CDK4/6 inhibitors in HR-positive, HER2-negative advanced breast cancer: A systematic review. Future Oncology. 2022;18(3):199–209. doi: 10.2217/fon-2020-1264
3. Messina C, Cattrini C, Buzzatti G, Cerbone L, Zanardi E, Messina M, et al. (2018). CDK4/6 inhibitors in advanced hormone receptor-positive/HER2-negative breast cancer: a systematic review and meta-analysis of randomized trials. Breast Cancer Research and Treatment. 2018;172(1):9–21. Doi: 10.1007/s10549-018-4901-0

P16 – CHARACTERISTICS OF PATIENTS WITH MEDICATION-RELATED OSTEONECROSIS OF THE JAW INDUCED BY ANTIRESORPTIVE THERAPY

LAURA BARTA[1], Hrvoje Blažević[1], Klaudia Babić[1], Filip Jakov Klisović[1], Tomislav Bubalo[3], Roko Bjelica[2], Sven Bival[5], Marija Križić[4], Marko Granić[2], Tajana Silovski[1,4]

[1]*University of Zagreb School of Medicine, Zagreb, Croatia*
[2]*School of Dental Medicine, University of Zagreb, Zagreb, Croatia*
[3]*Department of Surgery, University Hospital Centre Zagreb, Zagreb, Croatia*
[4]*Department of Oncology, University Hospital Centre Zagreb, Zagreb, Croatia*
[5]*Bival Private Dental Clinic, Zagreb, Croatia*

Introduction: Antiresorptive drugs, such as bisphosphonates and denosumab, are used in the treatment of osteoporosis and malignant diseases, usually advanced, involving bone, with the aim of reducing the risk of skeletal-related events. Antiangiogenic drugs, like bevacizumab and sutinib, inhibit angiogenesis, and are used in the treatment of various advanced malignant diseases. Although both drug classes help patients improve their outcomes, quality of life and prognosis, they also have some serious adverse effects such as increased risk of Medication– Related Osteonecrosis of the Jaw (MRONJ).

Methods: This retrospective study investigated the characteristics of patients treated at the University Hospital Center Zagreb for MRONJ since January 2020 to December 2024. The inclusion criterion was the development of MRONJ upon application of antiresorptive therapy, without previous radiation therapy and/or metastases in the jaws.

Results: The conducted study analysed total of 145 patients treated for MRONJ in UHC Zagreb. There were more women (69%, 100/145) with median age of 68 years than men (31%, 45/145), median age of 67 years. Among all patients, in 24.8% (36/145), antiresorptive therapy was used for treating osteoporosis, and in 75.2% (109/145) for treating malignant disease. The malignant disease diagnoses included 28.3% (41/145) cases of breast cancer, 23.5% (34/145) multiple myeloma, 7.6% (11/145) prostate cancer, 6.9% (10/145) lung cancer, 4.9% (7/145) kidney cancer, and 9.6% (2/145) of thyroid cancer, osteosarcoma, and lymphoma each.

The most prescribed drug was zoledronate, used in 53.1% of patients, with an average time to MRONJ development of 32.8 months from the beginning of therapy, while only 2.1% of patients received pamidronate and developed MRONJ after 48.7 months. Denosumab was administered to 20% of patients, who developed MRONJ after an average of 35 months. Ibandronate was prescribed in 19.2%, risedronate in 3.5% and alendronate in 2.1% of patients with MRONJ diagnosed after an average of 41.2, 33.5 and 38.9 months respectively.

Conclusions: Although antiresorptive therapy is a cornerstone of treatment in patients with malignant diseases and bone affection and is therefore often inevitable, this study emphasizes the need for regular dental check-ups before and during treatment. Additionally, it suggests exploring possible strategies to reduce the frequency of MRONJ, such as shortening the duration of antiresorptive therapy or implementing treatment interruptions. Such measures could contribute to reducing the risk of developing MRONJ while ensuring effective therapy and maintaining quality of life in patients with malignant disease.

Keywords: malignant disease, MRONJ, antiresorptive drugs

REFERENCES

1. Ebina K, Etani Y, Noguchi T, Nakata K, Okada S. Clinical effects of teriparatide, abaloparatide, and romosozumab in postmenopausal osteoporosis. J Bone Miner Metab. 2025 Jan;43(1):3-9.
2. Gupta M, Gupta N. Bisphosphonate related jaw osteonecrosis. [Updated 2023 Jul 24]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan.Available on: https://www.ncbi.nlm.nih.gov/books/NBK534771/
3. Byrne H, O'Reilly S, Weadick CS, Brady P, Ríordáin RN. How we manage medication– related osteonecrosis of the jaw. Eur J Med Res. 2024 Aug 2;29(1):402.

P17 – IMPACT OF CKD4/6 INHIBITORS SWITCH IN HR+/HER2– METASTATIC BREAST CANCER TREATMENT: A SINGLE-CENTER EXPERIENCE

KRISTINA KANCELJAK[1], Katarina Čular[1], Ana Kelečić[1], Martina Matec[1], Marija Križić[1], Marina Popović[1], Natalija Dedić Plavetić[1,2], Tajana Silovski[1,2]

[1]*Department of Oncology, University Hospital Center Zagreb, Zagreb, Croatia*
[2]*School of Medicine, University of Zagreb, Zagreb Croatia*

Introduction: CDK4/6 inhibitors (CDK4/6i) have significantly improved outcomes in hormone receptor-positive HER2-negative (HR+/HER2-) metastatic breast cancer (mBC). Although generally well tolerated, differences in toxicity profiles can lead to treatment discontinuation or switching between agents. This study aimed to analyze reasons for switching of CDK4/6i, characterize the adverse events (AEs) by severity, and assess treatment duration before and after the switch.

Methods: Retrospective analysis of 389 patients with HR+/HER2– mBC treated between 2019 and 2024 in University Hospital Center Zagreb was conducted with prior Ethics Committee approval. Among them, 48 patients (12.3%) underwent a switch from one CDK4/6i to another. Data were collected on AE type and grade (CTCAE v5.0), treatment duration with each CDK4/6i, and reasons for discontinuation.

Results: Among the 48 patients who underwent a CDK4/6i switch, the most common first-line agent was ribociclib (n=28), followed by abemaciclib (n=15) and palbociclib (n=5). The majority of switches were due to adverse events (n=42), and minority due to oligoprogression (n=3) or patient choice (n=1). The most common toxicities leading to discontinuation of the first CDK4/6i were hepatotoxicity in 12 (28.6%), diarrhea in 9 (21.4%), cardiotoxicity in 7 (16.7%), hematologic toxicity in 4 (9.5%) patients. Grade 4 toxicities were reported exclusively with ribociclib in overall 11.9% (5/42) of cases (hepatotoxicity in 4 and cardiotoxicity 1 patient). Grade 3 toxicities were reported in 47.6% (20/42) of all patients most frequently with ribociclib in 65% (13/20) of cases (most often hepatotoxicity in 6 and cardiotoxicity in 4 patients), followed by abemaciclib in 30% (6/20) of patients (most often diarrhea in 2 and hematologic toxicity in 2 cases). Palbociclib showed the lowest incidence of grade ≥3 toxicity, with a single case of grade 3 hematologic toxicity. The median treatment duration on the first CDK4/6i was 5 cycles (mean 10.19), while on the second CDK4/6i it was longer, 13.5 cycles (mean 16.08), indicating better tolerability or disease control after switching. At the time of data cut-off, 16 patients were still receiving the second CDK4/6i. Discontinuation of the second agent occurred due to disease progression (n=19), deterioration in general condition (n=5), hepatotoxicity, pulmonary embolism, sepsis, death, or loss to follow-up.

Conclusions: Switching between CDK4/6i is a legitimate strategy in patients experiencing toxicity or oligoprogression. The collected data suggest that patients may benefit from second CDK4/6i, even after discontinuation of the first due to toxicity. These data support a tailored approach for CDK4/6i selection and sequence in routine clinical practice.

Keywords: CDK4/6 inhibitors, metastatic breast cancer, adverse events

REFERENCES

1. Garufi C, et al. Advancing treatment choices: CDK4/6 inhibitor switching in HR+/HER2– metastatic breast cancer. ESMO Open. 2024;9(1):10024.
2. Gamucci T, et al. Late onset toxicities associated with the use of CDK4/6 inhibitors in metastatic breast cancer: A real-world experience. Breast. 2023;66:1-7.

P18 – FIRST EXPERIENCE WITH ANTIBODY-DRUG CONJUGATES TRASTUZUMAB DERUXTECAN AND SACITUZUMAB-GOVITECAN IN HEAVILY PRETREATED PATIENTS WITH METASTATIC BREAST CANCER

LAZAR POPOVIĆ[1,2], Maja Popović[1,2], Stela Novak[1], Ivana Kolarov-Bjelobrk[1,2], Bojana Vranjković[1], Stefan Đurić[1], Teodora Urošević[1], Nemanja Maletin[2], Gorana Matovina-Brko[1]

[1]*Oncology Institute of Vojvodina, Sremska Kamenica, Serbia*
[2]*Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia*

Introduction: Antibody-drug conjugates (ADCs) represent the standard of care for different subtypes of breast cancer. Trastuzumab-deruxtecan (T-Dxd) has shown benefit in the treatment of both HER2–positive and HER2-low breast cancer. Sacituzumab-govitecan (SG) is registered for the treatment of metastatic triple-negative (TNBC) and HR+/HER2– breast cancer. In our country, the use of ADC is reimbursed in heavily pretreated patients (Article 9).

Methods: In our institution, ADC received 28 patients, 17 T-Dxd, 11 SG. In the T-Dxd group, 14 were treated for HER2-positive cancer, while three patients were HER2-low (2 TNBC, 1 HR+). SG was received by 11 patients with TNBC.

Results: The median age of patients treated with T-Dxd was 55 years (31-74). The median number of previously received lines in metastatic disease was 4 (1-7). Two patients had brain metastases. The objective response rate (ORR) was 35.2% (5.8% CR 29.4% PR) in the total patient population, while in the HER2-positive group it was 42.8% (7.1% CR, 35.7% PR). The clinical benefit rate (CBR) was 52.9% in the overall and 50% in the HER2-positive population. The median time to disease progression (PFS) was 7 months in both populations. Diarrhea G1 was recorded in one patient, fatigue G1 in one, and anemia G4 in one. There were no patients with interstitial lung disease. The median age of patients treated with SG was 56 (35-66). Median previously received therapies in metastatic disease was 5 (3-8). Two patients had metastases in the CNS. The ORR was 9% (no CR). CBR was 36.4%. Median PFS was 4 months. Two patients had nausea, two fatigue, one diarrhea, one G4 neutropenia and one G4 anemia.

Conclusions: ADCs represent an effective option in pretreated patients with mBC, however, the inclusion of ADCs in earlier therapeutic lines would lead to better treatment outcomes for our patients.

Keywords: antibody-drug conjugates (ADCs), trastuzumab-deruxtecan (T-Dxd), sacituzumab-govitecan (SG)

REFERENCES

1. Cortés J, Kim SB, Chung WP, Im SA, Park YH, Hegg R, et al. Trastuzumab deruxtecan versus trastuzumab emtansine for breast cancer. N Engl J Med. 2022 Mar 24;386(12):1143– 1154.
2. Saura C, Modi S, Krop I, Park YH, Kim SB, Tamura K, et al. Trastuzumab deruxtecan in previously treated patients with HER2-positive metastatic breast cancer: updated survival results from a phase II trial (DESTINY-Breast01). Ann Oncol. 2024 Mar;35(3):302-307.
3. Modi S, Jacot W, Yamashita T, Sohn J, Vidal M, Tokunaga E, et al. Trastuzumab deruxtecan in previously treated HER2-low advanced breast cancer. N Engl J Med. 2022 Jul 7;387(1):9-20.
4. Bardia A, Hurvitz SA, Tolaney SM, Loirat D, Punie K, Oliveira M, et al. Sacituzumab govitecan in metastatic triple-negative breast cancer. N Engl J Med. 2021 Apr 22;384(16):1529-1541.
5. Rugo HS, Bardia A, Marmé F, Cortés J, Schmid P, Loirat D, et al. Overall survival with sacituzumab govitecan in hormone receptor-positive and human epidermal growth factor receptor 2-negative metastatic breast cancer (TROPiCS-02): a randomised, open-label, multicentre, phase 3 trial. Lancet. 2023 Oct 21;402(10411):1423-1433.

P19 – CORRELATION BETWEEN ADJUVANT CHEMOTHERAPY TREATMENT DECISION IN HR+/HER2– EARLY BREAST CANCER BEFORE AND AFTER MAMMAPRINT TEST: TWO-CENTER EXPERIENCE REPORT

LAZAR POPOVIĆ[1,2], Ana Cvetanović[3,4]

[1]*Oncology Institute of Vojvodina, Sremska Kamenica, Serbia*
[2]*Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia*
[3]*Clinic for Oncology, Clinical Center Niš, Niš, Serbia*
[4]*Faculty of medicine, University of Niš, Niš, Serbia*

Introduction: In patients with early HR+/HER2– stage T2 and/or N1, the decision on adjuvant chemotherapy is not always uniform. In MINDACT study Mammaprint test showed that in patients with T2 and/or N1 in low genomic risk group, do not benefit from addition of adjuvant chemotherapy to standard endocrine therapy. Because of this, mammaprint is used as a standard diagnostic procedure in the globally. In this paper, we tried to show in which percentage of patients mammaprint changes the decision on adjuvant therapy and in how it affects our regular practice.

Methods: We performed a total of 56 mammaprint tests in two centers, of which we have complete data for 47 patients. Two experienced oncologists with 15 (AC) and 20 (LP) years of experience in the treatment of breast cancer initially declared the need for adjuvant chemotherapy based on clinical parameters (age, T, N stage, receptor status, Ki67) before the mammaprint test, and then after receiving the results of the mammaprint test. The primary objectives were the level of correlation between the decisions of two oncologists before and after mammaprint testing, and the percentage of decision changes in terms of de-escalation

and escalation of therapy after mammaprint testing. Also, in the secondary objectives, we measured the degree of correlation of the progesterone receptor (PR) and the Ki67 index with the mammaprint result.

Results: In our series of 47 female patients, the median age was 50 (34-68), 34% were premenopausal, breast conserving surgery was performed in 61.7% of patients. The median tumor size was 18 mm (6-50), the median number of positive axillary lymph nodes (LN) was 1 (0-4), 13 patients had 0 positive LNs, 18 one, 11 two, 4 three and one patient 4 lymph nodes. Median Allred score for ER was 8 (6-8), PR 7 (0-8). The average Ki67 was 17% (7-55), 57.4% of patients had a Ki67 lower than 20%. Mammaprint result was Ultralow in one patient, low in 26 and high in 20 patients. All mammaprint high risk patients received chemotherapy, low and ultralow did not. Oncologist 1 (O1) had the decision to apply chemotherapy before mammaprint in 46.8% of cases, while oncologist 2 (O2) in 48.9%. Before mammaprint, chemotherapy decisions correlated within O1 and O2 in 80.9% of cases, after mammaprint in 100%. O1 changed the decision after mammaprint in 46.8% of cases, 28.8% in terms of chemotherapy de-escalation and 17% of cases in terms of escalation. O2 changed the decision in 53.2% of cases, 31.9% and 21.3% in terms of de-escalation and escalation, respectively. The Mammaprint result does not correlate with Ki67 values (cut off 20%) (rho=0.0968, p=0.5174), while it correlates with PR Allred score values less than 7 (rho=-0.385, p=0.0075).

Conclusions: In our series of patients, we demonstrated the importance of mammaprint testing, which can change the oncologist's decision in up to 53% of cases. Mammaprint significantly influences the decision on adjuvant therapy, and it is necessary that it be available in all countries of the region.

Keywords: adjuvant chemotherapy early breast cancer, mammaprint

REFERENCES

1. Cardoso F, Veer LJ, Bogaerts J, Slaets L, Viale G, Delaloge S, et al. 70-gene signature as an aid to treatment decisions in early-stage breast cancer. N Engl J Med. 2016 Aug 25;375(8):717-29.
2. Loibl S, André F, Bachelot T, Barrios CH, Bergh J, Burstein HJ, et al. ESMO Guidelines Committee. Early breast cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol. 2024
3. Piccart M, Veer LJ, Poncet C, Lopes Cardozo JMN, Delaloge S, Pierga JY, et al. 70-gene signature as an aid for treatment decisions in early breast cancer: updated results of the phase 3 randomised MINDACT trial with an exploratory analysis by age. Lancet Oncol. 2021 Apr;22(4):476-488.

P20 – SUSPECTED IPMN-B IN PATIENT WITH PSC/AIH OVERLAP SYNDROME

LEA BURILO[1], Ivan Romić[2], Hrvoje Silovski[2]

[1]*School of Medicine Zagreb, University of Zagreb, Zagreb, Croatia*
[2]*Department of Surgery, University Hospital Centre Zagreb, Zagreb, Croatia*

Introduction: Intraductal papillary mucinous neoplasm of the bile duct (IPMN-B) is a rare pre-cancerous lesion of the bile duct, a precursor to a biliary cholangiocarcinoma. It is considered to be analogous to intraductal papillary mucinous neoplasm of the pancreas (IPMN-P). Even though IPMN-P is well described, IPMN-B is, due to its rarity, not. Overlap syndrome of primary sclerosis cholangitis (PSC) and autoimmune hepatitis (AIH) is autoimmune liver disease with characteristics of both PSC and AIH, but

disease outcomes are usually similar to classical PSC phenotype. Thus, patients with PSC/AIH-overlap have higher chances of developing biliary tract tumors.

Case report: Here we present a 22-year-old female patient with overlap syndrome of PSC/AIH and suspected IPMN-B. The patient underwent magnetic resonance cholangiopancreatography (MRCP) and contrast-enhanced magnetic resonance imaging (MRI) which showed diffuse multifocal strictures of intrahepatic bile ducts characteristic for PSC, but also multilocular complex and smaller simple cystic lesions that communicate with the intrahepatic bile duct in both hepatic lobes. The biggest and most suspicious lesions were found in segments II and III of left lobe. Intraductal papillary mucinous neoplasm of bile duct was suspected. Liver resection of those two segments was performed and tissue samples were sent for histopathological diagnosis. Ultimately, pathohistological analysis revealed described changes are not characteristic to IPMN– B and instead indicate overlap syndrome of PSC/AIH. This case illustrates the difficulty of diagnosing IPMN-B, especially in patients with overlap syndrome of PSC/AIH. Even though IPMN-B was suspected due to radiological findings, the final diagnosis was related to changes of liver parenchyma as a result of PSC/AIH.

Conclusions: The presented case highlights the importance of meticulous clinical, radiologic and histopathological investigation when dealing with non– specific liver lesions.

Keywords: bile duct neoplasm, cholangitis, hepatitis, autoimmune

REFERENCES

1. Kraus M, Klang E, Soffer S, Inbar Y, Konen E, Sobeh T, Apter S. MRI features of intraductal papillary mucinous neoplasm of the bile ducts, *The myth about the cyst*: A systematic review. Eur J Radiol Open. 2023 Aug 12;11:100515. doi: 10.1016/j.ejro.2023.100515.
2. Rodríguez Vargas D, Parada Blázquez MJ, Vargas Serrano B. Intraductal papillary neoplasm of the bile duct: Radiologic findings in a new disease. Radiologia (Engl Ed). 2020 Jan-Feb;62(1):28-37. doi: 10.1016/j.rx.2019.07.003.
3. Ricciuto A, Kamath BM, Hirschfield GM, Trivedi PJ. Primary sclerosing cholangitis and overlap features of autoimmune hepatitis: A coming of age or an age-ist problem? J Hepatol. 2023 Aug;79(2):567-575. doi: 10.1016/j.jhep.2023.02.030.
4. Silveira MG, Lindor KD. Primary sclerosing cholangitis. Can J Gastroenterol. 2008 Aug;22(8):689-98. doi: 10.1155/2008/824168.

P21 – IMMUNOTHERAPY MAINTENANCE VERSUS IMMUNOTHERAPY AFTER PROGRESSION ON PLATINUM-BASED CHEMOTHERAPY IN THE TREATMENT OF LOCALLY ADVANCED OR METASTATIC UROTHELIAL CANCER

LAZAR POPOVIĆ[1,2], Maja Popović[1,2], Stefan Đurić[1], Nemanja Maletin[2], Teodora Urošević[1], Stela Novak[1], Gorana Matovina-Brko[1]

[1]*Oncology Institute of Vojvodina, Sremska Kamenica, Serbia*
[2]*Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia*

Introduction: Checkpoint inhibitors immunotherapy is a standard part of treatment for locally advanced or metastatic urothelial carcinoma (mUC). Initial clinical trials showed benefit of atezolizumab or pembrolizumab immunotherapy after progression to platinum-based chemotherapy. A few years later,

Javelin Bladder 100 (JB100) study was demonstrated longer progression-free survival (PFS) and overall survival if avelumab immunotherapy maintenance was added in patients without progression on platinum-based chemotherapy. In our institution, we initially treated patients with immunotherapy after progression, and after the appearance of the JB100 study, we included avelumab in the maintenance therapy. In this paper, we compared two forementioned strategies.

Methods: In our study, 56 subjects were included, 35 received atezolizumab after progression, while 21 patients were treated with avelumab in maintenance therapy. There were 41 male patients in the study, the median age was 65 years (41-78). We defined four endpoints PFS1 calculated from the start of immunotherapy to progression or death, PFS2 from the start of chemotherapy to progression to immunotherapy (as second line or maintenance) or death, OS1 from the start of immunotherapy to death and OS 2 from the start of chemotherapy to death.

Results: PFS2 and OS2 did not differ in relation to patient gender, age, diagnosis of synchronous or metachronous metastases, presence of mixed histology, presence of bone and lung metastases. Patients with lymph node metastases had a longer PFS2, while patients without liver metastases had a longer OS. PFS1 and PFS 2 were longer in the group treated with maintenance therapy with avelumab 7 vs. 3 months; p=0.0002 HR 0.27 (CI 0.14-0.53) and 17 vs. 10 months; p=0.021 HR 0.47 (CI 0.25-0.89), respectively. Also, OS 1 and OS 2 were longer in the group that received maintenance therapy: 10 vs 5 months; p=0.0006 HR 0.32 (CI 0.16-0.61) and 19 vs. 11 months; p=0.0251 HR 0.47 (CI 0.24-0.91), respectively. Two-year OS1 was 44% vs 8% in the maintenance therapy group versus the second-line immunotherapy group.

Conclusions: In our group of patients, the maintenance therapy strategy showed benefits in terms of PFS and OS compared to the second line of treatment. The reason is probably not a difference in the effectiveness of immunotherapy agents, but a better performance of patients after stabilization with chemotherapy, more time for immunotherapy to start working, and a certain number of platinum-refractory patients in the second-line group.

Keywords: checkpoint inhibitors, immunotherapy, urothelial carcinoma

REFERENCES

1. Powles T, Durán I, van der Heijden MS, Loriot Y, Vogelzang NJ, De Giorgi U, et al. Atezolizumab versus chemotherapy in patients with platinum-treated locally advanced or metastatic urothelial carcinoma (IMvigor211): a multicentre, open-label, phase 3 randomised controlled trial. Lancet. 2018 Feb 24;391(10122):748-757.
2. Bellmunt J, de Wit R, Vaughn DJ, Fradet Y, Lee JL, Fong L, et al. Pembrolizumab as Second– Line Therapy for Advanced Urothelial Carcinoma. N Engl J Med. 2017 Mar 16;376(11):1015– 1026.
3. Powles T, Park SH, Voog E, Caserta C, Valderrama BP, Gurney H, et al. Avelumab maintenance therapy for advanced or metastatic urothelial carcinoma. N Engl J Med. 2020 Sep 24;383(13):1218-1230.
4. Powles T, Bellmunt J, Comperat E, De Santis M, Huddart R, Loriot Y, et al. ESMO Guidelines Committee. Bladder cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol. 2022 Mar;33(3):244-258.
5. Popovic LS, Matovina-Brko G, Popovic M. Checkpoint inhibitors in the treatment of urological malignancies. ESMO Open. 2017 Jun 23;2(2):e000165.

P22 – ADJUVANT PEMBROLIZUMAB FOR CLEAR-CELL RENAL CELL CARCINOMA – A SINGLE CENTRE EXPERIENCE

LEA TOULA[1], Marko Lovrić[1], Zrna Antunac Golubić[1,2], Iva Nikles[1], Šime Bušelić[1], Ivan Vičić[1], Milena Gnjidić[1], Marija Gamulin[1,2]

[1]*Departmet of Oncology, University Hospital Centre Zagreb, Zagreb, Croatia*
[2]*University of Zagreb, School of Medicine, Zagreb, Croatia*

Introduction: Since the beginning of 2024, adjuvant pembrolizumab treatment has been available in the Republic of Croatia, for patients with clear-cell renal cell carcinoma who are at increased risk for disease recurrence after nephrectomy. This abstract aims to present the experience from the University Hospital Centre Zagreb.

Methods: Between January 1st 2024 and April 1st 2025, 24 patients commenced adjuvant pembrolizumab therapy. The median age of the patients was 65 years, and the majority of patients (66%) were male. Only 4 patients were surgically treated at a non-clinical hospital, with a total of 16/24 patients receiving radical surgical treatment at the University Hospital Centre Zagreb. Three out of 24 patients were classified as NED (no evidence of the disease), representing patients with metastatic disease (stage IV) who underwent complete surgical resection.

Results: Eighteen out of 21 patients (85%) were T stage 3a. The median tumor size was 6.4 cm. Regarding additional histopathological characteristics, the most frequent tumor grade was grade 2 (11/24), followed by grade 3 (7/24) and grade 4 (5/24). Tumor necrosis was present in 10/24 patients, and a sarcomatoid component in only 4/24 patients. The median time from surgery to the start of treatment was 98 days. To date, two patients have completed all 17 planned applications. Disease recurrence was verified in four patients during adjuvant treatment, all with lung localization. Seven patients experienced treatment-related adverse events. The most common adverse event was thyroid dysfunction (3/7), followed by skin reactions, hepatitis, pneumonitis, and myositis. Only one patient experienced more than one immune-mediated adverse event (concomitant myositis and hypothyroidism). Adjuvant treatment was discontinued in two patients after 4 and 6 cycles due to pneumonitis and myositis, respectively. In the remaining patients, treatment was continued after the management of adverse events. The median time to the onset of adverse events was 67 days.

Conclusions: This single-centre experience from the University Hospital Centre Zagreb provides initial insights into the use of adjuvant pembrolizumab for clear cell renal cell carcinoma in the Croatian setting. Further follow-up is needed to assess long-term outcomes and the impact of these early findings.

Keywords: adjuvant immunotherapy, adverse effects, pembrolizumab, renal cell carcinoma

REFERENCES

1. Choueiri TK, Tomczak P, Park SH, et al. Adjuvant pembrolizumab after nephrectomy in renal-cell carcinoma. N Engl J Med. 2021; 385(8):683-694.
2. Pal SK, Uzzo R, Karam JA, et al. Adjuvant atezolizumab versus placebo for patients with renal cell carcinoma at increased risk of recurrence following resection (IMmotion010): a multicentre, randomized, double-blind, phase 3 trial. Lancet. 2022;400(10359):1103– 1116.
3. Choueiri TK, Tomczak P, Park SH, et al. Overall survival results from the phase 3 KEYNOTE-564 study of adjuvant pembrolizumab vs placebo for the treatment of clear cell RCC. J Clin Oncol. 2024; 42(4_suppl) LBA 359.
4. Choueiri TK, Tomczak P, Park SH, et al. Overall survival with adjuvant pembrolizumab in renal-cell carcinoma. N Engl J Med. 2024;390:1359-1371.

P23 – OLAPARIB MAINTENANCE THERAPY IN BRCA 1/2-MUTATED OVARIAN CANCER PATIENTS WITH RENAL INSUFFICIENCY: A SINGLE-INSTITUTION EXPERIENCE

LIDIJA PAVLOVIĆ, Andjela Karaferic, Milana Matovic, Simonida Bobic, Slobodan Kutić, Jovana Mijucic, Teodora Novakovic, Marijana Milović-Kovačević

Instute for Oncology and Radiology of Serbia, Belgrade, Serbia

Introduction: Olaparib maintenance therapy following chemotherapy has significantly improved progression-free survival (PFS) in patients with BRCA1/2-mutated ovarian cancer, both in newly diagnosed and recurrent cases. However, data on its safety in specific patient populations, particularly those with renal insufficiency (RI), remain limited.

Aim: This study aimed to evaluate the safety and efficacy of olaparib in patients with renal insufficiency and to assess the impact of dose reduction on treatment effectiveness in this population.

Methods: In this study we have included patients with newly diagnosed or recurrent BRCA1/2-mutated ovarian carcinoma (OC), treated with olaparib maintenance therapy following response to platinum-based chemotherapy at Clinic for Medical Oncology, Institute for Oncology and Radiology of Serbia. Olaparib was administered at 300 mg (tablets) or 400 mg (capsules) twice daily (BID) between November 2019 and April 2025. Renal function was assessed using estimated glomerular filtration rate (eGFR) calculated by the Cockroft-Gault equation and serum creatinine levels. Plasma creatinine concentration (PCR) was used as surrogate marker for GFR. Adverse events (AEs) were recorded at each cycle and graded according to the Common Terminology Criteria for Adverse Events (CTCAE v 5.0).

Results: A total of 74 patients were included, with 41 (55 %) receiving olaparib for recurrent disease, and 33 (45 %) for newly diagnosed disease. Three patients (4%) had pre-existing chronic renal failure: one with newly diagnosed OC and two with recurrent disease. Following platinum-based therapy, two patients achieved no evidence of disease (NED), while one experienced partial remission (PR). Baseline eGFR values for these three patients with renal insufficiency were in the moderate range (30-44 ml/min). In consultation with nephrology specialists, in these three patients olaparib treatment was initiated at a reduced dose of 400 mg daily. Renal function ,including eGFR and serum creatinine levels were monitored monthly during treatment. Over the one-year follow-up period, no further decline in eGFR or worsening of renal insufficiency was observed. Patients who achieved NED at treatment initiation remained disease-free after one year, while the patient with residual disease exhibited disease stabilisation Renal function remained stable in all three patients. Regarding safety in these three patients, no serious (grade 3/4) AEs occurred. During the first six months of treatment, all three patients experienced grade 1 fatigue, while one patient developed grade 2 anemia, which did not necessitate treatment modification.

Conclusions: These findings suggest that a reduced olaparib dose of 400 mg daily is safe and effective for patients with renal insufficiency, with no significant deterioration in renal function or severe treatment-related AEs observed over the follow-up period.

Keywords: olaparib, ovarian cancer, renal insufficiency, eGFR, safety, tratment dosage

REFERENCES

1. Moore K, Colombo N, Scambia G, et al. Maintenance olaparib in patients with newly diagnosed advanced ovarian cancer. N Engl J Med 2018;379(26):2495–2505.
2. Pujade-Lauraine E, Ledermann JA, Selle F, et al. Olaparib tablets as maintenance therapy in patients with platinum-sensitive, relapsed ovarian cancer and a BRCA1/2 mutation (SOLO2/ENGOT-Ov21): a double-blind, randomised, placebo-controlled, phase 3 trial. Lancet Oncol 2017;18(9):1274–1284.
3. Baum J, Zickler D, Bolbrinker J, Richter R, Braicu EI, Grabowski J, et al. Olaparib in an ovarian cancer patient with end-stage renal disease and hemodialysis. Cancer Chemother Pharmacol. 2023 Apr;91(4):325-330. doi: 10.1007/s00280-023-04514-x.
4. Edelstein CL. (ed). Biomarkers of kidney disease (2nd ed.). Elsevier, 2017

P24 – TREATMENT PATTERNS IN ELDERLY PATIENTS WITH METASTATIC COLORECTAL CANCER DURING COVID-19 PANDEMICS

MIRJANA PAVLOVIĆ MAVIĆ[1], Petra Jakšić[2], Petra Sertić[2], Ljubica Vazdar[2], Robert Šeparović[2], Ana Tečić Vuger[2]

[1]*UPMC Hillman Cancer Center Croatia, Zabok, Croatia*
[2]*Medical Oncology Department, University Hospital for Tumors, Sestre milosrdnice University Hospital Center, Zagreb, Croatia*

Introduction: During the COVID-19 pandemic, elderly patients have been identified as one of the most vulnerable categories. In that period, the treatment landscape for metastatic colorectal cancer (mCRC) underwent several notable changes. Treatment of elderly patients faced unique challenges and treatments were modified on individual basis to balance cancer control and infection risk. Following global and European official guidelines and expert recommendations treatment patterns were changed in the way that pReferences was given to home-based care, including oral chemotherapy with less aggressive regimens when feasible. Balancing efficacy and toxicity were crucial with goals shifted from best response to treatment to maintaining best quality of life.

Methods: We conducted a retrospective analysis of elderly patients (≥65 years old) with mCRC who initiated their systemic treatment in period from 01/2016 to 02/2020 (pre-pandemic group), and compared them to patients whose treatment was initiated during the pandemic (03/2020 to 12/2020 – pandemic group). We collected the data for a total of 239 patients.

Results: We included 149 (62.1%) patients before the COVID-19 pandemic and compared them to 91 (37.9%) patients whose treatment plans were initiated during the pandemic. The mean age of all patients was 64.4±9.8, and 145 (60.4%) of them were men. There were no differences in the occurrence of the initially metastatic presentation in pre-pandemic vs pandemic time (60.4 vs 68.1%, P=0.228), while the multiple metastases were marginally insignificant (45.6 vs 58.2%; P=0.058). The number of applied treatment cycles before the pandemic of 6.33±2.35 vs 5.66±2.98 during the pandemic did not differ significantly (P=0.070). In contrast, when stratified by age 64 and over, we detected a significantly higher share of patients treated with deescalated and less aggressive protocols: 11 (7.4%) patients before COVID and 19 (20.9%) during COVID (P=0.002). Lastly, we utilized the Cox regression model, adjusted for the effects of gender and age, and showed that elderly patients did not experience a significant increase in hazard ratios during COVID-19 pandemics, with HR=1.29 [95% CI 0.93-1.79].

Conclusions: The results of this study demonstrate some differences in the oncologic treatment patterns related to the COVID pandemic, marked by a growing share of less aggressive treatment options. In addition, we managed to maintain the case fatality rates at the comparable level, probably due to strict adherence to anti-pandemic measures, yielding no net mortality differences in this groups of patients.

Keywords: colorectal cancer, metastatic, treatment, COVID-19, pandemics

P25 – CORRELATION BETWEEN NUTRITIONAL STATUS EVALUATED BY NUTRITIONAL SCREENING TOOLS AND LABORATORY NUTRITION ASSESSMENTS IN PATIENTS WITH METASTATIC COLON CANCER

MIRTA PEČEK[1], Sanja Langer[2], Milica Vrbančić[2], Petra Jakšić[1], Ljiljana Mayer[2,3], Ljubica Vazdar[1,4], Robert Šeparović[1,5,6]

[1]*Division for Medical Oncology, University Hospital for Tumors, Sestre milosrdnice University Hospital Center, Zagreb, Croatia*
[2]*Department of Medical Biochemistry in Oncology, University Hospital for Tumors, Sestre milosrdnice University Hospital Center, Zagreb, Croatia*
[3]*School of Medicine, Catholic University of Croatia, Zagreb, Croatia*
[4]*School of Medicine, University of Zagreb, Zagreb, Croatia*
[5]*Faculty of Medicine Osijek, University of J. J. Strossmayer Osijek, Osijek, Croatia*
[6]*Juraj Dobrila University of Pula, Pula, Croatia*

Introduction: Malnutrition and sarcopenia are highly prevalent among patients with metastatic colorecta cancer (mCRC), correlating with diminished treatment tolerance, heightened systemic inflammation, and worse clinical outcomes. Early identification and management of these risks are essential components of comprehensive oncologic care, although dynamic changes in biomarkers over time remain insufficiently explored.

Aim: This study evaluated the correlation between nutritional risk status and laboratory biochemical markers in patients with mCRC between high-risk and low-risk groups.

Methods: We conducted a cross-sectional retrospective observational study between January and April 2024 at University Hospital for Tumors Zagreb. The study included 43 patients with mCRC who were treated with first-line doublet chemotherapy in combination with bevacizumab between July 2021 and April 2025. Nutritional risk was assessed using the NRS-2002, while the risk for sarcopenia was evaluated using the SARC-F questionnaire. Based on NRS-2002 scores, patients were categorized into two groups: high nutritional risk (score ≥3) and low nutritional risk (score <3). Also, according to the SARC-F questionnaire, patients were divided into two groups: those with a high risk of developing sarcopenia (score ≥ 4) and those not at risk of developing sarcopenia (score <4). All patients identified as being at risk received nutritional support. Laboratory nutrition assessments tested biochemical indicators, including total serum protein (TP), albumin, C-reactive protein, neutrophils, and platelet count (PLT), at three points: start of treatment, end of treatment, and disease reactivation. Statistical comparisons between the two groups were made to identify significant differences associated with nutritional and sarcopenia risk and to determine whether the nutritional intervention affected these parameters.

Results: The research involved 28 men and 15 women. During the evaluation period, 31 patients experienced disease progression on first-line therapy. In the high nutritional risk (H-NR) group, there were 12 patients, and 31 in the low nutritional risk (L-NR) group. In a group with a high risk of developing sarcopenia (H-SARC) were four patients, while most of them were those with a low risk of developing sarcopenia (L-SARC). Serum albumin was significantly higher in the L-NR group compared to the H-NR group at the end of treatment (44.4 g/L vs. 41.2 g/L, p= 0.0245). PLT was higher in the H-NR group than in L-NR at the time of disease reactivation (243.0 x10^9/L vs.194.5 x10^9/L, p = 0.0451). Albumin and TP were significantly lower in H-SARC than in L-SARC (p = 0.0226 and p = 0.0419) at the end of treatment. TP, PLT, and neutrophils demonstrated statistically significant changes over time (p <0.01), with marked reductions at the end of treatment in H-SARC.

Conclusions: The combination of NRS-2002 and SARC-F screening tools provides a practical approach to identifying patients with mCRC at increased risk of malnutrition and sarcopenia. Patients at high nutritional or sarcopenia risk exhibit more unfavorable biochemical profiles, with lower protein and albumin levels and higher inflammatory markers, despite receiving nutritional support. Systematic monitoring of nutritional status and laboratory indicators throughout specific oncologic treatment is essential for identifying vulnerable individuals and optimizing management for improved clinical outcomes.

Keywords: malnutrition, metastatic colorectal cancer, sarcopenia

REFERENCES

1. Benedek Z, Coroş MF. The impact of sarcopenia on the postoperative outcome in colorectal cancer surgery. Med Pharm Rep. 2023;96(1):20-27. doi:10.15386/mpr-2483
2. Vergara-Fernandez O, Trejo-Avila M, Salgado-Nesme N. Sarcopenia in patients with colorectal cancer: A comprehensive review. World J Clin Cases. 2020 Apr 6;8(7):1188–1202.
3. Zhang X, Wang Y, Liu C, et al. Sarcopenia as a prognostic indicator in colorectal cancer: an updated meta-analysis. Front Oncol. 2023;13:10642225.

P26 – PROGNOSTIC FACTORS OF OVERALL SURVIVAL AND PROGRESSION FREE SURVIVAL IN HODGKIN LYMPHOMA PATIENTS

MAJA POPOVIĆ[1,2], Gorana Matovina-Brko[2], Dragana Petrović[2], Stefan Đurić[2], Lazar Popović[1,2]

[1]*Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia*
[2]*Oncology Institute of Vojvodina, Sremska Kamenica, Serbia*

Introduction: Hodgkin's lymphoma accounts for 10% of all lymphomas and is treated with chemotherapy or a combination of chemotherapy and radiation therapy, depending on the stage of the disease. In this way, about 80% of patients are cured, however 20% of patients do not respond to therapy or have a relapse of the disease after the initial response. Disease stage, age, presence of extranodal disease, bulky disease, B symptoms, laboratory findings such as leukocyte count, platelet count, hemoglobin level are prognostic factors of time to disease progression and overall survival of patients with Hodgkin's lymphoma.

Methods: We conducted study that included 157 patients diagnosed classic Hodgkin's lymphoma at the Oncology Institute of Vojvodina. We investigated the prognostic significance of the patient's age, sex,

stage of the disease, number of leukocytes, number of platelets, hemoglobin level, presence of disease in the bones.

Results: Patients in stage I and II of the disease had a longer progression free survival (PFS) (3-year 84% vs 59%, median not reached vs. 131 months; HR 0.47; p=0.006). Patients who had bone disease at initial staging had a shorter PFS (no 3-year 69%, median NR; yes 3-year 51%, median 87 months; p=0.02). Patients who had a platelet count greater than 400x10 9 before starting treatment had a shorter overall survival (<400x10 9 3-year 94%, median NR; > 400x10 9 3-year 87%, median NR; HR 0.28, p=0.017). Other evaluated factors did not significantly affect progression free survival or overall survival.

Conclusions: In the multivariate analysis of overall survival, the studied parameters had no significant influence.

Keywords: Hodgkin disease, lymphoma, prognosis, progression-free survival

REFERENCES

1. Agostinelli C, Gallamini A, Stracqualursi L, Agati P, Tripodo C, Fuligni F et al. The combined role of biomarkers and interim PET scan in prediction of treatment outcome in classical Hodgkin's lymphoma: a retrospective, European, multicentre cohort study. Lancet Haematol. 2016;3(10):e467-e479.
2. Eichenauer DA, Aleman BMP, André M, Federico M, Hutchings M, Illidge T et al. Hodgkin lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2018 ;29(Suppl 4):iv19-iv29.
3. Oki Y, Chuang H, Chasen B, Jessop A, Pan T, Fanale M et al. The prognostic value of interim positron emission tomography scan in patients with classical Hodgkin lymphoma. Br J Haematol. 2014;165(1):112-6
4. Radford J, Illidge T, Counsell N, Hancock B, Pettengell R, Johnson P, et al. Results of a trial of PET-directed therapy for early-stage Hodgkin's lymphoma. N Engl J Med. 2015 ;372(17):1598-607
5. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209-249.

P27 – POSITRON EMISSION TOMOGRAPHY AFTER TWO CYCLES OF CHEMOTHERAPY IN THE TREATMENT OF HODGKIN'S LYMPHOMA

MAJA POPOVIĆ[1,2], Gorana Matovina-Brko[2], Dragana Petrović[2], Stefan Đurić[2], Lazar Popović[1,2]

[1]*Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia*
[2]*Oncology Institute of Vojvodina, Sremska Kamenica, Serbia*

Introduction: Positron emission tomography after two cycles of chemotherapy (PET/CT2) evaluates early therapeutic response in the treatment of Hodgkin's lymphoma. In this way, patients with a negative or positive result are identified. Deescalation of treatment in patients with a negative result, and escalation of therapy in patients with a positive result aims to improve the outcome of the treatment and reduce toxicities.

Methods: We conducted a retrospective-prospective study at the Oncology Institute of Vojvodina and included 157 patients diagnosed with classic Hodgkin's lymphoma. All patients were treated with ABVD protocol. Positron emission tomography 2 (PET/CT2) was performed in 66 patients.

Results: The population of patients who underwent PET/CT2 was divided into two groups: the first group consisted of patients with a negative PET/CT2 result, the second group consisted of patients with a

positive PET/CT2. We evaluated the prognostic significance of PET/CT2 results on overall survival and time to disease progression. Negative result was identified in 52 (78.7%) patients, 14 (21.3%) patients had a positive PET/CT2. Patients with a negative PET/CT2 had a significantly longer progression free survival (PFS) (negative PET/CT2, 3-year 88%, median not reached; positive PET/CT2, 3-year 36%, median 3 months, p<0.0001). Patients with a negative PET/CT2 had significantly longer overall survival (negative PET/CT2 finding, 3-year 100%, median not reached; positive PET/CT2, 3-year 73%, median not reached, p=0.0004).

Conclusions: In the multivariate analysis, PET/CT2 also had a significant impact on overall survival. The result of PET/CT2 in patients with Hodgkin's lymphoma is a significant prognostic factor.

Keywords: Hodgkin disease, lymphoma, prognosis, positron emission tomography computed tomography, treatment outcome

REFERENCES

1. Johnson P, Federico M, Kirkwood A, Fosså A, Berkahn L, Carella A, et al. Adapted treatment guided by interim PET-CT scan in advanced Hodgkin's lymphoma. N Engl J Med. 2016 Jun 23;374(25):2419-29.
2. Eichenauer DA, Aleman BMP, André M, Federico M, Hutchings M, Illidge T, et al. Hodgkin lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2018 ;29(Suppl 4):iv19-iv29.
3. Radford J, Illidge T, Counsell N, Hancock B, Pettengell R, Johnson P et al. Results of a trial of PET-directed therapy for early-stage Hodgkin's lymphoma. N Engl J Med. 2015 ;372(17):1598-607
4. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209-249.
5. Yoo KH. Staging and response assessment of lymphoma: a brief review of the Lugano classification and the role of FDG-PET/CT. Blood Res. 2022;57(S1):75-78.

P28 – SECOND LINE TREATMENT OF CLEAR CELL RENAL CELL CARCINOMA AFTER PROGRESSION ON A TYROSINE KINASE INHIBITOR

MAJA POPOVIĆ[1,2], Nemanja Maletin[2], Gorana Matovina-Brko[1], Stefan Đurić[1], Stela Novak[1], Teodora Urošević[1], Svetlana Salma[1], Lazar Popović[1,2]

[1]*Oncology Institute of Vojvodina, Sremska Kamenica, Serbia*
[2]*Faculty of medicine, University of Novi Sad, Novi Sad, Serbia*

Introduction: Tyrosine kinase inhibitors (TKIs) and immunotherapy (IO) are the standard of care for metastatic clear cell renal-cell carcinoma (ccRCC). For many years, before the new studies which combined IO or IO plus TKI, the standard of first-line treatment for ccRCC were TKIs sunitinib or pazopanib. After progression on these agents, patients were offered three treatment options: nivolumab, axitinib, or cabozantinib. In this paper, we present our experience of treating ccRCC with a second line therapy.

Methods: In our study, we analyzed data for 58 patients with a median follow-up of 21 months (1-59). The median age of the patients was 62 (39-79).

Results: Median progression-free survival (PFS) first-line TKI was 14 months (2-107). In the second line of treatment, 29 patients received nivolumab, 16 cabozantinib, 13 axitinib. The median PFS was 7 months. There was no difference in PFS depending on patient age and sex, presence or absence of bone,

liver, or lung metastases. There was no difference in PFS by drug choice. Median PFS for nivolumab was 7, axitinib 8, cabozantinib 6 months (p=0.9). PFS was influenced by MSKCC (p=0.0004) and IMDC score (p=0.0006) calculated at the beginning of the second line, while there was borderline statistical significance for sincronous or metachronous metastatic disease among diagnosis. In the multivariate analysis, those three factors were statistically significant.

Conclusions: In our retrospective study, all three drugs showed efficacy similar to registrational studies. There was no difference in PFS between three drugs. Prognostic scores that are commonly used to predict the outcome of first-line treatment: MSKCC and the IMDC score, in our study have been shown to be useful in predicting the outcome of second-line PFS.

Keywords: tyrosine kinase inhibitors (TKIs), immunotherapy (IO), metastatic clear cell renal-cell carcinoma (ccRCC).

REFERENCES

1. Popovic M, Matovina-Brko G, Jovic M, Popovic LS. Immunotherapy: A new standard in the treatment of metastatic clear cell renal cell carcinoma. World J Clin Oncol. 2022 Jan 24;13(1):28-38.
2. Powles T, Albiges L, Bex A, Grünwald V, Porta C, Procopio G, ESMO Guidelines Committee. ESMO Clinical Practice Guideline update on the use of immunotherapy in early stage and advanced renal cell carcinoma. Ann Oncol. 2021 Dec;32(12):1511-1519.
3. Motzer RJ, Escudier B, McDermott DF, George S, Hammers HJ, Srinivas S, et al. Nivolumab versus everolimus in advanced renal-cell carcinoma. N Engl J Med. 2015 Nov 5;373(19):1803-13.
4. Rini BI, Escudier B, Tomczak P, Kaprin A, Szczylik C, Hutson TE, et al. Comparative effectiveness of axitinib versus sorafenib in advanced renal cell carcinoma (AXIS): a randomised phase 3 trial. Lancet. 2011 Dec 3;378(9807):1931-9.
5. Choueiri TK, Escudier B, Powles T, Mainwaring PN, Rini BI, Donskov F, et al. Cabozantinib versus everolimus in advanced renal-cell carcinoma. N Engl J Med. 2015 Nov 5;373(19):1814-23.

P29 – INTERNATIONAL ANALYSIS OF THE LEVEL OF KNOWLEDGE ABOUT HUMAN PAPILLOMAVIRUS INFECTIONS IN THE POPULATION OF YOUNG ATHLETES IN A VOLLEYBALL CAMP

Marija Živković Radojević[1,2], KATARINA JANKOVIĆ[2,6], Aljoša Mandić[3,4], Miloš Grujić[2,6], Katarina Krasić[2,6], Vladimir Grbić[5], Nevena Folić[7,8], Marko Folić[9,10], Ksenija Bošnjaković[6], Aleksandra Marković[11], Dragan Lončar[12], Neda Milosavljević[1,2]

[1]*Department of Clinical Oncology, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia*
[2]*Center for Radiation Oncology, University Clinical Center Kragujevac, Kragujevac, Serbia*
[3]*Department of Gynecology and Obstetrics, Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia*
[4]*Clinic for Surgical Oncology, Oncology Institute of Vojvodina, Sremska Kamenica, Serbia*
[5]*Sports Association 'Vladimir Vanja Grbić'*
[6]*Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia*
[7]*Department of Pediatrics, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia*
[8]*Clinic for Pediatrics, University Clinical Center Kragujevac, Kragujevac, Serbia*
[9]*Clinical Pharmacology Department, University Clinical Center Kragujevac, Kragujevac, Serbia*
[10]*Center for Pharmaceutical and Pharmacological Research, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia*
[11]*Institute for Information Technologies, University of Kragujevac, Kragujevac, Serbia*
[12]*Department of Gynecology and Obstetrics, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia*

Introduction: Infection with human papillomavirus (HPV) contributes to the development of 4.5% of cancers, primarily cervical cancer. Although the high efficacy and safety of the HPV vaccine have been confirmed, low uptake of HPV vaccination is observed in developing countries, which may be associated with a low level of knowledge about HPV infection. The aim was to investigate and compare the level of knowledge about HPV infection in a cohort of international athletes from different countries.

Methods: A cross-sectional clinical observational study was conducted at the international volleyball camp "VG Camp" in Valjevo, from June to September 2023. The level of knowledge about HPV infection among volleyball players was assessed by the Human Papillomavirus Knowledge Questionnaire (HPV-KQ), available in Serbian and English. The ANOVA test was used to examine the differences in total scores of correct answers between groups.

Results: The study included 514 volleyball players from 21 countries, aged 13.3±2.3 years, predominantly female (88%), who voluntarily completed the HPV-KQ questionnaire. The maximum score for correct answers was 18. Knowledge level about HPV infection correlated with the country of origin of the athletes, educational level, age, duration of sports involvement, and sources of information about HPV infection (<0.05). No statistical significance was found concerning residence, comorbidities, HPV vaccination status, and the number of doses administered (>0.05). The highest scores were achieved by athletes from Sweden (11.0±0.5), Hungary (8.0±1.2), and Macedonia (7.2±0.1), while the lowest scores were recorded for athletes from Serbia (4.82±2.9), Bosnia and Herzegovina (5.3±3.4), and Montenegro (4.72±2.6).

Conclusions: Participants from European countries with well-developed primary and secondary prevention programs demonstrated a high level of knowledge about HPV infection, in contrast to participants from countries with the highest incidence of cervical cancer, which are characterized by very low levels of knowledge about HPV infection. For the purpose of creating a quality prevention policy, a clear strategy is needed to raise awareness and knowledge about the importance of primary and secondary

prevention, leveraging accessible methods to inform the younger generation through appropriate media and platforms.

Keywords: HPV infection, HPV vaccination, prevention

Acknowledgment: The realization of this study was supported by the head of the *VG Camp*, PhD Vladimir Grbić, a renowned Serbian volleyball player and former national team member, along with his team. The co-authors of this paper express their gratitude for his invaluable contribution to the scientific research and promotion of healthy lifestyles.

REFERENCES

1. St Laurent J, Luckett R, Feldman S. HPV vaccination and the effects on rates of HPV-related cancers. Curr Probl Cancer 2018;42(5):493-506.
2. Venetianer R, Clarke MA, van der Marel J, Tota J, Schiffman M, Dunn ST, et al. Identification of HPV genotypes causing cervical precancer using tissue-based genotyping. Int J Cancer 2020;146(10):2836-44.
3. Kasymova S, Harrison SE, Pascal C. Knowledge and awareness of Human Papillomavirus among college students in South Carolina. Infect Dis (Auckl) 2019;12:1178633718825077.
4. Adjei Boakye E, Tobo BB, Rojek RP, Mohammed KA, Geneus CJ, Osazuwa-Peters N. Approaching a decade since HPV vaccine licensure: Racial and gender disparities in knowledge and awareness of HPV and HPV vaccine. Hum Vaccin Immunother 2017;13(11):2713-22.
5. Lei J, Ploner A, Elfström KM, Wang J, Roth A, Fang F, et al. HPV Vaccination and the risk of invasive cervical cancer. N Engl J Med 2020;383(14):1340-8.

P30 – SYNCHRONOUS OCCURRENCE OF HEPATOCELLULAR CARCINOMA AND LUNG ADENOCARCINOMA: A FAVORABLE RESPONSE TO COMBINED SYSTEMIC THERAPY WITH ATEZOLIZUMAB AND BEVACIZUMAB – A CASE REPORT

MARKO MARJANOVIĆ[1], Jelena Radić[1,2], Nemanja Petrović[1,2], Aleksandar Đurić[1,2], Stela Novak[1], Nikola Anđelić[2,3], Bojana Damjanović[4]

[1]*Clinic for Internal Oncology, Institute of Oncology of Vojvodina, Sremska Kamenica, Serbia*
[2]*Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia*
[3]*Department for Radiological Diagnostics, Institute of Oncology of Vojvodina, Sremska Kamenica, Serbia*
[4]*Clinic for Radiation Oncology, Institute of Oncology of Vojvodina, Sremska Kamenica, Serbia*

Introduction: The synchronous manifestation of two primary malignancies originating from distinct histogenetic lineages represents a rare and complex clinical scenario. Advances in systemic therapy, particularly immune checkpoint inhibitors and anti-angiogenic agents, have expanded therapeutic horizons in the management of advanced solid tumors.

Case Report: We describe the case of a 63-year-old female with a history of chronic smoking and successfully treated hepatitis C virus (HCV) infection, who presented with vague right upper quadrant discomfort and a persistent, non-productive cough. Clinical evaluation revealed hepatomegaly and bilateral reduction in breath sounds. Cross-sectional imaging (abdominal MRI and chest CT) identified a dominant

hepatic lesion in segments VI and VII (maximal dimension 100 mm) with right portal vein branch thrombosis and multiple satellite nodules. Concurrently, a 39 mm subpleural mass was noted in the left lower lung lobe, without mediastinal lymphadenopathy or thoracic dissemination. Histopathological examination confirmed two distinct primary tumors: a moderately differentiated hepatocellular carcinoma (HCC) via percutaneous liver biopsy, and a poorly differentiated non-small cell lung carcinoma (NSCLC) via transbronchial biopsy. Immunohistochemistry supported this distinction, with the liver lesion expressing HepPar1, arginase, and glypican-3, and the lung lesion positive for TTF-1 and napsin A. Serum alpha-fetoprotein (AFP) was significantly elevated (3049 ng/mL), reinforcing the diagnosis of active HCC. The patient's hepatic function was preserved (Child-Pugh class A), and upper GI endoscopy excluded esophageal varices. Following multidisciplinary tumor board review, the patient commenced combination therapy with Atezolizumab and Bevacizumab, selected for its proven efficacy in advanced HCC and potential benefit for NSCLC. This regimen was approved through national reimbursement pathways. From August 2024 to March 2025, the patient completed eight treatment cycles with excellent tolerance and maintained performance status (ECOG 0). Clinically, hepatomegaly resolved, and respiratory symptoms improved. Follow-up imaging revealed regression of the hepatic mass (from 73×100×82 mm to 40×69×49 mm), decreased vascularity, and partial recanalization of the portal vein. The pulmonary lesion remained radiologically stable. AFP levels normalized (1.74 ng/mL), indicating a robust biochemical response. The patient remains on treatment, with plans to continue until disease progression or unacceptable toxicity.

Conclusions: This case underscores the potential efficacy of combination regimens based on immune checkpoint inhibition and anti-angiogenic therapy in managing synchronous primary malignancies of distinct origins, particularly when guided by multidisciplinary evaluation and patient-specific considerations.

Keywords: hepatocellular carcinoma; lung adenocarcinoma; immunotherapy; atezolizumab; bevacizumab

REFERENCES

1. Cheng AL, Qin S, Ikeda M, Galle PR, Ducreux M, Kim TY, et al. Updated efficacy and safety data from IMbrave150: Atezolizumab plus bevacizumab vs. sorafenib for unresectable hepatocellular carcinoma. J Hepatol. 2022 Apr;76(4):862-873. doi: 10.1016/j.jhep.2021.11.030.
2. Socinski MA, Nishio M, Jotte RM, Cappuzzo F, Orlandi F, Stroyakovskiy D, et al. IMpower150 final overall survival analyses for atezolizumab plus bevacizumab and chemotherapy in first-line metastatic nonsquamous NSCLC. J Thorac Oncol. 2021 Nov;16(11):1909-1924. doi: 10.1016/j.jtho.2021.07.009.
3. Egawa T, Masuzawa K, Nakayama S, Maeda I, Tsunematsu S, Suzuki Y, et al. Synchronous primary lung adenocarcinoma and hepatocellular carcinoma successfully treated with a combination of atezolizumab, bevacizumab, carboplatin, and paclitaxel. Intern Med. 2021 Oct 15;60(20):3273-3277. doi: 10.2169/internalmedicine.6442-20.

P31 – TREATMENT OF BRAF MUTANT MELANOMA WITH BRAFi/MEKi COMBINATION THERAPY IN CLINICAL PRACTICE IN MONTENEGRO

NIKOLA MILAŠEVIĆ, Nevenka Lukovac-Janjić, Dijana Bošković, Nikola Peulić

Institute of Oncology, Clinical Center of Montenegro, Podgorica, Montenegro

Introduction: Melanoma is an aggressive form of skin cancer that often leads to metastasis and high mortality. BRAF mutations are present in a significant number of melanoma cases, leading to the development of targeted therapies. This abstract presents the results of treating patients with metastatic BRAF mutant melanoma using the combination therapies of dabrafenib + trametinib (TAF/MEK) and vemurafenib + cobimetinib (VEM/COB) in clinical practice in Montenegro.

Methods: The analysis included 14 patients with metastatic BRAF mutant melanoma diagnosed between January 2022 and December 2024. Of the total number of patients, 11 were treated with the combination of dabrafenib + trametinib, while 3 patients were treated with the combination of vemurafenib + cobimetinib. All patients received first-line therapy.

Results: The median age of the patients was 58 years (range 47-81). The localization of metastases among the patients was as follows: 29% of patients (5/14) had multiple metastases, 28% of patients (4/14) had lymph node metastases, 21% of patients (3/14) had multiple metastases with CNS involvement, 14% of patients (2/14) had visceral metastases. Progression-Free Survival (PFS): The Kaplan-Meier curve for progression-free survival (PFS) shows that the median PFS has not yet been reached, with 43% (6/14) events. After 12 months, 69% of patients had no disease progression, while after 24 and 34 months, this percentage was 60%. Regarding the response to therapy: 50% of patients (7/14) had stable disease (SD), 29% of patients (4/14) had a partial response (PR), In 3 patients, the response was not defined. Overall, 79% of patients (11/14) had some form of response to the therapy.

Conclusions: The results of this analysis indicate that the combination therapies of dabrafenib + trametinib and vemurafenib + cobimetinib can be effective first-line treatment for patients with metastatic BRAF mutant melanoma. The majority of patients had a positive response to the therapy, and the median progression-free survival has not yet been reached, indicating the long-term efficacy of these treatments. Further follow-up is needed to confirm these findings and optimize the treatment strategy for this patient population.

Keywords: BRAF mutations, dabrafenib, melanoma, trametinib

REFERENCES

1. Robert C, Grob JJ, Stroyakovskiy D, Karaszewska B, Hauschild A, et al. Five-year outcomes with dabrafenib plus trametinib in metastatic melanoma. 2019, New England Journal of Medicine. 2019; 381(7):626-636. doi.10.1056/NEJMoa1904059.
2. Stoff R, Markovic SN, McWilliams RR, Kottschade LA, Montane HN, Dimou A, et al. Real-world evidence on efficacy and toxicity of targeted therapy in older melanoma patients treated in a tertiary-hospital setting. Melanoma Res. 2024 Dec 1;34(6):510-518. doi: 10.1097/CMR.0000000000000997.
3. Piejko K, Cybulska-Stopa B, Ziętek M, Dziura R, Galus Ł, Kempa-Kamińska N, et al. Long-term real-world outcomes and safety of vemurafenib and vemurafenib + cobimetinib therapy in patients with BRAF-mutated melanoma. Target Oncol. 2023 Mar;18(2):235-245. doi: 10.1007/s11523-023-00954-w.

P32 – CASE REPORT: PULMONARY HYPERTENSION AS THE FIRST MANIFESTATION OF MALIGNANT DISEASE

NEVENKA LUKOVAC-JANJIĆ, Ivana Vukovic, Dragana Ognjenovic Nikcevic, Bojana Golubovic

Institute of Oncology, Clinical Center of Montenegro, Podgorica, Montenegro

Introduction: Pulmonary hypertension (PH) is a complex and progressive condition characterized by elevated blood pressure in the pulmonary arteries (greater than 25 mmHg). While commonly associated with a variety of underlying causes, including left heart disease, lung diseases, and chronic thromboembolic conditions, it can also emerge as a paraneoplastic syndrome.

Case presentation: A 41-year-old female patient presented to the Niksic General Hospital due to sudden onset of severe dyspnea. Workup revealed acute respiratory failure with an oxygen saturation (sO2) of 84% requiring oxygen support. Clinical examination showed diminished heart tones, reduced voltage of the QRS complex on the electrocardiogram and palpation confirmed the presence of a tumor in the right breast and axilla (cT3N3). A cardiologist at Niksic General Hospital performed echocardiography, indicating high mean pressure in the right heart chambers-evidence of right ventricular strain with pulmonary artery pressure (SPDK) of 95 mmHg, tricuspid regurgitation TR 3+ and established a diagnosis of pulmonary hypertension of unclear etiology. ECOG was 3.

The patient was referred to Clinical Center of Montenegro for cardiology evaluation and further workup. A multidetector computed tomography (MDCT) of the pulmonary arteries excluded pulmonary thromboembolism; however, based on imaging and clinical findings concerning the right breast, secondary PH due to malignancy was suspected. A chest and abdominal CT showed no clear signs of infiltration in the lungs, but a large tumor was found in the right breast with axillary lymphadenopathy. The liver appeared voluminous and congested, with Th3 changes noted as metastatic deposits. Given the suspicion of secondary PH, right heart catheterization was not performed. A bone scan was conducted, revealing a metastatic deposit at Th3 and a suspicious lesion in the right fifth rib.

A core biopsy from the right breast lesion was performed and showed invasive ductal carcinoma of the breast, ER+++, PR++, HER2 2+, Ki67 40%. FISH testing for HER2 showed no amplification. Tumor markers: CEA 9.6, Ca 15-3 75.4.

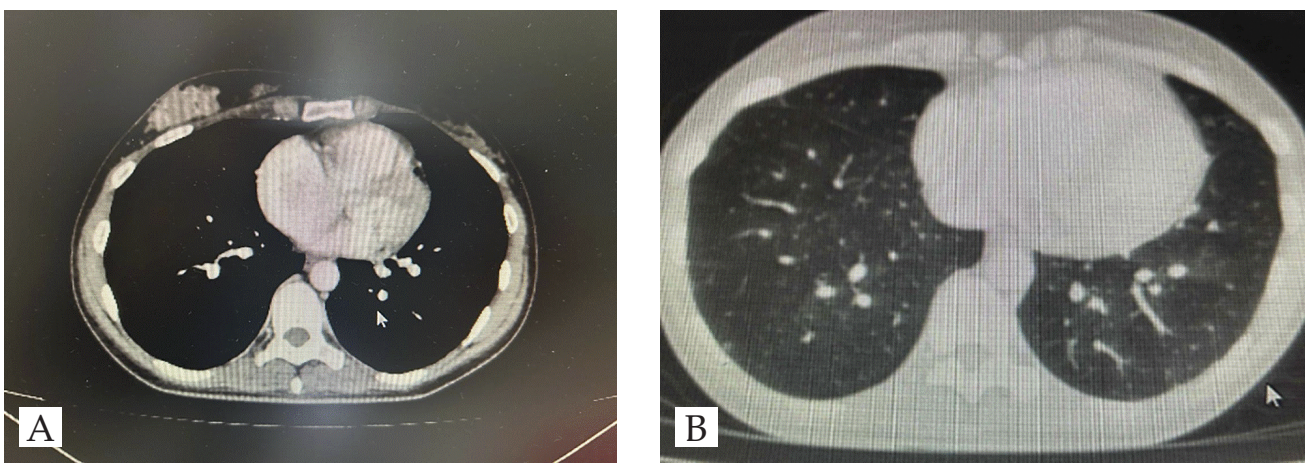

Figure 1: *Large tumor in the right breast and reticular exchange in lung with cardiomegaly*

Specific PH treatment was initiated by the cardiologist (macitentan, a potent endothelin receptor antagonist and sildenafil, a phosphodiesterase-5 inhibitor).

Due to respiratory distress, the risk of heart failure, and significant symptomatic burden, it was decided to initiate systemic chemotherapy (Taxol) with intensive oncologist monitoring. After twelve cycles of Taxol, ECOG performance status remained 1, with no complaints: echocardiography in February 2025 revealed SPDK of 25 mmHg and ejection fraction of 64%. Chest CT on March 11, 2025, showed significant regression of the right breast and axillary changes, with metastatic deposits at Th3.

Given the significant improvement in the overall condition, and improvement in echocardiographic findings (SPDK 25 mmHg), the patient's treatment continued with CDK4/6 inhibitors + Femozol and LHRH analogs, along with bisphosphonate therapy.

Conclusions: PH rarely occurs in the context of malignant disease but is a sign of poor prognosis. At the KCCG, this is the first patient with this clinical presentation.

Keywords: pulmonary hypertension, malignant disease

REFERENCES

1. Albaba I, Medarov BI. A case of severe cancer-related pulmonary hypertension; An unexpected resolution. Respiratory Medicine Case Reports, 2022 May 23:38:101671. doi: 10.1016/j.rmcr.2022.101671.
2. Ali HJ, Sahay S, Deswal A, Faiz SA. Evaluation of pulmonary hypertension in patients with cancer. American College of Cardiology, Mart 11, 2025. Available from: https://www.acc.org/Latest-in-Cardiology/Articles/2025/03/10/17/02/Evaluation-of-Pulmonary-Hypertension-in-Patients-With-Cancer
3. McHugh S, et al. Malignancy-related pulmonary hypertension presenting as a pulmonary veno-occlusive–like syndrome, JACC Case Rep. 2021 Jul 7;3(7):1044–1050. doi:10.1016/j.jaccas.2021.04.008

P33 – EFFICACY OF PEMBROLIZUMAB IN CLINICAL PRACTICE FOR METASTATIC MELANOMA IN MONTENEGRO

NIKOLA MILAŠEVIĆ, Nada Cicmil Sarić, Nevenka Lukovac-Janjić, Dijana Bošković

Institute of Oncology, Clinical Center of Montenegro, Podgorica, Montenegro

Introduction: This study aims to evaluate the efficacy of pembrolizumab in routine clinical practice for patients with metastatic melanoma (mM) in Montenegro.

Methods: A total of 30 patients diagnosed with mM between January 2022 and December 2024 were included in the analysis. The median age of the patients was 66 years (range 43– 84). The cohort consisted of 30% females (9/30) and 70% males (21/30). Pembrolizumab was administered as a first-line treatment in 77% (23/30) of patients and as a second-line treatment in 23% (7/30) of patients. All patients were tested for BRAF mutation, with 9 out of 30 patients being BRAF positive. Among these, 2 were treated in the first line, and 7 were treated in the second line following COMBO therapy. Elevated lactate dehydrogenase (LDH) levels were observed in 23% (7/30) of patients, while LDH levels were unknown in 53% (16/30) of patients.

Results: Localization of metastasis at diagnosis: 30% (9/30) had visceral metastases, 27% (8/30) had multiple metastases including CNS involvement, 23% (7/30) had lymphatic involvement, and 20% (6/30)

had multiple metastatic sites. Efficacy in First-Line Treatment: Median Progression-Free Survival (PFS) was 8 months. Patients treated in the first line were generally older, with a median age of 70 years. The majority had multiple metastases (26%, 6/23) and multiple metastases with CNS involvement (26%, 6/23). Additionally, 66% (4/6) of patients with CNS metastases received radiotherapy. Efficacy in Second-Line Treatment: Median PFS was 13 months. All patients treated in the second line were BRAF positive and had previously received COMBO therapy in the first line.

Conclusions: Pembrolizumab demonstrates significant efficacy in the treatment of metastatic melanoma in clinical practice in Montenegro.

Keywords: clinical practice, melanoma, pembrolizumab

REFERENCES

1. Long GV, Carlino MS, McNeil C, Ribas A, et al. Pembrolizumab versus ipilimumab for advanced melanoma: 10-year follow-up of the phase III KEYNOTE– 006 study. Annals of Oncology. 2024;35(12):1191-1199. Doi: 10.1016/j.annonc.2024.08.2330.
2. Zhang Q, Huo GW, Zhang HZ, Song Y. Efficacy of pembrolizumab for advanced/metastatic melanoma: a meta-analysis. Open Med (Wars). 2020 Jun 10;15(1):447-456. doi: 10.1515/med-2020-0110.
3. Liu FX, Ou W, Diede SJ, Whitman ED. Real-world experience with pembrolizumab in patients with advanced melanoma: A large retrospective observational study. Medicine (Baltimore). 2019 Jul;98(30):e16542. doi: 10.1097/MD.0000000000016542.

P34 – EFFICACY AND SAFETY OF RIBOCICLIB IN PATIENTS WITH HR+/HER2 ADVANCED BREAST CANCER – CLINICAL PRACTICE IN MONTENEGRO

SANJA LEKIC, Milan Sorat, Bojana Golubovic, Ivana Vukovic

Institute of Oncology, Clinical Center of Montenegro, Podgorica, Montenegro

Introduction: Cyclin-dependent kinase 4/6 (CDK4/6) inhibitors combined with endocrine therapy (ET) have become the standard first-line treatment for patients with hormone receptor-positive (HR+)/human epidermal growth factor receptor 2-negative (HER2-) metastatic breast cancer (MBC). Ribociclib, a CDK4/6 inhibitor, has been available in Montenegro since 2020., including both premenopausal and postmenopausal women treated in the first and second lines of therapy.

Methods: This retrospective study included 144 patients who started ribociclib treatment between January 2021 and December 2024. The primary endpoint was progression-free survival (PFS), defined as the time from the initiation of ET plus ribociclib to disease progression or death. Patient characteristics, including age, menopausal status, and metastatic sites, were recorded. Safety was assessed by monitoring adverse events (AEs) such as leukopenia, anemia, neutropenia, thrombocytopenia, and others.

Results: The median age of the patients was 57 years (range 30-83). De novo metastatic disease was present in 33% of patients. Premenopausal and postmenopausal patients comprised 27% and 72% of the cohort, respectively. Liver metastases were observed in 26% of patients, while bone metastases were present in 74%. For the PFS analysis, 105 patients who started treatment between January 2021 and December 2023 were included. The overall median PFS was 20 months, with 48% of patients experiencing progres-

sion or death. When stratified by the year of treatment initiation, the median PFS was 31.5 months for patients who started in 2021 (58% events), 20 months for those who started in 2022 (48% events), and 18 months for those who started in 2023 (46% events). The safety profile of ribociclib was consistent with clinical trial data. Leukopenia was the most common AE, occurring in 42% of patients (Grade 1: 80%, Grade 2: 48%, Grade 3: 5%). Other AEs included anemia (8%), neutropenia (3%), thrombocytopenia (3%), pancytopenia (1%), elevated transaminases (3%), increased ejection fraction (1%), fatigue (1%), nausea (1%), pancreatitis (1%), and Grade 2 skin allergy (1%).

Conclusions: Ribociclib, in combination with ET, demonstrates significant efficacy and a manageable safety profile in HR+/HER2– MBC patients in real-world clinical practice in Montenegro. The observed median PFS is consistent with the results from the MONALEESA trials, supporting the use of ribociclib as a standard treatment option in this patient population. However, longer follow-up is needed to achieve mature PFS data and to analyze overall survival (OS) outcomes.

Keywords: ribociclib, clinical practice, efficacy, safety

REFERENCES

1. Hortobagyi GN, Stemmer SM, Burris HA, et al. Overall survival with ribociclib plus letrozole in advanced breast cancer-MONALEESA-2. New England Journal Med 2022;386:942-950, DOI: 10.1056/NEJMoa2114663
2. Sammons S, Sharma P, Abdou Y, et al. Tolerability of first-line treatment with ribociclib for metastatic breast cancer using two large US data sources. Presented at San Antonio Breast Cancer Symposium; December 10-13; San Antonio, TX, USA. 2024.
3. Slamon DJ, Neven P, Chia S, Fasching PA, De Laurentiis M, et al. Phase III randomized study of ribociclib and fulvestrant in hormone receptor–positive, human epidermal growth factor receptor 2–negative advanced breast cancer: MONALEESA-3. Journal of Clinical Oncology, 2018 Aug 20;36(24):2465-2472. doi: 10.1200/JCO.2018.78.9909.

P35 – EFFICACY AND SAFETY OF PALBOCICLIB IN PATIENTS WITH HR+/HER2 ADVANCED BREAST CANCER – CLINICAL PRACTICE IN MONTENEGRO

SANJA LEKIC, Milan Sorat, Ivana Vukovic, Bojana Golubovic

Institute of Oncology, Clinical Center of Montenegro, Podgorica, Montenegro

Introduction: Palbociclib was approved, combined with hormone therapy (letrozole/fulvestrant), as first-line treatment of hormone receptor-positive, HER2-negative locally advanced or metastatic breast cancer (MBC) based on the results of the PALOMA-2 and PALOMA-3 clinical trial. Palbociclib, a CDK4/6 inhibitor, has been available in Montenegro since 2020., including both premenopausal and postmenopausal women treated in the first and second lines of therapy.

Methods: This retrospective study included 115 patients who started palbociclib treatment between January 2021 and December 2024. The primary endpoint was progression-free survival (PFS), defined as the time from the initiation of ET plus palbociclib to disease progression or death. We also analized patient characteristics such as age, menopausal status, metastatic sites and safety profile of palbociclib. Safety was analyzed by monitoring adverse events (AEs) such as hematotoxicity, skin toxicity, hepatotoxicity and others.

Results: The median age of the patients was 65 years (in most cases, therapy was initiated in elderly patients, among postmenopausal women – 94%). Bone is the most frequent site of metastasis, occurring in approximately 80% of cases. Liver metastases were observed in 15 patients (13%) and only 7% of patients presented with metastases at other sites, such as the lungs, pleura, mediastinal lymph nodes, supraclavicular lymph nodes… Palbociclib in combination with endocrine therapy (ET) was administered to the majority of patients (76%) as first-line treatment for metastatic disease, while 28 patients (24%) received it as second-line treatment (after chemotherapy or therapy with letrozol in the metastatic setting). For Progression-Free Survival (PFS) we included patients who initiated therapy between January 2021 and December 2024. Out of 115 patients, at the time of data cutoff, 66 (57%) had experienced a progression event. The median PFS was 14 months (range: 3–51 months). The analysis demonstrated that palbociclib has an acceptable safety profile in clinical practice. The most common adverse effect was neutropenia, which was recorded in 44 patients (38%), primary in Grade 1 and 2 (only 11 patients experienced Grade 3 or 4). Anemia was reported in 10 patients (9%) – (Grade 3 in 1 patients). Thrombocytopenia was observed in 7 patients (6%) – Grade 3 in 1 patient. Elevated transaminases occurred in 4 patients (3%). Pancytopenia was reported in 3 patients (3%), all Grade 1. A maculopapular rash was observed in 1 patient (1%) and others AE are rare about 1% (decreased ejection fraction, fatigue, nausea, renal impairment).

Conclusions: This analysis indicates that in clinical practice, the drug palbociclib in combination with ET demonstrates an acceptable safety profile, with a m-PFS of approximately 14 months. These results are consistent with findings reported in the available literature. Compared to the PALOMA-2 and PALOMA-3 studies, these outcomes may be explained by the fact that palbociclib was predominantly administered to older, postmenopausal women with cardiovascular comorbidities (only 6% were premenopausal women). Additionally, a significant proportion of patients (50%) received this CDK4/6 inhibitor in combination with fulvestrant, which may account for the consistency of these results with those observed in the PALOMA-3 study.

Keywords: palbociclib, clinical practice, efficacy, safety

REFERENCES

1. Turner NC, Finn RS, Martin M, et al. Clinical considerations of the role of palbociclib in the management of advanced breast cancer patients with and without visceral metastases, Annal of Oncology, 2018 Jan 11;29(3):669–680. doi: 10.1093/annonc/mdx797.
2. Cristofanilli M, Turner NC, Bondarenko I, et al. Fulvestrant plus palbociclib versus fulvestrant plus placebo for treatment of hormone-receptor-positive, HER2– negative metastatic breast cancer that progressed on previous endocrine therapy (PALOMA-3): final analysis of the multicentre, double-blind, phase 3 randomised controlled trial. The Lancet Oncology. 2016;17(4):425-439.
3. Im SA, Mukai H, Park IH, et al. Palbociclib plus letrozole as first-line therapy in postmenopausal asian women with metastatic breast cancer: results from the phase III, randomized PALOMA-2 study. J Glob Oncol. 2019;5:1-19. doi: 10.1200/JGO.18.00173.
4. Fernández-Cuerva C, del Rio Valencia JC, Tamayo Bermejo R. Effectiveness and safety of palbociclib plus endocrine therapy in hormone receptor–positive, HER2-negative metastatic breast cancer: real-world results. The Canadian Journal of Hospital Pharmacy, 2022;75(1):26–33. doi: 10.4212/cjhp.v75i1.3252.

P36 – HERENA: REAL-WORLD EXPERIENCE WITH ADJUVANT CHEMOTHERAPY AND HER2 BLOCKADE AFTER UPFRONT SURGERY FOR STAGE II AND III HER2– POSITIVE BREAST CANCER

SANJA LEKIC[1], Ivana Vukovic[1], Bojana Golubovic[1], Milica Radisavljevic[2]

[1]*Institute of Oncology, Clinical Center of Montenegro, Podgorica, Montenegro*
[2]*Roche d.o.o. Belgrade, Serbia*

Introduction: The discovery of Human Epidermal Growth Factor Receptor 2 (HER2)-targeted therapies has significantly improved the prognosis for patients with HER2 positive breast cancer. A meta-analysis conducted by the Early Breast Cancer Trialist Collaborative Group (EBCTCG) between 2000 and 2005, encompassing data from over 13,800 women, demonstrated a significant reduction (nearly one-third) in both mortality and recurrence risk with the addition of trastuzumab to chemotherapy.

Aim: This study aims to analyze real-world clinical data to understand the treatment patterns for stage II and III HER2-positive breast cancer, focusing on both the proportion of patients initially treated surgically who received adjuvant chemotherapy and HER2 blockade and the most frequently utilized type of surgical procedure within this subset of patients.

Methods: This study retrospectively analyzed data from all patients with HER2-positive breast cancer (stage II and III) in Montenegro during 2022 who underwent initial surgical treatment and subsequently required adjuvant chemotherapy alongside HER2-targeted therapy. The data were sourced through a review of multidisciplinary team decisions, medical reports, and pathological findings.

Results: In 2022 at the Institute of Oncology at the Clinical Center of Montenegro (KCCG), 58 patients were diagnosed with early-stage (II or III) HER2-positive breast cancer, with 63.79% also positive for Estrogen Receptor (ER) and Progesterone Receptor (PR). Initial surgical treatment was performed in 22 patients (37.93%), with radical mastectomy (50%) being the most common, followed by breast-conserving surgery with SLNB (45.45%).Notably, a high proportion (77.27%, 17 patients) of these surgically treated individuals required adjuvant chemotherapy with dual HER2 blockade (13.6% receiving trastuzumab + pertuzumab, 9.09% trastuzumab alone), with an average of 17.4 cycles administered. The majority (77.27%) were postoperatively staged as II (primarily IIA).

Conclusions: Considering that HER2 positive breast cancer was once among the more aggressive forms of breast cancer with poor prognosis, and that we now have innovative drugs that significantly change the prognosis for our patients, we must work on multidisciplinary collaboration to ensure that our patients receive adequate treatment and improve survival rates. It is concerning that in Montenegro, there is still a significant number of high-risk, early-stage HER2-positive breast cancer patients undergoing initial surgery without multidisciplinary consent.

Keywords: HER2 positive breast cancer, high-risk tumor, adjuvant chemotherapy, adjuvant HER2 blockade.

REFERENCES

1. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Trastuzumab for early-stage, HER2-positive breast cancer: a meta-analysis of 13 trials. The Lancet Oncology, 2021;22(8):1139-1150.
2. Slamon D, Eiermann W, Robert N, et al. Adjuvant trastuzumab in HER2-positive breast cancer. New England Journal of Medicine. 2011;365(14):1273-1283.
3. Burstein HJ, Winer EP. Adjuvant systemic therapy for HER2-positive breast cancer, UpToDate, 2025, February 27.
4. Loibl S, André F, Bachelot T, et al. Early breast cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Annals of Oncology. 2024;35(2):159-182.

P37 – HERENA: REAL-WORLD TREATMENT PATTERNS OF EARLY HER2+ BREAST CANCER IN MONTENEGRO

SANJA LEKIC[1], Ivana Vukovic[1], Bojana Golubovic[1], Milica Radisavljevic[2]

[1]*Institute of Oncology, Clinical Center of Montenegro, Podgorica, Montenegro*
[2]*Roche d.o.o. Belgrade, Serbia*

Introduction: Approximately 20-25% of breast cancer (BC) cases are characterized by HER2 amplification. Current standard of care for this subtype of breast cancer, particularly in patients with locally advanced, inflammatory, and initially inoperable stages of the disease involves chemotherapy in combination with dual HER2 blockade. One of the aims of neoadjuvant treatment is to downstage the disease to facilitate safe surgery, with evidence indicating that achieving a pathological complete response (pCR) following this therapy is associated with a better prognosis in terms of disease-free survival (DFS) and overall survival (OS).

Aim: To assess our institution's experiences with neoadjuvant therapy for early HER2– positive breast cancer through data from real clinical practice during one year of patient follow– up at Clinical Center of Montenegro (KCCG).

Methods: The analysis included all patients with HER2-positive breast cancer (stage II and III) who were eligible for neoadjuvant treatment during 2022. Data were obtained retrospectively through analysis of medical reports and pathological findings. A pCR was defined as the absence of invasive cancer in both breast tissue and axillary lymph nodes (ypT0/is ypN0).

Results: In 2022, 58 patients were diagnosed with early-stage (II or III) HER2-positive breast cancer at the Institute of Oncology at KCCG with 63.79% also exhibiting ER and PR positivity. A total of 36 patients (62.06%) predominantly with stage II disease (72.22%), received neoadjuvant therapy. The most frequently used neoadjuvant treatment protocol in Montenegro is THP (taxanes (T) along with trastuzumab (H) and pertuzumab (P)) with a median of 5 therapy cycles, while only a small portion received the AC-THP sequence (anthracyclines (A) and cyclophosphamide (C) followed by taxanes and trastuzumab (H) and pertuzumab (P)) was used in 16.6% of cases. Neoadjuvant treatment resulted in a pathological complete response (pCR) in 75% of patients (n=27). Notably, patients with a Ki-67 index ≥ 20 exhibited the highest pCR rate (96.30%). Despite this high response rate,,83.33% of patients underwent radical surgery (mastectomy in 30 patients) and the majority (77.7%) received postoperative radiation therapy.

Conclusions: Neoadjuvant chemotherapy with dual HER2 blockade represents the gold standard in the treatment of early HER2 positive breast cancer at stages II and III. The most commonly used protocol in Montenegro is THP demonstrating high pCR rates while avoiding the AC– basedsequence. The highest percentage of pCR was achieved in patients with tumors exhibiting high Ki-67. It is concerning that despite a high pathological complete response (pCR) rate to neoadjuvant treatment, classical radical surgical procedures continue to be performed in Montenegro, in contrast to global practices.

Keywords: HER2 positive BC, HER2 blockade, neoadjuvant chemotherapy, pCR

REFERENCES

1. Sevcikova K, Vertakova-Krakovska B, Spanik S. Neoadjuvant treatment in patients with HER2 positive breast cancer. ISRN Oncol. 2013;2013:362467.
2. Wuerstlein R, Harbeck N. Neoadjuvant therapy for HER2-positive breast cancer. Rev Recent Clin Trials. 2017;12(2):81-92.
3. Baskin AS, Huppert LA, Kelil T, Singer L, Mukhtar RA. The neoadjuvant approach to treatment of breast cancer: Multidisciplinary management to improve outcomes. Surg Oncol Insight. 2024;1(2):100059.
4. Loibl S, André F, Bachelot T, et al. Early breast cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol. 2024;35(2):159-182.

P38 – CASE REPORT: MYOEPITHELIAL TUMOR OF THE NASOPHARYNX

SANJA LEKIC, Ivana Vukovic, Bojana Scekic

Institute of Oncology – Clinical Center of Montenegro, Podgorica, Montenegro

Introduction: Myoepithelial tumors of the head and neck are extremely rare neoplasms. These lesions are predominantly benign in nature; small subset present as an aggressive variant – myoepithelial carcinoma, which exhibits a high propensity for local recurrence and distant metastasis. The most frequent site of origin is the salivary glands. Studies suggest that onset typically occurs around the sixth decade of life, with equal distribution between sexes. Prognosis is primarily influenced by the potential for surgical resection, histological grade, and the presence of distant metastases. Given the rarity of this entity, uncertainties remain regarding its biological behavior and optimal therapeutic management.

Case presentation: A 40-year-old female presented in May 2015 to the Otorhinolaryngology Department at the Clinical Center of Montenegro with right-sided cervical swelling and hypernasal speech. Clinical examination revealed a tumor mass in the epipharyngeal region. A biopsy of the lesion was performed, and histopathological evaluation confirmed malignant soft tissue myoepithelioma. Radiological assessment via CT scan of the head and neck identified a tumor mass involving the naso-, oro-, and hypopharynx measuring 80×46 mm, along with a right-sided cervical lymph node conglomerate measuring 44×20 mm. No evidence of visceral metastases was observed. Initial treatment involved chemotherapy (carboplatin + paclitaxel; doxorubicin + ifosfamid), but no objective response was achieved, suggesting chemoresistance. Given the inoperability of the tumor, the patient underwent intensity-modulated radiation therapy (IMRT) in November 2016 – 25 fractions, total dose 50 Gy. This led to disease stabilization, which persisted until August 2017, at which point disease progression was confirmed via repeat CT (tumor dimensions: 90×50×35 mm; lymphadenopathy: 45×35×27 mm).

A multidisciplinary tumor board review recommended targeted therapy with pazopanib. The drug was well tolerated, with only grade I–II neutropenia, a performance status of 0, and no need for dose reduction. In October 2017, after two months of treatment, imaging revealed >60% tumor regression. A PET-CT scan performed in April 2019 at Acibadem Hospital demonstrated complete disease remission.

In November 2021, a follow-up biopsy was performed and no residual neoplastic tissue was identified histologically. Given the complete therapeutic response, and due to cumulative hematologic toxicity, the patient chose not to continue therapy after three years and was placed on clinical surveillance.

In February 2022, a disease relapse was confirmed, prompting re-initiation of pazopanib therapy. After three months, significant progression of the primary lesion and right-sided cervical lymphadenopathy was observed. The patient ultimately decided not to pursue further treatment.

Conclusions: Myoepithelial carcinoma is an exceptionally rare malignancy. According to available literature, the incidence of nasopharyngeal myoepithelial carcinoma ranges from 0.3% to 0.5%. This case represents the first documented instance of this diagnosis at the Oncology Institute of the Clinical Center of Montenegro. The objective of this case presentation is to highlight the significant therapeutic efficacy of pazopanib, with a complete response maintained over a 3-year treatment period.

Keywords: myoepithelial tumor, nasopharynx, pazopanib

REFERENCES

1. WangJQ, Deng RX, Liu H, et al. Malignant myoepithelioma of the head and neck: demographics, clinicopathological characteristics, treatment, and prognosis. Front Oncol. 2022;12:754967. doi: 10.3389/fonc.2022.754967
2. Xu T, Liao Z, Tang J, Guo L, Qiu H, Gao Y, Hu W. Myoepithelial carcinoma of the head and neck: A report of 23 cases and literature review. Cancer Treatment Communications. 2014;2(2–3):24–29.
3. Xu B, Katabi N. Myoepithelial carcinoma. Surg Pathol Clin. 2021;14(1):67-73. doi: 10.1016/j.path.2020.09.008.

P39 – PRURIGO NODULARIS INDUCED BY ANTI-HER2 THERAPY: A RARE BUT CHALLENGING SKIN REACTION IN BREAST CANCER MANAGEMENT

SANJA LEKIC[1], Ana Popovic[2], Milica Bojic[2], Tanja Nenezic[3]

[1]*Institute of Oncology, Clinical Center of Montenegro, Podgorica, Montenegro*
[2]*Clinical od Dermatovenereology, Clinical Center of Motenengro, Podgorica, Montenegro*
[3]*Department of Pathology, Clinical Center of Montenegro, Podgorica, Montenegro*

Introduction: Breast cancer is the most commonly diagnosed malignancy among women and remains the leading cause of cancer-related mortality in the female population worldwide. Despite continuous progress in early detection and the increasing availability of adjuvant therapies leading to improved outcomes, approximately 20–30% of patients treated with curative intent will eventually develop distant metastases. Moreover, around 5–10% of patients present with metastatic disease at the time of diagnosis.

Therapeutic decisions in breast cancer are guided by both patient and disease characteristics, particularly hormone receptor and HER2 status. Approximately 15–20% of breast cancers exhibit overexpression or gene amplification of the human epidermal growth factor receptor 2 (HER2), a marker associated with aggressive tumor behavior and poor prognosis prior to the introduction of targeted therapy.

However, as with many targeted therapies, anti-HER2 agents are not without adverse effects. While the majority of side effects are well-documented and manageable, rare and unexpected cutaneous toxicities can pose diagnostic and therapeutic challenges. Prurigo nodularis (PN), a chronic pruritic dermatosis characterized by hyperkeratotic nodules and intense itching, represents a rare skin reaction linked to anti-HER2 therapy. Due to its chronic nature and impact on quality of life, timely recognition and appropriate management of PN are essential, requiring close collaboration between oncology and dermatology specialists.

Case presentation: A 61-year-old woman presented to the outpatient dermatology clinic with intensely pruritic, hyperkeratotic, and excoriated nodules ranging from 0.5 to 2 cm in diameter, accompanied by weeping or crusted erosions, primarily located on the back and limbs and confined to the trunk. She reported severe burning and itching, resulting in a significant reduction in quality of life. Her medical history includes HER2-positive early breast carcinoma, stage IIIB, for which initial treatment involved neoadjuvant therapy with taxanes in combination with dual HER2 blockade, followed by mastectomy with axillary dissection, postoperative radiotherapy, adjuvant hormonal therapy and adjuvant dual HER2 blockade. During the dermoscopic examination by a dermato-oncologist, a "white starburst pattern" was observed surrounding brown reddish to brown-yellowish crusts, erosions, and areas of hyperkeratosis or scaling findings that were consistent with the clinical diagnosis of prurigo nodularis. Skin biopsy demonstrated histologic features consistent with prurigo nodularis (PN), including parakeratosis, psoriasiform

epidermal hyperplasia, and a dermal inflammatory infiltrate composed of lymphocytes, histiocytes, and eosinophils. Despite initial topical treatment (fusidic acid/betamethasone cream and triamcinolone ointment), the patient's condition worsened. Due to the severe and persistent skin lesions, anti-HER2 therapy was discontinued as it was suspected to be the causative agent. Sonly after, a combination of topical, systemic, and intralesional corticosteroids led to rapid symptomatic improvement within four weeks. After one month, skin lesions resolved, allowing safe reintroduction of anti-HER2 therapy. Dermatological management will continue with narrow-band UVB phototherapy twice weekly and topical calcipotriene/betamethasone dipropionate foam.

Conclusions: This case highlights a rare skin reaction of prurigo nodularis associated with anti-HER2 therapy in breast cancer treatment. A multidisciplinary approach, involving close collaboration between oncologists, dermatologists, as well as pathologists, is essential for early recognition and management of such advents. Temporary cessation of therapy, combined with dermatological treatment, may enable reintroduction of life-prolonging anti– HER2 agents without compromising oncologic outcomes.

Keywords: anti-HER2 therapy, skin reaction, breast cancer

REFERENCES

1. Drucker AM, Wu S, Dang CT, Lacouture ME. Risk of rash with the anti-HER2 dimerization antibody pertuzumab: a meta-analysis. Breast Cancer Res Treat. 2012; 135:347–354. doi: 10.1007/s10549-012-2157-7
2. Ensslin CJ, Rosen AC, Wu S, Lacouture ME. Pruritus in patients treated with targeted cancer therapies: systematic review and meta-analysis. J Am Acad Dermatol. 2013; 69:708–720. doi: 10.1016/j.jaad.2013.06.038
3. Gianni L, Pienkowski T, et al. Efficacy and safety of neoadjuvant pertuzumab and trastuzumab in women with locally advanced, inflammatory, or early HER2– positive breast cancer (NeoSphere): a randomised multicentre, open-label, phase 2 trial. Lancet Oncol. 2012;13:25–32. doi: 10.1016/s1470-2045(11)70336-9

P40 – MASSIVE HEMOPERITONEUM AS THE INITIAL PRESENTATION OF METASTATIC TESTICULAR GERM CELL TUMOR: A CASE REPORT

SARA FILIPOVIĆ[1], Jovana Trifunović[1], Perica Jockić[2], Nemanja Trifunović[2], Miroslav Kreačić[1], Nebojša Mitrović[2]

[1]*Oncology Hospital, Clinical Hospital Center Zemun, Belgrade, Serbia*
[2]*Department of Surgery, Clinical Hospital Center Zemun, Belgrade, Serbia*

Introduction: Testicular tumors are relatively rare, comprising only 1% of all male malignancies, yet they represent the most common cancer in men aged 15 to 35 years. Histologically, the majority (95%) are of germ cell origin, further classified into seminomatous and non-seminomatous germ cell tumors (NSGCTs). NSGCTs generally carry a poorer prognosis due to their tendency for early hematogenous and lymphatic dissemination, most commonly to the lungs and retroperitoneum. Although metastatic disease is present at diagnosis in approximately 20% of cases, massive hemoperitoneum is an exceptionally rare presentation, with few cases reported in the literature. Spontaneous hemoperitoneum, when it occurs, is usually triggered by the initiation of chemotherapy.

Case presentation: We present the case of a 28-year-old male with no previous medical or surgical history, who arrived at the emergency department with acute abdominal pain and distension. Contrast-

enhanced computed tomography revealed a large hemorrhagic retroperitoneal mass. The patient underwent emergency laparotomy, during which active bleeding from the retroperitoneum was identified and controlled. Histopathological analysis of the resected tissue confirmed a mixed non-seminomatous germ cell tumor. The patient recovered well postoperatively and subsequently initiated chemotherapy with the BEP regimen (Bleomycin, Etoposide, Cisplatin), followed by radical orchiectomy.

Conclusions: NSGCTs are aggressive tumors that require prompt recognition and a multidisciplinary treatment approach. This case emphasizes the importance of considering retroperitoneal hemorrhage as a rare but potentially life-threatening initial manifestation of metastatic testicular cancer, even before the onset of chemotherapy.

Keywords: non-seminomatous germ cell tumor (NSGCT), retroperitoneal mass, testicular cancer, hemoperitoneum

REFERENCES

1. Motzer RJ, Bosl GJ. Hemorrhage: a complication of metastatic testicular horiocarcinoma. Urology. 1987;30(2):119–122.
2. Rodier JM, Pujade-Lauraine E, Guillonneau B, et al. Haemoperitoneum due to necrosis of bulky retroperitoneal metastases: an unusual complication of chemotherapy for testicular cancer. Br J Urol. 1996;77(6):919–920.
3. Gimeno Argente V, Bosquest Sanz M, Ramírez Backhaus M, Trassierra Villa M, Arlandis Guzmán S, Jiménez Cruz JF. Spontaneous retroperitoneal hemorrhage: our experience at last 10 years. Actas Urologicas Espanolas. 2007;31(5):521–527.
4. Filho LHCP, Silva TA, Beal PR, Buonfiglio VB, Sadi MV. Spontaneous rupture of a retroperitoneal lymph node metastasis causing massive hemorrhage in a patient with advanced mixed germ cell tumor. Urol Case Rep. 2022 Aug 4;45:102180.
5. Moore K, Imbeault A, Roy G, Bolduc S. Massive hemorrhage from spontaneous rupture of a retroperitoneal lymph node in patient with metastatic mixed germ cell tumor. Urology. 2010 Jul;76(1):159-61.

P41 – COMPARATION BETWEEN TREATMENT OUTCOMES AMONG PATIENTS WITH DIFFUSE-LARGE B-CELL LYMPHOMA TREATED BETWEEN 2003-2010 AND 2017-2021 TREATED WITH RITUXIMAB-BASED IMMUNOCHEMOTHERAPY

STEFAN ĐURIĆ[1], Maja Popović[1,2], Dragana Petrović[1], Gorana Matovina-Brko[1], Teodora Urošević[1], Nemanja Maletin[2], Stela Novak[1], Lazar Popović[1,2]

[1]*Oncology Institute of Vojvodina, Sremska Kamenica, Serbia*
[2]*Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia*

Introduction: Rituximab-based immunochemotherapy has been the standard of care for Diffuse Large B– Cell Lymphoma (DLBCL) for over 25 years. Except for patients with more aggressive subtypes of this disease, the absolute majority of patients are treated with 6 cycles of R-CHOP chemotherapy. Eleven years ago, we published the results of the first 140 patients treated with this combination in our Institution between 2003-2010.

Methods: In this paper, we will present the treatment results of 148 patients treated in the period between 2017-2021 and compare them with the historical control from the period 2003-2010.

Results: In our series of 148 patients, 50.6% were male, median age 60 years (20-89). 36.2% of patients had an IPI score of low risk, medium-low 25%, medium-high 30% and high risk 8.7%. Non-GCB subtype

was present in 57.4% of patients, 21.6% had GCB and 20.9% were unclassified. Complete response (CR) was achieved in 74.8% of patients, partial (PR) in 13.3% while 11.9% had disease progression (PD). The 3-year progression-free survival (PFS) was 69.1%, while the 3-year overall survival (OS) was 73.9%. If we compare the results from the period 2003-2010, the three-year PFS and OS were then 56.5% and 64%, respectively, which is numerically lower than in the new cohort 2017-2021 where the PFS was 69.1% and OS 73.9%. These results were achieved despite a greater number of low-risk patients (IPI score 0 and 1) 44.7% versus 36.2% in the 2003-2010 and 2017-2021 cohorts, respectively.

Conclusions: Although systemic therapy for DLBCL is basically similar, better treatment outcomes were achieved in the cohort treated an average of 13 years later. The reason probably lies in the greater utilization of PETCT imaging, more precise utilization of radiotherapy, better pathohistological and molecular diagnostics, and potentially more adequate symptomatic therapy.

Keywords: DLBCL, rituximab-based immunochemotherapy, treatment outcomes

REFERENCES

1. Popović, L. Ekspresija molekulskih markera kao faktorprognoze lečenja difuznog B-krupnoćelijskog limfoma imunohemioterapijom. Diss. University of Novi Sad (Serbia), 2013.
2. Melchardt T, Egle A, Greil R. How I treat diffuse large B-cell lymphoma. ESMO Open. 2023 Feb;8(1):100750.
3. Popovic LS, Matovina-Brko G, Popovic M, Popovic M, Cvetanovic A, Nikolic I, et al. Immunotherapy in the treatment of lymphoma. World J Stem Cells. 2021 Jun 26;13(6):503-520. doi: 10.4252/wjsc.v13.i6.503.

P42 – ADJUVANT PEMBROLIZUMAB FOR RENAL CELL CARCINOMA: ONE – YEAR EXPERIENCE AT UNIVERSITY HOSPITAL CENTRE ZAGREB

ŠIME BUŠELIĆ[1], Marija Gamulin[1,2], Milena Gnjidić[1], Zrna Antunac Golubić[1,2], Borislav Belev[1,2], Iva Nikles[1], Ana Koši Kunac[1], Lea Toula[1], Marko Lovrić[1]

[1]*Department of Oncology, University Hospital Centre Zagreb, Zagreb, Croatia*
[2]*School of Medicine, University of Zagreb, Zagreb, Croatia*

Introduction: The search for an effective adjuvant therapy for renal cell carcinoma has been marked by failures with absence of overall survival benefit in clinical trials. Keynote-564 is the first phase 3 trial to show a survival benefit with the use of adjuvant therapy over placebo in kidney cancer 1. In the trial, an immune-checkpoint inhibitor pembrolizumab was given for one year after nephrectomy to participants with an increased risk of disease recurrence, according to defined pathological criteria, as well as those with completely resected metastatic disease.

Methods: Here we present the early experience at UHC Zagreb with adjuvant pembrolizumab for patients with kidney cancer. During one-year period that pembrolizumab has been available as adjuvant therapy for kidney cancer patients, 26 patients have started treatment at UHC Zagreb.

Results: The average age at diagnosis was 62 years and 69% of patients were male. All but one patient underwent radical nephrectomy. The majority (77%) had a pathological stage T3a tumor. The most frequently described grades were 2 and 3. Three patients started treatment after resection of metastatic disease (M1, with no evidence of disease). So far, only two patients have completed all 17 cycles. Four patients (15.4%) experienced disease recurrence during adjuvant immunotherapy. All recurrences were detected in

the lungs, and in one patient additionally in the bones. All-grade adverse events were noted in 7 patients (27%), most often skin toxicity and thyroid dysfunction. Grade 3 adverse events (hypothyroidism and myositis) were reported in only one patient (3.8%). Two patients (7.7%) reported more than one adverse event. Permanent discontinuation of treatment due to adverse events occurred in two patients (one due to pneumonitis and one due to hypothyroidism and myositis).

Conclusions: One year of adjuvant pembrolizumab is a new option for kidney cancer patients with high risk of disease recurrence after nephrectomy. Limited experience at UHC Zagreb indicates a favorable tolerability with well-known adverse event profile. An individualized approach with risk and benefit assessment on a case-by-case basis is crucial for decision making on the use of adjuvant immunotherapy.

Keywords: renal cell carcinoma, adjuvant immunotherapy, adverse events

REFERENCES

1. Powles T, et al. Renal cell carcinoma: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Annals of Oncology. 2024;35(8):692 – 706

P43 – MONITORING OF ESTRADIOL VALUES IN PREMENOPAUSAL WOMAN RECEIVING OVARIAN FUNCTION SUPPRESSION IN COMBINATION WITH ANASTROZOLE AND ABEMACICLIB FOR HR POSITIVE HER2 NEGATIVE EARLY BREAST CANCER TREATMENT

LUKA BALOG[1¥], LOVRO BALEN[1¥], Katarina Čular[2], Natalija Dedić Plavetić[1,2], Tajana Silovski[1,2]

[1]*School of Medicine, University of Zagreb, Zagreb, Croatia*
[2]*Department of Oncology, University Hospital Centre Zagreb, Zagreb, Croatia*
[¥]*equal contribution*

Introduction: HR positive HER2 negative (HR+/HER2-) is the most common subtype of early breast cancer (eBC), and the backbone of its treatment represents endocrine therapy (ET). Recently, cyclin dependent kinase inhibitors (CDK4/6i), abemaciclib and ribociclib, along with ET, became standard of care in the adjuvant treatment of high-risk HR+/HER2– eBC. Aromatase inhibitors (AI) are most common ET combined with CDK4/6i, and in premenopausal women, must be given together with ovarian function suppression (OFS) using Gonadotropin-Releasing Hormone agonists (GnRHa). Adequate OFS measuring estradiol (E2) and follicle stimulating hormone (FSH) levels should be determined every few months.

Case presentation: 44-year-old premenopausal woman was diagnosed with high-risk, HR+/HER2– eBC. Due to the initial clinical and radiological tumor stage, patient underwent neoadjuvant chemotherapy followed by surgery with histopathological confirmation of partial therapeutic response. Further treatment was continued by adjuvant radiotherapy and ET consisted of OFS with GnRH a goserelin and AI anastrozole. Three months after starting goserelin and anastrozole therapy, menopausal status was checked confirming adequate OFS with low value of E2 and FSH. After completion of adjuvant RT, due to high-risk disease, abemaciclib was added to ET. Three months later, laboratory results revealed failure of OFS with E2 measuring 300 pmol/L and FSH 13.2 IU/L, although gynecological ultrasound showed no evidence of ovarian activity. After consultation with endocrinologist and no other reason found to cause

elevated E2 but inadequate OFS, the patient underwent bilateral salpingo-oophorectomy (BSO). Treatment with anastrozole and abemaciclib was continued and four months later, another check-up of E2 and FSH levels was done showing surprisingly elevated E2 value of 398 pmol/L, with FSH level of 30.6 IU/L being in postmenopausal range. At that point, doubt considering applied laboratory method (chemiluminescent microparticle immunoassay (CMIA) from Abbott Diagnostic) accuracy was raised. Meanwhile, following urinary tract infection, patient stopped taking abemaciclib and after two-week therapy holiday, E2 measurement was in postmenopausal range. In cooperation with biochemist on the same sample, measurement of E2 level was done by LC– MS/MS chromatographic method which found significantly different values of E2 being in the postmenopausal range.

Conclusions: Supposed interference of abemaciclib with determination of E2 by CMIA method could have profound implications on HR+/HER2– eBC patients' care provoking potential therapy interruptions and discontinuation with possible subsequent reduction in anticancer treatment efficacy. Therefore, in pursuit of assessing hormonal status in premenopausal women taking abemaciclib, chromatographic method LC-MS/MS should be used in monitoring E2 levels.

Keywords: early breast cancer, abemaciclib, estradiol, ovarian function suppression

REFERENCES

1. D Johnston SR, Harbeck N, Hegg R et al. Abemaciclib combined with endocrine therapy for the adjuvant treatment of HR1, HER22, node-positive, high-risk, early breast cancer (monarchE). J Clin Oncol 2020;38:3987–3998.
2. Cao L-Q, Sun H, Xie Y, et al. Therapeutic evolution in HR+/HER2– breast cancer: from targeted therapy to endocrine therapy. Front Pharmacol 2024;15:1340764.
3. Kessler AJ, Patel R, Gallagher EJ et al. Monitoring of estradiol levels in premenopausal women receiving adjuvant abemaciclib and ovarian function suppression. Breast Cancer Res Treat 2024;207(3):529-532.

P44 – IMMUNE-RELATED ADVERSE EVENTS IN METASTATIC MELANOMA PATIENTS TREATED WITH COMBINATION IMMUNOTHERAPY

VIKTOR ŠABARIĆ[1], Kata Međugorac[1], Krešimir Blažičević[1], Luka Simetić[1], Slaven Stanojlović[2], Gordana Horvatić Herceg[3], Davorin Herceg[1,4]

[1]*Department of Oncology, University Hospital Centre Zagreb, Zagreb, Croatia*
[2]*Medicol Polyclinic, Zagreb, Croatia*
[3]*Department of Nuclear Medicine and Radiation Protection, University Hospital Centre Zagreb, Zagreb, Croatia*
[4]*School of Dental Medicine, University of Zagreb, Zagreb, Croatia*

Introduction: According to National Cancer Registry, melanoma is 6th most common malignancy in Croatia, with a steady increase in incidence both nationally and globally. Despite the rising incidence, melanoma-related mortality is decreasing due to prompt diagnosis and potent treatment modalities. Immune checkpoint inhibitors (anti-PD-1 and anti-CTLA4), especially combination treatment with nivolumab and ipilimumab, have revolutionized metastatic melanoma treatment and demonstrated high response rates with durable response time. Compared with monotherapy combination immunotherapy with dual checkpoint inhibitors has shown surge in immune-related adverse events (irAE) which could lead to treatment discontinuation and permanent deterioration of patient life quality. The aim of our study

was to determine the incidence and characteristcs of irAE in metastatic melnoma patients treated with ipilimumab and nivolumab at UHC Zagreb.

Methods: From 1st of January 2024. to 1st of April 2025. at the Department of Oncology at UHC Zagreb 33 metastatic melanoma patients were treated with combination immunotherapy ipilimumab (3mg/kg) plus nivolumab (1mg/kg) for 4 cycles every 3 weeks which was continued with nivolumab monotherapy (3mg/kg) every two weeks based on Checkmate 067 study. Patients were closely monitored and screened for potential irAE. All irAE were stratified by affected organ, grade and time of onset.

Results: Of the 33 patients, 10 were female (31%) and 22 were male (69%) with a median age of 59.5 years at therapy initiation.The most frequent irAE was hepatitis (41%) followed by dermatitis (19%), thyroiditis (13%), hypophysitis (9%), nephritis (9%) and colitis (6%). Single cases of pneumonitis, meningitis, arthritis, type I diabetes and immune thrombocytopenia were also recorded. All irAEs occured within 22 weeks of treatment initiation. Most were grades 2 and 3 and no irAE-related deaths were reported.

Conclusions: Even though combination immunotherapy regimen ipilimumab and nivolumab demonstrated admirable long-term overall survival benefits in metastatic melanoma patients, irAE remain a major concern during and after the treatment. In this small cohort of patients we detected irAE in 22 of them (81%). This data emphasizes constant clinical alert in patients treated with ipilimumab and nivolumab combination. Continued clinical research is essential to optimize combination immunotherapy regimens and to develop strategies that minimize irAE incidence and severity as novel treatments emerge.

Keywords: metastatic melanoma, combination immunotherapy, checkpoint inhibitors, irAE

REFERENCES

1. Wolchok JD, Chiarion-Sileni V, Rutkowski P, Cowey CL, Schadendorf D, Wagstaff J, et al. Final, 10-year outcomes with nivolumab plus ipilimumab in advanced melanoma. N Engl J Med. 2025 Jan 2;392(1):11-22. doi: 10.1056/NEJMoa2407417.
2. Carlino MS, Larkin J, Long GV. Immune checkpoint inhibitors in melanoma. Lancet. 2021 Sep 11;398(10304):1002-1014. doi: 10.1016/S0140-6736(21)01206-X.
3. Sun Y, Shen Y, Liu Q, Zhang H, Jia L, Chai Y, et al. Global trends in melanoma burden: A comprehensive analysis from the Global Burden of Disease Study, 1990-2021. J Am Acad Dermatol. 2025 Jan;92(1):100-107. doi: 10.1016/j.jaad.2024.09.035.

P45 – CHARACTERISTICS OF PATIENTS WITH HIGH-RISK HR-POSITIVE, HER2– NEGATIVE EARLY BREAST CANCER TREATED WITH ADJUVANT ABEMACICLIB: A SINGLE-CENTRE EXPERIENCE

LOVRO BALEN[1¥], LUKA BALOG[1¥], Marija Križić[2], Katarina Čular[2], Martina Matec[2], Natalija Dedić Plavetić[1,2], Marina Popović[1,2], Tajana Silovski[1,2]

[1]*School of Medicine, University of Zagreb, Zagreb, Croatia*
[2]*Department of Oncology, University Hospital Centre Zagreb, Zagreb, Croatia*
[¥]*equal contribution*

Introduction: Hormone receptor-positive, HER2-negative (HR+/HER2-) early breast cancer (eBC) represents the most prevalent eBC subtype. Endocrine therapy (ET) is the cornerstone of its treatment.

Recently, cyclin-dependent kinase 4/6 inhibitors (CDK4/6i), initially abemaciclib and later ribociclib, in combination with ET, have become standard of care for high-risk HR+/HER2– eBC. Following the results of the MonarchE study, in October 2022, abemaciclib was reimbursed in Croatia.

Methods: This retrospective study aimed to present characteristics of the patients receiving abemaciclib, as the part of adjuvant treatment, in the University Hospital Center (UHC) Zagreb between October 2022 and March 2025. The study was approved by the Ethics Committee.

Results: A total of 59 patients with the median age of 51.8 years, started treatment with adjuvant abemaciclib in combination with ET. Of those, 31 patients (51.7%) were premenopausal women with a median age of 47.1 years. Neoadjuvant chemotherapy (NACT) was administered in 74.6% (44/59) while 3,4% (2/59) patients underwent neoadjuvant ET and 22% (13/59) underwent primary surgery. Tumor stage, prior to NACT, determined clinically and radiologically, was most often T2 (52,3%), followed by T3 (29.5%) and T1 (18.2%), while positive axillary lymph nodes were confirmed in 95.5% of patients. Following NACT, 61.4% (27/44) of patients still fulfilled MonarchE criteria, as pathohistology revealed, either 4 or more (81.5%, 22/27), or 1-3 positive axillary lymph nodes in combination with grade 3 (5/27) or tumor larger than 5 cm (1/27). In 38.6% (17/44) of patients, those criteria were not met. If the tumor was larger than 5 cm prior to NACT or if the sum of positive and negative lymph nodes showing therapy response (fibrous changes and lymphocyte depletion) after NACT was 4 or greater, patients were considered high-risk and treatment with abemaciclib was started. Among patients who underwent primary surgery, 23.1% (3/13) had T3 and 15.4% (2/13) had grade 3 tumors, while 1–3 positive lymph nodes were found in 38,5%, whereas four or more were found in 61.5% (8/13) of patients. Among the entire cohort, only 6.8% (4/59) of patients did not receive chemotherapy in either the neoadjuvant or adjuvant setting.

Conclusions: Adjuvant abemaciclib combined with ET is increasingly used in high-risk HR+/HER2– eBC. The described cohort of patients demonstrates consistent, somewhat broader, high-risk patient selection in comparison to MonarchE study criteria, with substantial neoadjuvant chemotherapy use and significant residual tumor burden. These findings support the real-world applicability of abemaciclib in managing biologically aggressive disease with pronounced importance of individualized, risk-adapted adjuvant strategies.

Keywords: early breast cancer, adjuvant therapy, abemaciclib

REFERENCES

1. Johnston SRD, Harbeck N, Hegg R, et al. Abemaciclib combined with endocrine therapy for the adjuvant treatment of HR+, HER2-, node-positive, high-risk, early breast cancer (monarchE). J Clin Oncol. 2020 Dec 1;38(34):3987-3998.
2. Rastogi P, O'Shaughnessy J, Martin M, et al. Adjuvant abemaciclib plus endocrine therapy for hormone receptor-positive, human epidermal growth factor receptor 2-negative, high-risk early breast cancer: results from a preplanned monarchE overall survival interim analysis, including 5-year efficacy outcomes. J Clin Oncol. 2024 Mar 20;42(9):987-993
3. Johnston SRD, Toi M, O'Shaughnessy J, et al. Abemaciclib plus endocrine therapy for hormone receptor-positive, HER2-negative, node-positive, high-risk early breast cancer (monarchE): results from a preplanned interim analysis of a randomised, open-label, phase 3 trial. Lancet Oncol. 2023 Jan;24(1):77-90.