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KARCINÓM PRSNÍKA

De Giorgi U, **Mego M**, Scarpi E, Giordano A, Giuliano M, Valero V, Alvarez RH, Ueno NT, Cristofanilli M, Reuben JM.

Association between circulating tumor cells and peripheral blood monocytes in metastatic breast cancer

Ther Adv Med Oncol. 2019 Aug 14;11:1758835919866065.

Background: We retrospectively evaluated the correlation between a baseline measurement of circulating tumor cells (CTCs) and inflammation-based scores in patients with metastatic breast cancer (MBC).

Methods: The optimal value of inflammation-based scores as the neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), monocyte-lymphocyte ratio (MLR) and systemic immune-inflammation index (SII) to predict survival was determined and compared with CTC <5 or ≥ 5 per 7.5 ml of blood.

Results: In the overall population of 516 women with MBC, CTCs correlated with peripheral blood monocytes ($p = 0.008$) and neutrophils ($p = 0.038$). In triple-negative tumors, CTCs correlated with monocyte count ($p = 0.009$); in HER2+ tumors, CTCs correlated with neutrophil count ($p = 0.009$), with a trend versus monocyte count ($p = 0.061$), whereas no correlation was found in HER2-estrogen receptor-positive (ER+) tumors. In multivariate analysis only monocytes were associated with ≥ 5 CTCs (OR = 2.72, 95% CI 1.09-6.80, $p = 0.033$). In multivariable analysis for predictors of overall survival, CTC (≥ 5 versus <5), number of metastatic sites (>1 versus 1), tumor subtypes (triple-negative versus HER2- ER+ tumors) and MLR only remained significant.

Conclusions: CTC and MLR are predictors of overall survival in MBC. CTC correlates with monocytes, in particular in triple-negative tumors.

GENITOURINÁRNE MALIGNITY

Hires M, Jane E, **Mego M**, **Chovanec M**, Kasak P, Tkáč J.

Glycan Analysis as Biomarkers for Testicular Cancer

Diagnostics (Basel). 2019 Oct 22;9(4). pii: E156.

The U.S. Preventive Services Task Force does not recommend routine screening for testicular cancer (TC) in asymptomatic men, essentially because serological testicular cancer (TC) biomarkers are not reliable. The main reason is that two of the most important TC biomarkers, α -fetoprotein (AFP) and human chorionic gonadotropin (hCG), are not produced solely due to TC. Moreover, up to 40% of patients with TC do not have elevated serological biomarkers, which is why serial imaging with CT is the chief means of monitoring progress. On the other hand, exposure to radiation can lead to an increased risk of secondary malignancies. This review provides the first comprehensive account of the applicability of protein glycoprofiling as a promising biomarker for TC with applications in disease diagnostics, monitoring and recurrence evaluation. The review first deals with the description and classification of TC. Secondly, the limitations of current TC biomarkers such as hCG, AFP and lactate dehydrogenase are provided together with an extensive overview of the glycosylation of hCG and AFP related to TC. The final part of the review summarises the potential of glycan changes on either hCG and AFP as TC biomarkers for diagnostics and prognostics purposes, and for disease recurrence evaluation. Finally, an analysis of glycans in serum and tissues as TC biomarkers is also provided.

Chovanec M, **Kalavska K**, **Mego M**, Cheng L.

Liquid biopsy in germ cell tumors: biology and clinical management

Expert Rev Mol Diagn. 2019 Oct 29:1-8.

Introduction: Liquid biopsy is an increasingly studied approach for optimal and minimally invasive diagnostics of malignant tumors. The aim of this review

is to provide evidence and discuss the utility of liquid biopsy in the management of germ cell tumors (GCTs).

Areas covered: Herein, we summarize the evidence on liquid biopsy in GCTs including serum tumor markers, circulating tumor cells, microRNA and cell-free DNA. The search of literature was conducted from Pubmed/Medline, ASCO-meeting library searching for terms 'liquid biopsy', 'germ cell tumors', 'circulating tumor cells', 'microRNA', 'cell-free DNA'. Obtained original studies were included. Reference lists of review articles and key original articles were searched for additional original studies. We included articles published between 1990 and 2019.

Expert opinion: Liquid biopsy is a minimally invasive tool using body fluids for diagnostic purposes in cancer. The established value of serum tumor markers may be already considered a liquid biopsy technique in diagnosis of GCTs. Possible near-future refinements in diagnosis of GCTs are emerging. Further information on diagnosis, prognosis and resistance is added with recently described microRNAs, circulating tumor cells and cell-free DNA. While great promise is shown, further large-scale validation is needed to incorporate these novel liquid biopsies into clinical practice.

Schmidtova S, **Kalavska K**, Gercakova K, Cierna Z, Miklikova S, Smolkova B, Buocikova V, Miskovska V, Durinikova E, Burikova M, **Chovanec M**, Matuskova M, **Mego M**, Kucerova L.

Disulfiram Overcomes Cisplatin Resistance in Human Embryonal Carcinoma Cells

Cancers (Basel). 2019 Aug 22;11(9). pii: E1224.

Cisplatin resistance in testicular germ cell tumors (TGCTs) is a clinical challenge. We investigated the underlying mechanisms associated with cancer stem cell (CSC) markers and modalities

circumventing the chemoresistance. Chemoresistant models (designated as CisR) of human embryonal carcinoma cell lines NTERA-2 and NCCIT were derived and characterized using flow cytometry, gene expression, functional and protein arrays. Tumorigenicity was determined on immunodeficient mouse model. Disulfiram was used to examine chemosensitization of resistant cells. ALDH1A3 isoform expression was evaluated by immunohistochemistry in 216 patients' tissue samples. Chemoresistant cells were significantly more resistant to cisplatin, carboplatin and oxaliplatin compared to parental cells. NTERA-2 CisR cells exhibited altered morphology and increased tumorigenicity. High ALDH1A3 expression and increased ALDH activity were detected in both refractory cell lines. Disulfiram in combination with cisplatin showed synergy for NTERA-2 CisR and NCCIT CisR cells and inhibited growth of NTERA-2 CisR xenografts. Significantly higher ALDH1A3 expression was detected in TGCTs patients' tissue samples compared to normal testicular tissue. We characterized novel clinically relevant model of chemoresistant TGCTs, for the first time identified the ALDH1A3 as a therapeutic target in TGCTs and more importantly, showed that disulfiram represents a viable treatment option for refractory TGCTs.

HEMATOLOGICKÉ MALIGNITY

Kral Z, Michalka J, Mocikova H, Markova J, Sykorova A, Belada D, Jungova A, Vokurka S, Lukasova M, Prochazka V, Duras J, Hajek R, Dusek L, **Drgona L, Ladicka M, Ballova V, Vranovsky A.**

Treatment of Relapsed/Refractory Hodgkin Lymphoma: Real-World Data from the Czech Republic and Slovakia *J Cancer*. 2019 Aug 28;10(21):5041-5048.

Introduction: Clinical trials have demonstrated the effectiveness of the CD30-targeted antibody-drug conjugate brentuximab vedotin (BV) for the treatment of relapsed/refractory Hodgkin lymphoma (R/R HL). In this study, we report on outcomes with BV in a real-world setting using data collected in clinics in the Czech Republic and Slovakia. Patients and Methods: Clinical and epi-

demiological data for patients with R/R HL who received treatment with BV at eight centers across the Czech Republic and Slovakia were examined. Data were amalgamated and analyzed retrospectively. Results: Clinical data for 58 patients (median age: 30.5 years) with R/R HL who received BV during the course of their treatment were collected and analyzed. Patients had received a median of 3 prior treatment regimens and most (91%) were treated with BV after relapse following autologous stem cell transplantation. Therapeutic responses after BV included 19 (33%) complete responses (CRs) and 8 (14%) partial responses. CRs occurred more frequently in patients who had received fewer prior treatment regimens. The 1-, 2-, and 3-year overall survival (OS) rates from initiation of BV were 78%, 62%, and 41%, respectively. Conclusion: Response rates and OS in this analysis of BV in real-world settings in the Czech Republic and Slovakia were consistent with those reported for pivotal clinical trials and from previous studies outside the clinical trial setting. The results support the efficacy of BV for treatment of R/R HL in real-life clinical practice.

Suportívna liečba

Cornely OA, Alastruey-Izquierdo A, Arenz D, Chen SCA, Dannaoui E, Hochhegger B, Hoenigl M, Jensen HE, Lagrou K, Lewis RE, Mellinshoff SC, Mer M, Pana ZD, Seidel D, Sheppard DC, Wahba R, Akova M, Alanio A, Al-Hatmi AMS, Arikan-Akdagli S, Badali H, Ben-Ami R, Bonifaz A, Bretagne S, Castagnola E, Chayakulkeeree M, Colombo AL, Corzo-León DE, **Drgona L**, Groll AH, Guinea J, Heussel CP, Ibrahim AS, Kanj SS, Klimko N, Lackner M, Lamoth F, Lanternier F, Lass-Floerl C, Lee DG, Lehrnbecher T, Lmimouni BE, Mares M, Maschmeyer G, Meis JF, Meletiadiis J, Morrissey CO, Nucci M, Oladele R, Pagano L, Pasqualotto A, Patel A, Racil Z, Richardson M, Roilides E, Ruhnke M, Seyedmousavi S, Sidharthan N, Singh N, Sinko J, Skiada A, Slavin M, Soman R, Spellberg B, Steinbach W, Tan BH, Ullmann AJ, Vehreschild JJ, Vehreschild MJGT, Walsh TJ, White PL, Wiederhold NP, Zaoutis T, Chakrabarti

A; Mucormycosis ECMM MSG Global Guideline Writing Group.

Global guideline for the diagnosis and management of mucormycosis: an initiative of the

European Confederation of Medical Mycology in cooperation with the Mycoses Study Group Education and Research Consortium

Lancet Infect Dis. 2019 Dec;19(12):e405-e421. doi: 10.1016/S1473-3099(19)30312-3.

Mucormycosis is a difficult to diagnose rare disease with high morbidity and mortality. Diagnosis is often delayed, and disease tends to progress rapidly. Urgent surgical and medical intervention is lifesaving. Guidance on the complex multidisciplinary management has potential to improve prognosis, but approaches differ between health-care settings. From January, 2018, authors from 33 countries in all United Nations regions analysed the published evidence on mucormycosis management and provided consensus recommendations addressing differences between the regions of the world as part of the „One World One Guideline“ initiative of the European Confederation of Medical Mycology (ECMM). Diagnostic management does not differ greatly between world regions. Upon suspicion of mucormycosis appropriate imaging is strongly recommended to document extent of disease and is followed by strongly recommended surgical intervention. First-line treatment with high-dose liposomal amphotericin B is strongly recommended, while intravenous isavuconazole and intravenous or delayed release tablet posaconazole are recommended with moderate strength. Both triazoles are strongly recommended salvage treatments. Amphotericin B deoxycholate is recommended against, because of substantial toxicity, but may be the only option in resource limited settings. Management of mucormycosis depends on recognising disease patterns and on early diagnosis. Limited availability of contemporary treatments burdens patients in low and middle income settings. Areas of uncertainty were identified and future research directions specified.