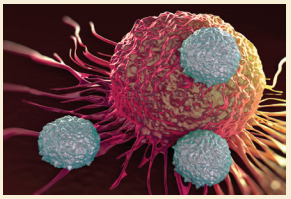
■ Article

Understanding Immune Checkpoint Inhibitors for Effective Patient Care

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Background: Immune checkpoint inhibitors represent a paradigm change in the treatment of melanoma and other advanced cancers. These agents manipulate key immune-regulating pathways to restore immune responses against tumors. The success of this approach is demonstrated by ipilimumab (Yervoy®) for the treatment of advanced melanoma, with improvement in three-year survival rates of about 20%. Newer checkpoint inhibitors targeting the programmed death-1 (PD-1) pathway have been approved and may have higher response rates and improved tolerability.

Objectives: This article aims to educate nurses and increase their comfort level with these new therapies.

Methods: The mechanism of action of immune checkpoint inhibitors is reviewed, and insight is provided on how nurses can use this knowledge to more effectively care for patients receiving these therapies.

Findings: The use of immuno-oncology agents is increasing. Oncology nurses must understand the basic immune mechanism of action responsible for the novel toxicity profile characterized by immune-related adverse events (irAEs) and clinical response patterns. Managing irAEs with immune checkpoint inhibitors is not necessarily more difficult than with conventional agents, but a difference does exist. Nurses and other healthcare providers must consider the underlying cause of toxicity with immune checkpoint inhibitors when making management decisions.

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Metastatic melanoma has historically been considered an incurable cancer. However, the treatment landscape for metastatic or unresectable melanoma and other advanced malignancies is undergoing rapid change. New immunotherapies, termed *immune checkpoint inhibitors*, work by reactivating an immune response against tumors (Pardoll, 2012). Immune checkpoint inhibitors for treating melanoma include ipilimumab (Yervoy®), pembrolizumab (Keytruda®), and nivolumab (Opdivo®). The checkpoint inhibitor ipilimumab, which targets the cytotoxic T-lymphocyte antigen 4 (CTLA-4) pathway, was approved for use in 2011 (Bristol-Myers Squibb, 2015b). Agents targeting the programmed death-1 (PD-1) pathway (i.e., pembrolizumab and nivolumab) are approved for the treatment of patients with unresectable or advanced melanoma that has progressed after ipilimumab (and, if positive for *BRAF V600* mutation, a BRAF inhibitor). Nivolumab was recently approved for the treatment of non-small cell lung cancer (NSCLC) with progression after platinum-based chemotherapy on or after targeted therapy (Bristol-Myers Squibb, 2015a), and pembrolizumab was also recently approved for the same indication, but for those whose tumors express PD-L1 (a biomarker) (Merck & Co., 2015). In addition, the U.S. Food and Drug Administration approvals included the combination of nivolumab and ipilimumab as a first-line treatment for patients with metastatic melanoma and wild-type *BRAF*, as well as the approval of ipilimumab as an adjuvant therapy for stage III melanoma following surgery (Bristol-Myers Squibb, 2015b). Most oncology nurses will likely be caring for patients receiving these agents in the near future. To optimize patient care, nurses must have a basic

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