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GENITOURINÁRNE MALIGNITY

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Molecular mechanisms of resistance in testicular germ cell tumors - clinical implications

Curr Cancer Drug Targets. 2018 Jan 1. (In press)

Testicular germ cell tumors (TGCTs) represent the most common malignancy in men aged 15-35. Due to these tumors' biological and clinical characteristics, they can serve as an appropriate system for studying molecular mechanisms associated with cisplatin-based treatment resistance. This review describes treatment resistance from clinical and molecular viewpoints. Cisplatin resistance is determined by various biological mechanisms, including the modulation of the DNA repair capacity of cancer cells, alterations to apoptotic cell death pathways, deregulation of gene expression pathways, epigenetic alterations and insufficient DNA binding. Moreover, this review describes TGCTs as a model system that enables the study of the cellular features of cancer stem cells in metastatic process and describes experimental models that can be used to study treatment resistance in TGCTs. All of the abovementioned aspects may help to elucidate the molecular mechanisms underlying cisplatin resistance

and may help to identify promising new therapeutic targets.

PODPORNÁ LIEČBA

Mikulska M, Lanini S, Gudiol C, Drgona L, Ippolito G, Fernández-Ruiz M, Salzberger B.

ESCMID Study Group for Infections in Compromised Hosts (ESGICH) Consensus Document on the safety of targeted and biological therapies: an Infectious Diseases perspective (Agents targeting lymphoid cells surface antigens [I]: CD19, CD20 and CD52).

Clin Microbiol Infect. 2018 Feb 12.

Background: The present review is part of the ESCMID Study Group for Infections in Compromised Hosts (ESGICH) Consensus Document on the safety of targeted and biological therapies.

Aims: To review, from an Infectious Diseases perspective, the safety profile of agents targeting CD19, CD20 and CD52 and to suggest preventive recommendations.

Source: Computer-based MEDLINE searches with MeSH terms pertaining to each agent or therapeutic family.

Content: Although CD19-targeted agents (blinatumomab or inebilizumab) are not associated with an increased risk of infection, they may cause IgG hypogammaglobulinemia and neutropenia. The requirement for prolonged intra-

venous infusion of blinatumomab may increase the risk of catheter-associated bloodstream infections. Infection remains the most common non-hematological adverse effect of anti-CD20 monoclonal antibodies (mAbs), including severe respiratory tract infection, hepatitis B virus (HBV) reactivation and varicella-zoster virus infection. Screening for chronic or resolved HBV infection is recommended for patients receiving anti-CD20 mAbs. Antiviral prophylaxis should be offered for 12-18 months to hepatitis B surface antigen (HBsAg)-positive and HBsAg-negative/anti-hepatitis B core antibody (HBc)-positive patients. Anti-Pneumocystis prophylaxis should be considered in patients receiving concomitant chemotherapy, particularly steroids. Alemtuzumab (anti-CD52) increases the risk of infections, in particular among leukaemia and solid organ transplant patients. These populations benefit from anti-Pneumocystis prophylaxis, prevention strategies for cytomegalovirus infection, and screening for HBV, HCV and tuberculosis. Antiviral prophylaxis for at least 6-12 months should be provided for HBsAg-positive patients.

Implications: Since there are limited clinical data for many of the reviewed agents, special attention must be put to promptly detect and report emerging infectious complications.