Avelumab Immunotherapy

Management of adverse events associated with new treatment for Merkel cell carcinoma

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BACKGROUND: Metastatic Merkel cell carcinoma (mMCC) is a rare skin cancer with poor prognosis. Avelumab is the first approved treatment option for patients with mMCC. Immune checkpoint inhibitors, such as avelumab, are associated with unique toxicities that can be effectively addressed with prompt recognition and appropriate management.

OBJECTIVES: This article discusses the use of avelumab for the treatment of mMCC and management of associated toxicities.

METHODS: Literature on mMCC disease state and clinical trial data for avelumab were reviewed.

FINDINGS: Avelumab has been investigated in patients with mMCC either following disease progression after one or more prior lines of chemotherapy or no prior systemic therapy. These patients experience clinically meaningful benefit. About 70% of patients receiving avelumab experience treatment-related adverse events. Given the limited benefit of chemotherapy, managing symptoms related to avelumab is key to administering this effective treatment to patients with mMCC.

KEYWORDS
carcinoma; Merkel cell; avelumab; drug-related side effects; adverse reactions

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MERKEL CELL CARCINOMA (MCC) IS A RARE, AGGRESSIVE SKIN MALIGNANCY that occurs mainly in older adults or immunosuppressed patients (Lebbe et al., 2015; Schadendorf et al., 2017). Patients with MCC experience a high rate of regional mtastasis, and survival outcomes for patients with advanced-stage MCC are worse than those for patients with melanoma (Schadendorf et al., 2017).

Risk factors for MCC include ultraviolet (UV) radiation and infection with Merkel cell polyomavirus (MCPyV) (Feng, Shuda, Chang, & Moore, 2008; Schadendorf et al., 2017). About 80% of MCC tumors are positive for MCPyV (Feng et al., 2008). MCPyV-negative tumors have a high mutational burden, likely resulting from chronic UV exposure (Harms et al., 2015; Wong et al., 2015). The identification of mechanisms for virus- and UV-mediated tumorigenesis provides insight into the immunogenicity of MCC: viral proteins and UV-induced mutations cause the production of neoantigens, which activate the host immune response (Goh et al., 2016).

Historically, for patients with distant metastases (stage IV), standard care for MCC is enrollment in a clinical trial (Lebbe et al., 2015; National Comprehensive Cancer Network, 2018). Updated practice guidelines also recommend treatment with programmed cell death protein 1 (PD-1) and programmed cell death protein ligand 1 (PD-L1) immune checkpoint inhibitors (ICIs) unless contraindicated; systemic therapies, such as platinum-based chemotherapy regimens; or clinical trial participation if the disease progresses after PD-1/PD-L1–directed treatment (National Comprehensive Cancer Network, 2018). Although MCC is considered chemosensitive, responses to chemotherapy in patients with metastatic MCC (mMCC) are seldom durable (Becker et al., 2017; Cowey et al., 2017; Iyer et al., 2016; Lebbe et al., 2015). Some patients receiving chemotherapy for mMCC experienced serious side effects, including a high incidence of treatment-related death, reported in one series as 7.7% (Voog, Biron, Martin, & Blay, 1999). ICIs represent an alternative strategy for treating patients with advanced MCC.

Approval of the ICI avelumab, an anti–PD-L1 antibody, represents the first drug approval for patients with mMCC in several countries, including the United States, Canada, Australia, Israel, and Japan, as well as Europe