Patients with advanced melanoma have few treatment options, and survival is poor. However, improved understanding of how the immune system interacts with cancer has led to the development of novel therapies. Ipilimumab is a monoclonal antibody that inhibits cytotoxic T-lymphocyte antigen–4 (CTLA-4), a key negative regulator of host T-cell responses. This article presents cases of patients receiving ipilimumab in clinical trials along with a discussion of their significance and relevance to nursing practice. The patients showed different response patterns to ipilimumab and also had various typical immune-related adverse events (irAEs), which were managed successfully. The atypical response patterns produced by ipilimumab likely reflect its mechanism of action, which requires time for the immune system to mount an effective antitumor response. Meanwhile, lesions may appear to enlarge as a consequence of enhanced T-cell infiltration, although this may not necessarily be true disease progression. Patients receiving ipilimumab may respond very differently compared to how they might react to chemotherapy. Responses can take weeks or months to develop; therefore, clinicians should not terminate treatment prematurely, providing the patient’s condition allows for continuation. Early recognition of irAEs combined with prompt management will ensure that events are more likely to resolve without serious consequences.