POSTER PRESENTATIONS

P1 – 1 COHORT, 2 MINISTRIES, 3 SPECIALTIES: SYNERGY OF SYSTEMS IN THE TREATMENT OF PATIENTS WITH RADIATION-INDUCED HEMORRHAGIC CYSTITIS WITH HYPERBARIC OXYGEN THERAPY

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Introduction: Radiotherapy (RT) is a key method of treatment for many pelvic malignancies, including cancer of the prostate, bladder, cervix, endometrium and rectum(1-3). Although the effectiveness of RT in controlling tumor growth is significant, it can cause numerous late side effects, among which radiation-induced hemorrhagic cystitis (RIHC) is one of the most severe and persistent complications(4).

RIHC refers to damage to the bladder caused by ionizing radiation, which usually occurs months or years after the end of therapy, and is manifested by hematuria, pain, and difficulty urinating. The pathophysiological mechanism involves progressive vascular damage, fibrosis, and chronic ischemia of the detrusor and bladder mucosa, which leads to the loss of normal tissue regeneration and the development of chronic inflammation(5). The incidence of RIHC varies depending on the type and dose of RT, the techniques used, and the comorbidities of the patients. Despite the development of modern RT methods such as IMRT (Intensity-Modulated Radiation Therapy), which allow for more precise targeting of the tumor while sparing surrounding healthy tissue, the risk of bladder damage still exists, especially with high cumulative doses or combined therapies (e.g. external beam radiation + brachytherapy)(6). Due to the limited efficacy of conventional therapeutic approaches (bladder lavage, intravesical agents, and coagulation), the role of hyperbaric oxygen therapy (HBOT) as an alternative and adjuvant method of treating this serious complication(7).

Materials and methods: A cohort of patients treated at the Split University Hospital Center, who received HBOT due to radiation sequelae, is presented.

From September 2020 to July 2025, 29 patients were identified and referred to the Institute of Maritime Medicine in Split for HBOT.

3 patients were excluded from further analysis: 1 patient with a contraindication in the form of pulmonary embolism, 1 patient for whom the end date of radiotherapy and data on the applied dose are missing, and 1 patient who was referred for HBOT, but then did not report to UHC Split. One patient was referred to HBOT for post-radiation treatment proctitis, previously unsuccessfully treated with APC (argon plasma coagulation). Among the remaining 25 patients, 22 were treated with radiotherapy for prostate cancer, 1 patient was treated with chemobrachyradiotherapy for cervical cancer, 1 patient was treated with a bladder sparing approach for bladder cancer, and 1 patient was treated with radiotherapy for uterine corpus cancer.

All referred patients, prior to referral to HBOT, underwent at least one cystoscopy, which determined hyperemia/vulnerable bladder mucosa/ post-radiation cystitis, and confirmed the absence of secondary bladder cancer by cytology or trans-urethral resection. Most patients received at least 1 transfusion prior to referral to HBOT.

Results: The median time from the end of radiation to the onset of hematuria was 34.7 months.

The average prescribed dose was 67 Gy (range 61-76 Gy), in the majority of patients (96%), administered in conventional daily fractions of 200 cGy.

Two patients (8%) are currently undergoing HBOT treatment, one (4%) has no therapeutic effect from HBOT, and one patient (4%) did not report to the Clinical Hospital after completing treatment. Partial/complete regression of RIHC was achieved in 21 patients (84%) – complete regression of RIHC in 18 patients (72%), and partial regression in 3 patients (12%), of which three patients underwent double HBOT treatment, after which partial/complete regression of RIHC occurred. Among the side effects, only one high– grade side effect was recorded – unilateral hearing loss in one patient (4%).

HBOT has shown high efficacy with a favorable toxicity profile in patients with RIHC, in our patient cohort. The results achieved are in line with international publications on the subject. HBOT is a valuable therapeutic option in patients in whom conservative treatment methods are ineffective.

Keywords: radiation, side effects, radiation cystitis, hyperbaric oxygen therapy

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P2 – ADJUVANT PEMBROLIZUMAB IN CLEAR CELL RENAL CELL CARCINOMA (CCRCC): SINGLE-INSTITUTION AND TERTIARY CANCER CENTER EXPERIENCE.

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Background: Clear cell renal cell carcinoma (ccRCC) is the most prevalent subtype of kidney cancer, and patients with intermediate-high or high risk of recurrence following surgery face a substantial chance of disease recurrence[1]. Adjuvant pembrolizumab has been shown to improve survival outcomes in this population, most notably in the KEYNOTE-564 study, which demonstrated a significant overall survival benefit (hazard ratio (HR) 0.62) compared with placebo[2,3]. Subsequent real-world evidence from the multinational ARON-1 study has supported the feasibility of this strategy[4]. We report outcomes from a single Croatian center to further characterize real-world implementation in routine clinical practice.

Materials and methods: We conducted a retrospective single-center observational cohort study of patients with histologically confirmed ccRCC who initiated adjuvant pembrolizumab between January 1, 2024, and December 31, 2025, at the Department of Oncology and Radiotherapy, University Hospital Split, Croatia. Eligible patients met intermediate-high or high-risk criteria according to KEYNOTE-564, defined as: pT2 grade 4 or sarcomatoid differentiation, N0M0; pT3 any grade, N0M0; pT4 any grade, N0M0; any pT, N+ M0, M1 with no evidence of disease following metastasectomy (M1 NED)[3]. Radiologic assessment was performed every 12–16 weeks. Disease recurrence was defined as radiologically confirmed local or distant relapse. Endpoints included treatment exposure, completion rate, discontinuation patterns, immune-related adverse events (irAEs; graded per Common Terminology Criteria for Adverse Events (CTCAE)), and recurrence characteristics. Data were analyzed using descriptive statistics; median follow-up was calculated using the reverse Kaplan–Meier method.

Results: The cohort included 25 patients; 24% were female, and the median age was 65 years (IQR 60–70). Most patients had an ECOG performance status of 0 (96%). A sarcomatoid component was present in 8% of tumors, and tumor necrosis in 48%. Tumor grade distribution was as follows: grade 2 (40%), grade 3 (32%), and grade 4 (28%), respectively. At data cutoff, 10/25 patients (40%) remained on therapy. The median number of administered cycles was 8 (range 1–17), and 5/25 patients (20%) had completed the planned course of pembrolizumab. Adverse events were reported in 13 patients (52%), with 8 (32%) requiring treatment for toxicity. Grade ≥3 toxicity occurred in 4 patients (16%), leading to treatment discontinuation in 5 patients (20%). The most common toxicities were thyroid dysfunction, skin toxicity, and colitis. Among these five patients, one experienced disease progression. Overall, early treatment discontinuation occurred in 10 of 25 patients (40%). After a median follow-up of 11.2 months (range 2.9–21.4), disease recurrence occurred in 7 patients (28%): 5 during ongoing pembrolizumab therapy and 2 following treatment discontinuation. Lung metastases were the predominant site of relapse (71%). Median time to recurrence was 5.6 months (range 2.1–9.4). With a median follow-up of 11.2 months, the estimated 12-month DFS rate was 72%.

Conclusion: In this single-center Croatian cohort, adjuvant pembrolizumab demonstrated safety comparable to that observed in pivotal trials and real-world studies. Although recurrence rates appeared numerically higher than those reported in KEYNOTE-564, interpretation is limited by shorter follow-up and the small sample size. Notably, relapse during ongoing therapy in five patients may suggest primary

resistance or suboptimal pre-adjuvant staging in a subset of cases. These real-world data confirm the manageable safety profile of adjuvant pembrolizumab in routine practice. However, high recurrence rates highlight the need for improved risk stratification, better staging procedures (stage migration), and predictive biomarkers.

Keywords: carcinoma, renal cell; immune checkpoint inhibitors; immune-related adverse events; real-world performance

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P3 – ANTI-ANGIOGENIC THERAPY BEYOND CHEMORESISTANCE: BEVACIZUMAB IN ADVANCED LOW-GRADE SEROUS OVARIAN CARCINOMA – REAL-WORLD EXPERIENCE FROM SERBIA

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Background: Low-grade serous ovarian carcinoma (LGSOC) accounts for less than 10% of epithelial ovarian malignancies and is characterized by an indolent clinical course, pronounced chemoresistance, and a distinct molecular profile. Standard first-line therapy includes paclitaxel and carboplatin, while bevacizumab, a monoclonal antibody targeting vascular endothelial growth factor (VEGF), has increasingly been incorporated to prolong progression-free survival (PFS).

Objective: To evaluate the efficacy of bevacizumab combined with carboplatin and paclitaxel as first-line therapy in patients with advanced LGSOC FIGO stage IIIC/IV, with analysis of surgical status and postoperative findings as potential predictors of therapeutic response.

Methods: A retrospective study included 27 patients with histologically confirmed LGSOC FIGO IIIC/IV treated at the Institute for Oncology and Radiology of Serbia between December 2017 and October 2025. All patients received paclitaxel (175 mg/m^2) and carboplatin (AUC 5) plus bevacizumab (7.5 mg/kg) for up to 17 cycles. Parameters evaluated included surgical status, postoperative findings, number of bevacizumab cycles, response according to RECIST criteria, progression-free survival (PFS), and overall survival (OS).

Results: Suboptimal cytoreduction was achieved in 19 patients (70.4%), 4 (14.8%) were inoperable, and optimal cytoreduction (<1 cm residual disease) was achieved in 4 (14.8%). The most frequent postoperative finding was peritoneal carcinomatosis (15; 55.6%). The mean number of bevacizumab cycles was

10.3. The overall response rate (RR) was 48.1%, with an additional 14.8% achieving NED, indicating clinical benefit in 62.9% of patients. Median PFS was 21.6 months, and median OS was 32 months, suggesting potential long-term benefit in this selected population.

Conclusion: Bevacizumab combined with paclitaxel and carboplatin demonstrated clinical benefit in patients with LGSOC FIGO IIIC/IV despite a high rate of suboptimal cytoreduction. A median PFS of 21.6 months and OS of 32 months are comparable with published data, supporting the efficacy of anti-angiogenic therapy in this specific population.

Keywords: low-grade serous ovarian carcinoma; bevacizumab; progression-free survival; response rate; cytoreduction

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P4 – BASELINE METABOLIC RISK FACTORS AND ADJUSTED TREATMENT EFFECTS ON GRADE 3–4 HYPERGLYCEMIA DURING ALPELISIB THERAPY: COVARIATE MODELS FROM THE ITACA RANDOMIZED PHASE IIB TRIAL

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Background: Alpelisib plus fulvestrant is a validated treatment option for patients with PIK3CA-mutated, HR-positive/HER2-negative metastatic breast cancer; however, hyperglycemia remains the dominant on-target toxicity that can jeopardize sustained treatment delivery (1–3). Severe events often occur early, and standardized algorithms emphasize monitoring and pharmacologic intervention (2,4–6). In practice, clinically available baseline metabolic characteristics may meaningfully determine who develops grade 3–4 hyperglycemia and could therefore be leveraged for preventive, risk-adapted supportive care.

Methods: ITACA was a multicenter, open-label, randomized phase IIb trial conducted at three Croatian university hospitals and registered in the European Union Clinical Trials Register (EudraCT 2021-000845-42). Postmenopausal women with HR-positive, HER2-negative, PIK3CA-mutated metastatic breast cancer progressing on endocrine therapy were randomized 1:1 to alpelisib 300 mg once daily as either standard morning dosing or evening dosing at 22:00 after a ≥5-hour fasting interval with low-carbohydrate dietary guidance, both with fulvestrant. This analysis used the safety population (≥1 alpelisib dose). The endpoint was the first CTCAE v4.03 grade 3–4 hyperglycemia within 90 days of initiation or 30 days after discontinuation. Exposure-adjusted incidence rates (EAIR) were estimated and Poisson regression models with log(person-time) offset were fitted. Adjusted incidence rate ratios (aIRR) were derived using a protocol-specified covariate set (study center, age, metastatic distribution, prior chemotherapy, baseline HbA1c, baseline BMI). A prespecified sensitivity analysis redefined time at risk from Day 2 to remove Day-1 dosing-time asymmetry.

Results: In adjusted modeling from Day 1, evening dosing with fasting and dietary guidance was associated with a lower incidence of grade 3–4 hyperglycemia versus morning dosing (aIRR 0.37; 95% CI 0.13–1.08; p=0.058). Baseline HbA1c and BMI were independently associated with severe hyperglycemia risk: HbA1c was strongly associated with risk (aIRR 4.38; 95% CI 1.87–10.56; p=0.001), and BMI contributed additional risk (aIRR 1.24 per kg/m²; 95% CI 1.07–1.42; p=0.003). When analyses began on Day 2, the adjusted treatment association strengthened (aIRR 0.28; 95% CI 0.10–0.83; p=0.017) and BMI remained predictive (aIRR 1.16 per kg/m²; 95% CI 1.01–1.33; p=0.037).

Conclusion: Baseline HbA1c and BMI were strong independent predictors of grade 3–4 hyperglycemia during alpelisib therapy, and an evening dosing strategy with a short fasting interval plus low-carbo-

hydrate guidance was associated with a lower adjusted incidence of severe events–particularly in sensitivity analyses starting from Day 2. Because HbA1c and BMI are routinely available before treatment initiation, these findings support a pragmatic risk-stratified approach in which patients at higher metabolic risk are prioritized for intensive glucose monitoring and early integration of dosing-context optimization alongside guideline-based management.

Keywords: alpelisib; hyperglycemia; HbA1c; body mass index; risk stratification; Poisson regression

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P5 – BIOCHEMICAL AND METASTASIS-FREE SURVIVAL AFTER POST-PROSTATECTOMY SALVAGE RADIOTHERAPY: UPDATED ANALYSIS AND IMPACT OF CONCOMITANT ADT AND FRACTIONATION IN A SINGLE-CENTRE RETROSPECTIVE COHORT

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Introduction: Post-prostatectomy salvage radiotherapy (sRT) for biochemical failure (BF) is frequently combined with androgen deprivation therapy (ADT) and delivered using different fractionation schemes (moderately hypofractionated and conventionally fractionated). We assessed biochemical failure-free survival (BFFS) and metastasis-free survival (MFS) and explored associations with concomitant ADT and radiotherapy treatment factors.

Patients and Methods: This is retrospective updated analysis of 378 patients treated with post-prostatectomy sRT (database cutoff: 02-Mar-2026). BF and metastasis were coded as binary events; time-to-event used BFF duration and MFS duration (months). Kaplan–Meier (KM) estimated BFFS/MFS; median

follow-up was calculated by reverse KM. Baseline comparisons between ADT and no-ADT used Mann–Whitney U and χ^2 tests. Multivariable Cox proportional hazards regression for BFFS adjusted for Gleason sum, pT group (≤T2 reference; T3a; ≥T3b), pN (N0 reference; N1), RT volume (prostate bed reference; pelvis), margins, ECE, SVI, log(pre-RT PSA), fractionation (52.5(Gy)/20(fractions) reference vs 66/33 or 70/35), and concomitant ADT (yes/no).

Results: Median age at prostatectomy was 65.0 years (range 44–80). Major pathological findings: Gleason 7 predominated (n=284, 75.1%); pT group: ≤T2 n=173 (45.8%), T3a n=75 (19.8%), ≥T3b n=113 (29.9%), 17 patients had unknown pT stage (4.5%); pN1, n=38 (10.1%). Positive margins were present in 195/347 (56.2%), ECE in 172/358 (48.0%), and SVI in 115/358 (32.1%). Prostate-bed RT was delivered in n=337 (89.2%); pelvic RT in n=41 (10.8%). RT scheme was 66/33 or 70/35 in n=243 (64.3%), 52.5/20 in n=121 (32.0%), and early interrupted or other regimens in 14 patients (3.7%). Concomitant ADT was used in 226/378 (59.8%) (long 49.6%, short 50.4% among ADT). Overall BF occurred in 147/378 (38.9%), metastasis in 73/378 (19.3%), and RT side effects of any grade were recorded in 103/378 (27.2%). Whole-cohort KM estimates showed 6-year BFFS 54.87% and 6-year MFS 79.30%; reverse-KM median follow-up was 71.0 months. At 5 years, KM BFFS was 55.39% with ADT vs 70.90% without ADT; KM MFS was 81.75% with ADT vs 89.98% without ADT. ADT patients had higher-risk features and earlier RT (RP-to-RT interval median 8 vs 22 months; p<0.0001; pT distribution p<0.0001; SVI p<0.0001; Gleason sum p<0.0001; pre-RT PSA p<0.0001). In multivariable Cox analysis for BFFS, significant predictors were log(pre-RT PSA) (HR 1.269, 95%CI 1.104–1.459; p=0.000806), conventional fractionation vs 52.5/20 (HR 0.567, 95%CI 0.378–0.852; p=0.006282), and concomitant ADT (HR 1.686, 95%CI 1.037–2.743; p=0.035170).

Discussion: Multivariable Cox analysis for BFFS showed that higher pre-RT PSA increased biochemical failure risk, and conventional fractionation (66/33 or 70/35) reduced failure when compared with hypofractionation (52.5/20) (HR 0.567, p=0.006). Unadjusted KM comparisons suggested worse outcomes with concomitant ADT, but ADT was preferentially used in patients with higher-risk pathology and shorter RP-to-RT intervals, indicating confounding by indication; KM estimates by ADT status should therefore be viewed cautiously. Deficiencies of this study are its retrospective, non-randomized design and treatment-selection bias for both ADT and fractionation; baseline risk imbalance, treatment era/technique effects, and unmeasured clinical factors that may have produced residual confounding. These findings support earlier sRT at lower PSA, but need validation

Keywords: prostate cancer; biochemical failure; salvage radiotherapy; androgen deprivation therapy; hypofractionation; radical prostatectomy

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P6 – CDK4/6 INHIBITORS AS ADJUVANT THERAPY IN THE TREATMENT OF EARLY-STAGE BREAST CANCER – SINGLE INSTITUTION EXPERIENCE

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Introduction: Hormone-dependent, HER2-negative breast cancer accounts for 70-75% of all breast cancers and is often diagnosed early. Some patients with resected stage II and III disease are treated with CDK4/6 inhibitors (abemaciclib or ribociclib) and endocrine therapy due to higher risk of recurrence. This study aims to describe the characteristics of patients treated with this therapy, their experience of side effects and their compliance with the treatment regimen.

Methods: A retrospective cohort study was conducted, including all patients with early-stage breast cancer treated with adjuvant ribociclib or abemaciclib and endocrine therapy in the period from 2023 to February 2026. The data were analysed using descriptive statistics.

Results: Thirty-one patients received adjuvant CDK4/6 inhibitors: 19 (61.3%) received ribociclib and 12 (38.7%) abemaciclib. Median age of patients treated with ribociclib was 58 years, lymph node involvement (1–3 lymph nodes) was determined in 13 (68.4%) patients, and 10 (52.6%) patients were treated with chemotherapy, of whom 1 patient received neoadjuvant and 9 received adjuvant treatment. The median age of patients treated with abemaciclib was 57.5 years. All of the patients had lymph node involvement, while 9 (75%) had four or more lymph nodes affected (N2 disease). Six (50%) patients received chemotherapy, 4 of them as neoadjuvant and 2 as adjuvant treatment. In the ribociclib group, the median number of cycles received was 6. Adverse events were reported in 13 (68.4%) patients, of which grade 3 or 4 events were reported in 4 (21.1%) patients. The most prevalent were hepatotoxicity (36.8%), nausea (26.3%), fatigue (21.1%) and neutropenia (10.5%). QTc interval prolongation was reported in a single patient (5.3%). Ribociclib dosage was reduced in 3 patients (15.8%) due to adverse events. In 5 patients (26.3%), therapy

was temporarily interrupted, and in 4 (21.1%), permanently discontinued. In two cases, patients discontinued the medication due to adverse effects, specifically nausea, and did not consent to a dose reduction. This occurred after Cycle 1 and after Cycle 4. In the other two cases, the drug was discontinued due to the development of grade 4 hepatitis (after Cycle 10) and cardiac surgery. In the abemaciclib group, the median number of cycles received was 15. Adverse events were reported in 11 (91.7%) patients, but there were no grade 3 or 4 adverse events. The most prevalent adverse events were diarrhoea (66.7%), neutropenia (33.3%), thrombocytopenia (8.3%), and anaemia (8.3%). The abemaciclib dose was reduced due to adverse events in 5 (41.7%) patients, of whom one had a dose reduction twice due to renal function deterioration. In 6 patients (50%), therapy was temporarily interrupted, and one patient died during abemaciclib therapy (the cause of death was not recorded).

Conclusion: Adjuvant ribociclib or abemaciclib with endocrine therapy is indicated for patients according to the results of the NATALEE and MonarchE studies, respectively. The observed adverse events do not fully correspond to those reported in the studies due to the small number of patients. Further investigation is required over time to evaluate disease-free survival and overall survival. It is essential to collect real-world data from one's own centre to facilitate informed, evidence-based decisions.

Keywords: ribociclib; abemaciclib; adjuvant therapy; adverse events

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P7 – CHARACTERISTICS AND OUTCOMES OF PATIENTS WITH GASTROINTESTINAL TUMORS UNDER 50 YEARS OF AGE – A SINGLE-CENTER EXPERIENCE

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Introduction: According to GLOBOCAN, the incidence and mortality of gastrointestinal (GI) cancers are projected to double by 2050. Early-onset GI cancers, typically defined as cancer diagnosed in individuals younger than 50 years, are among the largest subset of early-onset cancers globally. These tumors are predominantly associated with genetic alterations and hereditary syndromes (e.g., Lynch syndrome and familial adenomatous polyposis). However, a growing number of cases are reported as sporadic, with yet uncertain early detection and treatment strategies for this group of patients. The aim of this work is to analyze characteristics and treatment patterns of our patient cohort.

Methods: This was a single-center retrospective analysis of 30 patients (19 female (63.33%) and 11 male (36.67%)) who were younger than 50 years at the time of diagnosis of a malignant gastrointestinal tumor and were treated from March 2021 to February 2026 in Sestre milosrdnice University Hospital Centre. Data was analyzed using descriptive statistics and Python v. 3.14.3.

Results: The median age of the patients at the time of diagnosis was 44 years (range: 33-50). A significant majority (83.33%) of the patients were diagnosed with colorectal carcinoma, colon (21 patients) and rectum (4 patients) respectively. Three patients were diagnosed with gastric cancer and 2 patients with pancreatic cancer. A positive family history of malignancy was identified in 18 cases, 13 of whom had a family history of gastrointestinal cancer. Comprehensive genomic profiling revealed targetable genetic alterations in two patients. In one case findings suggest an association with hereditary Lynch syndrome. Nine individuals had a negative family history of malignancy, while data were unavailable for three individuals. At the time of the diagnosis, 20 patients (67%) presented with metastatic disease. Treatment course and outcomes of these patients are shown graphically on swimmer-plot.

Conclusion: Given that 60% of patients with young-onset gastrointestinal cancer had a positive family history of malignancy, screening strategies for this target population should be improved. The high prevalence of patients presenting with metastatic disease at initial diagnosis further supports this rationale.

Keywords: early-onset gastrointestinal cancer, positive family history

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P8 – COMPARATIVE PERFORMANCE OF LARGE REASONING MODELS AND HUMAN MULTIDISCIPLINARY TEAMS IN LUNG CANCER DECISION-MAKING

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Background: Multidisciplinary teams (MDTs) are the cornerstone of lung cancer decision-making, providing integrated diagnostic and therapeutic recommendations. However, MDT performance may vary due to workload, time constraints, and heterogeneity in expertise. Large reasoning models (LRMs), an advanced class of large language models designed for multi-step clinical reasoning, have recently demonstrated strong performance in oncology-related tasks. Direct head-to-head comparisons between different LRMs and real-world MDT decisions remain limited, particularly in consecutive clinical cases. This study aimed to compare the performance of two LRMs (GPT-5-Thinking and DeepSeek-v3-r1) with each other and with human MDT decisions in real-world lung cancer care.

Methods: This single-centre real-world study included 100 consecutive lung cancer cases discussed at a tertiary thoracic oncology MDT. Fifty cases were analyzed retrospectively (retrograde phase), reflecting MDT decisions made without awareness of AI evaluation, and fifty cases were analyzed prospectively (anterograde phase), where MDT members were informed that their decisions would be compared with AI-generated recommendations. For each case, anonymized structured clinical summaries excluding MDT conclusions were submitted to both LRMs. Models generated structured recommendations for radiologic diagnostics, pathologic diagnostics, and oncologic therapy. Two independent experienced lung oncologists evaluated MDT decisions and model outputs using standardized 1–5 Likert scales. An average recommendation score (avg_rec) was calculated as the mean of the three recommendation domains.

Results: Both LRMs generated high-quality recommendations across diagnostic and therapeutic domains, with GPT-5-Thinking consistently outperforming DeepSeek-v3-r1. In paired case-level comparisons, GPT-5-Thinking achieved significantly higher ratings than DeepSeek-v3-r1 for radiologic diagnostics and oncologic therapy, particularly in the retrograde phase, while maintaining superiority in key diagnostic domains in the anterograde phase. When compared with MDT decisions, GPT-5-Thinking demonstrated significantly higher overall recommendation quality in both phases. In the retrograde phase, GPT-5-Thinking achieved a mean avg_rec of 4.90 compared with an MDT score of 4.14, while DeepSeek-v3-r1 also exceeded MDT performance (4.56 vs 4.14). In the anterograde phase, GPT-5-Thinking again outperformed MDT decisions (4.79 vs 4.34), whereas DeepSeek-v3-r1 no longer demonstrated a statistically significant advantage over MDT outputs. Overall, GPT-5-Thinking was the highest-performing decision-support system across phases and domains.

Conclusion: In real-world lung cancer MDT cases, large reasoning models generated recommendations that were rated as equal or superior to human MDT decisions. GPT-5-Thinking consistently outperformed both DeepSeek-v3-r1 and expert MDT outputs, indicating a higher level of completeness, diagnos-

tic accuracy, and therapeutic appropriateness. These findings suggest that if artificial intelligence is to be integrated into routine MDT workflows, GPT-based reasoning models should be preferred over alternative LRM systems. AI tools should be implemented as structured decision-support systems under explicit clinical oversight, with the potential to improve consistency and quality of multidisciplinary cancer care.

Keywords: multidisciplinary team; artificial intelligence; decision quality; lung cancer; benchmarking

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P9 – COMPLEMENTARY THERAPIES IN EARLY BREAST CANCER: EVIDENCE-BASED DECISIONS OF CROATIAN ONCOLOGISTS

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Background: Complementary therapies are increasingly integrated into oncology care, but real-world use may diverge from evidence-based recommendations. We evaluated the extent to which Croatian oncologists' decisions regarding complementary therapies in early breast cancer align with current evidence.

Methods: We conducted a cross-sectional online survey incorporating a randomized vignette experiment. Participants were presented with multiple clinical scenarios simulating both neoadjuvant and adjuvant treatment settings, and were asked to classify each therapy-indication pair as *prohibit*, *allow*, or

recommend. A total of 48 oncology specialists and residents from Croatia met the inclusion criteria and provided complete paired responses for analysis. Participants evaluated 28 complementary therapy–indication pairs in both neoadjuvant and adjuvant settings. The primary outcome was the proportion of evidence-concordant decisions across therapy–indication pairs. Correctness was evaluated using a strict definition (only the single evidence-supported action was considered correct) and an expanded definition (both *allow* and *recommend* were considered correct when supported by evidence).

Results: Median accuracy was 52.7% (95% CI 49.1–56.2) under the strict definition and 69.6% (95% CI 66.9–72.6) under the expanded definition. Evidence-based interventions, such as physical exercise, relaxation techniques, and cognitive behavioral therapy, were most frequently recommended, whereas many other complementary therapies were rarely endorsed. Under the strict definition, accuracy was lowest for therapies supported for active recommendation (median 50%), while higher accuracy was observed for therapies supported to be allowed but not recommended (median 65.6%) and for those where evidence advised against use (median 61.5%).

Conclusion: Croatian oncologists show moderate alignment with evidence when making decisions on complementary therapies, with a tendency to allow rather than actively recommend them. These findings underscore the need for targeted educational interventions, standardized guidelines, and greater dissemination of evidence-based recommendations to ensure safe integration of complementary therapies in clinical practice.

Keywords: Integrative medicine, integrative oncology, breast neoplasms, complementary therapies

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P10 – COMPREHENSIVE GENOMIC PROFILING (CGP) OF GASTROINTESTINAL CANCERS: UPDATED SINGLE INSTITUTION EXPERIENCE FROM CROATIA

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Introduction: Nextgeneration sequencing (NGS)-based comprehensive genomic profiling (CGP) is increasingly used in gastrointestinal (GI) cancers, complementing standard biomarker testing and enabling detection of uncommon but targetable alterations. We report an updated singleinstitution experience in advanced GI malignancies at "Sestre Milosrdnice" University Hospital Center. This larger dataset refines and confirms patterns from our previous analysis, with similar distributions of tumor types, actionability and use of matched therapies.

Patients and methods: This retrospective study included 144 patients with advanced or metastatic GI tumors profiled by CGP between 1 January 2020 and 26 February 2026 (82 females, 56.9%; median age 56.2 years). Main tumor types were colorectal carcinoma (CRC, 74/144, 51.4%), pancreatic (21/144, 14.6%), gastric (17/144, 11.8%), biliary tract (14/144, 9.7%), small intestine (9/144, 6.2%), esophageal (5/144, 3.5%) and others (4/144, 2.8%). CGP was mostly tissuebased (112/144, 77.8%), with 32/144 (22.2%) plasma tests; among tissue samples, 80/112 (71.4%) derived from primary tumors and 32/112 (28.6%) from metastases, consistent with Croatian multicenter metastatic CRC practice where tissue CGP predominates.

Results: At least one actionable therapeutic option was found in 80/144 patients (55.6%). Actionability was highest in biliary tract (10/14), CRC (49/74) and small intestine tumors (6/9), intermediate in esophageal (3/5) and gastric cancer (9/17), and low in pancreatic (2/21) and other tumors (1/4), in line with Croatian CRC and international data. Primarytumor tissue biopsies more often yielded options than metastatic samples (57/80 vs 13/32). Among 32 liquid biopsies, 9/32 (28.1%) had low ctDNA fraction (<1%) and were considered unreliable, whereas 10/23 (43.5%) samples with ctDNA ≥1% were actionable, underscoring the importance of sample quality and timing for liquid CGP. Although actionable alterations were found in over half of patients, after exclusion of 20 CRC patients with RASwt and BRAFwt tumors that received targeted treatment according to routine clinical practice, only 14/144 (9.7%) received CGPguided therapy, i.e. 17.5% (14/80) of those with at least one option. Among 60 patients with tumortype-specific options, 14 did not start recommended treatment due to ECOG deterioration, confirming performancestatus decline as a key barrier alongside access and reimbursement limitations reported in Croatian CRC and other national GI series.

Conclusion: This larger cohort confirms that CGP detects actionable alterations in over half of Croatian patients with advanced GI cancer (particularly CRC, biliary tract and small intestine tumors). However, only 17.5% of those with at least one therapeutic option received matched therapy. Tumor distribution, subgroup actionability and the modest use of CGPguided treatment closely mirror our previous singleinstitution analysis and other Croatian CGP reports. To better exploit CGP in GI malignancies, it should be integrated earlier and more systematically into treatment algorithms, with a focus on highquality tissue and proactive strategies to overcome performancestatus and access barriers.

Keywords: gastrointestinal cancers; comprehensive genomic profiling; actionable mutations; precision oncology

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P11 – COMPREHENSIVE GENOMIC PROFILING IN ADVANCED PROSTATE CANCER: SECOND UPDATE FROM CROATIAN URO-ONCOLOGY GROUP (CUOG)

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Background: Comprehensive genomic profiling (CGP) is a fundamental tool for identifying genetic alterations in advanced prostate cancer, enabling the personalized use of PARP inhibitors and other targeted therapies. Although CGP testing is increasingly available, its real-world application and clinical

impact in Croatia have not been systematically assessed. This study represents the second analysis of the Croatian uro-oncology group (CUOG) aiming to establish feasibility and impact of CGP in real life setting.

Methods: Data were retrospectively analyzed from 6 centers covering patients tested between 2020 and 2025.The spectrum of mutations in clinically relevant genes, as well as outcomes of patients treated according to CGP findings after exhaustion of standard therapeutic options were evaluated.

Results: A total of 242 patients with advanced prostate cancer were profiled. The median age of patients was 70 years. CGP using the Foundation Medicine platform was performed in 145 patients, while a targeted gene panel (ATM, BARD1, BRCA1, BRCA2, CDK12, CHEK2, FANCD2, MRE11, NBN, PALB2, PPP2R2A, RAD51B, RAD54L, TP53) was used in 97 patients**.** Profiling was conducted in the castration-resistant phase in 122 patients and hormone-sensitive phase in 120 patients.

Profiling was performed using liquid biopsy in 85 patients (35.1%) and tissue-based testing in 157 patients (64.9%).

Comparison of genomic alterations between hormone-sensitive prostate cancer (HSPC) and castration-resistant prostate cancer (CRPC) revealed a higher overall mutation frequency in CRPC. Clinically significant (Tier I) alterations were found in 52,47% overall, more frequently in mCRPC (58%) than mHSPC (26%).

The most common mutations were TP53 (22.31%), PTEN (14.88%) AR (11.16%), ATM (10.74%), PIK3CA (5.37%), BRCA2 (5.79%), CHEK2 (4.96%), BRCA1 (3.31%), CDK12 (2.89%), and RB1 (2.07%).

Median follow up of all patients was 21 months. Median OS of all patients calculated from the date of CGP was 16 months.

Twenty-five patients (10,33%) received targeted therapy (19 PARPi, 3 PARPi+ARPI, 1 everolimus, 1 alpelisib, 1 Entrectinib**).**

Median progression-free survival (PFS) from the start of PARP therapy was 8 months, and median overall survival (OS) was 10 months.

Targeted therapy was most commonly initiated in later treatment lines, with a median introduction in the 4th line, indicating its use after previous standard systemic treatments.

Conclusion: Our national-wide analysis revealed that CGP is feasible in real-world setting and leads to identification of clinically actionable alterations in significant proportion of patients with advanced prostate cancer. While percentage of patients who received targeted treatment is relatively low, it is expected that moving testing to earlier phases of disease will increase its impact and improve patients outcomes.

Keywords: genomic profiling, prostate cancer, targeted therapy, PARPi

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P12 – DECISION-MAKING ON COMPLEMENTARY THERAPIES IN EARLY BREAST CANCER: EVIDENCE ALIGNMENT AMONG BOSNIA AND HERZEGOVINA ONCOLOGISTS

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Background: The extent to which oncologists' decisions regarding complementary therapies reflect evidence-based guidance in Bosnia and Herzegovina remains unclear. Although complementary therapies are increasingly used by breast cancer patients globally, little is known about how evidence shapes clinical decisions in transitional healthcare systems. This study examined evidence-aligned clinical decisions among oncologists in both neoadjuvant and adjuvant breast cancer settings. Understanding these patterns is essential to inform targeted educational interventions and support patient-centered integrative oncology practices.

Methods: We conducted a cross-sectional online survey incorporating randomized clinical vignettes to explore decision-making among oncology specialists and residents. A total of 34 participants from Bosnia and Herzegovina fulfilled the inclusion criteria and completed all required paired responses for analysis. Each respondent assessed 28 therapy–indication combinations in both neoadjuvant and adjuvant breast cancer settings. The main outcome measured was the proportion of responses in agreement with current evidence. Decision accuracy was examined using a strict definition (only the single evidence-supported option counted as correct) and an expanded definition (both "allow" and "recommend" were considered correct when supported by evidence). Descriptive statistics, including medians, interquartile ranges (IQR), and 95% bootstrap confidence intervals (CI), were calculated to summarize the results.

Results: Median accuracy under the strict definition was 50% (95% CI 46.2–56.2). When responses were evaluated using the expanded definition, the median increased to 67.0% (95% CI 62.4–70.8). Looking specifically at the strict definition categories, therapies supported for active recommendation achieved a median concordance of 50% (95% CI 38.81–58.81), therapies intended to be allowed but not recommended showed higher concordance with a median of 62.5% (95% CI 54.02–73.18), and therapies where evidence advised against use reached a median of 61.5% (95% CI 46.23–67.35). Evidence-based interventions such as physical exercise, relaxation techniques, and cognitive behavioral therapy were the most frequently recommended by respondents. No statistically significant difference was found between neoadjuvant and adjuvant settings. Overall, these findings indicate that Bosnian oncologists tend to permit rather than actively recommend complementary therapies, with notable variation depending on the strength and type of supporting evidence.

Conclusion: Oncologists in Bosnia and Herzegovina show moderate alignment with evidence, with a preference for allowing rather than actively recommending complementary therapies. These results emphasize the need for educational initiatives to improve knowledge translation and the safe integration of evidence-based complementary therapies into routine oncology care.

Keywords: Integrative medicine, integrative oncology, breast neoplasms, complementary therapies

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P13 – DEVELOPMENT AND IMPLEMENTATION OF THE FIRST DEDICATED INTENSIVE CARE UNIT FOR ONCOLOGY PATIENTS IN CROATIA

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The continuous rise in the incidence of malignant diseases, together with prolonged survival outcomes has significantly increased the overall burden on healthcare system and the complexity of cancer care. Contemporary oncologic treatment involves higly differentiated and often multimodal treatment aproaches – which, while improving survival outcomes, are associated with a higher risk of severe and potentially life-threatening complications. The use of more aggresive treatment regimens, particularly in patients with advanced disease and multiple comorbidities, predictibly leads to increased incidence of sepsis, acute respiratory failure, hemodynamic instability and other acute conditions requiring specialised intensive care management.

In this context, the establishment of dedicated Intensive Care Unit (ICU) for oncology patients represents both a clinical and organisational strategic advacement. Such a model enables continuum of cancer care, rappid access to specialised interventions, standardized treatment protocols, and multidisciplinary collaboration between oncologists and intensivists. Centralising care in this manner enhances patient safety, improves clinical outcomes and provides a structured response to the evolving demands to modern oncolgy practice(1).

In April 2025, Tumor Clinic in Clinical Hospital Centre Rijeka has established Intensive Care Unit dedicated to oncological emergencies and cancer treatment related complications and adverse events,

representing the first and only unit of its kind in Croatia. The unit consists of five fully equipped beds enabling continuous invasive and non-invasive monitoring of vital functions, not requiring invasive ventilation. To ensure optimal care for immunocompromised patients, two beds are located in an isolation section. Eligibility criteria for ICU admission included confirmed malignancy, ongoing active treatment, life expectancy >6 months, no urgent need for surgical or endoscopic intervention, and absence of infection requiring isolation unless directly related to the malignancy or its treatment.

This abstract outlines the most common diagnoses treated in our unit, categorized into therapy-related adverse events; hematologic, infectious, respiratory, neurological, cardiovascular, and metabolic emergencies; and late radiotherapy complications(1,2).

Systemic therapy complications include immunotherapy-related autoimmune toxicities such as colitis, pneumonitis, nefritis, hepatitis, Guillan-barre like syndroms, encephalitis, as well es chemotherapy-induced allergic or anaphylactic reactions. The most frequent emergencies are febrile neutropenia, pancytopenia, and sepsis. Other critical conditions include malignant airway obstruction, spinal cord compression, increased intracranial pressure, metabolic disturbances (including tumor lysis syndrome), superior vena cava syndrome, therapy-related acute heart failure, arrhythmias, thromboembolism, and malignant pericardial effusion(3,4).

We analyzed the first 13 months of activity in our unit, including 111 hospitalized patients. Lung cancer was the most frequent diagnosis (20.7%), followed by breast (9.0%), gastrointestinal (8.1%), melanoma and pancreatic (7.2% each), and endometrial cancer (5.4%).

The main reasons for admission were febrile neutropenia (16.2%), immune-related adverse events (13.5%), respiratory complications (9.0%), and bacteremia/sepsis (4.5%). The mean ICU stay was 6 days. Most patients (89.2%) were discharged home, 1.8% were transferred to another ward, and overall mortality was 3.6%.

Our initial experience demonstrates that establishing a dedicated intensive care unit for oncology patients is feasible, supports effective multidisciplinary care, and highlights the ongoing need for specialized training in intensive care oncology according to growing burden of cancer.

Keywords: ICU; oncology emergencies; Croatia

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P14 – DIVERGENT TEMPORAL TRENDS IN EARLY NON-BREAST SECOND PRIMARY MALIGNANCIES FOLLOWING BREAST CANCER: A 25-YEAR SEER ANALYSIS

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Background: Second primary malignancies (SPMs) represent an important concern among breast cancer survivors. An increased risk of second primary breast cancer has been well established, and current follow-up strategies focus on the detection of loco-regional recurrence and new breast cancer. While the excess risk for non-breast malignancies has been established, it remains unclear whether early SPM risk has evolved across treatment eras.

Methods: A population-based retrospective cohort study was conducted using SEER 12 registries (1992–2016), applying a multiple primary standardized incidence ratio (MP-SIR) approach. To minimize detection bias from synchronous tumours, early SPMs were defined as those occurring 6-59 months after breast cancer diagnosis. Five-year diagnosis eras were constructed, spanning from 1992-1996 to 2012-2016. The year 2016 was selected as the final diagnosis year to ensure uniform follow-up across eras. Observed and expected counts were pooled within eras, and standardized incidence ratios (SIRs) and 95% confidence intervals (95% CI) were calculated. Temporal trends were evaluated using Poisson regression models, yielding incidence rate ratios (IRRs) per 5-year era, reflecting the relative change in SIR between consecutive eras.

Results: Across all sites excluding non-melanoma skin cancer, early SPM risk declined significantly over time (IRR per era 0.94, 95% CI 0.93-0.95; p<0.001). Site-specific analyses demonstrated divergent trends. Thyroid cancer risk increased significantly across eras from SIR of 1.34 (95% CI 0.88-1.95) in 1992-1996 to 1.92 (95% CI 1.70-2.17) in 2012-2016 (IRR 1.17 per era, 95% CI 1.10-1.24; p<0.001). Acute myeloid leukaemia (AML) exhibited persistently elevated risk (SIR 2.94, 95% CI 2.67-3.24), without significant temporal change (IRR 0.99 per era; p=0.74). In contrast, corpus and uterine cancers demonstrated a significant decline in early risk across eras, with SIR decreasing from 1.61 (95% CI 1.37-1.88) in 1992-1996 to 0.86 (95% CI 0.77-0.96) in 2012-2016 (IRR 0.83 per era, 95% CI 0.80-0.87; p<0.001).

Conclusions: The overall risk of early SPM among breast cancer patients has declined over time. However, site-specific trends differ substantially, with increasing thyroid cancer risk, stable excess AML risk, and declining uterine cancer risk. These findings likely reflect the evolution of treatment paradigms and surveillance practices. Recognition of these trends may inform further refinement in follow-up strategies.

Keywords: breast cancer; second primary cancer; SEER program; population-based analysis; temporal trends; early second cancer

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P15 – DOES REDUCING HYPERINSULINEMIA FEEDBACK IMPROVE OUTCOMES OF PI3KA INHIBITION? EXPLORATORY EFFICACY SIGNALS FROM THE ITACA TRIAL

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Background: Alpelisib, a selective PI3Kα inhibitor, combined with fulvestrant improves outcomes in patients with HR-positive, HER2-negative, PIK3CA-mutated metastatic breast cancer(1). However, its clinical benefit is frequently limited by on-target metabolic toxicity, particularly hyperglycemia, which leads to compensatory hyperinsulinemia(2,3). Preclinical studies have demonstrated that insulin-mediated feedback can reactivate PI3K–mTOR signaling and attenuate the antitumor efficacy of PI3K inhibitors(4). These findings raise the hypothesis that strategies aimed at reducing postprandial glucose and insulin excursions may not only improve tolerability but also preserve or enhance antitumor activity(5). The ITACA trial explored whether modifying the metabolic context of alpelisib administration through evening dosing and short fasting could influence both metabolic toxicity and efficacy outcomes(6).

Methods: ITACA was an open-label, randomized, phase IIb pilot trial conducted at three Croatian university hospitals. Postmenopausal women with HR-positive, HER2-negative, PIK3CA-mutated metastatic breast cancer progressing on prior endocrine therapy, typically after or with a CDK4/6 inhibitor, were randomized 1:1 to receive alpelisib plus fulvestrant either as standard morning dosing or as evening dosing following a ≥5-hour fasting interval with low-carbohydrate dietary guidance. While the primary endpoint focused on metabolic toxicity, key exploratory efficacy endpoints included objective response rate (ORR) and progression-free survival (PFS). Tumor responses were assessed according to RECIST criteria by local investigators and PFS was defined as time from randomization to radiographic progression or death. Analyses were performed using Kaplan–Meier curves and Cox models adjusted for the base covariate set

Results: Forty-two patients were randomized (21 per arm). Baseline tumor characteristics and prior treatment exposure were broadly comparable between treatment groups. Among evaluable patients, ORR

was numerically higher in the evening-dosing arm (18.2%, 2/11) compared with the standard morning-dosing arm (8.3%, 1/12). Progression-free survival analyses showed fewer progression or death events in patients receiving evening dosing (6/21, 28.6%) than in those receiving morning dosing (10/21, 47.6%). Median PFS was not reached in the evening-dosing arm during the observed follow-up, whereas median PFS in the morning-dosing arm was 8.0 months. In exploratory multivariable Cox regression adjusted for key baseline covariates, evening dosing was associated with a lower hazard of disease progression compared with morning dosing (hazard ratio 0.20, 95% CI 0.04–0.92). Although based on a limited number of events, the direction and magnitude of the effect were consistent with preserved or potentially enhanced efficacy.

Conclusion: In this randomized phase IIb pilot trial, metabolic optimization of alpelisib administration through evening dosing and short-term fasting was not associated with reduced antitumor efficacy and demonstrated exploratory signals of improved progression-free survival. These findings suggest that attenuation of hyperinsulinemic feedback may enhance the therapeutic index of PI3Kα inhibition while improving metabolic tolerability. In the context of prior clinical trials, where metabolic toxicity frequently necessitated dose modifications and treatment interruptions, strategies that improve metabolic tolerability may indirectly support sustained drug exposure and therapeutic benefit. Importantly, the ITACA trial was not powered to detect differences in efficacy, and all efficacy results should be interpreted as hypothesis-generating, requiring validation in larger, adequately powered randomized studies.

Keywords: alpelisib; hyperglycemia; breast cancer, PIK3CA mutation, diet

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P16 – DURVALUMAB IN THE FIRST-LINE TREATMENT OF ADVANCED BILIARY TRACT CANCER: SINGLE CENTER EXPERIENCE AT THE DEPARTMENT OF ONCOLOGY AND RADIOTHERAPY, UNIVERSITY HOSPITAL SPLIT

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Background: Biliary tract cancer (BTC) is an aggressive malignancy with limited therapeutic options in the advanced setting. The phase III TOPAZ-1 trial demonstrated that the addition of durvalumab to first-line cisplatin and gemcitabine (CG) significantly improves progression-free survival (PFS) and overall survival (OS) compared with chemotherapy alone. Based on these results, the combination of CG plus durvalumab has become the new standard of care for patients with advanced BTC. The aim of this study was to evaluate real-world outcomes of CG combined with durvalumab in patients with advanced BTC treated at the Department of Oncology and Radiotherapy, University Hospital Split.

Methods: We retrospectively analyzed the medical records of 22 consecutive patients with histologically confirmed advanced BTC who received at least one cycle of CG plus durvalumab between January 2023 and December 2025. Durvalumab was administered at a fixed dose of 1500 mg intravenously on day 1 of each 3-week cycle in combination with cisplatin and gemcitabine, followed by maintenance durvalumab monotherapy every 4 weeks until disease progression, unacceptable toxicity, or completion of a maximum of 2 years of treatment. Data were analyzed using descriptive statistics in Microsoft Excel and OriginPro 9.0.0 (OriginLab Corp, Northampton, MA, USA).

Results: The study cohort comprised 7 males and 15 females, with a median age of 71 years (range, 39–85). All patients had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. Two or more comorbidities were present in 45% of patients.

Intrahepatic cholangiocarcinoma was the predominant tumor location (n = 14), while 8 patients had extrahepatic disease, including gallbladder carcinoma. Twenty patients presented with de novo advanced disease, whereas two had recurrent disease following prior surgical resection.

At a median follow-up of 7.8 months, the median number of administered CG cycles was 6 (range, 1–9), and the median number of durvalumab cycles was 7 (range, 1–18). The disease control rate (DCR) was 77%, with partial response observed in 18% of patients and stable disease in 59%. The median PFS was 6.2 months. Median OS was not reached at the time of analysis; 14 patients (63.6%) were alive.

Treatment was generally well tolerated. The most common grade ≥3 treatment-related adverse events were hematologic, including neutropenia in 4 patients (18%) and thrombocytopenia in 1 patient (4%). No grade 3 or 4 immune-related adverse events were observed. Grade 1 hypothyroidism occurred in two patients. No patient discontinued treatment due to toxicity.

Conclusion: In this real-world cohort, first-line CG plus durvalumab demonstrated effectiveness consistent with the results of the TOPAZ-1 trial, with a manageable safety profile. The main limitations of this analysis include the small sample size, relatively short follow-up period, and its retrospective design.

Keywords: durvalumab; advanced biliary tract cancer; first-line treatment; real-world experience; progression free survival

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P17 – EFFICACY AND SAFETY OF IMMUNOTHERAPY IN PREVIOUSLY CHEMOTHERAPY TREATED PATIENTS WITH RECURRENT ENDOMETRIAL CANCER

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Introduction: Therapeutic options for patients with recurrent endometrial cancer (EC) who have previously received chemotherapy are limited. According to the KEYNOTE 158, the GARNET and the PHAEDRA trials, immunotherapy (immune checkpoint inhibitors) has a promising role in the management of these patients, characterised by improved objective response rate (ORR) and more durable responses, especially in the mismatch repair-deficient/microsatellite instability-high (dMMR/MSI-h) population or in patients with high tumor mutational burden (TMB) tumors.

Methods: We retrospectively analysed the archive data of eight patients with MSI-h or high TMB recurrent EC who had already been treated with chemotherapy and subsequently started immunotherapy at the Department of Gynecologic Oncology, University Hospital Centre Zagreb between December 2020 and July 2025.

Results: The median age of the patients at the time of diagnosis was 58 years (range 43-75). ECOG status 0 was observed in 75% of patients. All patients had prior platinum exposure and four patients (50%) had prior radiotherapy. Five patients (62.5%) had MSI-h/TMB high tumors, and three patients (37.5%) had TMB high and microsatellite stable tumor. Four patients (50%) were treated with pembrolizumab, 37.5%

with dostarlimab and 12.5% with atezolizumab. The median number of immunotherapy cycles was eight (range 3-58). Disease control was achieved in 62.5% of patients, with an ORR of 25 % (one patient achieved a complete response, and one a partial response). Median progression free survival was 5 months, and median overall survival from the time of including immunotherapy was not reached. The patient who had a complete response is off therapy and remains disease-free and two patients (25%) are still on therapy. Five patients (63%) discontinued therapy due to disease progression. Possible immunotherapy-related serious adverse events included thyroiditis (37%), pneumonitis (25%) and rash (25%).

Conclusions: Our experience in treating patients with immunotherapy showed good results with acceptable toxicity.

Keywords: endometrial cancer, immunotherapy, side effects.

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P18 – ESTABLISHING A STEREOTACTIC RADIOTHERAPY PROGRAM: INITIAL EXPERIENCE OF THE TUMOR CLINIC AT CLINICAL HOSPITAL CENTER RIJEKA

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Abstract: Radiotherapy remains a vital component of modern oncologic treatment, and ongoing technological advances brought us to the development of stereotactic techniques (1). Stereotactic radiotherapy is characterized by the delivery of very high, ablative doses of radiation in a limited number of fractions, and is primarily used to treat small, well-defined tumor lesions while maximally sparing surrounding healthy tissue. The term includes both stereotactic radiosurgery (SRS) and stereotactic body radiotherapy (SBRT). SRS uses single-session delivery of a high radiation dose, whereas SBRT refers to treatment administered in one to five fractions(2,3). In the treatment of oncology patients, stereotactic radiotherapy is most often used for brain metastases, where it achieves high local control rates while largely preserving cogni-

tive function and quality of life compared with whole-brain irradiation, then for oligometastatic disease with the intent of achieving long-term remission or potential cure, and for oligoprogression, where it targetes progressive changes while maintaining the ongoing systemic therapy, which is particularly important for patients with limited therapeutic options(3-5).

In response to the evolving demands of modern oncology, the Tumor Clinic at the Clinical Hospital Center Rijeka became the first public healthcare institution in Croatia to introduce stereotactic treatment for oncologic patients. Also, given the complexity and demands of advanced radiotherapy techniques, a special Department for Advanced Radiotherapy Techniques and Stereotaxy was recently established within the Tumor Clinic. Each case considered for stereotactic treatment is first discussed at an expert meeting of radiation oncologists, where dose prescription and fractionation schedules are defined, after which the case is reviewed by a multidisciplinary tumor board, which confirms the indication for this approach. Prior to the initiation of the program, an internal protocol outlining the safe implementation of stereotactic radiotherapy was developed through close collaboration among radiation oncologists, radiologic technologists, and medical physicists.

Methods: Between December 2025 and March 2026, a total of three SRS procedures for brain lesions (HyperArc technique, total dose 2400 cGy in a single fraction), two SBRT treatments for lung lesions (VMAT technique, total dose 5000 cGy in five fractions), and five SBRT treatments for liver lesions (VMAT technique, total dose 5400 cGy in three fractions) were performed at the Clinic for Tumors of the Clinical Hospital Center Rijeka. As for treatment indiciation, all patients were undergoing systemic oncologic treatment, and oligoprogression was detected on prior follow-up examinations.

Results: The patients tolerated radiotherapy well, with no reported acute adverse events. One patient who underwent SRS for a brain lesion had a follow-up examination, which demonstrated good local disease control.

Conclusion: Radiotherapy represents a vital component in the treatment of oncology patients. Stereotactic radiotherapy has shown great results as ablative therapy in achieving long-term local control of individual. Well-established treatment protocols and the leadership of trained radiation oncologists, radiologic technologists, and medical physicists ensure the safe delivery of therapy, as well as good clinical.

Keywords: stereotactic radiotherapy, radiosurgery, modern oncology, brain metastases, oligoprogression

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P19 – EVALUATING LARGE REASONING MODELS VERSUS HUMAN MULTIDISCIPLINARY TEAMS IN LUNG CANCER DECISION-MAKING: A REAL-WORLD STUDY

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Background: Recent advances in artificial intelligence, particularly large language models (LLMs), have shown strong performance in medical applications, including oncology, positioning them as potential clinical decision-support tools(1,2). The development of large reasoning models (LRMs) has further enhanced this potential by enabling multi-step clinical reasoning (3). In lung cancer care, advanced AI models have demonstrated performance comparable to expert clinicians in retrospective and simulated settings, occasionally surpassing junior oncologists. However, persistent reasoning errors, ethical concerns, and performance plateaus currently limit their use as autonomous decision-makers(4,5). Multidisciplinary team (MDT) decision-making remains the standard of care in lung cancer management, yet real-world MDT decisions show variability in guideline adherence and personalization, and systematic evaluation of decision quality is limited. Most existing AI studies rely on retrospective datasets or simulated cases, providing little insight into how AI compares with MDT decision-making in routine clinical practice(6). Given the growing complexity of lung cancer care and rapid AI development, real-world comparative evidence is urgently needed. This study addresses this gap by evaluating two advanced LRMs–GPT-5-Thinking and DeepSeek-v3-r1–against MDT decisions in consecutive real-world lung cancer cases

Methods: We conducted a real-world study involving 100 consecutive lung cancer cases discussed at an MDT. Two large reasoning models (GPT-5-Thinking and DeepSeek-v3-r1) independently generated radiologic, pathologic, and therapeutic recommendations for each case. MDT decisions and AI-generated recommendations were assessed by two independent expert clinicians, blinded to the source, using 5-point Likert scales. Fifty cases were analyzed retrospectively, during which MDTs operated without AI monitoring, and fifty cases were analyzed prospectively, with MDT members aware that their decisions would be compared with AI outputs. Non-parametric statistical analyses were used to compare AI performance, MDT decision quality, and the effect of AI monitoring

Results: The study included 100 real-world lung cancer cases, with 50 evaluated retrospectively and 50 prospectively. Most cases were discussed in the pre-staging phase (70%), while 30% were staged, with pT1cN0 being the most common stage (22%). Both LRMs achieved high expert ratings across diagnostic and therapeutic domains, demonstrating ceiling effects. In the retrospective phase, GPT-5-Thinking achieved mean scores of 4.89 for radiologic diagnostics, 4.88 for pathologic diagnostics, and 4.82 for oncological therapy, with an aggregate score of 4.90 (95% CI 4.84–4.95). DeepSeek-v3-r1 showed slightly lower performance, with domain scores of 4.76, 4.73, and 4.18, and an aggregate score of 4.56 (95% CI 4.40–4.72). In the prospective, AI-monitored phase, GPT-5-Thinking maintained high performance with an aggregate score of 4.79

(95% CI 4.69–4.89), while DeepSeek-v3-r1 achieved 4.54 (95% CI 4.41–4.67). AI performance remained stable across phases. Mean MDT case-level scores were 4.14 (95% CI 3.96–4.33) retrospectively and 4.34 (95% CI 4.16–4.52) prospectively, with no statistically significant difference between phases (p = .13).

Conclusion: This real-world study demonstrates that state-of-the-art LRMs can generate diagnostic and therapeutic recommendations in lung cancer care that closely match the quality of expert MDT decision-making. AI performance was consistent across domains and clinical contexts, supporting the robustness of LRMs as independent clinical reasoning systems. MDT decision quality did not significantly change when clinicians were aware of AI evaluation, suggesting that high-performing MDTs may already operate near a decision-making ceiling. Rather than primarily influencing clinician behavior, LRMs may be most valuable as continuous, independent benchmarks that enhance transparency, consistency, and decision safety. These findings support integrating AI as a parallel second-opinion and quality assurance layer at the MDT level, offering a scalable approach to maintaining high-quality cancer care in increasingly complex healthcare systems.

Keywords: large reasoning models, large language models, clinical decision making, lung cancer, artificial intelligence

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P20 – FECAL MICROBIOTA TRANSPLANTATION FOR THE TREATMENT OF IMMMUNE-MEDIATED COLITIS AS A CONSEQUENCE OF IMMUNOTHERAPY – A SINGLE CENTER EXPERIENCE

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Immune checkpoint inhibitors (ICIs) have substantially improved survival outcomes in malignant diseases but are associated with immune-related adverse events, among which immune-mediated colitis (IMC) is frequent. IMC occurs in up to 32% of patients, with severe forms in up to 21%(1). It typically presents with diarrhea, abdominal pain, and endoscopic signs of mucosal inflammation, while histology may resemble inflammatory bowel disease (2). Management is based on immunosuppression: systemic corticosteroids are first-line therapy, and infliximab or vedolizumab are used in steroid-refractory cases. Nonetheless, a considerable proportion of patients remain refractory or become steroid-dependent, and no consensus exists regarding third-line treatment(3). Emerging evidence highlights the role of the intestinal microbiota in IMC pathogenesis, positioning fecal microbiota transplantation (FMT) as a potential strategy to restore microbial balance and induce remission, although robust controlled data are limited(4,5).

We report five patients with IMC treated with FMT. The first two, a woman and a man, received FMT as third- and second-line therapy, respectively, for grade 3 IMC refractory to corticosteroids and, in the woman, also to infliximab. The female patient had metastatic lung adenocarcinoma treated with durvalumab, while the male patient had metastatic melanoma treated with pembrolizumab. Both received two cycles of FMT via colonoscopic instillation of 300 mL of donor stool into the cecum. Marked clinical improvement followed, including reduced inflammatory markers, improved quality-of-life scores, and regression of endoscopic inflammation. Based on these outcomes, FMT was applied as second-line therapy in two additional patients. One was a man with multiple primary malignancies and pre-existing Crohn's disease on maintenance immunosuppression, considered treatment of the underlying condition rather than acute IMC. The other was a woman with lung cancer who experienced IMC relapse one year after corticosteroid therapy for it. Two FMT cycles were administered in the former and one in the latter, resulting in clinical and laboratory improvement and reduced gastrointestinal symptoms. The fifth patient, with breast cancer, developed pancolitis after chemoimmunotherapy. Following initial corticosteroid treatment, she underwent FMT, with an early reduction in diarrhea frequency to one bowel movement per 24 hours during hospitalization. In the first four patients, sustained clinical control was achieved without additional immunosuppression, and a similar response is anticipated in the fifth.

This case series suggests that FMT may be an effective therapeutic option for IMC refractory to corticosteroids and other immunosuppressive agents. The favorable clinical, laboratory, and endoscopic outcomes support further prospective controlled studies to clarify its role in treatment algorithms.

Keywords: colitis; immunotherapy; FMT

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P21 – FIRST MULTIDISCIPLINARY TOXICITY TEAM FOR CANCER IMMUNOTHERAPY–RELATED ADVERSE EVENTS IN CROATIA – CENTRE FEASIBILITY AND CLINICAL EXPERIENCE

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Background: Immune checkpoint inhibitors (ICIs) are associated with immune-related adverse events (irAEs) that may involve multiple organ systems and require specialized multidisciplinary input(1,2). Some studies suggest that the incidence of irAEs ranges between 54% and 76% frequency and presentation depending on ICIs type(3). The most common irAEs affect the skin, gastrointestinal tract, liver, endocrine organs and lungs and while often mild, severe irAEs may require coordinated management by multiple healthcare providers(4). The body of evidence on methods to obtain real-time multidisciplinary input for irAEs requiring subspecialist care is scarce. We evaluated the feasibility, utilization, and clinical characteristics of referrals to a multidisciplinary immunotherapy team at Clinical Hospital Centre Rijeka, Croatia.

Methods: Data were collected from February 2, 2024, through August 1, 2025. All referrals to the multidisciplinary immunotherapy team were reviewed. Feasibility was defined as provision of recommendations within 24 hours of referral. Referral indications, patient characteristics, suspected and confirmed irAEs, and grading according to Common Terminology Criteria for Adverse Events (CTCAE) were analyzed descriptively(5).

Results: Over the study period, 493 patients received ICIs. The multidisciplinary immunotherapy team received 176 referrals concerning 146 patients. Recommendations were provided within 24 hours in

100% of cases. Most referrals concerned suspected irAEs (n = 170; 96.6%), whereas a minority concerned cases representing evaluation of ICI eligibility 6 (3.4%) before initiation of immunotherapy. Team evaluation confirmed suspected irAEs in 116 of 140 patients and in 140 of 170 total referrals, corresponding to confirmation rates of 82.9% and 82.3%, respectively. Other cases were reclassified as non–irAEs. Similar reclassification occurred among other suspected toxicities following radiologic, laboratory, or clinical evaluation, or when causality could not be definitively established. The most frequently suspected irAE prompting referral was hepatitis (in 57 referred patients), followed by endocrinological (mostly thyroid-related) events, colitis, and myositis. Multidisciplinary referral characteristics and associated management recommendations based on individual / combined irAEs and associated CTCAE criteria will be summarized in Table 1.

Conclusions: According to our best knowledge this is the first and only multidisciplinary team for adverse events of immunotherapy in Croatia. A multidisciplinary immunotherapy team was feasible to implement at our centre, consistently providing recommendations within 24 hours. Most referrals involved suspected irAEs, and a substantial proportion were reclassified after specialist review, underscoring the value of multidisciplinary evaluation in toxicity attribution and management.

Keywords: cancer; immune-related adverse events; multidisciplinary approach

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P22 – GENOMIC DETERMINANTS OF OUTCOMES DURING AVELUMAB MAINTENANCE IN ADVANCED UROTHELIAL CARCINOMA: REAL-WORLD GENOMIC INSIGHTS FROM THE CROATIAN URO-ONCOLOGY GROUP

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Background: Maintenance therapy with Avelumab following platinum-based chemotherapy has become the standard of care for patients with advanced Urothelial Carcinoma who achieve disease control after first-line treatment, based on the phase III JAVELIN Bladder 100 study. Despite demonstrated improvements in overall survival, a substantial proportion of patients experience early disease progression, and robust predictive biomarkers of benefit remain lacking. Comprehensive genomic profiling (CGP) is increasingly used in clinical practice and may provide insight into molecular determinants of response or resistance to immune checkpoint inhibition. We aimed to evaluate associations between tumor genomic alterations and clinical outcomes during avelumab maintenance therapy in a national real-world cohort.

Methods: We conducted a multicenter retrospective study within the Croatian Uro-Oncology Group (CUOG) including patients with advanced or metastatic urothelial carcinoma treated with avelumab maintenance after achieving disease control following platinum-based chemotherapy. Clinical character-

istics and treatment outcomes were collected from participating institutions. A subset of patients underwent comprehensive genomic profiling using next-generation sequencing panels. The genomic landscape of the cohort was characterized, and exploratory analyses were performed to evaluate associations between genomic alterations and clinical outcomes. Progression-free survival (PFS) and overall survival (OS) were assessed using Kaplan–Meier methodology.

Results: A total of 141 patients treated with avelumab maintenance were included in the CUOG cohort, of whom 67 (47%) had available genomic profiling data. Among these patients, 63% underwent radical surgery, and visceral metastases were present in 42% of patients at initiation of maintenance therapy. Sixty-eight % of patients had ECOG performance status 0, and variant histology was observed in a 25% of analyzed primary tumors.

The genomic landscape of the cohort was consistent with previously reported data in advanced urothelial carcinoma. The ten most frequent genomic alterations were TERT promoter (68.7%), TP53 (61.2%), FGFR3 (25.4%), RB1 (25.4%), CDKN2A (23.9%), PIK3CA (17.9%), KMT2D (16.4%), ARID1A (14.9%), KDM6A (13.4%), and ERBB2 (11.9%).

All tumors were microsatellite stable (MSS). Tumor mutational burden (TMB) was available for 66 patients, with a median TMB of 7 mutations/Mb, and 23 patients (34.8%) demonstrated high TMB (≥10 mutations/Mb).

Exploratory analyses identified several genomic alterations associated with inferior outcomes during avelumab maintenance therapy. FGFR3–TACC3 fusion and NOTCH1 mutations were associated with shorter progression-free survival, while FGFR3–TACC3 fusion, NOTCH1, and PTEN alterations were associated with inferior overall survival. Furthermore, none of the patients harboring FGFR3–TACC3 fusion or PTEN alterations achieved treatment duration exceeding the cohort median. In contrast, no significant associations between clinical outcomes and alterations in FGFR3, ERBB2, or other evaluated cancer-related genes were observed, suggesting that treatment outcomes are unlikely to be driven by a single genomic event.

Conclusions: In this national real-world cohort, specific genomic alterations were associated with poorer outcomes during avelumab maintenance therapy in advanced urothelial carcinoma. These findings suggest that tumor genomic profiling may help identify molecular subgroups with reduced benefit from immune checkpoint inhibitor maintenance strategies. The observed signals involving FGFR3-TACC3 fusion, NOTCH1, and PTEN alterations warrant further investigation in larger prospective studies integrating genomic and clinical biomarkers.

Keywords: urothelial cancer; avelumab maintenance

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P23 – HEALTH-RELATED QUALITY OF LIFE AMONG WORKING-AGE WOMEN WITH BREAST CANCER IN CROATIA: A MULTICENTRE CROSS-SECTIONAL STUDY USING EQ-5D-5L AND EORTC QLQ-BR23

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Background: Breast cancer survival has improved substantially, resulting in a growing population of women living for many years after diagnosis. Consequently, health-related quality of life (HR-QoL) has become a key survivorship outcome, as persistent physical symptoms, psychological distress and disruptions in social roles may continue beyond primary treatment(1,2). These issues are particularly relevant for women of working age, for whom breast cancer intersects with active family and social life stages, and may affect intimate relationships, future plans and everyday functioning.

However, HR-QoL evidence is uneven across Europe. Data from Central and Eastern Europe remain limited despite documented gaps in cancer care and supportive infrastructure compared with Western Europe, and benchmarking against population norms is scarce(3,4). In Croatia, multicentre data on HR-QoL among working-age women with breast cancer are lacking. We quantified HR-QoL in this population and benchmarked generic outcomes against national female population norms.

Methods: We conducted a multicentre cross-sectional study in 2024 at two Croatian tertiary oncology centres. Women aged 18–65 years attending outpatient oncology care completed the EQ-5D-5L and the EORTC QLQ-BR23. EQ-5D-5L utilities were derived using the Slovenian value set due to the absence of a Croatian tariff(5). Patient outcomes were compared with age-stratified Croatian female population norms (2022). Group differences by age and metastatic status were analysed using non-parametric tests. Clinical relevance of utility differences was interpreted using published minimally important difference (MID) estimates for cancer populations(6,7).

Results: A total of 266 women were included (mean age 51.4 years; range 24–65), spanning a broad survivorship spectrum (year of diagnosis 1999–2024); 19.2% had metastatic disease. Socioeconomic strain was frequent: 45.3% reported negative effects of breast cancer on household finances, providing important context for patient-reported outcomes.

Complete EQ-5D-5L data were available for 233 participants. Mean utility was 0.76 (SD 0.19) compared with 0.91 (SD 0.14) in Croatian female population norms, yielding a decrement of 0.15–well above established MID ranges [6,7]. Mean EQ-VAS was also lower (66.2 vs 84.0; $p<0.01$). Patients reported significantly more problems across all EQ-5D-5L dimensions than the general population (all $p<0.01$), with the greatest burden in pain/discomfort (mean 2.12 vs 1.53) and anxiety/depression (2.08 vs 1.46), consistent with persistent symptom and distress profiles described in survivorship literature [1,2].

Utility declined with age from 0.82 (24–43 years) to 0.70 (60–65 years) ($p=0.03$) and was lower in metastatic compared with non-metastatic disease (0.70 vs 0.77; $p=0.03$). On EORTC QLQ-BR23, the most impaired functional domains were future perspective (mean 40.6/100) and sexual functioning (26.0/100;

sexual enjoyment 50.0/100), while symptom burden was notable for systemic therapy side effects (32.3/100) and arm and breast symptoms (33.2/100 and 26.2/100).

Conclusion: Working-age Croatian women with breast cancer experience substantial and clinically meaningful HR-QoL impairment compared with population norms, with prominent deficits in pain/discomfort, anxiety/depression, future perspective, and sexual functioning. Older age and metastatic disease are associated with greater utility loss. These findings support routine patient-reported outcome monitoring and strengthened survivorship care focusing on symptom management, psychosocial support, rehabilitation, and sexual health.

Keywords: breast cancer; health-related quality of life; EQ-5D-5L; EORTC QLQ-BR23; population norms; Croatia

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P24 – HOW DID ONCOLOGY PATIENTS IN CROATIA EXPERIENCE ONCOLOGY CARE PATHWAY IN 2025?

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Patient-centered care (PCC) in oncology means putting the patient's values, preferences, and needs at the core of decision-making, addressing not only the tumor but the whole person going through the process of oncology care.

Studies show PCC improves quality of care, patient satisfaction, trust in providers, and self-efficacy. Emotional support, effective communication, and shared decision-making contribute to better clinical outcomes such as reduced anxiety and improved symptom management. Patient involvement in their care enhances adherence and engagement throughout treatment. Holistic cancer care combines medical treatment with different aspects of quality of life support. It integrates psychooncology and expert psychological support when needed, nutrition counseling, caregiver support, and community resources. Together, these elements create a cancer care experience that respects the whole person, improves health outcomes, and fosters strong patient-provider relationships.

The term *oncology care pathway* is for the purpose of this survey defined as formal sequence of care services organized by the healthcare system in Croatia to ensure access, coordination, and support from the moment of diagnosis. It also reflects the subjective reality of those who live through it. This dual perspective highlights the potential misalignments between what was planned and actual lived experiences.

This survey aimed to explore the lived experiences of individuals undergoing cancer treatment in Croatia to identify gaps and potential improvements in the oncology care pathway. It seeks to address the challenges faced during diagnosis, treatment and beyond treatment emphasizing the need for patient-centered care.

To present the experiences of oncology patients in Croatia in 2025, an online survey was conducted, using a specially constructed questionnaire "Experiences of Oncology Patients in Croatia in 2025", designed to assess various aspects of the experience. The survey included 355 oncology patients undergoing active treatment and patients undergoing follow-up after treatment in Croatia.

The questionnaire included sociodemographic data (gender, age, region of treatment, type of diagnosis, treatment status) and questions related to: diagnostics and access to treatment, information and communication with healthcare staff, involvement in decision-making, psychological support, organization of healthcare, perception of equality of access to treatment, and financial aspects of treatment.

When asked about overall satisfaction, 64,8% of patients stated that they were completely or mostly satisfied with their oncology care. Among the suggestions for improvement, the most prominent are: more time with health providers, more information about treatment and self-care, better involvement in treatment, one/leading oncologist in treatment and monitoring, better communication, reduced waiting lists, a better defined and coordinated patient pathway, faster access to radiotherapy, lack of professional psychological support, advice on nutrition and supplementation, difficulties in achieving rehabilitation, etc.

Looking to the future, the need for a holistic approach to treatment and quality of life, including patient experiences in outcome monitoring, better organization of care, developing partnerships at all levels, and fulfilling the promises made through strategic documents is emphasized.

Keywords: oncology patients experience, oncology care pathway, holistic approach

P25 – HYPOFRACTIONATED RADIOTHERAPY FOR PROSTATE CANCER – EXPERIENCE FROM THE DEPARTMENT OF ONCOLOGY AND RADIOTHERAPY, UNIVERSITY HOSPITAL CENTER SPLIT

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Background: Primary radiotherapy is a well-established local treatment option for patients with localized prostate cancer, particularly in men older than 70 years or in those who are unsuitable or unwilling to undergo surgery. Moderately hypofractionated radiotherapy delivers higher daily doses (2.5–4 Gy) over a shorter treatment duration (4–6 weeks) compared with conventional fractionation. Due to the low α/β ratio of prostate cancer, hypofractionation may achieve comparable or improved oncologic outcomes with similar toxicity profiles while improving treatment accessibility.

Objectives: The aim of this study was to evaluate the effectiveness and safety of primary hypofractionated radiotherapy for prostate cancer at the Department of Oncology and Radiotherapy, University Hospital Center Split, and to compare the results with previously published data.

Materials and Methods: A retrospective analysis was performed on 36 patients with prostate cancer (34 with localized and 2 with locoregional disease) treated with primary moderately hypofractionated radiotherapy. Treatment was delivered using 3D conformal image-guided radiotherapy (IGRT) on a linear accelerator with 18 MV photon energy, with a total dose of 68.04 Gy administered in 27 fractions. Outcomes included PSA response, biochemical progression-free survival (BPFS), radiological progression-free survival (RPFS), clinical progression-free survival (CPFS), overall survival (OS), cancer-specific survival (CSS), disease control rate (DCR) and treatment-related toxicities. Data were collected from medical records and analyzed using descriptive statistics.

Results: The median follow-up time was 23 months, and most patients had unfavorable intermediate-risk disease. The median duration of radiotherapy was 41 days. A PSA reduction greater than 90% from baseline was observed in 63.9% of patients, while most of the remaining patients achieved reductions between 75% and 90%. PSA response did not correlate with tumor aggressiveness or baseline functional status. None of the responders developed metastatic or castration-resistant disease, while only one very high-risk patient experienced disease progression.

Median BPFS, RPFS, and OS were 23 months. BPFS was achieved in 83.3% of patients, while RPFS and CPFS were observed in 88.9% of patients. Patients with disease progression had more aggressive baseline characteristics. Treatment-related toxicities were mostly mild to moderate, and 22.2% of patients experienced no adverse events. Occasional treatment interruptions occurred in patients with comorbidities but did not prevent treatment completion. All four patients receiving androgen deprivation therapy responded to treatment and did not develop castration-resistant disease. The disease control rate was 80.6%. Four patients died during follow-up; however, cancer-specific survival remained 100%.

Conclusion: Moderately hypofractionated radiotherapy demonstrated high effectiveness and an acceptable safety profile, with significant PSA reductions, favorable disease control rates and encouraging survival outcomes. These findings are consistent with previous studies and support the use of hypofractionated radiotherapy as an effective treatment option for prostate cancer in routine clinical practice. The study also provides real-world data from a consecutive patient population, including individuals with multiple comorbidities.

Keywords: prostate cancer; hypofractionated radiotherapy; PSA response; progression-free survival; toxicity

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P26 – IMMUNE-RELATED ADVERSE EVENTS AND CLINICAL OUTCOMES OF FIRST-LINE PEMBROLIZUMAB IN ADVANCED CERVICAL CANCER

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Introduction: The addition of pembrolizumab to first-line therapy for metastatic, recurrent, or persistent cervical cancer has significantly improved progression-free survival (PFS) and overall survival (OS) [1,2]. However, its integration into standard regimens raises concerns about immune-related adverse events (irAEs), which require vigilant monitoring and appropriate management [3,4,5]. This study aimed to characterize the incidence, spectrum, and management of irAEs in patients receiving first-line pembrolizumab-based therapy at our institution, while also evaluating early treatment efficacy and clinical outcomes.

Methods: A retrospective descriptive study included 39 patients treated with pembrolizumab combined with chemotherapy, without bevacizumab, between January 2025 and February 2026.

Results: The median age of the cohort was 53 years (range, 33–74). Histologically, 29 patients (74.4%) had squamous cell carcinoma, 8 (20.5%) had adenocarcinoma, and 2 (5.1%) had mixed histology. Most patients (31; 78.8%) were treated for relapsed disease, 6 (15.4%) had persistent disease, and 2 (5.1%) presented with de novo metastatic cancer. Prior radiotherapy with concomitant cisplatin had been administered in 94.9% of patients.

After a median follow-up of 8 months (range, 3–17), disease progression had occurred in 15 patients (38.5%), and median PFS had not yet been reached. Among the 31 patients who underwent radiologic response evaluation, stable disease was observed in 10 (25.6%), partial response in 11 (28.2%), and complete response in 2 (5.1%), while 8 patients (20.5%) had progressive disease as their best response. Six patients (15.4%) were awaiting evaluation at data cutoff, and therapy was discontinued due to toxicity prior to response assessment in 2 patients (5.1%). In the evaluable population, the objective response rate was 41.9%, and the clinical benefit rate was 74.2%.

Suspected irAEs were reported in 11 patients (28.2%), with confirmed irAEs in 9 cases (23%). Gastrointestinal toxicity was most frequent, including five cases (12.8%) of grade 2–3 diarrhea. In three patients (7.7%), fecal calprotectin levels exceeded 1000 mcg/g, and colonoscopy confirmed grade 3 immune-related colitis, leading to permanent treatment discontinuation. All three patients were treated with intravenous methylprednisolone followed by an oral prednisone taper, resulting in normalization of bowel movements and calprotectin levels.

Thyroid dysfunction occurred in three patients (7.7%), and two patients (5.1%) developed grade 2 skin toxicity. One case of grade 3 immune-related rheumatoid arthritis was observed; after corticosteroid therapy, pembrolizumab was successfully reintroduced without recurrence of symptoms. Grade 2–3 transaminase elevations occurred in two patients (5.1%), both of whom had previously experienced another irAE. Three patients (7.7%) developed two or more distinct irAEs.

A single case of duodenal ulcer was reported, with causality still under investigation. Overall, therapy was permanently discontinued due to irAEs in four patients (10.2%). Additionally, chemotherapy was discontinued in one patient due to severe febrile neutropenia complicated by sepsis and prolonged neutropenia.

Conclusion: In this real-world cohort, first-line pembrolizumab-based therapy showed encouraging antitumor activity in metastatic, recurrent, or persistent cervical cancer. Immune-related adverse events

were frequent but generally manageable with prompt recognition and appropriate immunosuppressive therapy, although treatment discontinuation was occasionally required. Continued follow-up is essential to define the durability of response and long-term safety outcomes.

Keywords: pembrolizumab; cervical cancer; first-line therapy; immune-related adverse events (irAEs); clinical outcome

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P27 – IMMUNOTHERAPY IN PD-L1–HIGH METASTATIC NON–SMALL CELL LUNG CANCER: REAL-WORLD RESULTS FROM A SINGLE CROATIAN ACADEMIC CENTER

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Background: The introduction of immune checkpoint inhibitors has addressed a major unmet need in the treatment of patients with advanced non-small cell lung cancer (NSCLC) who don't have actionable driver mutations. In randomized clinical trials, pembrolizumab demonstrated superior efficacy compared with standard platinum-based chemotherapy in patients whose tumors exhibit high PD-L1 expression. Specifically, pembrolizumab was associated with higher objective response rates and significantly prolonged progression-free survival (PFS) and overall survival (OS) in patients with PD-L1 tumor proportion score ≥50%. These findings established pembrolizumab as a standard first-line treatment option in this population. However, real-world data, particularly from Central and Eastern Europe, remain limited and are essential to confirm clinical trial outcomes in routine practice settings.

Methods: This retrospective, single-center study conducted at the University Hospital Center Zagreb, Croatia, evaluated the real-world effectiveness and safety of pembrolizumab in patients with metastatic NSCLC and high PD-L1 expression (≥50%). A total of 246 patients treated between March 2018 and April 2020 were included in the analysis. Patients with known EGFR mutations, ALK rearrangements, or ROS1

fusions were excluded. Treatment outcomes assessed median progression-free survival (mPFS), median overall survival (mOS), objective response rate (ORR), and disease control rate (DCR). Safety was evaluated by analyzing the incidence and severity of treatment-related adverse events, including those leading to treatment discontinuation or death.

Results: The mean age of the study population was 65 years, and 30% of patients were female. A history of smoking was reported in 92.9% of patients, including 52.7% current smokers and 40.2% former smokers. The predominant histological subtype was adenocarcinoma (67.5%). Brain metastases were present at diagnosis in 21% of patients. The median PFS was 22 months, and the median OS was 32 months. At 12 months, 60.6% of patients remained alive without evidence of disease progression. The ORR was 48.1%, while the DCR reached 75.8%. No statistically significant differences in PFS or OS were observed according to tumor histology, smoking status, or the method used for PD-L1 assessment. The only statistically significant difference was found in overall survival between patients with central nervous system (CNS) metastases and those without ($p = 0.013$; HR = 1.80; 95% CI 1.04–3.15), indicating worse survival outcomes in patients with CNS involvement. Adverse events led to treatment discontinuation in 44 patients (18.1%), and treatment-related death occurred in 7 patients (2.9%). The most frequent treatment-related adverse events of any grade leading to discontinuation were pneumonitis (47.2%) and dermatitis (20.4%). Among serious adverse events (grade 3–5), pneumonitis was the most common, occurring in 13.6% of patients who discontinued therapy due to toxicity.

Conclusion: This real-world study confirms that pembrolizumab is an effective and generally safe first-line treatment for patients with metastatic NSCLC and high PD-L1 expression. The observed clinical outcomes are consistent with results from pivotal clinical trials and provide valuable real-world evidence from Croatia.

P28 – IMPACT OF STEROID DAILY DOSE AT START OF RADIOTHERAPY ON SURVIVAL IN PATIENTS WITH GLIOBLASTOMA: A SINGLE-CENTER RETROSPECTIVE ANALYSIS

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Background: Glioblastoma remains the most aggressive primary malignant brain tumor in adults, with poor survival despite maximal safe resection followed by radiotherapy with concomitant and adjuvant temozolomide. Corticosteroids, particularly dexamethasone, are frequently administered to control peritumoral edema and neurological symptoms during the perioperative period and throughout chemoradiotherapy. However, emerging evidence suggests that corticosteroid exposure may adversely affect oncologic outcomes(1). Subsequent systematic review and meta-analysis confirmed a negative prognostic impact of dexamethasone administration in glioblastoma patients(2). Experimental and translational data further indicate that corticosteroids induce lymphopenia and impair anti-tumor immune responses, potentially attenuating the efficacy of radiotherapy(3-5).

Methods: We retrospectively analyzed 94 patients diagnosed with glioblastoma between 2020 and 2024 at University Hospital Centre Split. Patients were divided according to daily corticosteroid dose at

initiation of chemoradiotherapy (CRT): group 1 (≤4 mg dexamethasone daily; n=48; 51.1%) and group 2 (>4 mg daily; n=46; 48.9%). Baseline characteristics included age, ECOG performance status, extent of surgery (resection vs biopsy), tumor multicentricity, radiotherapy fractionation (standard 60 Gy in 30 fractions vs hypofractionated schedules), and time from surgery to initiation of CRT (≤8 vs >8 weeks). Survival outcomes were estimated using Kaplan–Meier analysis and compared using the log-rank test.

Results: The median age was 64.4 years in the lower-dose group (≤4 mg) and 65.6 years in the higher-dose group (>4 mg). An ECOG performance status of 0–1 was more frequently observed in the lower-dose group (95.8%) compared with the higher-dose group (69.6%). Tumor resection was also performed more commonly among patients receiving ≤4 mg (93.8% vs 69.6%), whereas biopsy-only procedures were more frequent in the higher-dose group.

Regarding radiotherapy technique, standard fractionation was delivered to 81.3% of patients in the lower-dose group and 63.0% in the higher-dose group. Multicentric tumors were observed in 16.7% of patients in the lower-dose group and in 28.3% of those in the higher-dose group.

In terms of survival outcomes, patients receiving ≤4 mg of dexamethasone at the start of chemoradiotherapy demonstrated significantly improved results. Median PFS was 9.8 months in the lower-dose group compared with 4.4 months in the higher-dose group ($p < 0.05$). Median OS was 14.3 months versus 5.7 months, respectively ($p < 0.05$). Overall, lower steroid exposure at treatment initiation was associated with significantly better survival outcomes.

Study limitations are a small sample size, the retrospective nature of the study, and the unbalanced distribution of major prognostic factors between the two cohorts of the study.

Conclusions: In this real-world single-center cohort, a lower dexamethasone dose (≤4 mg daily) at the initiation of chemoradiotherapy was significantly associated with improved progression-free and overall survival. These findings are consistent with previous reports suggesting a negative prognostic impact of corticosteroid exposure in patients with glioblastoma(1,2). The observed survival differences may be partly explained by the immunosuppressive effects of corticosteroids, including treatment-induced lymphopenia and interference with anti-tumor immune responses described in translational studies(3–5).

While corticosteroids remain essential for the management of peritumoral edema and neurological symptoms, our results suggest that their use should be carefully individualized, with efforts to minimize exposure whenever clinically feasible during definitive oncologic treatment.

Keywords: glioblastoma; steroid dose; chemoradiotherapy;overall survival; progression-free survival

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P29 – IMPACT OF TIME TO POSTOPERATIVE CHEMORADIOTHERAPY ON SURVIVAL IN PATIENTS WITH GLIOBLASTOMA: A SINGLE-CENTER RETROSPECTIVE ANALYSIS

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Background: Glioblastoma is the most aggressive primary malignant brain tumor in adults. Standard treatment consists of maximal safe surgical resection followed by radiotherapy with concomitant and adjuvant temozolomide. Despite multimodal therapy, prognosis remains poor, with a median overall survival (OS) of approximately 14–16 months in contemporary series(1). Given the rapid proliferative capacity of glioblastoma, the interval between surgery and initiation of postoperative chemoradiotherapy (CRT) may influence outcomes. Several large retrospective analyses suggest that radiotherapy initiated within approximately 4–8 weeks after surgery is associated with improved survival, whereas delays beyond this interval may negatively affect prognosis(2,3). However, results across studies remain heterogeneous, warranting further real-world evaluation(4,5).

Methods: We retrospectively analyzed 94 patients diagnosed with glioblastoma between 2020 and 2024 at University Hospital Centre in Split. Patients were divided according to the interval from surgery or biopsy to initiation of CRT: group 1 (early) <8 weeks (n=43; 45.7%) and group 2 (late) ≥8 weeks (n=51; 54.3%). Surgical management was categorized as biopsy only or tumor resection, with the the resection group including maximal tumor reduction, subtotal resection, and gross total resection. Survival outcomes were estimated using Kaplan–Meier analysis and compared using the log-rank test.

Results: Median age was 61.8 years in the earlier-treated group and 66.4 years in the later-treated group. In the earlier-treated group, 79.1% of patients had an ECOG performance status of 0 or 1, compared with 86.3% in the later-treated group. Standard fractionation (60 Gy in 30 fractions) was delivered to 76.7% of patients in the earlier-treatment group and 68.6% in the later-treatment group, whereas hypofractionated schedules were administered in 23.3% and 31.4% of patients, respectively. Regarding corticosteroid use, lower doses (≤4 mg) were more frequently observed in the later-treatment group (58.8%) compared with the earlier-treatment group (41.9%). Conversely, higher doses (>4 mg) were more common among earlier-treated patients (58.1% vs 41.2%).

Tumor resection was more frequent in the late group (92.1%) compared with the early group (69.8%), whereas biopsy-only procedures were more common in the early group (30.2% vs 7.9%). Patients undergoing resection initiated CRT significantly later than those treated with biopsy alone (p=0.019).

Median progression-free survival (PFS) was 7 months in the early group and 6 months in the late group (p=0.529). Median OS was 13 months versus 10 months, respectively (p=0.157). Although these differences did not reach statistical significance, Kaplan–Meier analysis demonstrated a consistent numerical advantage in both PFS and OS for patients who initiated CRT within 8 weeks.

Study limitations are a small sample size, the retrospective nature of the study, and the unbalanced distribution of major prognostic factors between the two cohorts of the study.

Conclusions: In this real-world cohort, patients who started chemoradiotherapy within 8 weeks demonstrated numerically longer PFS and OS, despite the early group containing a higher proportion of biopsy-

only patients and fewer resections. Importantly, resection (including maximal tumor reduction, subtotal, and gross total resection) was significantly associated with delayed initiation of adjuvant therapy.

While maximal safe resection remains a cornerstone of glioblastoma management, our findings suggest that the timely initiation of definitive oncologic treatment may be critically important, potentially regardless of whether the patient undergoes extensive resection or biopsy only. These observations align with prior evidence indicating that excessive delay beyond the 4–8 week window may compromise outcomes(2, 3). Streamlined multidisciplinary coordination aimed at minimizing avoidable postoperative delays should therefore be prioritized in routine clinical practice.

Keywords: glioblastoma; chemoradiotherapy; treatment timing; overall survival; progression-free survival

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P30 – INDIRECT ECONOMIC BURDEN OF BREAST CANCER AMONG WORKING-AGE WOMEN IN CROATIA: PRODUCTIVITY LOSSES, INFORMAL CARE AND MONETISED MORBIDITY-RELATED WELFARE LOSS

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Background: Beyond direct healthcare expenditure, breast cancer generates substantial societal costs through morbidity-related productivity losses and reliance on informal caregiving, particularly among women of working age(1,2). These indirect components can represent a major share of the overall cancer burden because symptoms and treatment sequelae affect attendance, performance at work and day-to-day activities, while families often compensate through unpaid support. Yet these costs are frequently absent from routine reporting and decision-making.

Evidence from Central and Eastern Europe remains sparse despite regional differences in labour markets, wage structures and survivorship support, limiting health-policy and health-technology assess-

ment that adopt a broader societal perspective(3,4). In Croatia, robust estimates of morbidity-related productivity losses and informal care are scarce. We estimated the indirect economic burden of breast cancer among working-age women receiving outpatient oncology care in Croatia.

Methods: A multicentre cross-sectional study was conducted in 2024 at two Croatian tertiary oncology centres. Women aged ≤65 years receiving ambulatory oncology care or follow-up within 24 months of active treatment were included. Work productivity impairment over the previous 7 days (absenteeism, presenteeism, overall work impairment) was assessed using the Work Productivity and Activity Impairment instrument and standard scoring rules(5,6). Productivity losses were annualised and valued using the human-capital approach(7) with Croatian female net hourly earnings (€7.46/hour; Q4 2024) and annual paid working time (2,076 hours) (national statistics). Informal care receipt and frequency over 12 months were converted to annual time and valued using the opportunity-cost approach(8). Morbidity-related welfare loss was monetised using a Croatian willingness-to-pay value per QALY with scenario analyses(9). Deterministic one-way sensitivity analyses assessed uncertainty in valuation inputs.

Results: We enrolled 266 women (mean age 51.4 years); 19.2% had metastatic disease. Among employed participants (165/233; 70.8%), mean overall work impairment was 43.9%, corresponding to ≈911 lost work hours and €6,799 productivity loss per employed patient-year. Absenteeism averaged 35.8% of scheduled work time and presenteeism 37.1%, indicating that reduced performance while working contributed substantially to total productivity loss rather than labour-market exit.

Informal care was reported by 54.7% (129/236) and averaged 22.5 eight-hour workdays/year, valued at €1,343 per patient-year, demonstrating a sizeable transfer of burden to households consistent with prior evidence on informal caregiving in cancer (2,8). Monetised morbidity-related welfare loss was €2,550 per patient-year (base case). Total indirect burden was €10,692 per patient-year, with sensitivity analyses yielding €9,063–€12,642. National-level contextualisation suggested an annual indirect burden of approximately €80 million among working-age women with breast cancer in Croatia.

Conclusion: Breast cancer imposes substantial indirect societal costs among working-age women in Croatia, driven predominantly by productivity losses that persist despite high employment, and reinforced by extensive reliance on informal caregiving. These findings support incorporating indirect costs into survivorship planning and health-technology assessment and prioritising interventions that improve functional recovery, work ability, and caregiver support in Croatia and comparable Central and Eastern European settings(3,4).

Keywords: breast cancer; indirect costs; productivity loss; absenteeism; presenteeism; informal caregiving; cost of illness; Croatia

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P31 – LYMPHOCYTIC INFILTRATION IN PROSTATE CANCER

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Lymphocytic infiltration within prostate cancer has emerged as an important prognostic and predictive biomarker due to its central role in the tumor microenvironment and host immune response. The interaction between tumor cells and infiltrating lymphocytes regulates anti-tumor immunity and may influence disease progression, therapeutic response, and clinical outcomes. Understanding the distribution, density, and functional phenotype of tumor-infiltrating lymphocytes (TILs) is therefore critical for assessing patient prognosis and guiding potential immunotherapeutic strategies.

In this study, we analyzed $CD3^+$ and $CD8^+$ lymphocytic infiltration in 90 patients diagnosed with prostate adenocarcinoma. The cohort included 30 patients with localized disease, 30 with locally advanced disease, and 30 with metastatic disease. Immunohistochemical evaluation was performed both at the invasive tumor margin (peritumoral compartment) and within the tumor tissue itself (intratumoral compartment). Lymphocyte density was determined using the hotspot method, whereby the area exhibiting the highest concentration of lymphocytes was counted. This approach allowed precise quantification of immune cell infiltration in the most immunologically active regions of the tumor.

Analysis demonstrated that high peritumoral $CD3^+$ infiltration was an independent predictor of shorter progression-free survival (PFS) and overall survival (OS) (log-rank $P < 0.001$). $CD3^+$ infiltration at the invasive margin was significantly associated with baseline prostate-specific antigen (PSA), nadir PSA, and perineural invasion ($p < 0.05$), while no significant correlations were observed with Gleason score, ISUP grade, or patient age. Receiver operating characteristic (ROC) analysis established $CD3^+$ infiltration thresholds predictive of cancer-specific mortality (AUC = 0.681; P = 0.0017), OS (AUC = 0.634; P = 0.0173), and PFS (AUC = 0.657; P = 0.0062). In contrast, $CD3^+$ infiltration within tumor tissue and $CD8^+$ infiltration in both tumor and invasive margin compartments did not exhibit significant prognostic value.

These results emphasize the importance of spatial immune distribution within the tumor microenvironment, highlighting the differential prognostic relevance of peritumoral versus intratumoral immune responses. The findings also underscore the heterogeneity of lymphocyte subsets, as variations in density and composition may be influenced by tumor molecular subtypes and genetic drivers. For instance, $CD3^+$ T-cells are often enriched in the stromal compartment, and higher numbers can be observed in ERG-positive tumors, suggesting that molecular profiling may be necessary for accurate interpretation of immune infiltration patterns. Overall, our study supports the concept that TIL assessment, particularly in the peritumoral region, provides valuable prognostic information and may guide immunotherapeutic decision-making.

Further research is required to elucidate the functional roles of different T-cell subsets, including $CD4^+$ and $CD8^+$ lymphocytes, in prostate cancer progression and response to therapy. Standardized methods for quantifying lymphocyte density and distribution, along with integration of molecular tumor characteristics, will be essential for translating these observations into clinical practice.

Keywords: prostate cancer; tumor-infiltrating lymphocytes; $CD3^+$ T cells; $CD8^+$ T cells; tumor microenvironment

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P32 – METASATIC LAESIONS IN URINARY BLADDER: CASE SERIES AND LITERATURE REVIEW

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Introduction: Secondary urinary bladder tumors comprise approximately 2% of all neoplasms at this site. Metastatic involvement most frequently originates from adjacent genitourinary organs, including the prostate, cervix, and colon. In this case series, however, we describe comparatively uncommon presentations of bladder metastases arising from primary lung cancer and renal cell carcinoma. Despite their low prevalence, secondary bladder tumors should be considered in the differential diagnosis when evaluating patients presenting with urological symptoms.

Patients: The first patient was a 68-year-old male with a history of primary renal cell carcinoma diagnosed three years prior to the most recent admission. Postnefrectomy histopatological examination confirmed clear cell renal carcinoma with sarcomatoid component. Alongside, he was diagnosed with prostate cancer year after having nefrectomy, followed by radical prostatectomy which was confirmed as prostate adenocarcinoma Gleason score (3+4). His presenting complaint was asymptomatic gross haematuria. Cystoscopic evaluation raised a strong suspicion of a bladder neoplasm, and transurethral endoscopic resection of the laesion was performed. Histopathological analysis confirmed metastatic clear cell renal

cell carcinoma involving the urinary bladder. The second patient was a 77-year-old female with previously diagnosed primary lung adenocarcinoma who likewise presented with gross hematuria. Transurethral electroresection of the bladder tumor was done. Intraoperatively, the lesion morphologically resembled a primary urothelial carcinoma. However, histopathological examination of the biopsy specimen established the diagnosis of metastatic lung adenocarcinoma to the urinary bladder. Following the procedure, the patient underwent palliative chemotherapy and radiotherapy.

Literature review: Metastatic involvement of the urinary bladder from extravesical primaries is rare, with available evidence limited to case reports and small series. The true incidence, metastatic pathways, and long-term outcomes remain unclear due to restricted data. Diagnosis is challenging and requires careful histopathologic, immunohistochemical, and clinicoradiologic correlation to differentiate metastatic lesions from primary bladder tumors. The lack of large studies precludes standardized treatment guidelines, resulting in individualized management strategies based mainly on the primary malignancy and overall disease burden. Importantly, accurate recognition of bladder metastasis may significantly influence therapeutic decisions and overall patient management.

Conclusion: In conclusion, secondary involvement of the urinary bladder by distant primary malignancies is rare but clinically significant and may closely mimic primary urothelial carcinoma both clinically and endoscopically. These case series underscore the importance of thorough histopathological evaluation in patients with a history of extravesical malignancy who present with haematuria and bladder lesions. Accurate identification of metastatic disease is essential for appropriate therapeutic planning and prognostic assessment.

Keywords: haematuria; lung carcinoma; renal carcinoma; urinary bladder metastatic laesions

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P33 – METASTATIC CLEAR CELL RENAL CELL CARCINOMA: REAL WORLD EVIDENCE FROM COMPREHENSIVE ONCOLOGY CENTRE IN CROATIA

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Metastatic clear cell renal cell carcinoma (mccRCC) is the most common subtype of kidney cancer, accounting for 75–80% of renal cell carcinomas and the majority of advanced cases. Despite significant therapeutic advances over the past two decades, mccRCC remains associated with substantial morbidity and mortality. The introduction of immune checkpoint inhibitors (ICIs) and vascular endothelial growth factor receptor (VEGFR) tyrosine kinase inhibitors (TKIs) has reshaped the treatment landscape and improved survival outcomes in these patients. The aim of this study was to evaluate real world evidence regarding outcomes in mccRCC from a tertiary oncology centre in Croatia. From January 2023 to January 2026 Dubrava University Hospital treated 27 patients with mccRCC. Of the total 27 patient, 19 were male and 8 were female, with their median age being 65 years (range 45 – 79 years). 15 patients were initially diagnosed with metastatic disease (de novo metastatic disease). The remaining 12 developed metastatic disease in a metachronous manner after being previously treated for localized renal cell carcinoma, 3 of whom progressed during adjuvant pembrolizumab therapy. Cytoreductive nephrectomy was performed in 11 out of the 15 patients as a part of multimodal therapy in metastatic setting. 9 out of 11 patients had pT3a stage on the pathology report. There were single cases of stage pT2a and stage pTa tumors. The first-line treatment for 15 patients was dual imunotherapy with nivolumab and ipilimumab, while 12 patients received TKIs, out of those, 10 patients received pazopanib and 2 patients cabozantinib. The number of patients undergoing second-line treatment was 16. Out of these, 10 patients received TKIs (7 patients cabozantinib, 2 patients axitinib, and 1 patient pazopanib). The other 6 patients received nivolumab. After the median follow-up of 14 months the median OS has still not been reached. Estimated 24-month OS for entire cohort was 58.7%, with 19 patients who were still living at the time of analysis and 8 who died. The patients treated with TKI had a numerically higher 24-month overall survival (OS, 71.4%) than the patients receiving immunotherapy (48%). The TKI group had not yet achieved the median OS, while in the immunotherapy group it was 17 months (range 3-17). However, the difference was not statistically significant ($p = 0.0844$). These results are comparable with most retrospective studies from large oncology centres. The information collected in practice demonstrates that mccRCC presents in different clinical scenarios and that selecting the most suitable treatment should be done on an individual basis through multidisciplinary approach. Also, it seems that some patients with symptomatic metastatic disease needing faster response might benefit from TKI rather than dual immunotherapy. In conclusion, metastatic clear cell renal cell carcinoma is a heterogeneous disease with encouraging results in real world setting. Further investigation are needed in order to address controversies and improve outcome in population with high-risk mccRCC.

Keywords: metastatic clear cell renal carcinoma; immune checkpoint inhibitors; tyrosine kinase inhibitors

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P34 – MRI RESTAGING AFTER TOTAL NEOADJUVANT THERAPY: HOW ACCURATE IS IT IN LOCALLY ADVANCED RECTAL CANCER?

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Background: The management of locally advanced rectal cancer (LARC) has evolved toward total neoadjuvant therapy (TNT), shifting systemic chemotherapy to the preoperative setting to improve distant control and survival. TNT has demonstrated reductions in distant metastases and improved disease-free and overall survival, while enabling organ-preservation strategies such as *watch-and-wait* in selected patients. Magnetic resonance imaging (MRI) plays a pivotal role in primary staging and restaging. Accurate MRI assessment is essential for selecting patients for neoadjuvant treatment and tailoring surgical strategies. However, post-TNT MRI interpretation is challenging due to fibrosis and treatment-related changes that may mimic residual tumor. This raises the question of potential overstaging or downstaging before surgery and its impact on clinical decision-making.

Methods: A retrospective analysis included 71 patients with rectal cancer treated with TNT (49 males, 22 females; mean age 62.5 ± 9.5 years). Regarding treatment sequencing, 28 patients received chemotherapy before chemoradiotherapy (CRT), 13 both before and after CRT, and 30 after CRT. Most regimens consisted of CAPOX (65 patients) and FOLFOX (6 patients). Long-course CRT was administered in 58 patients and short-course in 13. Overall, 37 patients received six cycles of neoadjuvant chemotherapy and 34 received ≤5 cycles. Post-treatment MRI staging (yT, yN) was compared with pathological staging (ypT, ypN) in the 59 patients who underwent surgical resection, while 12 patients were managed with a watch-and-wait strategy due to a favorable clinical response. Agreement between MRI and pathological staging was assessed using Cohen's kappa statistics and the Wilcoxon signed-rank test. Diagnostic performance metrics were calculated for detection of residual tumor, nodal metastases, and pathological complete response (pCR).

Results: Among 59 operated patients, agreement between MRI-assessed and pathological tumor stage was limited (accuracy 33.9%, $\kappa = 0.12$), indicating slight agreement. Nodal staging showed higher concordance (accuracy 74.6%, $\kappa = 0.28$; fair agreement). MRI overstaged tumors in 17 patients and under-

staged in 22, with 20 correctly staged; for nodal staging, 44 were correctly staged, with 7 overstaged and 8 understaged. MRI sensitivity and specificity were 73.5% and 30.0% for detecting residual tumor (T0 vs ≥T1) and 42.9% and 88.9% for nodal metastases (N0 vs N+). pCR occurred in 10/59 patients (16.9%). MRI predicted pCR with 30.0% sensitivity, 73.5% specificity, 18.8% positive predictive value, 83.7% negative predictive value, and 66.1% accuracy.

Conclusion: MRI shows limited accuracy for post-treatment tumor staging and prediction of pCR, although nodal staging demonstrates moderate concordance with pathology. These findings highlight limitations of MRI-based restaging in rectal cancer and the need for cautious interpretation when considering organ-preserving strategies such as watch-and-wait.

Keywords: rectal neoplasm; neoadjuvant chemoradiation therapy; neoadjuvant chemotherapy; magnetic resonance imaging

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P35 – NEOADJUVANT THERAPY OF TRIPLE – NEGATIVE BREAST CANCER – A FIVE – YEAR SINGLE – CENTER EXPERIENCE

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Introduction: Triple – negative breast cancer is the most aggressive subtype of breast cancer. Studies have demonstrated a favorable response to neoadjuvant chemotherapy in these patients. Furthermore, based on the KEYNOTE-522 trial, the addition of pembrolizumab has further improved the treatment of early – stage triple – negative breast cancer. In this study, we analyzed treatment data at our institution.

Methods: In this retrospective study, we analyzed data from 46 female patients with early-stage triple – negative breast cancer who were treated with neoadjuvant therapy at University Hospital Center Osijek between 2021 and 2025. The patients were divided into three groups according to HER2 expression (0, 1+, and 2+), and differences in treatment response according to the RCB (*Residual Cancer Burden*) classification were analyzed between the groups.

Results: In the study sample of 46 patients, 33 (72%) had tumors with HER2 – negative (0) expression, 12 (26%) patients had HER2 1+ expression, and 1 patient (2%) had HER2 2+ expression. Four patients (9%) received pembrolizumab. Overall, 18 patients (39%) achieved pCR (complete pathologic response; RCB 0), 7 patients (15%) achieved RCB I, 19 patients (41%) achieved RCB II, and 2 patients (4%) achieved RCB III. Differences in the distribution of RCB categories between the groups were not statistically significant, although the highest proportion of pCR (RCB 0) was observed in the HER2 1+ group (7 patients; 58%), compared to 11 patients (33%) in the HER2 – negative (0) group (Fisher's exact test, $p = 0.54$).

Conclusion: According to a comprehensive meta – analysis, the pCR rate after neoadjuvant chemotherapy for triple – negative breast cancer was 28.9%, and according to the experience of one European center, it was 32.5%, while in our sample it was 39%, which is higher than the reported results. Studies show that patients with HER2 – negative (0) tumors have a higher pCR rate than those with HER2 low positivity (1+ and 2+). However, in our sample, patients with HER2 1+ had the highest pCR rate. A possible explanation is that, according to research, the visual assessment of immunohistochemical staining intensity depends on the pathologist, and the distinction between HER2 0 and HER2 1+ can be minimal. Furthermore, most studies that examined differences in pCR have grouped HER2 1+ and HER2 2+ tumors together in HER2 low positivity group. Therefore, we can conclude that our results are in line with worldwide research.

Keywords: triple – negative breast cancer; neoadjuvant therapy; RCB classification

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P36 – OPTIMIZING ALPELISIB TOLERABILITY THROUGH EVENING DOSING AND SHORT FASTING: RESULTS OF THE RANDOMIZED ITACA PHASE IIB TRIAL

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Background: Alpelisib combined with fulvestrant improves outcomes in patients with hormone receptor–positive (HR-positive), HER2-negative, PIK3CA-mutated metastatic breast cancer, but its use is frequently limited by on-target metabolic toxicity, particularly hyperglycemia(1,2). Severe hyperglycemia typically occurs early after treatment initiation and often leads to dose interruptions or discontinuation(2). Preclinical data suggest that insulin-mediated feedback following PI3Kα inhibition may exacerbate hyperglycemia and potentially attenuate antitumor efficacy(3). Pharmacologic and metabolic context, including timing of drug administration and nutritional status, may therefore influence both toxicity and therapeutic index(4). The ITACA trial evaluated whether modifying alpelisib dosing time and metabolic context could improve tolerability without compromising efficacy.

Methods: ITACA was an open-label, randomized, phase IIb trial conducted at three Croatian academic centers. Postmenopausal women with HR-positive, HER2-negative, PIK3CA-mutated metastatic breast cancer progressing on endocrine therapy were randomized 1:1 to receive alpelisib plus fulvestrant either as standard morning dosing or as evening dosing following a ≥5-hour fasting interval with low-carbohydrate dietary guidance. The primary endpoint was the exposure-adjusted incidence rate (EAIR) of first grade 3–4 hyperglycemia during the prespecified 90-day risk window (or up to 30 days after discontinuation). Secondary endpoints included time to first grade 3–4 hyperglycemia, objective response rate (ORR), progression-free survival (PFS), and quality of life (QoL). Glycemic monitoring included baseline and early-treatment 7-point glucose profiles and continuous glucose monitoring.

Results: Forty-two patients were randomized (21 per arm), and 41 received at least one dose of alpelisib. Median age was 60 years in the evening-dosing arm and 63 years in the morning-dosing arm. Within the prespecified risk window, evening dosing with short fasting was associated with a lower exposure-adjusted incidence rate (EAIR) of first grade 3–4 hyperglycemia compared with standard morning dosing (378 vs 742 per 100 person-years; unadjusted IRR 0.51, 95% CI 0.23–1.12). Adjusted Poisson regression models consistently favored evening dosing, with adjusted incidence rate ratios ranging from 0.25 to 0.37.

Evening dosing substantially delayed the onset of severe hyperglycemia. Median time to first grade 3–4 hyperglycemia was 73 days with evening dosing versus 9.5 days with morning dosing, and fewer patients experienced grade 3–4 events (52.4% vs 70.0%). Exploratory efficacy analyses showed no evidence

of compromised antitumor activity, with fewer progression events observed in the evening-dosing arm and no deterioration in quality of life.

Conclusion: Evening alpelisib dosing following a brief fasting interval was associated with a reduced incidence and delayed onset of severe hyperglycemia in this randomized study. Importantly, improved metabolic tolerability did not compromise antitumor activity or quality of life. Consistency across exposure-adjusted incidence-rate and time-to-event analyses supports the hypothesis that metabolic context at dosing influences PI3K inhibitor–related toxicity. These findings extend prior observations on the temporal dynamics of alpelisib-induced hyperglycemia(5) and provide prospective evidence that simple behavioral interventions may optimize host metabolic state. This pragmatic strategy warrants validation in larger trials and may improve the therapeutic index of alpelisib

Keywords: alpelisib, hyperglycemia, fasting, metabolic tolerability, PI3K inhibition

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P37 – PREVALENCE OF IDH MUTATED GLIOMAS, PATIENT CARACTERISTICS AND TREATMENT MODALITIES

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In 2025, 89 patients with gliomas were referred to Department of oncology and radiotherapy University hospital center Zagreb. Most of the patients were surgically treated at University hospital center Zagreb (65). 11 patients were referred from Clinical hospital Dubrava, eight from Clinical hospital center Sestre milosrdnice, four from General hospital Varaždin and one from Children's hospital Zagreb. Median patient's age was 64 (range 20 –84). 38 patients were female (43%).

Most of the patients (69) had IDH WT high-grade gliomas. Median patient's age was 67 (range 25 –84). One patient had pleomorphic xanthoastrocytoma, one patient had pilocytic astrocytoma and one patient had low-grade glial/glioneuronal tumor.

17 patients had IDH-mutant gliomas based on IHC staining. Median age of these patients was 40 (range 25 – 59). Seven patients were female (41%).

Based on molecular analysis 7 patients had oligodendroglioma (41%): 5 patients oligodendroglioma grade 2 and two patients oligodendroglioma grade 3. 8 patients (47%) had astrocytoma: three patients

astrocytoma grade 2, three patients astrocytoma grade 3 and two patients astrocytoma grade 4. Two patients had diffuse high-grade glioma. Four patients had CDKN2A hemizygote deletion. In five patients, CDKN2A status was unknown. Remaining eight patients did not have CDKN2A deletion.

Ten patients underwent radiotherapy, out of which nine proceeded with adjuvant chemotherapy (temozolomide or PCV). In one patient chemotherapy was not indicated due to comorbidities. In case of tumor progression upon radiochemotherapy, targeted therapy with IDH inhibitor would be considered in further therapy lines.

In seven patients, watchful waiting was initially planned. Due to residual tumor not requiring chemo-radiotherapy, targeted therapy with vorasidenib is currently planned in three patients.

In two patients FMI confirmed IDH1 mutation; in one p.R132H and in one IDH1 p.R132C. In both patients, according to FMI results targeted therapies includes vorasidenib or ivosidenib. In two more patients, FMI results are awaited in order to start with targeted therapy in accordance with INDIGO trial results.

Keywords: gliomas; IDH-mutant gliomas; targeted therapy, IDH inhibitor

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P38 – PROGNOSTIC VALUE OF BASELINE NEUTROPHIL-TO-LYMPHOCYTE RATIO IN PATIENTS WITH HEPATOCELLULAR CARCINOMA, TREATED WITH ATEZOLIZUMAB PLUS BEVACIZUMAB: A SINGLE-CENTER REAL-WORLD ANALYSIS

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Background: Immune checkpoint inhibitors have substantially improved outcomes across several solid tumors; however, clinical benefit remains heterogeneous, highlighting the need for reliable and easily applicable prognostic biomarkers. Systemic inflammation has emerged as an important host-related determinant of immunotherapy outcomes. The neutrophil-to-lymphocyte ratio (NLR) is a simple biomarker reflecting the balance between pro-tumor inflammatory activity and anti-tumor immune response and has been consistently associated with survival outcomes in patients treated with immunotherapy(1–3).

In hepatocellular carcinoma (HCC), chronic inflammation related to underlying liver disease and cirrhosis plays a central role in tumor development and progression. Several studies have demonstrated the prognostic value of baseline NLR in patients with advanced HCC treated with immune checkpoint inhibitor monotherapy(4–6). However, data on the prognostic relevance of NLR in patients receiving combination therapy with atezolizumab and bevacizumab in real-world clinical practice remain limited.

Methods: We retrospectively analyzed consecutive patients with unresectable or metastatic HCC treated with atezolizumab plus bevacizumab between 2020 and 2025 at a single tertiary center. Baseline neutrophil and lymphocyte counts were used to calculate NLR. Overall survival (OS) and progression-free survival (PFS) were defined from treatment initiation and estimated using the Kaplan–Meier method. Associations between baseline NLR and OS or PFS were evaluated using Cox proportional hazards models. NLR was analyzed as a continuous variable and using predefined cut-off values of ≥3 and ≥5. Survival was further explored across clinically relevant strata.

Results: Median baseline NLR was 3.18 (interquartile range (IQR) 1.90–5.18); 59.6% of patients had NLR ≥3 and 26.9% had NLR ≥5. Increasing NLR as a continuous variable was significantly associated with shorter OS (hazard ratio (HR) 1.15 per unit increase; 95% CI 1.02–1.28; $p < 0.05$) and shorter PFS (HR 1.11; 95% CI 1.00–1.23; $p<0.05$).

Patients with NLR ≥3 had inferior OS compared with those with NLR <3 (HR 2.13; 95% CI 1.06–4.29; $p<0.05$). Patients with NLR ≥5 represented a high-risk subgroup with markedly worse outcomes, including a median OS of 6.1 months compared with 19.4 months in patients with NLR <5, and a median PFS of 3.4 months versus 9.8 months, respectively. High NLR (≥5) was associated with a nearly four-fold increased risk of death (HR 3.70; 95% CI 1.74–7.89; $p<0.05$) and a three-fold increased risk of progression or death (HR 3.00; 95% CI 1.53–5.87; $p<0.05$). The adverse prognostic impact of elevated NLR was consistently observed across clinically relevant subgroups.

Conclusion: Baseline NLR is a strong and clinically relevant prognostic biomarker in patients with unresectable or metastatic HCC treated with atezolizumab plus bevacizumab. Both moderate (≥3) and high (≥5) NLR thresholds stratify patients into distinct risk groups, with NLR ≥5 identifying a population with particularly unfavorable survival outcomes. These real-world findings support the integration of inflammatory biomarkers into baseline risk assessment in patients receiving combination immunotherapy.

Keywords: hepatocellular carcinoma; neutrophil-to-lymphocyte ratio; inflammation; immunotherapy; atezolizumab; bevacizumab; prognostic biomarker

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P39 – REAL-WORLD IMPACT OF COMPREHENSIVE GENOMIC PROFILING – GUIDED THERAPY ON ADVANCED SOLID TUMORS: INSIGHTS FROM A SINGLE-INSTITUTION COHORT

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Background: Precision oncology is being revolutionized by comprehensive genomic profiling (CGP)-enabled personalization, now gradually integrating into routine clinical practice, where its utility has been validated in realworld cohorts, already demonstrating high actionability rates of around 80%(1). Furthermore, Molecular tumor board (MTB) recommended CGP-guided therapy demonstrated improved outcomes across different solid cancer types(2). Croatia has broad availability of molecular profiling and therapy in accordance to its results. Thus, realworld data are essential to fully capture clinical value of CGP-guided therapy beyond clinical trials(3). This singlecenter analysis reports outcomes of CGPguided therapy in all treated patients, aiming to characterize its clinical utility in everyday practice.

Methods: This retrospective study was carried out at UHC Split, including all patients who received (CGP-guided therapy between January 1, 2020, and December 31, 2025. CGP testing was conducted in an accredited laboratory (Foundation Medicine Inc., Cambridge, MA, USA). Therapy decisions were based on recommendations from the MTB. Progression-free survival (PFS) was defined as the time from starting CGP-guided therapy to disease progression, death from any cause, or last follow-up (with censoring as appropriate), whichever occurred first.

Results: A total of 69 patients received CGP-guided therapy. Median age was 64 years (IQR 53–74), and 52% of patients were women, while 48% were men. The most common cancer types treated were gastrointestinal, gynecologic and lung in 26%, 20% and 19% of patients. Majority of patients (94%) received at least one previous line of therapy, with 38% of patients who received at least 3 lines of therapy. Clinically relevant alterations were reported in 52 (75%) patients. The most commonly therapies used were PARP inhibitors, antibody-drug conjugate and immune checkpoint inhibitors in 22%, 20% and 16% patients.

Median PFS was 5.8 months (IQR 2.1–12.7), with 28% of patients achieving >12 months and 12% >18 months. As of January 20, 2026, 28% patients are still being treated. All treatments were well tolerated, with worst adverse events being pneumonitis and acute renal failure.

Conclusion: Our results have shown that demonstrates that CGP-guided therapy is feasible and clinically meaningful in a heterogeneous, predominantly heavily pretreated population. With clinically relevant alterations identified in 75% of patients and over one quarter achieving progression-free survival beyond 12 months, CGP-based treatment yielded durable disease control across multiple tumor types. Our experience underscores the importance of realworld evidence for future implementation of CGP-guided therapy in routine care.

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P40 – REAL-WORLD IMPLEMENTATION OF NEXT-GENERATION SEQUENCING IN GYNECOLOGICAL CANCERS: PRELIMINARY DATA FROM THE UNIVERSITY CLINICAL HOSPITAL MOSTAR

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Introduction: Next-generation sequencing (NGS) is a technology that enables the simultaneous analysis of a large number of genes. It facilitates a personalized treatment approach through the identification of predictive biomarkers and actionable genetic alterations that may be targeted therapeutically. Real-world evidence suggests that the clinical benefit of NGS testing may be greatest in patients with advanced cancers that routinely require multiple molecular markers, in patients with advanced rare malignancies, and in those screened for enrollment in biomarker-driven clinical trials.[1] We conducted a retrospective analysis of gynecologic cancer patients who underwent NGS testing at our institution to evaluate the prevalence of actionable genomic alterations and their impact on treatment decisions in a real-world setting.

Methods: We analyzed data from 27 patients with gynecologic malignancies who underwent NGS testing at the University Clinical Hospital Mostar (Bosnia and Herzegovina) between 2021 and 2025. Clinical data were collected through review of electronic or paper medical records. All genomic analyses were performed using Foundation Medicine Inc. (Cambridge, MA, USA) NGS assays.

Results: Out of 133 total NGS tests performed at our institution, 27 (20%) were conducted in patients with gynecologic cancers. Primary tumor sites included ovarian cancer (n = 19), endometrial cancer (n = 5), and cervical cancer (n = 3). The median age at testing was 58 years. Actionable predictive biomarkers (*BRCA1/2* mutation, HRD positivity, MSI-high status, TMB ≥10 Mut/Mb, and/or *ERBB2* mutations) were identified in 11/27 patients (40.7%). However, FMI-guided targeted therapies were administered in only 18.5% patients, all of whom received PARP inhibitor-based treatment.

Conclusions: Although a substantial proportion of patients harbored actionable genomic alterations, the real-world clinical impact of NGS testing in our cohort remains limited due to restricted availability and reimbursement of targeted therapies for gynecologic malignancies in the Federation of Bosnia and Herzegovina. Additional efforts are needed to address the challenges associated with precision oncology in the Federation of Bosnia and Herzegovina.

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P41 – QUALITY OF LIFE WITH EVENING ALPELISIB DOSING AND FASTING: PATIENT-REPORTED OUTCOMES FROM THE ITACA STUDY

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Backgroud: In hormone receptor–positive (HR-positive), HER2-negative metastatic breast cancer long-term disease control relies on sustained exposure to targeted therapies, while treatment-related toxicities may impair quality of life (QoL) and adherence. Alpelisib, a PI3Kα inhibitor, is associated with metabolic adverse events that can negatively affect patient-reported outcomes(1). Treatment-related symptoms and functional impairment are known to influence daily functioning and overall well-being in this population(2,3). The ITACA study evaluated whether modifying the timing and metabolic context of alpelisib administration could influence QoL outcomes.

Methods: ITACA was an open-label, randomized, phase IIb pilot trial conducted at three Croatian university hospitals (Split, Zagreb, Osijek) between September 2022 and February 2025. Postmenopausal women with HR-positive, HER2-negative, PIK3CA-mutated metastatic breast cancer were randomized to receive alpelisib plus fulvestrant as either standard morning dosing or evening dosing after a ≥5-hour fasting interval with low-carbohydrate dietary guidance. Quality of life, a predefined secondary endpoint, was assessed using the EORTC QLQ-C30 and QLQ-BR23 questionnaires at baseline and approximately three months.

Results: Of the patients included in the safety population, evaluable QoL data at baseline and end of study were available for 13 patients in the evening-dosing arm and 10 patients in the morning-dosing arm. Overall, evening dosing with fasting was not associated with deterioration in global health status or overall QoL. On the QLQ-C30, adjusted mean differences favored the evening-dosing arm for physical functioning (+9.5 points) and pain (–12.3 points), although confidence intervals were wide and did not consistently reach statistical significance. Global health status and other functional domains showed small between-group differences. On the breast cancer–specific QLQ-BR23, sexual functioning scores were significantly higher in the evening-dosing arm compared with standard dosing (+7.2 points). Most other symptom and functional scales, including body image and systemic therapy side effects, were similar between groups. A trend toward higher breast symptom scores was observed in the evening-dosing arm, but estimates were imprecise and based on small numbers. Importantly, no QoL domain showed a clinically meaningful deterioration associated with evening dosing.

Conclusion: Evening alpelisib dosing after a short fasting interval was not associated with deterioration in global quality of life and showed favorable trends in selected patient-reported outcomes, including

physical functioning, pain and sexual functioning. In breast cancer populations, changes in functional and symptom domains are clinically meaningful for daily functioning and overall well-being(4). Importantly, despite the known metabolic toxicity profile of alpelisib and the need for active glycemic management(5), no clinically meaningful deterioration in quality-of-life domains was observed with evening dosing and fasting. Taken together, these findings suggest that metabolic optimization of alpelisib administration may preserve overall quality of life and potentially improve selected aspects of patient-reported functioning without introducing additional QoL burden during long-term treatment for metastatic breast cancer.

Keywords: alpelisib; breast cancer, quality of life; patient-reported outcomes; evening dosing

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P42 – RADIOLOGICAL EVALUATION OF RESPONSE TO NEOADJUVANT THERAPY IN NON-SMALL CELL LUNG CANCER: RADIOLOGICAL–PATHOLOGICAL CORRELATION – EXPERIENCE FROM UNIVERSITY HOSPITAL CENTER OSIJEK

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Neoadjuvant therapy has become an important component of treatment for patients with resectable non-small cell lung cancer (NSCLC), particularly in stage II–III disease. Following the results of the KEYNOTE-671 trial, neoadjuvant chemo-immunotherapy with pembrolizumab in combination with platinum-based chemotherapy was approved by the European Commission in 2023 and has since been implemented

in clinical practice across European Union countries, including Croatia. Radiological imaging plays a key role in staging, treatment planning, and response assessment.

This study presents a retrospective analysis of 10 patients with NSCLC treated with neoadjuvant therapy at University Hospital Center Osijek. All patients underwent CT and/or PET/CT imaging before and after therapy, followed by surgical resection. Radiological response was evaluated according to RECIST 1.1 criteria and correlated with postoperative pathological findings.

Radiological evaluation demonstrated partial response or stable disease in most patients. However, in several cases, residual lesions observed on CT corresponded to fibrosis, necrosis, or inflammatory changes without viable tumor cells or < 1% of residual tumor on pathological analysis. These findings highlight the limitations of size-based radiological criteria in assessing treatment response.

Radiological–pathological correlation is essential for accurate evaluation of therapeutic efficacy. A multidisciplinary approach remains crucial for optimal interpretation of imaging findings and management of patients with NSCLC treated with neoadjuvant therapy.

Keywords: NSCLC, neoadjuvant therapy, CT, PET/CT, RECIST, pathological response

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P43 – REAL-WORLD CLINICAL OUTCOMES OF ATEZOLIZUMAB PLUS BEVACIZUMAB IN UNRESECTABLE OR METASTATIC HEPATOCELLULAR CARCINOMA: A SINGLE-CENTER RETROSPECTIVE STUDY

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Background: Atezolizumab plus bevacizumab is the established first-line systemic therapy for unresectable or metastatic hepatocellular carcinoma (HCC) following the IMbrave150 trial, which demonstrated superior overall survival (OS) and progression-free survival (PFS) compared with sorafenib(1,2). Subsequent updates and real-world studies confirmed the clinical benefit of this regimen, while also reporting variability in outcomes due to broader patient selection, more advanced disease, and limited access to post-progression therapy compared with randomized trials(3–6). Single-center real-world analyses provide important complementary evidence and allow detailed clinical characterization of treated populations.

Methods: We conducted a retrospective single-center cohort study including consecutive patients with unresectable or metastatic HCC treated with atezolizumab plus bevacizumab between 2020 and 2025. Base-

line data included age, sex, ECOG performance status, Barcelona Clinic Liver Cancer (BCLC) stage, presence of extrahepatic spread, liver cirrhosis, prior locoregional therapy, alpha-fetoprotein (AFP) level, and baseline laboratory parameters. Tumor response was assessed during routine follow-up and categorized as complete response, partial response, stable disease, progressive disease, or not evaluable. Overall survival (OS) and progression-free survival (PFS) were defined from treatment initiation to death or progression/death and estimated using the Kaplan–Meier method. Survival outcomes were stratified by BCLC stage, ECOG performance status, extrahepatic spread, AFP level, and receipt of second-line systemic therapy.

Results: Sixty-one patients were included (median age 71 years; interquartile range (IQR) 64–77), of whom 85.5% were male. BCLC stage was B in 41.8% and C in 54.5% of patients, while extrahepatic spread was present in 54.5%. ECOG performance status was 0–1 in 81.8% and 2 in 18.2%. AFP ≥400 μg/L was observed in 22.4%. Median follow-up was 26.2 months.

Median OS was 14.7 months (95% CI 6.6–21.6), and median PFS was 7.6 months (95% CI 4.2–11.4). Among evaluable patients (67.2%), objective response rate was 48.8% and disease control rate was 85.4%.

Median OS was longer in patients with BCLC B compared with BCLC C disease (not reached vs 11.9 months; log-rank $p<0.005$), absence versus presence of extrahepatic spread (18.4 vs 10.8 months; $p<0.005$), ECOG performance status 0–1 versus 2 (16.2 vs 8.1 months; $p<0.005$), and receipt versus no receipt of second-line systemic therapy (23.6 vs 12.9 months; log-rank $p<0.001$). No statistically significant difference in OS was observed according to AFP <400 versus ≥400 μg/L (16.8 vs 7.9 months; $p=0.587$).

Progression-free survival differed significantly by BCLC stage (log-rank $p=0.002$), ECOG performance status ($p=0.0025$, and presence of extrahepatic spread ($p=0.002$). No significant difference in PFS was observed according to AFP cutoff (<400 vs ≥400 μg/L; $p=0.430$). PFS was not stratified by receipt of second-line therapy, as second-line treatment was initiated after progression.

Conclusion: In this single-center real-world cohort, atezolizumab plus bevacizumab demonstrated clinically meaningful activity in unresectable or metastatic HCC. Survival outcomes were inferior (14.7 months) to pivotal trial results but closely aligned with other real-world series (3–6), reflecting advanced disease stage and limited access to subsequent therapy. These findings reinforce the effectiveness of atezolizumab plus bevacizumab in routine clinical practice and highlight the value of detailed single-center real-world analyses.

Keywords: hepatocellular carcinoma; atezolizumab; bevacizumab; real-world evidence; overall survival; progression-free survival; single-center study

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P44 – REAL-WORLD TREATMENT PATTERNS FOR ADVANCED UROTHELIAL CANCER IN THE ERA OF IMMUNOTHERAPY AND ANTIBODY-DRUG CONJUGATES: A SINGLE-INSTITUTION ANALYSIS

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Background: The therapeutic landscape of advanced urothelial carcinoma (aUC) has evolved substantially with the introduction of immune checkpoint inhibitors (ICIs), maintenance immunotherapy, and antibody–drug conjugates (ADCs). While randomized clinical trials have defined optimal treatment sequencing, real-world implementation remains heterogeneous, particularly in smaller national healthcare systems. Data describing contemporary treatment patterns, line attrition, and immunotherapy uptake in routine practice are limited. We conducted a single-institution analysis to characterize real-world treatment patterns for aUC in the immunotherapy era.

Methods: We retrospectively analyzed consecutive patients diagnosed with advanced or metastatic urothelial carcinoma and managed at our institution between 2020-2025. Clinical data were extracted from institutional records, including first-line (1L) systemic therapy, maintenance treatment, subsequent therapy lines, and treatment transitions. Regimens were categorized into platinum-based chemotherapy (gemcitabine/cisplatin, gemcitabine/carboplatin, ddMVAC), immune checkpoint inhibitor monotherapy (atezolizumab, nivolumab), maintenance avelumab, antibody–drug conjugates (enfortumab vedotin), and other systemic therapies. Treatment attrition was evaluated across sequential line.

Results: A total of 241 patients with advanced urothelial carcinoma were included. Prior neoadjuvant chemotherapy was administered in 17 patients (7%), and adjuvant chemotherapy in 28 patients (11%). Seventy-six patients (31%) did not receive systemic first-line therapy, reflecting comorbidity burden, performance status limitations, or early clinical deterioration, leaving 165 patients who received first line systemic treatment (69%). Among treated patients, platinum-based chemotherapy remained the dominant first-line strategy, administered in 127 (53%) patients. Of these, 57 (45%) received gemcitabine/cisplatin, 62 (49%) gemcitabine/carboplatin, and 8 (6%) ddMVAC. Immune checkpoint inhibitor monotherapy was used in 31 patients (13%), primarily in PD-L1 positive platinum-ineligible individuals, including atezolizumab in 19 patients (61%) and nivolumab in 12 patients (39%). Avelumab maintenance was administered in 54 patients (22% of the overall cohort and 43% of patients receiving first-line platinum-based chemotherapy. Thirteen patients (10% of all patients treated with chemotherapy) received chemotherapy during a period when avelumab maintenance therapy was not available in Croatia. Only 65 patients (27% of the total cohort, and 39% of those who received first line therapy) proceeded to second-line therapy. Among

second-line treatments, nivolumab was administered in 29 patients (45%), enfortumab vedotin in 19 patients (29%), atezolizumab in 8 patients (12%) and trastuzumab deruxtecan in 1 patient. Overall, immune checkpoint inhibitors (nivolumab or atezolizumab) were used in 37 patients (57%) in the second-line setting. In the third-line setting, 11 patients received systemic therapy (17% of patients who received second line, 5% of total cohort), of whom 1 patient (9%) was treated with enfortumab vedotin, 1 patient with erdafitinib, 4 patients with taxane chemotherapy, 3 with cyclofosfamide, and 2 with gemcitabine/carboplatin reinduction. Only three patients (1% of the total cohort) received fourth-line systemic therapy, including enfortumab vedotin, taxane chemotherapy, and erdafitinib (one patient each). Overall, fewer than one-third of patients exposed to first-line therapy reached a second-line regimen, underscoring the gap between clinical trial eligibility and real-world treatment feasibility. Among patients who underwent comprehensive genomic profiling (n = 59), the most frequently identified Tier 1 alterations were ERBB2 (13 patients, 22%), FGFR3 (12 patients, 20%), and ARID1A (8 patients, 14%). High TMB was present in 13 patients (22%) and 1 patient was MSI-H positive.

Conclusions: In this single-institution real-world cohort, platinum-based chemotherapy remains the backbone of first-line treatment for advanced urothelial carcinoma, with increasing integration of immunotherapy and enfortumab vedotin in subsequent lines. However, significant attrition between treatment lines persists, with only a minority of patients receiving second-line therapy and very few reaching later lines. These findings highlight the importance of optimizing first-line strategies and early integration of effective therapies in routine practice. Real-world data such as these are essential to contextualize clinical trial results and inform treatment sequencing in everyday oncology practice.

Keywords: advanced urothelial carcinoma (aUC); immune checkpoint inhibitors; antibody–drug conjugates.

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P45 – SHAPING GYNECOLOGIC TUMOR MANAGEMENT: COMPREHENSIVE GENOMIC-GUIDED THERAPY RESULTS FROM EVERYDAY CLINICAL PRACTICE ACROSS THE NATION

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Background: Gynecologic cancers remain a major cause of cancer-related mortality in women, and outcomes for some entities, such as uterine and cervical cancer, have not improved over the last few decades despite potential therapeutic advances(1). Genomic-guided therapy using comprehensive genomic profiling (CGP) is slowly finding its place in gynecologic oncology, with emerging real-world data from positive results of testing to molecular tumor boards showing improved outcomes in selected patients(2,3). Building on these experiences, Croatia's nationwide CGP program and centralized Molecular Tumor Board provide a unique setting to generate real-world evidence on the feasibility and clinical impact of CGP-guided treatment. We aimed to present real-world national outcomes of CGP-guided therapy in women with advanced gynecologic cancers.

Methods: The study was retrospective, conducted at the country level among all gynecologic patients who were administered with CGP-guided therapy from January 1, 2020, to December 31, 2025. The analysis was performed in an accredited laboratory (Foundation Medicine Inc., Cambridge, MA, USA, or Personalized Medicine Department, UHC Zagreb, Croatia). Patients were administered with CGP-guided therapy following recommendations from the Multidisciplinary Tumor Board (MTB). Progression-free survival (PFS) was measured from the initiation of either CGP-guided therapy to the occurrence of disease progression, death from any cause, or the most recent follow-up (with data censored accordingly), whichever event transpired first.

Results: A total of 89 patients received CGP-guided therapy. Median age was 62 years (IQR 52–67), with 35% presenting with initial stage IV disease. Ovarian cancer was most common (40 patients, 45%), followed by uterine (26, 29%) and cervical cancer (23, 26%). Clinically relevant alterations appeared in 82% of CGP reports; additionally, high tumor mutational burden occurred in 29%, microsatellite instability in 15%, and loss of heterozygosity >16% in 36% patients.

Median number of previous lines was 1 (IQR 1-3), with 18% of women who received at least 3 lines of therapy. PARP inhibitors were used most frequently (47 patients, 53%), followed by immune checkpoint inhibitors (36, 40%), everolimus (3, 3%), alpelisib (2, 2%), and trastuzumab-deruxtecan (1, 1%).

Median PFS was 5.9 months (IQR 3–12.2), with 12% achieving >12 months and 5.6% >18 months. As of February 25, 2026, 40.4% remained progression-free on therapy. All treatments were well tolerated, with most adverse events limited to grade 1–2 nausea or fatigue.

Conclusion: Our results have shown that CGP-guided therapy is feasible in everyday gynecologic oncology practice and can deliver clinically meaningful benefit even in a heavily pretreated population. Despite prior lines of therapy, results of a subset of patients experiencing prolonged disease control, while toxicity remained manageable, support the incorporation of precision oncology into routine care for women with advanced gynecologic cancers.

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P46 – SINGLE-CENTER EXPERIENCE WITH NEOADJUVANT CHEMOIMMUNOTHERAPY IN RESECTABLE NSCLC

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Background: Neoadjuvant chemoimmunotherapy has become a standard approach in resectable non-small cell lung cancer (NSCLC), resulting in higher rates of pathological response and survival in clinical trials. However, real-world evidence remains limited.

Methods: We performed a retrospective single-center analysis of patients with resectable NSCLC treated with neoadjuvant chemoimmunotherapy at the Department of Pulmonary Diseases, University Hospital Centre Zagreb, evaluating pathological response and nodal downstaging.

Results: Between March 2023 and December 2025, 59 patients with resectable NSCLC received two to four cycles of neoadjuvant chemoimmunotherapy and were assessed for surgery. The median age was 66 years (range 59–70), and 54% were male. The objective response rate according to RECIST 1.1 was 97%. Adequate staging, including PET-CT and endobronchial ultrasound, was done in the vast majority of patients. Most patients had stage III disease (IIIA 53%; IIIB 24%). Histology included adenocarcinoma in 64% and squamous cell carcinoma in 29%. Nine patients (15%) did not proceed to surgery despite surgical evaluation. Reasons included patient choice (33%), disease progression (33%), and comorbidity-related inoperability (33%). Among operated patients, the median interval to surgery was 9 weeks (range 7–12). Pathological evaluation of the primary tumor revealed complete pathological response (pCR) in 38% of patients and major pathological response (MPR) in an additional 16%. A complete pathological response

in both the primary tumor and lymph nodes was achieved in 30% of patients. Among those with baseline nodal involvement, 58% demonstrated nodal downstaging, with 46% achiving complete nodal clearance (ypN0). In the cN2 subgroup, 38% were downstaged to ypN0. Grade 3 treatment-related adverse events occurred in 7% (4/59) of patients.

Conclusions: Our data confirm the trial experience of high pCR rates after neoadjuvant chemoimmunotherapy. The proportion of patients not proceeding to surgery was consistent with rates reported in clinical trials, further supporting the feasibility of this approach in routine clinical practice. Additional real-world studies are needed to better define the impact of perioperative chemoimmunotherapy on long-term outcomes.

Keywords: NSCLC, neoadjuvant, single-centar, chemoimmunotherapy

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P47 – SODIUM HYALURONAN BUTYRATE FOR THE PREVENTION OF RADIATION PROCTITIS: A RANDOMIZED, PLACEBO-CONTROLLED STUDY

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Radiation proctitis is a frequent adverse effect in patients undergoing pelvic radiotherapy, leading up to 20% of patients to temporarily discontinue treatment until symptoms resolve. Preventive strategies and therapeutic options for radiation proctitis remain limited(1,2,5). We conducted a prospective study with the primary objective to evaluate whether sodium hyaluronan butyrate can prevent the onset of radiation proctitis in patients with prostate, bladder, cervical, or endometrial cancer receiving radiotherapy, compared to placebo. Secondary objectives included assessing whether sodium hyaluronan butyrate reduces the need for blood transfusions, parenteral iron administration, and hospitalizations. Proctosal, administered as a cream or microenema, contains sodium hyaluronan butyrate, which supports rectal mucosal restoration and integrity(3,6,8,9), and dimethicone, which forms a mucoadhesive gel barrier to protect rectal tissue(7).

This investigation was a prospective, double-blind, placebo-controlled study(3,4,6) with participants randomized 1:1. Group 1 received sodium hyaluronan butyrate microenemas, 8 g in the evening, beginning one week prior to radiotherapy, continuing throughout radiotherapy, and for one week following

completion. Group 2 received placebo microenemas with the same administration schedule. Inclusion criteria were: age 18 years or older, diagnosis of a localized pelvic tumor, and planned radical radiotherapy. Exclusion criteria included: other active bowel or anorectal diseases, prior colon or rectal surgery, topical hemorrhoid preparations within four weeks, metastatic disease or history of another primary tumor, previous radiotherapy or chemotherapy, and coagulopathies.

Follow-up assessments were conducted at baseline, week 3, end of radiotherapy (week 6), and six months post-radiotherapy. Assessments included blood count, serum iron, ferritin, fecal calprotectin, and a questionnaire evaluating quality of life and symptoms(6,8,9). Rectoscopy was undertaken at baseline, end of radiotherapy, and six months, with evaluation using the Vienna Rectoscopy Score (VRS)(3,6,8,9).

The primary endpoint was prevention of radiation proctitis, assessed by endoscopy, biopsies, and histopathology. Secondary endpoints included fecal calprotectin levels, frequency of transfusions, parenteral iron administration, and hospitalizations due to bleeding.

At the interim analysis with a six-month follow-up, 120 participants were enrolled. There were 10 dropouts, 9 cases of noncompliance, and 1 cerebrovascular insult, resulting in 100 participants analyzed (60 Proctosal and 40 placebo).μg

Fecal calprotectin (mean ± SD) in the Proctosal group was 97 ± 4 mcg/g at baseline, 82 ± 1.2 mcg/g after radiotherapy, and 25.8 ± 4.5 mcg/g at six months. In the placebo group, values were 101 ± 1 mcg/g, 131 ± 4 mcg/g, and 160 ± 7 mcg/g. Statistical significance was not reached at baseline (NS), but differences were significant after radiotherapy ($p = 0.05$) and at six months ($p = 0.01$).

VRS for the Proctosal group was 0 at baseline, 1 ± 0.5 after radiotherapy, and 1.1 ± 0.2 at six months. For placebo, scores were 0, 3 ± 1, and 5 ± 1.1. Statistical significance was observed at six months ($p = 0.01$)(3,6,8,9).

At interim analysis with six-month follow-up, the original Proctosal preparation demonstrated statistically significant improvements in laboratory parameters, the inflammatory marker calprotectin, RTOG score, and endoscopic findings.

Keywords: radiation proctitis; sodium hyaluronan butyrate; prevention; Vienna Rectoscopy Score (VRS);

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P48 – TARGETED THERAPY FOR PATIENTS WITH ADVANCED ALK-POSITIVE NON-SMALL CELL LUNG CANCER – SINGLE CENTER EXPERIENCE

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Background: Targeted therapy for patients with non-small cell lung cancer (NSCLC) and targetable genetic alterations has significantly improved treatment outcomes and the quality of life for these patients.

In this work we present the real-world results of targeted therapy with ALK TKIs in patients with advanced ALK-positive NSCLC at the Department of Oncology and the Clinic for Pulmonary Diseases of the University Hospital Split.

Methods: This retrospective analysis included all patients with advanced ALK-positive NSCLC who initiated targeted therapy at the University Hospital Split between November 2015, when the first targeted therapy for these patients was approved in the Republic of Croatia, and the end of December 2024.

Results: Of the 30 patients included, 16 were female and 14 were male. The median age of the patients was 62 years. The median follow-up period was 1052 days. In the first-line setting, 21 patients were treated with alectinib, eight patients with crizotinib, and one patient with lorlatinib. The choice of first-line treatment was primarily determined by the date of diagnosis of advanced disease and the available therapeutic options at that time. All patients treated with crizotinib had disseminated disease at the start of treatment, whereas among those treated with alectinib, four patients (19%) had locally advanced inoperable disease. Five patients (63%) initially treated with crizotinib had brain metastases, compared to only three patients (14%) initially treated with alectinib, representing a statistically significant difference (P=0.0075). In both groups, the majority of patients had not received prior chemotherapy for advanced disease before initiating targeted therapy (alectinib 81%, crizotinib 75%). The response rate to first-line treatment with alectinib was slightly higher than in those treated with crizotinib (76% vs. 63%). The median PFS was 1387 days (95% CI: 412–NR) in the first-line alectinib group, compared to 207 days (95% CI: 108–412) in the crizotinib group. Patients receiving first-line crizotinib had a more than threefold higher risk of disease progression or death compared to those initially treated with alectinib, even after adjustment for the differing stages of disease progression between the two groups (HR 3.12; 95% CI 1.04–9.35). The median overall survival was 2442 days; it was not reached for patients treated with first-line alectinib, while for those treated with crizotinib, it was 854 days.

Toxicity related to targeted therapy was observed in 29 patients (97%), predominantly of grade 1. Permanent discontinuation due to toxicity occurred in two patients (7%). Dose reduction due to toxicity was recorded in 25% of patients on crizotinib and 14% of those on alectinib.

Conclusion: The availability of modern therapy and the consequent choice of first-line treatment have the greatest impact on overall treatment outcomes. The more modest treatment outcomes with crizotinib, compared to the pivotal registration trial, are likely due to the more advanced disease stage of our patients at treatment initiation. The excellent treatment outcomes with alectinib have confirmed the value

of this therapeutic option in routine clinical practice. To draw firm conclusions, a larger sample size and longer follow-up are needed.

Keywords: targeted therapy, ALK rearrangement, non-small cell lung cancer, treatment outcomes

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P49 – TEN-YEAR FOLLOW-UP OF LUNG CANCER PATIENTS DIAGNOSED AT A TERTIARY CENTER IN CROATIA: A RETROSPECTIVE COHORT STUDY

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Background: Croatia has one of the highest incidences of lung cancer in Europe, with lung cancer remaining the leading cause of cancer-related mortality. Despite this, there is a substantial lack of long-term follow-up data regarding patient characteristics and subgroup-specific outcomes. In this study, we present a 10-year follow-up analysis of more than 1,300 patients.

Methods: We conducted a retrospective cohort study including all patients diagnosed with lung cancer between January 2012 and December 2013 at the University Hospital Center Zagreb, Department of Respiratory Diseases, Jordanovac.

Results: Adenocarcinoma was the most frequent histological subtype (45.9%), followed by squamous-cell carcinoma (27.4%) and small-cell lung cancer (13%). At diagnosis, 47.5% of patients had stage IV disease, 16.3% stage IIIB, and 20.8% stage IIIA, while only 10% presented with early-stage disease (I–II). Surgical treatment was performed in 58.2% of patients with stage I–II disease and was associated with significantly longer survival (median overall survival (mOS) 31 vs. 7 months). In stage IIIA disease, 20.4% underwent surgery, most combined with perioperative chemotherapy, 38.6% received chemoradiotherapy, and 37.8% chemotherapy alone, with an mOS of 12 months. Patients with stage IIIB and IV disease had poor outcomes, with mOS of 8 and 5 months, respectively. In NSCLC, paclitaxel–carboplatin and platinum–etoposide were the most common first-line regimens; 46.9% received second-line treatment, mainly pemetrexed or docetaxel, while 22% received third-line therapy, predominantly erlotinib. Small-cell lung cancer was primarily treated with platinum–etoposide doublets, with limited use of second– and third-line chemotherapy. Survival differed by histology, performance status, and stage, with better out-

comes in surgically treated patients, females, non-smokers, and those diagnosed at earlier TNM stages. The 5– and 10– year survival rates were 7.1 and 3.4%, respectively.

Conclusion: Our retrospective analysis highlights several challenges that hindered adequate treatment of lung cancer patients in Croatia a decade ago. Therapy options limited to platinum-based doublet chemotherapy and the scarce use of radiotherapy in curative-intent settings, with only a small proportion of patients diagnosed and surgically treated at an early stage, were the main factors contributing to the poor outcomes observed at that time. These findings provide an important baseline for the era preceding targeted therapy and immunotherapy, against which the effectiveness of modern lung cancer treatments can be more accurately evaluated.

Keywords: NSCLC; SCLC; long term survival; treatment outcomes

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P50 – THE DIFFERENCE IN KI67 BEFORE AND AFTER NEOADJUVANT CHEMOTHERAPY IN BREAST CANCER

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Introduction: Breast cancer is the most common type of cancer in women. When discovered, if in the local stage, it can be divided into two groups based on tumor size. If it's smaller than 2cm, preferred therapy is surgical intervention, but if it's bigger than 2cm, neoadjuvant oncological treatment is preferred. Ki67 is a nuclear protein noticed in proliferating cells. Ki67 is also a prognostic factor, bigger reduction in Ki67 after neoadjuvant chemotherapy can indicate a better prognosis. The main goal of the neoadjuvant chemotherapy is to make the tumor accessible for surgery, but also, at the same time, to make that surgery conservative, eg, quadrantectomy instead of mastectomy. This type of treatment can also provide assessment of treatment response(1–4).

Methods: In this retrospective study, we analyzed data from 157 patients who went through neoadjuvant chemotherapy at University Hospital Center Osijek between 2022 and 2025. Parameters that were recorded were immunohistochemistry results from core biopsy and from the operation sample, and patients were divided into molecular subgroups.

Results: In the study sample of 157 patients, the most common (43.9%) molecular type was the luminal B/HER2 negative group. Regarding the Ki67 in the core biopsy, 75.2% of patients had Ki67 >30%, while after the operation, most of the patients (45.2%) had Ki67<5%. There was a statistically significant lowering of the Ki67 from biopsy to operation (Wilcox test, *P*<0,001). Median of Ki67 in biopsy was 50%, while in operation, the median of Ki67 was only 5% (difference estimation is -35). The most significant reduction of Ki67 was noted in the triple-negative breast cancer and HER2-positive subgroup (Wilcox test, *P*<0,001).

Conclusion: There was a statistically significant reduction of Ki67 before and after neoadjuvant chemotherapy, especially in the triple-negative breast cancer and HER2-positive subgroups. This could be because of the complete pathological response in these groups. In a study by Matsubara et al. A reduction of Ki67 was observed in all groups, 70% of patients had a decrease, but their median of Ki67 pre-chemo was 20%, which is lower than in this study. Toli et al. had more similar findings to ours; Ki67 in core biopsy was 40%, while after chemotherapy, Ki67 was 12%(5–7).

Keywords: breast cancer, Ki67, neoadjuvant chemotherapy

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P51 – THE ROLE OF THE LUNG IMMUNE PROGNOSTIC INDEX (LIPI) IN REAL-WORLD PATIENTS WITH EXTENSIVE-STAGE SMALL-CELL LUNG CANCER

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Introduction: The Lung Immune Prognostic Index (LIPI), derived from lactate dehydrogenase (LDH) levels and the neutrophil-to-lymphocyte ratio, is a validated prognostic biomarker in lung cancer. The LIPI score stratifies patients into three prognostic groups: good, intermediate, and poor – based on baseline LDH levels above the upper limit of normal and a neutrophil-to-lymphocyte ratio greater than three1. Although the LIPI score was initially developed to predict response to immunotherapy in non-small-cell lung cancer (NSCLC), its prognostic role has also been investigated in patients with ES-SCLC treated with immunotherapy or chemotherapy2,3. Its role in patients with ES-SCLC in real-world clinical practice remains insufficiently characterized.

Patient and Methods: We performed a retrospective analysis of patients diagnosed with ES-SCLC and treated at University Clinical Hospital Mostar (Bosnia and Herzegovina) between 2013 and 2023. Patients were stratified by LIPI score into good, intermediate, poor, and unknown categories. Overall survival (OS) and progression-free survival (PFS) were analyzed according to the LIPI score. Associations between LIPI score, ECOG performance status, and administration of first-line platinum-based chemotherapy for ES-SCLC were also evaluated.

Results: Ninety-four patients were included. The majority were men (72%), with a median age of 64 years. Most patients were current (87%) or former smokers (13%). Poor LIPI was associated with impaired performance status, with only 32% of patients having ECOG 0-1 compared with 82% in the good LIPI group, while ECOG ≥2 was observed in 58% and 18% of patients, respectively. The likelihood of receiving systemic chemotherapy decreased with unfavorable LIPI: 100% of patients with good LIPI, 94% with intermediate LIPI, and 74% with poor LIPI received first-line chemotherapy for ES-SCLC. Median OS differed markedly across LIPI groups, demonstrating a clear prognostic gradient: eight months in LIPI good, seven months in LIPI intermediate, and only three months in LIPI poor patients. Similarly, median PFS was seven months, six months, and two months in the good, intermediate, and poor LIPI groups, respectively. Brain and liver metastases were more frequently observed in patients with poor LIPI compared with those with good or intermediate LIPI scores.

Conclusion: In this real-world cohort of patients with ES-SCLC, the LIPI score demonstrated a strong prognostic value for both OS and PFS. Higher LIPI scores were associated with worse performance status, reduced likelihood of receiving systemic chemotherapy, and inferior survival outcomes. These findings support the clinical utility of LIPI as a simple and informative prognostic biomarker in ES-SCLC.

Keywords: small-cell lung cancer; lung immune prognostic index, treatment, outcome

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P52 – DURATION OF CDK4/6 INHIBITOR THERAPY IN PATIENTS WITH METASTATIC BREAST CANCER AND SUBSEQUENT TREATMENT OPTIONS

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Introduction: Cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitors have significantly improved the treatment of hormone receptor-positive, HER2-negative metastatic breast cancer. According to current guidelines, they represent the standard first-line therapy in combination with endocrine therapy, except in cases of visceral crisis. Their benefit is reflected in prolonged progression-free survival (PFS), effective disease control, and a manageable toxicity profile, primarily including neutropenia, gastrointestinal symptoms, and fatigue. In clinical practice, Palbociclib, Ribociclib, and Abemaciclib are used. Their mechanism of action involves selective inhibition of cyclin-dependent kinases 4 and 6, thereby inducing cell cycle arrest (from the G1 to S phase) and slowing tumor growth. They are usually administered in combination with endocrine therapy, such as aromatase inhibitors (AIs) or selective estrogen receptor degraders (SERDs).

Aim: The aim of this study was to determine progression-free survival in patients treated with CDK4/6 inhibitors, to assess whether differences in PFS exist among individual CDK4/6 inhibitors, and to analyze therapeutic options applied after disease progression.

Methods: In this cross-sectional retrospective study, we analyzed data from patients who received CDK4/6 inhibitors for metastatic breast cancer at University Hospital Center Osijek between 2018 and the end of 2025. Variables of interest included progression-free survival, comparison of CDK4/6 inhibitors, types of therapy after progression, age, and sex.

Results: During the specified period, 260 patients received CDK4/6 inhibitor therapy for metastatic breast cancer. Of the total number, 98% were female, with a median age of 64 years at the diagnosis of metastatic disease. Ribociclib was administered to 50% of patients, Palbociclib to 29%, and Abemaciclib to 21%. In combination with CDK4/6 inhibitors, 55% of patients received a SERD and 45% received an AI. The mean progression-free survival was 17.6 months (median 13 months). After disease progression, most patients received capecitabine, followed by paclitaxel. Subsequent therapies, in decreasing order of fre-

quency, included fulvestrant, alpelisib, and "rechallenge" with palbociclib or abemaciclib (in combination with fulvestrant).

Discussion: The shorter median PFS compared to the MONARCH, PALOMA, and MONALEESA trials may be explained by the real-world population (older age, comorbidities, higher tumor burden, heterogeneity of treatment lines) and by the fact that 29% of patients were still receiving therapy at the time of analysis, which may have led to underestimation of the true median. No significant differences were observed among CDK4/6 inhibitors (14 months for ribociclib and palbociclib, and 13 months for abemaciclib). The higher use of chemotherapy after progression reflects the 2018–2021 period, prior to the broader availability of molecularly guided therapy.

Conclusion: CDK4/6 inhibitors have significantly improved the treatment of hormone receptor-positive, HER2-negative metastatic breast cancer. Upon disease progression, endocrine therapy combined with targeted agents is preferred, including alpelisib in cases of PIK3CA mutation, capivasertib (an AKT inhibitor) with fulvestrant in patients with PI3K/AKT/PTEN pathway alterations, as well as PARP inhibitors in those with germline BRCA mutations, while chemotherapy is reserved for hormone-refractory or clinically aggressive disease.

Keywords: breast carcinoma, ribociclib, palbociclib, abemaciclib

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P53 – TREATMENT OF PATIENTS WITH LOCALLY ADVANCED AND/OR METASTATIC CUTANEOUS SQUAMOUS CELL CARCINOMA (CSCC) WITH CEMIPLIMAB AS FIRST-LINE SYSTEMIC THERAPY – INITIAL EXPERIENCES FROM THE DEPARTMENT OF ONCOLOGY AND NUCLEAR MEDICINE AT SESTRE MILOSRDNICE UNIVERSITY HOSPITAL CENTER

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Introduction: Cemiplimab, a PD-1 immune checkpoint inhibitor, is the first-line systemic treatment for locally advanced and metastatic cutaneous squamous cell carcinoma (CSCC). Given the high tumor mutational burden and immunogenicity of CSCC, PD-1 blockade has demonstrated durable responses in clinical studies. The aim of this retrospective study was to present initial results of cemiplimab therapy in a real-world cohort of patients with CSCC treated at a single university hospital center.

Patients and methods: This retrospective analysis includes data from patients with locally advanced and metastatic CSCC who received cemiplimab. The data collected included patient characteristics (age, gender, ECOG performance status, comorbidities), primary tumor site, site of disease dissemination, objective response rate (ORR), progression-free survival (PFS), overall survival (OS) and safety.

Results: Between February 2021 and February 2025, 21 patients started treatment. 62% of them were male. The median patients' age was 70 years (range 43-99) and 86% had an ECOG PS of 0-1. Fifteen patients (71%) had comorbidities, most commonly arterial hypertension and diabetes, and 4 patients had a documented history of another malignancy in addition to CSCC. Nine patients (43%) presented with metastatic disease, with regional lymph nodes being the most common site of involvement. The median number of treatment cycles was 9 (range 1-31). Five patients achieved a partial response (PR) and 4 patients achieved a complete response (CR), resulting in an ORR of 42.9%. With a median follow-up of 13.1 months, 8 of 21 patients (38%) experienced disease progression or death. Median PFS was not reached. The estimated 12-month PFS rate was 53.3%. Median OS was not reached at the time of analysis. Immune-related adverse events (irAEs) were observed in 5 patients (24%). Four patients experienced grade 1–2 events, most commonly hepatotoxicity and hypothyroidism. 3 of these cases required no specific treatment, while 1 patient was treated with oral corticosteroids. One patient developed a grade 4 skin toxicity requiring hospitalization and treatment with intravenous corticosteroids. Treatment interruption due to toxicity occurred in 3 patients, with permanent discontinuation in 1 patient. No treatment-related deaths were observed.

Conclusion: Cemiplimab demonstrated meaningful effectiveness in patients with locally advanced and metastatic CSCC in this real-world cohort, with a manageable safety profile. These findings are consistent with previously reported clinical trial outcomes. Treatment proved feasible even in an elderly and comorbidity-burdened population.

Keywords: cemiplimab; cutaneous squamous cell carcinoma; PD-1 inhibitor; adverse events

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P54 – TREATMENT OUTCOMES OF PATIENTS WITH EXTENSIVE-STAGE SMALL CELL LUNG CANCER (ES-SCLC) TREATED WITH ATEZOLIZUMAB – A SINGLE CENTER EXPERIENCE

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Introduction: Small cell lung cancer (SCLC) is an aggressive, high-grade neuroendocrine carcinoma that accounts for approximately 10–15% of all lung cancers. It is characterized by rapid tumor growth, early metastatic spread, and initial sensitivity to chemotherapy and radiotherapy. At diagnosis, most patients have extensive-stage disease, commonly involving the brain, liver, bone, or adrenal glands. Extensive-stage disease is managed primarily with systemic therapy, including platinum–etoposide combined with immune checkpoint inhibitors such as atezolizumab or durvalumab. Although response rates are initially high, relapse is common, and prognosis remains poor, with a 5-year survival rate below 10% overall. The aim of the study was to analyse clinical outcomes (PFS, OS) of patients with extensive-stage SCLC treated with atezolizumab at University Clinical Hospital Osijek (University Hospital Center Osijek).

Methods: We retrospectively analysed medical data of patients with ES-SCLC treated with atezolizumab in University Hospital Center Osijek from September 2024 till January 2026. From medical records data were collected that included patients age, sex, ECOG status, smoking status, results of first evaluation, date of progression or death and appearance of immune-related adverse events (irAEs). Progression-free survival (PFS) and overall survival (OS) were calculated using the Kaplan Meier method.

Results: In the study data of total 40 patients were analysed. Median follow up time was 14,0 months. Majority of patients were men (75,0%) and were ECOG PS 0 (65,0%). 50,0% of the patients were smokers and 25,0% were former smokers. Results of first evaluation showed partial response in 21 (52,5%) patient, stable disease in 13 (32,5%) of the patents and 6 (15,0%) patients had disease progression. Median PFS was 7,2 months and median OS was 12,1 months. There were two cases of irAEs. One case of pneumonitis grade 3 and one case of colitis grade 3.

Conclusion: The results of our study show consistent survival results with those of the clinical study. Real-world data confirm the efficacy and safety of atezolizumab in the first line treatment of ES-SCLC.

Keywords: small cell lung cancer (SCLC), immunotherapy, atezolizumab

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P55 – WHAT DO WE LOSE WHEN DIBH FAILS? A SIX-MONTH RETROSPECTIVE ANALYSIS OF HEART, LAD AND LEFT LUNG DOSES IN LEFT-SIDED BREAST RADIOTHERAPY

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Background: Breast cancer is the most common cancer among women and the leading cause of cancer-related deaths in females(1). While radiation therapy enhances local control of the disease and improves survival rates, there are concerns about cardiac toxicities that may reduce survival benefits because of the higher risk of cardiac mortality(2). Deep inspiration breath hold (DIBH) is a standard cardiac-sparing technique in left-sided breast radiotherapy. By increasing thoracic volume and displacing the heart away from the irradiation field, DIBH significantly reduces radiation exposure to the heart and the left anterior descending coronary artery (LAD)(3,4). Darby et al demonstrated that for every 1 Gy increase in mean heart dose, the incidence of major coronary artery events rises by 7.4% (5). However, not all patients can reproducibly perform DIBH, necessitating treatment in free-breathing (FB). This study evaluates the dosimetric impact of DIBH failure over a 6-month follow-up period at the Tumor Clinic of the Clinical Hospital Center Rijeka.

Methods: A total of 106 breast cancer patients were indicated for adjuvant radiotherapy using the DIBH radiation technique and respiratory gating, with either the Varian Respiratory Gating for Scanners (RGSC) system or a surface-guided radiotherapy (SGRT) system. Among these, eight patients (7.5%) were unable to adequately perform or maintain DIBH throughout the treatment course. For these patients, treatment plans were adapted using a free-breathing (FB) approach, including recontouring of target volumes and organs at risk, so as a replanning. A paired dosimetric comparison between DIBH and FB plans was performed. Evaluated parameters included mean heart dose (Dmean), LAD mean dose (LAD Dmean), LAD maximum dose (LAD Dmax), and left lung mean dose. Statistical analysis was conducted using the Wilcoxon signed-rank test (two-sided, $\alpha = 0.05$).

Results: The median age of the cohort was 69.9 years. Compared with DIBH, FB plans result in higher organ-at-risk doses. The median difference in mean heart dose was 41.32 cGy (range from -13.9 to 204.0 cGy; T=3.0, p=0.039). For LAD Dmean, the median difference was 233.5 cGy (range 7.9 to 1359.8 cGy; T=0.0, p= 0.018), and for LAD Dmax, 1931.6 cGy (range 0.0-2755.3 cGy; T=0.0; p= 0.0180). The results indicate that DIBH in this cohort clearly and statistically significantly reduces cardiac and LAD exposure compared with FB. Left lung mean dose differences did not reach statistical significance within this subgroup.

Conclusions: Although the proportion of patients unable to perform DIBH was relatively small (7.5%), the dosimetric consequences are clinically relevant. Failure of DIBH primarily compromises cardiac and coronary artery protection, particularly affecting LAD exposure. Given the established linear relationship between mean heart dose and the long-term risk of ischemic heart disease, these findings underscore the importance of using DIBH to maintain overall health.

Keywords: deep inspiration breath hold (DIBH); free breathing (FB); left-sided breast cancer; radiotherapy; cardiac toxicity; dosimetric analysis

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P56 – WHOLE BRAIN RADIATION WITH HIPPOCAMPAL AVOIDANCE PLUS MEMANTINE: INITIAL EXPERIENCE OF THE TUMOR CLINIC AT CLINICAL HOSPITAL CENTRE RIJEKA

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Abstract: In adults, whole-brain radiation therapy (WBRT) is administered in cases of multiple brain metastases or prophylactically for small cell lung cancer, with the aim of prolonging survival. One of the side effects of WBRT is neurocognitive toxicity. Early toxicity occurs within four months after irradiation and primarily manifests as verbal neurocognitive impairment and short-term memory difficulties, with preliminary data suggesting possible late recovery. Late toxicity occurs several months to years after WBRT and is associated with the development of severe dementia(1). Studies have shown that 11% of long-term survivors (over 12 months) treated with WBRT develop severe dementia(2). Recent clinical studies have shown that radiation-induced damage to neural progenitor cells located in the subgranular zone of the hippocampus plays a significant role in neurocognitive decline after cranial irradiation. The main role of the hippocampus is consolidation and retrieval of information, as well as learning(1,2). Given the above, studies, such as prospective study RTOG 0933, have focused on investigating the implementation of hippocampal avoidance whole-brain radiation therapy (HA-WBRT). In these study, intensity-modulated radiotherapy (IMRT) was used, 30 Gy in 10 fractions, sparing the hippocampus with a 5-mm margin, while maintaining acceptable target coverage and homogeneity. Dosimetric recommendations for HA-WBRT (Dmedian < 7.8 Gy, D100% <10 Gy, and Dmax <15.3 Gy) were proposed for patients with brain

metastases and an expected survival greater than six months. The study reported that only 7% of patients experienced memory decline compared to 30% of patients in the historical cohort (p = 0.0003) four months after irradiation (3). Other studies investigated the introduction of memantine to HA-WBRT, a neuroprotective drug. Memantine was administered: 5 mg in the morning during week 1, 5 mg twice daily during week 2, 10 mg in the morning and 5 mg in the evening during week 3, and 10 mg twice daily during weeks 4–24. The study showed that the risk of cognitive failure was significantly lower after HA-WBRT plus memantine compared with WBRT plus memantine (adjusted hazard ratio 0.74; 95% CI 0.58–0.95; P = .02), with no difference in overall survival, intracranial progression-free survival, or toxicity(4,5).

Methods: Between September 2025 and January 2026, we treated two patients using the HAWBRT method combined with memantine. The patients were treated with the IMRT technique, with a total dose of 30 Gy in 10 fractions, along with the standard dose of memantine.

Results: The patients tolerated therapy well. Coverage of the target volume was achieved (PTV V95% = 98.88%; V100% = 91.26%) with an acceptable maximum dose (Dmax 109.76%). The maximum doses to the hippocampus were 15.17 Gy left and 15.39 Gy right, while the D100% values were 8.45 Gy and 8.32 Gy. Both patients underwent follow-up evaluation, which demonstrated excellent local disease control, being without acute clinical signs of neurological deterioration.

Conclusion: Whole-brain radiotherapy with hippocampal avoidance plus memantine represents an excellent treatment approach with the aim of preserving cognitive function, without compromising disease control.

Keywords: hippocampal avoidance radiotherapy, memantin, brain metastases, modern oncology

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