Abstract

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Immunotherapy in microsatellite instability metastatic colorectal cancer: current status and future perspectives

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Abstract

Background:

Colorectal cancer (CRC) is one of the most frequent and deadly malignancies worldwide. This specific pathology is composed of various molecular entities, with distinct immunological phenotypes. In addition to KRAS, NRAS, and BRAF mutation status, other druggable alterations such as those in HER2, MET, NTRK, ALK, and ROS1 have been identified in recent years offering new therapeutic options for some patients with CRC.

Aim: This review will focus on the molecular biology, immunological fingerprints, and current clinical evidence for the use of immunotherapy in patients with CRC.

Relevance for patients:

High microsatellite instability (MSI-H) and mutations in mismatch repair genes constitute a new molecular entity within CRC, which is characterized by a high mutational and neoantigen burden, frequent immune cell infiltration, and where immune checkpoint inhibitors have shown high response and survival rates compared to microsatellite stable (MSS) tumors. Indeed, the approval of pembrolizumab in MSI-H tumors was the first agnostic FDA approval in solid tumors. While monotherapy with anti-programmed cell death protein-1 agents achieves objective response rates (ORR) of around 30% and 1-year overall survival (OS) rates of 76%, anti-PD1, and anti-CTLA4 combinations achieve a 55% ORR and a 1-year OS rate of 85%. Several ongoing trials are evaluating the use of different immunotherapy combinations, both in the advanced and early settings and in MSI-h and MSS CRCs.

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Biography

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