

## Online Exclusive

# Immunotherapy for Advanced Melanoma: The Emerging Role of Therapeutic Antibodies Against CTLA-4 for Metastatic Melanoma

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The anticytotoxic T-lymphocyte antigen-4 (CTLA-4) monoclonal antibody ipilimumab was approved recently by the U.S. Food and Drug Administration for the treatment of patients with unresectable or metastatic melanoma. Anti-CTLA-4 treatment yields tumor responses or stable disease that may last months or years. Antitumor responses can occur within the first few weeks or even months after initiation of treatment, even as the disease appears to be progressing or new lesions are detected. Most side effects are immune related, consistent with the immune-based mechanism of action, and generally manageable with supportive measures and steroids. With anti-CTLA-4 therapy, patient response differs (both clinically and psychologically) to that generally observed with chemotherapy or other agents used to treat advanced cancer. Patients and caregivers require education about the likely patterns of response to treatment to help them understand why beneficial clinical outcomes may require weeks or months to occur and why continued treatment may be advisable, even when the disease may appear to be progressing. At the author's institution, the staff have noted that patients also need increased psychological support as a result of these clinical features and decisions. Patients and caregivers require instruction on recognition of potential side effects, the importance of reporting them in a timely manner, and their management.

**T**he incidence of melanoma has increased since the 1980s at a faster rate than that observed with any other cancer (Ries et al., 2007), and an expected 70,230 new cases of melanoma will be diagnosed and 8,790 deaths will be attributed to melanoma in the United States in 2011 (Siegel, Ward, Brawley, & Jemal, 2010). Patients with metastatic melanoma (stage IV) have an extremely poor prognosis, with one-year survival rates ranging from 41%–59%, depending on the extent of metastases (Balch et al., 2001).

In the face of limited efficacy with conventional cytotoxic therapy for advanced melanoma, much effort has been made to develop new therapeutic options for this disease. With increased understanding of the complex factors and pathways involved in tumor biology, targeted therapies against specific molecules

### At a Glance

- ◆ Anticytotoxic T-lymphocyte antigen-4 immunotherapy aids the immune system in mounting an effective immune response against solid tumors, such as advanced melanoma.
- ◆ Responses and stable disease resulting from ipilimumab treatment often are long lasting and may occur weeks to months after the start of treatment or after apparent progressive disease or new lesions.
- ◆ The side effects of ipilimumab are mainly immune-related adverse events and generally are responsive to supportive treatment or immunosuppressive steroids.

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