Adverse Effects of Denileukin Diftitox and Their Management in Patients With Cutaneous T-Cell Lymphoma

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Cutaneous T-cell lymphoma (CTCL) is a rare non-Hodgkin lymphoma with predominant skin manifestations and a relatively indolent course at early stages, but it can be fatal in advanced settings. In the absence of cure, the goal of therapy for CTCL is to induce long-term remissions without further compromising a patient’s immune system or quality of life. Denileukin diftitox (DD) is a fusion protein chemotherapeutic agent used for the treatment of persistent or recurrent CTCL. It binds selectively to the high- and intermediate-affinity interleukin-2 receptor (CD25+) on lymphocytes and is internalized by these cells. Inside the cells, the diphtheria toxin portion of fusion protein is cleaved by proteolytic enzymes, causing cell death. DD produces durable responses and may forestall disease progression. This article reviews DD phase III clinical trial data and summarizes one institution’s clinical experience in the management of the most frequent and clinically significant adverse effects of DD (e.g., acute infusion reactions, capillary leak syndrome, hypoalbuminemia, visual changes, constitutional symptoms, rash, hepatobiliary disorders). Many DD-associated adverse effects can be managed effectively without dose reduction or interruption of treatment with prudent use of supportive care measures.

The annual incidence of CTCL is estimated to be 0.6 cases per 100,000 individuals (Criscione & Weinstock, 2007) and has increased dramatically in the United States since the 1980s, such that CTCL now comprises about 4% of all NHLs (Criscione & Weinstock, 2007). An analysis of epidemiology data from 2001-2005 suggested that about 12,000 individuals in the United States may have been diagnosed with CTCL during this time frame (Bradford, Devesa, Anderson, & Toro, 2009).

CTCL prognosis depends on multiple factors, including the patient’s age at presentation, the type and extent of skin involvement, and the spread of disease to extracutaneous sites. The five-year rate of overall survival is significantly better for patients younger than 57 years versus older than 57 years (80% versus 56%, respectively) (Kim, Liu, Mraz-Gernhard, Varghese, & Hoppe, 2003). Prognosis is excellent for patients with limited patch or plaque disease (stages IA-IIA), less favorable for those with more advanced disease (stages IIB-IV), and poor for those with metastases (stage IVB) (de Coninck, Kim, Varghese, & Hoppe, 2003).