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GENITOURINÁRNE MALIGNITY

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Liquid biopsy in the clinical management of bladder cancer: current status and future developments

Expert Rev Mol Diagn. 2019 Oct 17:1-10.

Introduction: The use of liquid biopsy on the blood from solid malignancies provides a convenient way of detecting actionable mutations, monitoring treatment response, detecting early recurrence and prognosticating outcomes. The aim of this review is to discuss the current status and future direction of serum biomarkers in the clinical management of urinary bladder cancer.

Areas covered: This review provides an overview of blood liquid biopsy and bladder cancer using methods of circulating tumors cells, circulating RNA, serum metabolites and cell-free DNA. Recent clinical studies and advances in methodology are emphasized. We performed a literature search using PMC/PubMed with keywords including ‚liquid biopsy', ‚circulating tumor DNA', ‚cell-free DNA','biomarkers', ‚bladder cancer' ‚precision medicine'. Additional articles were obtained from the cited references of key articles. An emphasis was placed on recent studies published since 2018.

Expert opinion: Liquid biopsies represent a potential biomarker using cell-free DNA, metabolomic profiles of altered cellular metabolism, circulating cancer cells and RNA. Despite displaying tremendous clinical promise, the current status of the blood liquid biopsies has not reached fruition. However, future investigations should lead the evolution of liquid biomarker into clinical utility for the management of bladder cancer.

De Padova S, Casadei C, Berardi A, Bertelli T, Filograna A, Cursano MC, Menna C, Burgio SL, Altavilla A, Schepisi G, Prati S, Montalti S, **Chovanec M**, Banna GL, Grassi L, **Mego M**, De Giorgi U.

Caregiver emotional burden in testicular cancer patients: from patient to caregiver support

Front Endocrinol (Lausanne). 2019 May 28;10:318.

Testicular cancer is the most common tumor in young males aged 15-40 years. The overall cure rate for men with testicular cancer is >90%, so a huge number of these patients will become testicular cancer survivors. These people may feel some stress in the experience of diagnosis, treatment, and consequences that affects the quality of life, and during follow-up, especially when new issues and emotional distresses appear over time, such as late side-effects of treatments and emotional challenges including fear of tumor relapse, fertility and sexuality concerns, and social and workplace issues. The cancer experience has an impact not only on patients, but also on their relatives (e.g., spouses, parents, or siblings), who often have to assume a caregiving role for the duration of and following treatment for cancer. Moreover, the caregiver plays an important role in supporting a man with a testicular cancer, providing physical and emotional care. This review presents a summary of existing knowledge regarding the impact and the burden of testicular cancer on caregivers.

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Severe complications in testicular germ cell tumors: the choriocarcinoma syndrome

Front Endocrinol (Lausanne). 2019 Apr 12;10:218.

Testicular germ cell tumors (TGCTs) represent the most common solid tumor in young men and is a model of curable cancer. The effectiveness of cisplatin-based chemotherapy secures more than 95% of patients' 5-years survival rate. However, some high-risk patients with a very advanced disease develop choriocarcinoma syndrome (CS) connected with acute respiratory failure with poor prognosis and high mortality rate shortly after beginning systemic chemotherapy. CS was first described as a syndrome with hemorrhage from metastatic sites in patients with TGCTs with significantly high choriogonadotropin level. Acute hemorrhage to lung metastases is typical, but hemorrhage can occur from any metastatic site. Patognomic of choriocarcinoma cells is an invasion of small blood vessels within CS. The incidence of CS in patients with TGCTs are not well-defined and can vary across the world. To date, there are a few case reports and small retrospective series reporting a connection between systemic chemotherapy and the development of CS in metastatic TGCTs. CS is known to be triggered by massive tumor cell lysis as a result of chemotherapy and cytokine release, aggravated with alveolar hemorrhage. This can lead to a consecutive superinfection, furthered with neutropenia after chemotherapy, acute respiratory distress syndrome, rising to systemic inflammatory response, resulting in multiorgan failure and death. A reasonably effective approach in patients with extensive disease could be a shortened course of chemotherapy as well as a reduction of dosage in induction chemotherapy before full-dose chemotherapeutical regimen; however, current data regarding optimal treatment approach are limited. Patients' referral to tertiary centers and the administration of induction chemotherapy in an intensive care unit setting could further improve the treatment outcome.

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

Cancer stem cell niche and immune--active tumor microenvironment in testicular germ cell tumors

Adv Exp Med Biol. 2020;1226:111-121.

Testicular germ cell tumors (TGCTs) represent the most common neoplasia among young men. Management of TGCTs is an excellent example of curative outcomes in clinical oncology. The unique sensitivity to cisplatin-based chemotherapy regimens has led to establishing TGCTs as a „model of cancer cure." However, mechanisms and factors underlying pervasive growth of TGCTs are still poorly understood. It is suggested that unique cancer stem cell (CSC) niche exists in the testicular tumor microenvironment. CSC niche potentially contributes to the progression of germ cell tumors. Furthermore, rich infiltration of TGCTs with immune cells indicates involvement of immune system in biology of this cancer type. This review summarizes current knowledge regarding specific cancer microenvironment in TGCTs and discusses the role of cancer stem cells as well as immune mechanisms in these tumors.

Cierna Z, Miskovska V, Roska J, Jurkovicova D, Pulzova LB, Sestakova Z, Hurbanova L, Machalekova K, Chovanec M, Rejlekova K, Svetlovska D, Kalavska K, Kajo K, Babal P, Mardiak J, Ward TA, Mego M, Chovanec M.

Increased levels of XPA might be the basis of cisplatin resistance in germ cell tumours

BMC Cancer. 2020 Jan 6;20(1):17.

Background: Germ cell tumours (GCTs) represent a highly curable malignity as they respond well to cisplatin (CDDP)-based chemotherapy. Nevertheless, a small proportion of GCT patients relapse or do not respond to therapy. As this might be caused by an increased capacity to repair CDDP-induced DNA damage, identification of DNA repair biomarkers predicting inadequate or aberrant response to CDDP, and thus poor prognosis for GCT patients, poses a challenge. The objective of this study is to examine the expression levels of the key nucleotide excision repair (NER) factors, XPA, ERCC1 and XPF, in GCT patients and cell lines.

Methods: Two hundred seven GCT patients' specimens with sufficient follow-up clinical-pathological data and pairwise combinations of CDDP-resistant and -sensitive GCT cell lines were included. Immunohistochemistry was used to detect the ERCC1, XPF and XPA protein expression levels in GCT patients' specimen and Western blot and qRT-PCR examined the protein and mRNA expression levels in GCT cell lines.

Results: GCT patients with low XPA expression had significantly better overall survival than patients with high expression (hazard ratio = 0.38, 95% confidence interval: 0.12-1.23, p = 0.0228). In addition, XPA expression was increased in the non-seminomatous histological subtype, IGCCCG poor prognosis group, increasing S stage, as well as the presence of lung, liver and non-pulmonary visceral metastases. Importantly, a correlation between inadequate or aberrant CDDP response and XPA expression found in GCT patients was also seen in GCT cell lines.

Conclusions: XPA expression is an additional independent prognostic biomarker for stratifying GCT patients, allowing for improvements in decision-making on treatment for those at high risk of refractoriness or relapse. In addition, it could represent a novel therapeutic target in GCTs.

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Molecular characteristics of testicular germ cell tumors: pathogenesis and mechanisms of therapy resistance

Expert Rev Anticancer Ther. 2020 Jan 27:1-5.

KARCINÓM PĽÚC

Cufer T, Ciuleanu TE, **Berzinec P**, Galffy G, Jakopovic M, Jassem J, Jovanovic D, Mihaylova Z, Ostoros G, Thallinger C, Zemanova M, Zielinski C.

Access to novel drugs for non-small cell lung cancer in Central and Southeastern Europe: A Central European Cooperative Oncology Group Analysis.

Oncologist. 2019 Nov 29. pii: theoncologist.2019-0523.

Background: Treatment of non-small cell lung cancer (NSCLC) improved substantially in the last decades. Novel targeted and immune-oncologic drugs were introduced into routine treatment. Despite accelerated development and subsequent drug registrations by the European Medicinal Agency (EMA), novel drugs for NSCLC are poorly accessible in Central and Eastern European (CEE) countries.

Material and methods: The Central European Cooperative Oncology Group conducted a survey among experts from 10 CEE countries to provide an overview on the availability of novel drugs for NSCLC and time from registration to reimbursement decision in their countries.

Results: Although first-generation epidermal growth factor receptor tyrosine kinase inhibitors were reimbursed and available in all countries, for other registered therapies-even for ALK inhibitors and checkpoint inhibitors in first-line-there were apparent gaps in availability and/or reimbursement. There was a trend for better availability of drugs with longer time from EMA marketing authorization. Substantial differences in access to novel drugs among CEE countries were observed. In general, the availability of drugs is not in accordance with the Magnitude of Clinical Benefit Scale (MCBS), as defined by the European Society for Medical Oncology (ESMO). Time spans between drug registrations and national decisions on reimbursement vary greatly, from less than 3 months in one country to more than 1 year in the majority of countries.

Conclusion: The access to novel drugs for NSCLC in CEE countries is suboptimal. To enable access to the most effective compounds within the shortest possible time, reimbursement decisions should be faster and ESMO MCBS should be incorporated into decision making.