

Publikujeme v zahraničí

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GENITOURINÁRNE MALIGNITY

Palacka P, Slopovsky J, Obertova J, Chovanec M, Rejlekova K, Sycova-Mila Z, Kollarik B, Mardiak J, Mego M.

Survival prediction by baseline systemic immune-inflammation index and its changes during first-line platinum-based treatment in a Caucasian population of patients with metastatic urothelial carcinoma

Anticancer Res 2021; 41(11):5749-5759.

Background: Systemic immune-inflammation index (SII) predicts survival in patients with various malignancies. This study explores the prognostic value of SII in metastatic urothelial carcinoma (MUC) subjects.

Methods: We evaluated 181 consecutive MUC (148 bladder, 27 upper tract) patients (135 men) treated with first-line platinum-based therapy. Karnofsky performance status <80% and visceral metastasis were present in 18.2% and 46.4%, respectively. SII was based on platelet x neutrophil/lymphocyte counts. Study population was dichotomized by median into high SII and low SII groups before the initiation of chemotherapy (median 1326) and at week 6 (median 705). Progression-free survival (PFS) and overall survival (OS) were estimated by the Kaplan-Meier method and compared with log-rank test.

Results: At median follow-up of 9.6 months (range 1.7-191.1 months), 174 patients (96.1%) experienced disease progression and 173 (95.6%) died. Subjects with low SII at baseline and at week 6 had significantly better PFS (HR 0.58; $P = 0.0002$ and HR 0.55; $P < 0.0001$) and OS (HR 0.54; $P < 0.0001$ and HR 0.54; $P < 0.0001$) compared to patients with high SII. Independent prognostic value of SII was confirmed in a multivariate analysis. Patients with low SII at baseline and at week 6 had significantly better PFS and OS compared to patients with high SII at both timepoints ($P < 0.0001$).

Conclusion: High SII before chemotherapy that persists at week 6 negatively affects survival. SII at baseline can be used in stratification of patients within clinical trials and in clinical practice.

Mego M, Rejlekova K, Svetlovska D, Miskovska V, Gillis AJM, De Angelis V, Kalavska K, Obertova J, Palacka P, Reckova M, Sycova-Mila Z, Pindak D, Chovanec M, Looijenga LHJ, Mardiak J. **Paclitaxel, Ifosfamide, and Cisplatin in Patients with Poor-prognosis Disseminated Nonseminomatous Germ Cell Tumors with Unfavorable Serum Tumor Marker Decline After First Cycle of Chemotherapy. The GCT-SK-003 Phase II Trial.**

Eur Urol Open Sci. 2021 Sep 22;33:19-27.

Background: Germ cell tumors represent highly curable disease even in metastatic stage. However, poor-risk patients with an unfavorable serum tumor marker (STM) decline after the first cycle of chemotherapy represent a subgroup with dismal prognosis, with approximately 50% cure rate using bleomycin, etoposide, and cisplatin (BEP).

Objective: The aim of this study was to determine the efficacy and safety of paclitaxel, ifosfamide, and cisplatin (TIP) in this patient population.

Design setting and participants: This was an open-labeled, nonrandomized, single-center phase II trial to study the efficacy and toxicity of TIP in the first-line treatment of germ cell tumor patients with an unfavorable decline of STMs. Nineteen patients with a poor prognosis according to the International Germ Cell Cancer Collaboration Group classification and an unfavorable STM decline after the first cycle of chemotherapy were included in this phase II study (NCT02414685). The treatment regimen consisted of paclitaxel 250 mg/m² on day 1, ifosfamide 1200 mg/m² on days 1-5, and cisplatin 20 mg/m² on days 1-5, totally for four cycles.

Outcome measurements and statistical analysis: The primary endpoint was complete response (CR) rate. An optimal Simon two-stage design was used with a type I error of 5% and study power of 80%. If fewer than six CRs to study therapy have been observed among the first 19 patients, the study was to be terminated.

Results and limitations: A CR was achieved in four (21.1%) patients; therefore, the study was terminated in the first stage. A favorable response rate (CR or partial remission with negative tumor markers) was observed in 14 (78.9%) patients. At a median follow-up period of 35.2 mo (range, 5.6-62.1 mo), ten (52.6%) patients experienced disease progression and eight patients (42.1%) died. The 2-yr progression-free and overall survival was 41.2% (95% confidence interval [CI] 16.8-65.7) and 72.7% (95% CI 48.9-96.4), respectively. TIP was well tolerated, and no unexpected toxicity was observed. No informative biomarkers, including miR-371a-3p was identified.

Conclusions: Treatment modification from the BEP to the TIP regimen in patients with an unfavorable STM decline after the first cycle of chemotherapy was not associated with improved outcome, and four cycles of BEP remain the standard treatment option in this patient population.

Borszékóvá Pulzová L, Roška J, Kalman M, Kliment J, Slávik P, Smolková B, Goffa E, Jurkovičová D, Kulcsár L, Lešková K, Bujdák P, Mego M, Bhide MR, Plank L, Chovanec M.

Screening for the Key Proteins Associated with Rete Testis Invasion in Clinical Stage I Seminoma via Label-Free Quantitative Mass Spectrometry Cancers (Basel). 2021 Nov 8;13(21):5573.

Rete testis invasion (RTI) is an unfavourable prognostic factor for the risk of relapse in clinical stage I (CS I) seminoma patients. Notably, no evidence of difference in the proteome of RTI-

positive vs. -negative CS I seminomas has been reported yet. Here, a quantitative proteomic approach was used to investigate RTI-associated proteins. 64 proteins were differentially expressed in RTI-positive compared to -negative CS I seminomas. Of them, 14-3-3 γ , ezrin, filamin A, Parkinsonism-associated deglycase 7 (PARK7), vimentin and vinculin, were validated in CS I seminoma patient cohort. As shown by multivariate analysis controlling for clinical confounders, PARK7 and filamin A expression lowered the risk of RTI, while 14-3-3 γ expression increased it. Therefore, we suggest that in real clinical biopsy specimens, the expression level of these proteins may reflect prognosis in CS I seminoma patients.

Lamphar H, Kocifaj M, Limón-Romero J, Paredes-Tavares J, Chakameh SD, **Mego M**, Prado NJ, Baez-López YA, Diez ER.

Light pollution as a factor in breast and prostate cancer

Sci Total Environ. 2021 Oct 12:150918.

Light pollution is a global environmental issue that affects photosensitive organisms. For instance, several researchers have recognized melatonin suppression in humans as a direct cause of long-term exposure to high artificial light levels at night. Others have identified low melatonin levels as a risk factor for a higher prevalence of hormone-sensitive cancer. This paper analyzes the association between light pollution, estimated as the emission analysis of satellite worldwide nighttime light collections from 1999 to 2012, and 25,025 breast and 16,119 prostate cancer events from 2003 to 2012. Both types of cancer increased during the study period, but light pollution increased in urban and peri-urban areas and decreased in rural areas. Cumulative light pollution during 5 years showed a positive association with breast cancer but not with prostate cancer. The association between light pollution and breast cancer persisted when adjusted to age-standardized rates with a mean increase of 10.9 events per 100,000 population-year (95% confidence interval 7.0 to 14.8). We conclude that exposure to elevated light pollution levels could be a risk factor for breast

cancer in Slovakia. This work can interest researchers who study relationships between atmospheric pollutants and the growing cancer epidemic. The results and the methodology can be extrapolated to any country in the world if data is available.

GASTROINTESTINÁLNE MALIGNITY

Babela R, Orsagh A, Ricova J, Lansdorpvogelaar I, Csanadi M, De Koning H, Reckova M.

Cost-effectiveness of colorectal cancer screening in Slovakia

Eur J Cancer Prev. 2021 Nov 16.

Background: Colorectal cancer (CRC) is an ideal disease for screening due to known and detectable precursor lesions and slow progression from benign adenoma to invasive cancer. The introduction of organized population-based screening programs reduces the burden of colorectal cancer and increases the quality of the screening process with a more favorable harm to benefit ratio compared to opportunistic screening.

Methods: The study used the microsimulation screening analysis-colon simulation model for the estimation of the effect of various factors on cancer incidence and mortality. The model simulated the Slovakian population from 2018 to 2050. Study includes the analysis of two screening strategies the fecal immunochemical test (FIT) every 2 years and annual FIT. Cost-effectiveness parameters were evaluated comparing each simulated screening scenario with no screening.

Results: Compared to no screening, the biennial FIT would detect 29 600 CRC cases and annual FIT 37 800 CRC cases. Mortality due to CRC showed benefits for both strategies with 17,38% reduction in biennial FIT and 24,67% reduction in annual FIT approach. Both screening programs were more costly as well as more effective compared to no screening. The ICER for biennial FIT strategy was 1776 EUR per 1 QALY and for the annual FIT 3991 EUR per 1 QALY.

Conclusions: In summary, this is the first cost-effectiveness analysis focusing on multiple national CRC screening strategies in Slovakia. Both strategies

demonstrated cost-effectiveness compared to no screening. However, for optimal population-based programmatic screening strategy, the policymakers should also consider human resources availability, acceptability of screening test among the population or additional resources including the screening funding.

IMUNOTERAPIA

Reckova M, Mladosičovicova B.

An ongoing evolution of cardio-oncology with the rapid development of modern immunotherapy

Int J Cardiol. 2021 Nov 16:34798210

INÉ

Gvozdjaková A, Sumbalová Z, Kucharská J, Szamosová M, Čápková L, Rausová Z, Vančová O, Mojto V, Langsjoen P, **Palacka P.** Platelet mitochondrial respiration and coenzyme Q10 could be used as new diagnostic strategy for mitochondrial dysfunction in rheumatoid diseases **PLoS One** 2021; 16(9): e0256135.

Introduction: Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disorder affecting both small and large synovial joints, leading to their destruction. Platelet biomarkers are involved in inflammation in RA patients. Increased circulating platelet counts in RA patients may contribute to platelet hyperactivity and thrombosis. In this pilot study we evaluated platelet mitochondrial bioenergy function, CoQ₁₀ levels and oxidative stress in RA patients.

Methods: Twenty-one RA patients and 19 healthy volunteers participated in the study. High resolution respirometry (HRR) was used for analysis of platelet mitochondrial bioenergetics. CoQ₁₀ was determined by HPLC method; TBARS were detected spectrophotometrically.

Results: Slight dysfunction in platelet mitochondrial respiration and reduced platelet CoQ₁₀ levels were observed in RA patients compared with normal controls.

Conclusions: The observed decrease in platelet CoQ₁₀ levels may lead to platelet mitochondrial dysfunction in RA diseases. Determination of platelet mitochondrial function and platelet CoQ₁₀ levels could be used as new

diagnostic strategies for mitochondrial bioenergetics in rheumatoid diseases.

Furka S, Furka D, Dadi NCTCT, **Palacka P**, Hromníková D, Dueñas Santana JA, Pineda JD, Casas SD, Bujdák J.

Novel antimicrobial materials designed for the 3D printing of medical devices used during the COVID-19 crisis

Rapid Prototyping Journal 2021; 27(5): 890-904.

Purpose: This study aims to describe the preparation of antimicrobial material usable in 3D printing of medical devices. Despite the wealth of technological progress at the time of the crisis caused by SARS-CoV-2 virus Virus that causes current Pandemic situation (COVID-19), the global population had long been exposed beforehand to an acute absence of essential medical devices. As a response, a new type of composite

materials intended for rapid prototyping, based on layered silicate saponite (Sap), antimicrobial dye phloxine B (PhB) and thermoplastics, has been recently developed.

Design/methodology/ approach:

Sap was modified with a cationic surfactant and subsequently functionalized with PhB. The hybrid material in powder form was then grounded with polyethylene terephthalate-glycol (PETG) or polylactic acid (PLA) in a precisely defined weight ratio and extruded into printing filaments. The stability and level of cytotoxicity of these materials in various physiological environments simulating the human body have been studied. The applicability of these materials in bacteria and a yeast-infected environment was evaluated.

Findings: Ideal content of the hybrid material, with respect to ther-

moplastic, was 15 weight %. Optimal printing temperature and speed, with respect to maintaining antimicrobial activity of the prepared materials, were $T = 215^{\circ}\text{C}$ at 50 mm/s for PETG/SapPhB and $T = 230^{\circ}\text{C}$ at 40 mm/s for PLA/SapPhB. 3 D-printed air filters made of these materials could keep inner air flow at 63.5% and 76.8% of the original value for the PLA/SapPhB and PETG/SapPhB, respectively, whereas the same components made without PhB had a 100% reduction of airflow.

Practical implications: The designed materials can be used for rapid prototyping of medical devices. Originality/value The new materials have been immediately used in the construction of an emergency lung ventilator, Q-vent, which has been used in different countries during the COVID-19 crisis.