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Managing Immune-Related Adverse Events to Ipilimumab: A Nurse's Guide

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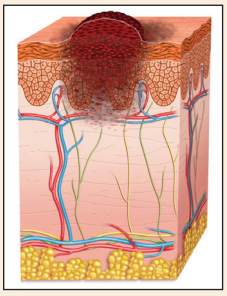

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Ipilimumab is a U.S. Food and Drug Administration–approved novel T-cell potentiator that improves survival in metastatic melanoma. Ipilimumab blocks cytotoxic T-lymphocyte antigen–4, a negative regulator of the immune response, thus promoting T-cell activation and prolonging a patient's antitumor response. However, that action may produce a mechanism-related spectrum of immune-related adverse events (irAEs), which can become severe and life-threatening if left unrecognized and untreated. This article describes the clinical properties of ipilimumab, specifically in regard to its unique profile of irAEs. Guidelines to manage irAEs are reviewed with a particular emphasis on the contribution of nurses to patient care and education. The nurse's role in facilitating communication among the oncology team, primary practice team, patients, and caregivers is fundamental to early recognition and effective management of irAEs so that patients can continue on therapy. As a regular, ongoing presence in patient care, the oncology nurse is well placed to deliver information, assess patients' understanding of that information, and support them through their cancer experience. Checklists of irAE symptoms may be useful for patients and nurses alike. In addition, education on ipilimumab's mechanism of action and how it contributes to irAEs should form an integral part of the patient treatment plan.

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The outlook for patients with advanced (unresectable stage III or stage IV) melanoma is poor. Single-agent dacarbazine remains the only chemotherapeutic agent approved for metastatic melanoma; however, an increase in overall survival has not been demonstrated when compared to supportive care. High-dose interleukin-2 (IL-2), a U.S. Food and Drug Administration–approved immunotherapy, is an option only for a select group of patients and requires care in specialty centers because it is associated with severe toxicity (National Comprehensive Cancer Network, 2011). Despite its limited use, IL-2 has demonstrated durable, ongoing responses in some patients, thus encouraging persistence with an immunotherapeutic approach to melanoma (Atkins, Kunkel, Sznol, & Rosenberg, 2000).

Immune Response in Cancer

In patients with advanced cancer, tumors fail to trigger an antitumor immune response strong enough to be clinically relevant. That failure may occur for many reasons because tumors can develop mechanisms to evade an antitumor immune response as they progress (Drake, Jaffee, & Pardoll, 2006). Antitumor T-cell responses require full cellular activation that involves two successive cell signals. Tumors are unable to trigger the second cell signal directly, so a surrogate cell called the antigen-presenting cell (APC) is needed to present tumor antigen to the T cell using specialized cellular equipment known as the major histocompatibility complex (MHC). MHC on the APC, carrying tumor antigen, binds to the T-cell receptor triggering the first signal; that primes the T cell, but it still is not activated fully. The second signal is initiated when the B7 molecule expressed on the surface of the APC binds with a different receptor on the T cell (CD28). The second signal fully activates the T cell, enabling it to attack tumor cells expressing the tumor antigen being presented by the MHC (Robert & Ghiringhelli, 2009).

However, as the T cell becomes activated, the molecule cytotoxic T-lymphocyte antigen–4 (CTLA-4), which serves as a checkpoint inhibitor, is produced gradually over time by the T cell and migrates to the cell surface. CTLA-4 is a key immunoregulatory molecule that deactivates the patient's T cells as the immune response builds to stop them from attacking healthy host tissues and producing unwanted autoimmunity. CTLA-4 is more efficient