

# Immune Modulation in Melanoma and Advanced Cancer Therapy: Anti-Cytotoxic T Lymphocyte-Associated Antigen 4 Monoclonal Antibodies

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Two fully human monoclonal antibodies (mAbs) that target cytotoxic T lymphocyte-associated antigen 4 (CTLA4), tremelimumab and ipilimumab, are in clinical development for the treatment of advanced cancers. The investigational agents enhance T-cell activation and are hypothesized to generate antitumor immunity. Clinical data have shown that treatment with an anti-CTLA4 mAb is tolerable in most patients. In addition, enhanced antitumor activity was observed in some patients. As expected with an agent that enhances the immune response, immune-related adverse events are observed frequently in treated patients. The immune-related adverse events are not observed with standard chemotherapy agents, so many nurses may be unfamiliar with their management. Early recognition and management of immune-related adverse events by oncology nurses is an essential component of effective treatment with an anti-CTLA4 mAb. As immunomodulatory agents such as anti-CTLA4 mAbs are introduced in oncology treatment, nurses will need a greater understanding of the complexities associated with the therapies. Knowledge of immune system functions and how altering the functions may affect the development of side effects will enhance safety and quality of care for patients receiving anti-CTLA4 mAbs.

Incidence of cutaneous melanoma rose at a rate of about 3% per year from 1981–2000; however, incidence has been stable since 2000 (American Cancer Society, 2009). In 2009, 68,720 new cases of melanoma are expected, and an estimated 8,650 patients will die from the disease (American Cancer Society). Risk factors for melanoma include family history of melanoma, presence and number of melanocytic moles on the body, sensitivity to sunburns, excessive exposure to natural sunlight or artificial ultraviolet light, and the immune status of individuals.

Prognosis for patients with melanoma depends largely on the stage of the disease, which most often is based on the American Joint Committee on Cancer staging system (National Cancer Institute, 2008). Although most cases of early-stage melanoma are curable with surgery, patients with inoperable and distant metastatic melanoma have an extremely poor survival rate (National Cancer Institute); the five-year survival rate is 6%, with a median survival time of 6–7.5 months (Bajetta et al., 2002). To date, dacarbazine is the only U.S. Food and Drug Administration (FDA)-approved chemotherapeutic agent to treat advanced melanoma; response rates range from 10%–20%, with a median response duration of four to six months (Bajetta et al.; Tarhini & Agarwala, 2006). In a randomized phase III trial of temozolomide versus dacarbazine, temozolomide demonstrated equivalent efficacy (Middleton et al., 2000). Cytokine-based therapies with

## At a Glance

- ◆ As increasing numbers of novel immunotherapy agents are in development, oncology nurses should continue to expand their knowledge of the immune system's role in the biology of cancer and cancer treatment strategies.
- ◆ Anti-cytotoxic T lymphocyte-associated antigen 4 monoclonal antibody (anti-CTLA4 mAb) therapy, which is designed to manipulate the regulatory mechanism of T-cell activation and T-cell peripheral tolerance, is associated with antitumor activity in some patients with cancer.
- ◆ Antitumor immunity may be augmented through treatment with anti-CTLA4 mAbs, but the associated increase in immune cell activation may cause immune-related adverse events.

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Digital Object Identifier:10.1188/09.CJON.547-554