Publikujeme v zahraničí

Onkológia (Bratisl.), 2020;15(5):378-380

GENITOURINÁRNE MALIGNITY

Slopovsky J, Kucharska J, **Obertova J, Mego M, Kalavska K, Cingelova S, Svetlovska D,** Gvozdjakova A, Furka S, **Palacka P.**

Plasma thiobarbituric acid reactive substances predicts survival in chemotherapy naïve patients with metastatic urothelial carcinoma

Transl Oncol. 2020 Oct 12;14(1):100890.

Oxidative stress plays a significant role in development and progression of cancer, including urothelial carcinomas. TBARS (Thiobarbituric acid reactive substances) represents a marker of oxidative stress increased in various diseases. In this prospective study, we tested the hypothesis of plasma TBARS concentration and correlation with survival in chemotherapy naïve MUC (metastatic urothelial carcinoma) patients. Most of subjects (N = 65) were treated with gemcitabine and cisplatin (GC) chemotherapy. Performance status ECOG ≥2 had 11 patients, visceral metastases were present in 43. Based upon the mean of plasma TBARS, subjects were dichotomized into low and high groups. Progression-free survival (PFS), overall survival (OS) and their 95% CI were estimated by Kaplan-Meier method and compared by log-rank test. At median follow-up of 9.6 months, 65 patients experienced progression and 64 died. Subjects with low TBARS had significantly better PFS (HR 0.51) and OS (HR 0.44) opposed to high TBARS. Patients with low TBARS had significantly higher rate of neutropenia G4 and less liver involvement. High TBARS correlated with BMI above 30 kg/m^2. Performance status and plasma TBARS were proven to be independent predictors of PFS and OS. In this study, high TBARS in MUC patients were associated with poor survival, likely due to more aggressive disease activity as reflected in increased liver involvement. Therefore, this biomarker could be used in clinical practice for early identification of patients with worse prognosis, better patient stratification, and treatment decision making.

Kalavska K, Schmidtova S, Chovanec M, Mego M.

Immunotherapy in testicular germ cell tumors

Front Oncol. 2020 Sep 24;10:573977.

Testicular germ cell tumors (TGCTs) are malignancies with very high curative potential even in metastatic settings, mainly due to the introduction of cisplatin in the treatment of this disease. However, in a group of patients with cisplatin-refractory disease or with progressive disease despite high-dose salvage chemotherapy treatment, the prognosis is typically dismal. The triple combination of gemcitabine, oxaliplatin, and paclitaxel (GOP) has reasonable efficacy and is considered to be standard care for this group of patients. It remains to be seen, however, whether refractory TGCTs may represent a potential target for immune checkpoint inhibition. This review will focus on the rationale of the use of immunotherapy for platinum-refractory TGCTs and summarize data reporting experiences with immune checkpoint inhibitor treatment for this malignancy.

Kozakova K, Mego M, Cheng L, Chovanec M.

Promising novel therapies for relapsed and refractory testicular germ cell tumors

Expert Rev Anticancer Ther. 2020 Nov 2:1-17.

Introduction: Germ cell tumors (GCTs) are the most common solid malignancies in young men. The overall cure rate of GCT patients in metastatic stage is excellent, however; patients with relapsed or refractory disease have poor prognosis. Attempts to treat refractory disease with novel effective treatment to improve prognosis have been historically dismal and the ability to predict prognosis and treatment response in GCTs did not sufficiently improve in the last three decades.

Areas covered: We performed a comprehensive literature search of PubMed/MEDLINE to identify original and review articles (years 1964-2020) reporting on current improvement salvage treatment in GCTs and novel treatment options including molecularly targeted therapy and epigenetic approach. Review articles were further searched for additional original articles.

Expert opinion: Despite multimodal treatment approaches the treatment of relapsed or platinum-refractory GCTs remains a challenge. High-dose chemotherapy (HDCT) regimens with autologous stem-cell transplant (ASCT) from peripheral blood showed promising results in larger retrospective studies. Promising results from in vitro studies raised high expectations in molecular targets. So far, the lacking efficacy in small and unselected trials do not shed a light on targeted therapy. Currently, wide inclusion of patients into clinical trials is highly advised.

Hulova S, Aziri R, Vulev I, Palacka P, Kolnikova G, Rejlekova K, Chovanec M, Mardiak J, Pindak D, Mego M.

Successful emergency endovascular aortic repair for intratumoral hemorrhage in extensive retroperitoneal mass of testicular origin

BMC Surg. 2020 Nov 7;20(1):272. doi

Background: Metastatic germ cell cancer of the testis is characterized by favorable prognosis since effective treatment methods are available even in cases of extensive disease. Retroperitoneal masses frequently encroach major blood vessels requiring a vascular intervention usually performed in association with the post-chemotherapy retroperitoneal lymph node dissection (RPLND). Reported clinical case describes a successful pre-treatment endovascular surgery for abdominal aortic rupture allowing for full-dose systemic chemotherapy administration, and subsequent radical surgical intervention at primary

tumor site as well as metastatic retroperitoneal lymph node dissection including the reconstruction of inferior caval vein.

Case presentation: Patient presented with left-sided testicular tumor and voluminous retroperitoneal mass with vascular involvement. Soon after the patient had been admitted for the first cycle of cisplatin-based chemotherapy, computed tomographic angiography (CTA) revealed a dorsal aortic wall rupture with active extravasation and irregular pseudoaneurysmatic dilatation of the aorta below the leak area. Retroperitoneal intratumoral hemorrhage associated with the bilateral iliac venous thrombosis required an endovascular repair procedure of infrarenal abdominal aorta.

Conclusions: Following the successful endovascular aortic repair 3 cycles of BEP (bleomycin, etoposide, cisplatin) regimen were administered with subsequent delayed left radical orchiectomy and RPLND associated with vena cava inferior (VCI) resection. Reconstruction of VCI was originally not deemed necessary as collateral blood flow appeared sufficient, however, intraoperative complications resulted in the need for unilateral VCI reconstruction, using the interposed bypass between right common iliac vein and infrarenal segment of VCI. Histopathologic examination of the attained specimen detected no vital cancer structures. The patient remains disease-free 18 months after the RPLND.

Cheng L, Mann SA, Lopez-Beltran A, **Chovanec M**, Santoni M, Wang M, Albany C, Adra N, Davidson DD, Cimadamore A, Montironi R, Zhang S.

Molecular characterization of testicular germ cell tumors using tissue microdissection

Methods Mol Biol. 2021;2195:31-47

Testicular germ cell tumors are among the most common malignancies seen in children and young adults. Genomic studies have identified characteristic molecular profiles in testicular cancer, which are associated with histologic subtypes and may predict clinical behavior including treatment responses. Emerging molecular technologies analyzing tumor genomics, transcriptomics, and proteomics may now guide precision management of testicular tumors. Laser-assisted microdissection methods such as laser capture microdissection efficiently isolate selected tumor cells from routine pathology specimens, avoiding contamination from nontarget cell populations. Laser capture microdissection in combination with next generation sequencing makes precise high throughput genetic evaluation effective and efficient. The use of laser capture microdissection (LCM) for molecular testing may translate into great benefits for the clinical management of patients with testicular cancers. This review discusses application protocols for laser-assisted microdissection to investigate testicular germ cell tumors.

KARCINÓM PRSNÍKA

Dobiasova B, Mego M.

Biomarkers for inflammatory breast cancer: diagnostic and therapeutic utility

Breast Cancer (Dove Med Press). 2020 Oct 14;12:153-163.

Inflammatory breast cancer (IBC) is a rare and highly aggressive subtype of advanced breast cancer. The aggressive behavior, resistance to chemotherapy, angiogenesis, and high metastatic potential are key intrinsic characteristics of IBC caused by many specific factors. Pathogenesis and behavior of IBC are closely related to tumor surrounding inflammatory and immune cells, blood vessels, and extracellular matrix, which are all components of the tumor microenvironment (TME). The tumor microenvironment has a crucial role in the local immune r09esponse. The communication between intrinsic and extrinsic components of IBC and the abundance of cytokines and chemokines in the TME strongly contribute to the aggressiveness and high angiogenic potential of this tumor. Critical modes of interaction are cytokine-mediated communication and direct intercellular contact between cancer cells and tumor microenvironment with a variety of pathway crosstalk. This review aimed to summarize current knowledge of predictive and prognostic biomarkers in IBC.

Mego M, Kalavska K, Karaba M, Minarik G, Benca J, Sedlackova T, Gronesova P, Cholujova D, Pindak D, Mardiak J, Celec P.

Plasma nucleosomes in primary breast cancer

Cancers (Basel). 2020 Sep 10;12(9):2587.

High-dose chemotherapy (HDCT) has curative potential in relapsed/refractory germ cell tumors (GCT). Due to the complexity of this population and the toxicity of HDCT, we evaluated the association between blood-based systemic inflammatory indexes and the outcome of GCT patients undergoing salvage treatment with HDCT in order to define additional prognostic factors able to orient clinical decision. Baseline characteristics, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and the systemic immune-inflammation index (SII) of 62 patients undergoing HDCT for GCT were retrospectively collected. The aim is to evaluate the correlation between each inflammatory marker (NLR, PLR, and SII) and response to HDCT, overall survival (OS), and progression-free survival (PFS). Using the receiver operating curve to identify the best cutoff values, it was found that patients with GCT with NLR ≥3.3 and SII ≥844,000 had shorter PFS and inferior OS. In the multivariable analysis including inflammatory markers, the International Prognostic Factor Study Group (IPFSG) risk group, age, and previous line of treatment, NLR ≥3.3 and SII ≥844,000 were identified to be independently associated with shorter PFS and OS. Moreover, NLR, PLR, and SII significantly correlate with overall response to HDCT. Associating IPFSG prognostic score to inflammatory markers at baseline of HDCT may improve prognostic information and could help physicians to make more personalized treatment decisions.

KARCINÓM PĽÚC

Tancos V, Farkasova A, Kviatkovska Z, Grendar M, Lisková A, Hutka Z, Plank L.

Non-small cell lung carcinomas with a minor sarcomatoid component and pleomorphic carcinomas are associated with high expression of programmed death ligand 1

Pathol Res Pract. 2020 Oct 2;216(12):153238. d

Pleomorphic carcinomas are known to be highly programmed death ligand 1 (PD-L1) positive non-small cell lung cancer (NSCLC) types. However, the level of PD-L1 expression in lung carcinomas with a minor sarcomatoid component, comprising less than 10 % of the tumor mass, has not been determined yet. We hypothesized that NSCLC with a minor sarcomatoid component is more closely related to pleomorphic carcinomas in terms of PD-L1 expression than to NSCLC types without sarcomatoid features. The surgical resections from 690 lung carcinoma patients were retrospectively analyzed for the presence of PD-L1 by means of immunohistochemistry using the 22C3 PharmDx assay. The tumor proportion score system was applied to quantify the level of PD-L1 expression. Membranous staining present in ≥ 1 % of tumor cells was chosen as the cut-off to define a positive result for PD-L1 expression. Tumors were allocated into one of four subgroups: „adenocarcinoma“, „squamous cell carcinoma“, „pleomorphic carcinoma“, or „NSCLC with a minor sarcomatoid component“. PD-L1 expression in pleomorphic carcinomas (26/32, 81.3 %) and in the subgroup of NSCLC with a minor sarcomatoid component (35/46, 76.1 %) was identified in a comparable proportion of cases. Pleomorphic carcinomas were significantly more often PD-L1 positive than adenocarcinomas ($p < 0.001$) or squamous cell carcinomas ($p = 0.0015$). Accordingly, the proportion of PD-L1 expressing NSCLC with a minor sarcomatoid component was significantly higher than that of the adenocarcinoma ($p < 0.001$) or squamous cell carcinoma ($p = 0.002$) subgroup. In summary, we identified a presumable new subgroup of highly PD-L1 positive neoplasms within the NSCLC spectrum that is related to pleomorphic carcinomas in terms of PD-L1 expression. Further investigation regarding genetic relation and mechanism of PD-L1 expression in these two NSCLC categories is recommended.

Abstrakty a príspevky z konferencií

KARCINÓM PĽÚC

D. Scepanovic, M. Dzongov, A. Hanicova, M. Lukacovicova Kolarcikova, M. Fekete, M. Pobijakova, A. Masarykova

Impact of radiotherapy timing after induction chemotherapy on survival of patients with locally advanced non small cell lung cancer

IASLC 2020 World Conference on Lung Cancer | Singapore, Worldwide Virtual Event (WCLC 2020), January 28 – 31, 2021.