

MANAGEMENT OF THE ADVERSE EFFECTS OF IMMUNE CHECKPOINT THERAPY

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Today immunotherapy with immune checkpoint inhibitors such as a-CTLA4, a-PD-1, and a-PD-L1 antibodies is standard for the treatment of many solid tumors and haematological malignancies. Side effects of these drugs can be general, non-specific (weakness, infusion-related reactions) or specific, so-called immune-related adverse effects (irAEs). Specific side effects are results of the mechanism of action of these drugs, which is non-specific activation of immune system. Clinically, they manifest as organ and tissue inflammation. Almost all organ and system can be affected by irAEs, although side effects on the gastrointestinal tract, skin, liver, endocrine glands and lungs are the most common. The side effects of checkpoint inhibitors are usually transient and mild, but can be also serious or even fatal. The lecture will present general principles for early identification, evaluation and control of irAEs, recommendations from published clinical practice guides, authors' previous clinical experience and open questions that still pose a challenge in clinical practice.

LEČENJE NEŽELJENIH DEJSTAVA IMUNSKE BLOKADE KONTROLNIH TAČAKA

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Imunološka terapija blokatorima tzv. kontrolnih tačaka (engl. *immune checkpoint inhibitor therapy*: a-CTLA4, a-PD-1, a-PD-L1) danas je standard lečenja mnogih solidnih tumora i hematoloških maligniteta. Neželjena dejstva ovih lekova mogu da budu opšta, nespecifična (slabost, malaksalost; reakcije vezane za infuziju) ili specifična (tzv. neželjena dejstva posredovana imunskim sistemom, engl. *Immune-related adverse effects*, irAEs). Specifična neželjena dejstva direktno proističu iz mehanizma dejstva ovih lekova, a to je nespecifična aktivacija imunskog sistema. Klinički se ispoljavaju kao inflamacija organa ili tkiva. Bilo koji organ ili tkivo mogu da budu zahvaćeni, iako se najčešće viđaju neželjena dejstva na gastrointestinalni trakt, kožu, jetru, žlezde sa unutrašnjim lučenjem i pluća. Neželjena dejstva inhibitora kontrolnih tačaka najčešće su prolazna i blaga, iako mogu da budu i ozbiljna i fatalna. Predavanje će predstaviti opšte principe za rano prepoznavanje, evaluaciju i kontrolu irAEs, preporuke iz publikovanih vodiča kliničke prakse, dosadašnje kliničko iskustvo autora i otvorena pitanja koja još uvek predstavljaju izazov u kliničkoj praksi.