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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.

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Cutaneous T-cell lymphomas (CTCLs) constitute a heterogeneous group of non-Hodgkin lymphomas (NHLs) characterized by skin infiltrates of malignant T memory lymphocytes (National Comprehensive Cancer Network [NCCN], 2012b; Olsen et al., 2007; Willemze et al., 2005). The two most common CTCL variants include mycosis fungoides (MF) and Sézary syndrome (SS). MF, named for the mushroom-shaped tumors that arise on the skin of some patients, accounts for about 60% of all new CTCL cases (NCCN, 2012b). This variant has a relatively indolent clinical course in its early stages and may slowly progress over years to decades. Patients with advanced MF also may have lymph node and visceral organ involvement. The rare SS variant comprises about 5% of all CTCLs. A more aggressive form of the disease, SS is characterized by the presence of malignant lymphocytes in the blood (leukemia) and generalized skin involvement (erythroderma) (Glass et al., 1998; NCCN, 2012b; Olsen et al., 2007; Willemze et al., 2005).

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–IVA), and poor for those with metastases (stage IVB) (de Coninck, Kim, Varghese,