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,
Nursing Strategies
Clinical Journal of Oncology Nursing • Volume 16, Number 5 • Adverse Effects of Denileukin Diftitox
& Hoppe, 2001; Kim, Bishop, Varghese, & Hoppe, 1995; Kim, Chow, Varghese, & Hoppe, 1999; Kim et al., 2003). Five-year survival rates range from 91% for patients with MF affecting less than 10% of total body area (stage IA) to 40% for patients with SS (Bradford et al., 2009). Infection constitutes the most common cause of death in CTCL, with more than 50% of deaths from complications of infection with Staphylococcus aureus, Pseudomonas aeruginosa, or Enterobacteriaceae species (Glass et al., 1998; Habermann & Pittelkow, 2008; Tsambiras, Patel, Greene, Sandin, & Vincent, 2001). As many as 47% of deaths are from cardiopulmonary disease (cause not explored in this study) and secondary malignancy (Habermann & Pittelkow, 2008).

The long-term nature of the disease, pruritus, ulceration of the tumors, secondary odorous pyogenic skin infection, and scaly skin lesions can have a profound negative effect on the quality of life of these patients. In addition, about 40% of patients report pain (Demierre, Gan, Jones, & Miller, 2006). Palmar and planter keratoderma often present with incapacitating, nonhealing fissures, which cause significant discomfort for the patient and are a site of entry for infection (Leukemia & Lymphoma Society, 2006). Intense pruritus, edema, and constant exfoliation often are associated with erythrodermic CTCL (Willemze et al., 2005). These symptoms may lead to sleep disturbance, missed days of work, limitations in normal daily activities, depression, feelings of frustration, anger, embarrassment, and shame, and may reduce intimacy with loved ones (Demierre et al., 2006) (see Table 1). The physical and psychosocial effects of CTCL on the patient have important implications for nursing care (see Table 2).

A number of therapies are available for CTCL (Lansigan & Foss, 2010; NCCN, 2012b; Prince, Whittaker, & Hoppe, 2009); however, none is curative. Patients with early-stage CTCL involving skin patches or plaques without lymph node involvement usually receive treatment with skin-directed therapies, such as light therapy and/or topically applied creams and ointments. Patients with tumors, lymph node involvement, visceral disease, and/or erythroderma (advanced-stage disease), as well as those who do not respond to skin-directed therapies, require systemic treatment with agents such as bexarotene, interferon-α, denileukin diftitox (DD), romidepsin, vorinostat, and single-agent chemotherapy (e.g., low-dose methotrexate, gemcitabine, pentostatin, temozolomide, bortezomib, doxorubicin) or multiagent chemotherapy (NCCN, 2012b).

Denileukin Diftitox Therapy for Cutaneous T-Cell Lymphoma

DD is indicated for the treatment of a select group of patients with persistent or recurrent CTCL (Eisai Inc., 2010). In the United States, DD is indicated for patients with CTCL with malignant T cells that express the alpha chain of the interleukin-2 (IL-2) receptor (CD25+), although recent data show that DD also is effective against disease considered to have low expression of CD25 (Negro-Vilar et al., 2008a; Prince, Duvic, Martin, & Fivenson, 2011).

Mechanism of Action

DD is a genetically engineered fusion protein composed of the enzymatically active domain of the diphtheria toxin, which lacks a receptor portion capable of infecting the cells, followed by sequences of human IL-2. It does not cause generalized diphtheria-related toxicity because the cell-binding parts were removed from the diphtheria molecule and replaced by the IL-2 segment targeting only those cells bearing the IL-2 receptor (Foss, 2000). DD binds to the IL-2 receptor and internalizes within cells, allowing the diphtheria toxin components to be released into the cell cytosol, leading to irreversible inhibition of protein synthesis and resulting in cell death (Bacha et al., 1988; Waters et al., 1990; Williams, Snider, Strom, & Murphy, 1990).

Administration and Efficacy

DD is administered at 9 or 18 mcg/kg per day as an IV infusion over 30–60 minutes for five consecutive days every 21 days. The prescribing information indicates that up to eight DD cycles may be administered (Eisai Inc., 2010).

DD showed efficacy in CTCL in three phase III clinical trials conducted to date (Negro-Vilar et al., 2008a; Olsen et al., 2001; Prince et al., 2010). In the first phase III trial (Study L-10), which compared two different doses of DD (9 and 18 mcg/kg per day) in extensively pretreated patients with CD25+ CTCL, TABLE 1. Addressing Impairment of ADL in Patients With CTCL

<table>
<thead>
<tr>
<th>ADL Impairment</th>
<th>Impact on Patient</th>
<th>Nursing Strategies</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperkeratosis, palms and soles</td>
<td>Decreased dexterity and fine motor skills (e.g., inability to button or pull zippers, difficulty holding pen or pencil); mobility issues (e.g., difficulty walking)</td>
<td>Consult occupational therapy for adaptive equipment and clothing; apply topical skin care therapies as prescribed (consult dermatology as needed).</td>
<td>Use of medicated ointments under occlusion (socks or gloves) may help to close fissures and to prevent or decrease hyperkeratotic skin build-up</td>
</tr>
<tr>
<td>Deconditioning</td>
<td>Weakness; at risk for falls</td>
<td>Consult physical therapy for assessment and strengthening program.</td>
<td>Assess independence, fall risk, and need for visiting nurses.</td>
</tr>
<tr>
<td>Extremity edema</td>
<td>Decreased mobility and comfort; increased risk of falls; increased inflammation or erythema in affected areas</td>
<td>Elevate extremities; utilize compression management; suggest adaptive shoes; assess nutritional status.</td>
<td>Monitor albumin and protein status; consider medications for gentle diuresis; consult nutritionist as needed.</td>
</tr>
<tr>
<td>Ectropion and dry eyes</td>
<td>Diminished visual acuity and comfort; increased tearing</td>
<td>Consult ophthalmology; suggest use of artificial tears as needed.</td>
<td>Surgical repair of ectropion may be an option*</td>
</tr>
</tbody>
</table>

*Vallabhanath & Carter, 2000

ADL—activities of daily living; CTCL—cutaneous T-cell lymphoma

TABLE 2. Nursing Care Concerns for Patients With Cutaneous T-Cell Lymphoma (CTCL)

<table>
<thead>
<tr>
<th>Nursing Care Issue</th>
<th>Patient Education</th>
<th>Assessment and Interventions</th>
</tr>
</thead>
</table>
| Alteration in skin integrity | **Skin care**  
• Emollients are important to maintain the skin barrier and to reduce symptoms of erythema, dryness, and pruritus.  
  – Ointment-based  
  – Ceramide creams  
  – Lotions or solutions for hair-bearing areas  
  • Prescribed topical medications  
  • Steroid examples include: triamcinolone 0.1% (for body-sparing face, groin, and axilla); hydrocortisone 1%–2% for face/intertriginous areas; clobetasol solution 0.05% for the scalp  
  • Chemotherapy (e.g., mechlorethamine)  
  • Antibacterials, such as mupirocin  
  • Application techniques  
  – Apply thin layer of medication or emollient in direction of hair growth; skin should feel slightly tacky but without any excess medication to the touch.  
  • Signs of skin infection  
  – Honey-colored crusts  
  – Multiple excoriated areas with erythematous base and inflammation  
  – Fever and chills | Nutrition and hydration  
• Monitor electrolytes, albumin, and protein levels.  
• Ensure diet is adequate to cover nutritional needs.  
• Monitor for edema and refer to compression management, as indicated.  
**Skin integrity—monitor for:**  
• Wounds  
• Ulcers  
• Excoriations (evidence of scratching)  
• Infection  
• Honey crust  
• Exudate  
• Febrile |
| Alteration in comfort: pruritus | **Antipruritic agents**  
• Sedating agents (use with caution in older adults)  
  – Diphenhydramine hydrochloride  
  – Hydroxyzine hydrochloride  
  • Non-sedating agents  
  – Cetirizine hydrochloride  
  – Fexofenadine  
  – Loratadine  
**Moisturization and humidification**  
• Skin  
• Home  
**Breaking the scratch/itch cycle**  
• Diversion  
• Distraction techniques  
• Cold compresses  
• Oatmeal baths  
• Mentholated or cooling topicals  
• Nonirritating clothing | Evaluate and address antipruritic effectiveness.  
• Assess for adequate skin moisturization.  
• Emphasize importance of moisture and assess patient compliance with prescribed regimen.  
• Discuss strategies with the patient to develop a plan of action to cope with intense pruritus. |
| Alteration in homeostasis: cold intolerance and/or inability to perspire | **Strategies to cope with cold intolerance**  
• Warm, draft-free environment  
• Layer clothing to hold body heat.  
• Avoid overexposure in hot weather if unable to perspire.  
• Adequate hydration | Ensure patient comfort.  
• Assess for infection.  
  – Low-grade fever may indicate a serious infection due to thermal dysregulation. |
| Alteration in comfort: pain | **Reported symptoms of pain**  
• Pain is treatable.  
• Skin pain is valid.  
• Utilization of skin protective and/or comfort measures  
• Adequate moisturization  
• Appropriate clothing choices  
• Petroleum-like dressings to cover ulcerated or denuded skin  
• Frequent position changes  
• Warm or cool compresses | Assess type and quality of pain.  
• Assess and treat for infection.  
• Utilize appropriate pain relief measures.  
  – Pain medications  
  – Adequate moisturization  
  – Special dressings  
  – Topical applications including occlusion to increase effectiveness of topical agents |
| Potential for infection | **Infection-prone skin**  
Vigilant skin care required to prevent bacterial overgrowth  
• Topical antibiotics to open areas  
• Bleach or vinegar baths  
• Dilute ¼ to ½ cup of bleach or vinegar to bath tub (as tolerated); patient should soak for 20–30 minutes, pat dry, and apply topical medications as prescribed. | Skin affected by CTCL is more prone to bacterial superinfection, especially with erythroderma, Sézary syndrome, and eroded plaques and tumors.  
• Skin cultures and oral antibiotics as appropriate  
• Avoidance of central lines due to increased risk of bacterial sepsis |

TABLE 2. Nursing Care Concerns for Patients With Cutaneous T-Cell Lymphoma (Continued)

<table>
<thead>
<tr>
<th>Nursing Care Issue</th>
<th>Patient Education</th>
<th>Assessment and Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychosocial issues of emotional distress (de-nial, anger, depression); self-image and sexuality; socioeconomic concerns</td>
<td>Coping strategies for cancer diagnosis and chronic illness</td>
<td>Provide appropriate mental health, social service, and support or networking referrals.</td>
</tr>
<tr>
<td></td>
<td>• Online support groups</td>
<td></td>
</tr>
<tr>
<td></td>
<td>— Cutaneous Lymphoma Foundation ([<a href="http://www.clfoundation.org">www.clfoundation.org</a>])</td>
<td></td>
</tr>
<tr>
<td></td>
<td>— Leukemia and Lymphoma Society ([<a href="http://www.lls.org">www.lls.org</a>])</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Patient education forums</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Resources (local, national, and patient assistance programs)</td>
<td></td>
</tr>
<tr>
<td>Knowledge deficits (disease, treatment options, chronic disease management)</td>
<td>• Disease process</td>
<td>• Provide written and oral instruction.</td>
</tr>
<tr>
<td></td>
<td>• Therapeutic options</td>
<td>• Ensure opportunity to review or ask questions.</td>
</tr>
<tr>
<td></td>
<td>• Required follow-up</td>
<td>• Refer to appropriate Internet information sources.</td>
</tr>
<tr>
<td></td>
<td>• Appropriate Internet information sources</td>
<td>• Evaluate need for reinforcement of information.</td>
</tr>
</tbody>
</table>


the overall response rate (ORR) was 30% (a 10% complete response rate and a 20% partial response); the median duration of response was 6.9 months (Olsen et al., 2001). Patients in that trial received a median of six DD cycles. In the second phase III trial (Study L-11), which compared the same two doses of DD (9 and 18 mcg/kg per day) versus placebo in a less heavily pretreated population, the ORR for both DD arms was 44% compared with 16% for placebo (Prince et al., 2010). In addition, progression-free survival was significantly longer for patients randomized to DD compared with patients randomized to placebo (794–971 versus 124 days, respectively; p ≤ 0.002). Patients in this study received a median of seven and six DD cycles of 9 mcg/kg per day and 18 mcg/kg per day, respectively. The third phase III trial (Study L-14) of DD, which was an open-label companion study to L-11 that enrolled patients assigned to the placebo arm, those with stable or relapsed disease after DD treatment, or those who were excluded from the study because of CD25-low expression status, identified ORRs (28% or higher) similar to those in the previous phase III trials, as well as median progression-free survival of 205 days (Negro-Vilar et al., 2008b).

Toxicities and Management

In phase III clinical trials involving a total of 234 patients, the most frequently reported adverse events (20% or higher) were pyrexia, nausea, rigors, fatigue, headache, vomiting, peripheral edema, diarrhea, cough, dyspnea, and pruritus, and the most common serious adverse events were capillary leak syndrome, infusion reactions, and visual changes (Eisai Inc., 2010) (see Table 3). The occurrence of adverse events tended to diminish in frequency and severity after the first two DD courses. The occurrence and management of select DD-associated adverse effects that may require additional patient monitoring by nursing staff are reviewed in this article. A summary of prevention and management strategies for those events is provided in Table 4.

Constitutional Symptoms

Constitutional or flu-like symptoms are commonly associated with DD administration and include fever, nausea, vomiting, fatigue, rigors, headache, and diarrhea. Premedication with acetaminophen, an antihistamine, and corticosteroid prior to each DD infusion can help limit the incidence and severity of these adverse events. These medications also can be administered postinfusion.

Fever typically develops 48–72 hours after DD administration. A complete blood count with differential, blood and urine cultures, and a chest X-ray in patients with a temperature exceeding 101ºF would be the next steps in determining a differential diagnosis, because infection is not an uncommon complication in patients with CTCL (Walker & Dang, 2004).

Antiemetic prophylaxis is needed only on a case-by-case basis. Given that 15%–35% of patients treated with DD experienced vomiting in phase III clinical trials, DD is considered to have a low (10%–30%) emetic risk; therefore, appropriate antiemetic prophylaxis involves dexamethasone (Kris et al., 2006; NCCN, 2012a). If nausea persists despite dexamethasone prophylaxis, the addition of a 5-HT₃ serotonin receptor antagonist (e.g., dolasetron, granisetron, ondansetron, palonosetron) and, in severe cases, aprepitant may help to limit those adverse effects (Kris et al., 2006). In the authors’ experience, appropriate pretreatment almost always alleviates nausea in patients.

DD-associated fatigue tends to be most severe during the first treatment cycle, subsiding in the weeks thereafter. Patients should be informed of this timing and encouraged to pace daily activities and allow for rest periods accordingly. Other approaches to managing fatigue include improving nutrition and ensuring adequate hydration. Unrelenting fatigue in a patient requires an evaluation of possible coexisting causes, such as anemia, drug-induced hepatitis, electrolyte imbalance, poor nutrition, depression, and hypothyroidism, among other causes.

Patient education and support during the first several cycles of DD is particularly important because of the increased likelihood
TABLE 3. Adverse Events Occurring in 15% or More of All Patients, Regardless of Relationship to Drug

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>DD-Treated Patients&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Grade</td>
<td>Grade 3 or 4</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td></td>
</tr>
<tr>
<td>Pyrexia</td>
<td>57</td>
</tr>
<tr>
<td>Fatigue</td>
<td>45</td>
</tr>
<tr>
<td>Rigors</td>
<td>45</td>
</tr>
<tr>
<td>Peripheral edema</td>
<td>23</td>
</tr>
<tr>
<td>Askenia</td>
<td>18</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>54</td>
</tr>
<tr>
<td>Vomiting</td>
<td>25</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>22</td>
</tr>
<tr>
<td>Anorexia</td>
<td>15</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>27</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>22</td>
</tr>
<tr>
<td>Pruritus</td>
<td>17</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td></td>
</tr>
<tr>
<td>Myalgia</td>
<td>19</td>
</tr>
<tr>
<td>Back pain</td>
<td>17</td>
</tr>
<tr>
<td>Respiratory, thoracic, and mediastinal disorders</td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>19</td>
</tr>
</tbody>
</table>

<sup>a</sup> N = 100, but more than one event per category may apply to each participant

DD—denileukin diftitox

Note. Based on information from Prince et al., 2010.

do side effects occurring during initial cycles. When patients are prepared for any expected side effects and are provided with supportive care, successful treatment adherence is more likely.

Liver Test Abnormality

Across the phase III trials, 84% of patients developed transient elevations from baseline in alanine aminotransferase or aspartate aminotransferase during treatment with DD (Eisai Inc., 2010). The majority of those events occurred during the first or second DD course and resolved within two weeks, without the need for medical intervention or discontinuation of DD. If transaminase levels are found to be elevated by liver function testing conducted prior to a course of DD, treatment should be held and the decision of when to resume DD is left to the discretion of the healthcare provider. A conservative approach is to delay DD administration until transaminase levels return to grade 1 (i.e., 2.5 times or less the upper limit of normal) or lower (Dang et al., 2004; Walker & Dang, 2004).

Acute Infusion Reactions

Acute infusion reactions associated with DD are defined as symptoms occurring within 24 hours of infusion and resolving within 48 hours of the last infusion within that course. Such symptoms may include acute back or chest pain, hypotension, dyspnea, angioedema, pruritus, or rash (Olsen et al., 2001). Seventy-one percent of patients experienced acute infusion reactions in the phase III trials after DD administration (Eisai Inc., 2010). Those events required emergent care in about 8% of patients. The incidence of infusion reactions was higher during the first two courses of DD compared with the third and fourth courses. In addition, infusion reactions resulting in death have been reported in postmarketing research (Eisai Inc., 2010).

Possible causes of acute infusion reactions include the release of cytokines and/or mast cell degranulation (Foss et al., 2001; Shao, Kuzel, Osann, & Foss, 2000). To limit infusion reactions, premedication with dexamethasone, acetaminophen, and an antihistamine was administered prior to each DD infusion (Dang et al., 2007; Lansigan & Foss, 2010). Premedication with a corticosteroid (dexamethasone 8 mg or prednisone 20 mg) can dramatically reduce the incidence of infusion-related events (Foss et al., 2001; Shao et al., 2000). In the pivotal trial, the use of steroids as premedication or concomitant medication generally was not permitted (Olsen et al., 2001). Corticosteroids do not interfere with the mechanism of action of DD or its efficacy and, in fact, combining DD with corticosteroids may improve overall responses to therapy (Foss et al., 2001). The authors prescribed a regimen of prednisone 20 mg by mouth daily two days prior to day one of each cycle and daily before each infusion.

Should infusion reactions occur, they may be managed by decreasing the rate of or interrupting the DD infusion. In the case of serious infusion reactions, such as anaphylaxis, DD infusion should be immediately and permanently discontinued (Eisai Inc., 2010). At the authors’ institution, rechallenge with DD may be considered on a case-by-case basis for serious infusion reactions other than allergic reactions, with the appropriate premedications, a lower dose, and a decreased rate of infusion. Resuscitative equipment should be available any time DD is administered, in the event that serious infusion reactions occur.

Capillary Leak Syndrome

DD-associated capillary leak syndrome is defined as the occurrence of at least two of the following three symptoms at any time during DD treatment: edema, hypotension, and serum albumin less than 3.0 g/dl (Eisai Inc., 2010). Using that definition, about 33% of patients treated with DD experienced capillary leak syndrome in phase III trials, and one-third of those patients required either hospitalization or medical intervention to prevent hospitalization (Eisai Inc., 2010). Symptoms of capillary leak syndrome usually appeared within the first two weeks following infusion. After the first two DD cycles, the occurrence of capillary leak syndrome typically is decreased. However, symptoms may persist or worsen even after DD cessation. Appropriate patient selection and monitoring are crucial in the management of these patients, as severe capillary leak syndrome resulting in death may occur.

The cause of capillary leak syndrome may be related to dehydration, hypoalbuminemia, and/or an increase in capillary permeability (Olsen et al., 2001). Therefore, low serum albumin levels prior to DD administration and preexisting edema are risk factors for the development of capillary leak syndrome (Eisai Inc., 2010). Precautionary measures should be taken when administering DD to patients with preexisting cardiovascular
disease (Olsen et al., 2001). At a minimum, patients with known cardiovascular disease should be well controlled and stabilized prior to initiating DD therapy. At the authors’ institution, patients with stable cardiovascular disease may receive a lower dose of DD at a decreased frequency during initial cycles of treatment to mitigate potential side effects, along with judicious use of diuretics and overall fluid and compression management as indicated. Additional monitoring includes careful assessment of electrocardiogram changes, electrolytes, and pulmonary status. The authors’ experience suggests that advanced patient age may further increase the risk for developing capillary leak syndrome. To mitigate that risk, outpatient monitoring of serum albumin, weight, edema, and blood pressure should be undertaken (Olsen et al., 2001). Electrolytes, liver function tests, albumin, and a complete blood count with differential should be checked weekly during the DD cycles to evaluate for potential risk factors. DD administration should be withheld for patients with serum albumin below 3 g/dl. Patients should be weighed daily during infusion weeks, and consideration should be given to withholding DD infusion if weight gain exceeds 1.5 kg from one day to the next. Patients should be instructed to weigh themselves daily at home and to report an overnight weight gain of 1 kg or more, along with unusual swelling or edema, increased coughing or difficulty breathing, or feelings of light-headedness. Pretreatment with dexamethasone or prednisone before each dose of DD has reduced the incidence of capillary leak syndrome, compared with that reported in trials that did not use steroid premedication (Foss et al., 2001), and decreased the incidence of grade 3 or 4 edema (Shao et al., 2000). Another way to decrease the risk for edema is

<table>
<thead>
<tr>
<th>TABLE 4. Prevention and Management Strategies for Adverse Effects of DD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adverse Effect</strong></td>
</tr>
<tr>
<td>Acute infusion reactions</td>
</tr>
<tr>
<td>Capillary leak syndrome</td>
</tr>
<tr>
<td>Constitutional symptoms</td>
</tr>
<tr>
<td>Hepatobiliary disorders</td>
</tr>
<tr>
<td>Hypoalbuminemia</td>
</tr>
<tr>
<td>Rash</td>
</tr>
<tr>
<td>Visual changes</td>
</tr>
</tbody>
</table>

CTCL—cutaneous T-cell lymphoma; DD—denileukin diftitox
Implications for Practice

- Treatment strategies for patients with cutaneous T-cell lymphoma (CTCL) aim to induce durable remission while preserving adequate quality of life, as no cure is available.
- One treatment option, denileukin diftitox, may elicit long-term responses in patients with persistent or recurrent CTCL.
- The oncology nurse can support patients with CTCL in managing anticipated adverse effects associated with denileukin diftitox, avoiding dose reductions or delays and ensuring each patient’s successful therapy.

administration of diuretics, although slow hydration may reduce the risk for developing hypotension (Olsen et al., 2001).

Management of capillary leak syndrome is symptom-driven and depends on whether hypotension or edema is the primary clinical problem (Olsen et al., 2001). IV fluid replacement with colloids may be warranted for patients who present with dehydration or intravascular fluid depletion. Harsh diuretics should be avoided to prevent the exacerbation of fluid shifts, particularly in patients with uncorrected intravascular depletion. In contrast, aggressive diuresis may be appropriate for patients who present primarily with edema, so long as careful monitoring of weight, blood pressure, and electrolytes is continued. In addition, supportive care including rest, oral hydration, and proper nutrition are key factors in maintaining good nutritional status and, therefore, serum protein level. Intensive care monitoring and use of vasopressive drugs may be warranted in the event of hemodynamic collapse.

Hypoalbuminemia

Hypoalbuminemia secondary to capillary leak syndrome as a consequence of vascular leakage typically occurs about one to two weeks after the initiation of DD therapy. In addition to the prevention and management strategies presented in this article, the authors encourage patients to drink high-protein shakes as a supplement to daily meals during DD therapy to help maintain adequate serum protein and albumin levels. Patients undergoing DD therapy who are experiencing hypoalbuminemia and having difficulty increasing protein in their diet may benefit from a referral for nutritional counseling to receive recommendations for palatable and practical high-protein foods and supplements.

Visual Changes

In the three clinical studies discussed, vision impairment following DD administration was reported in 4% of patients (Eisai Inc., 2010). Those events included loss of color vision, with or without retinal pigment mottling (Park et al., 2007; Ruddle, Harper, Hömemann, Seymour, & Prince, 2006). Visual changes resolved in some of the affected patients; however, one patient reported some degree of persistent visual impairment. The retinal antigen has been suggested to be highly immunogenic but remains invisible to the immune system, owing to the presence of regulatory CD25+ T cells suppressing an undesirable immune response. However, their depletion by DD may reveal the retinal antigen to the immune system, thereby causing retinal damage from attack by the immune cells (Park et al., 2007; Ruddle et al., 2006).

Color vision examination (pseudochromatic [Ishihara] plates) with routine ophthalmologic screening of patients receiving DD is important to establish and document baseline conditions and assess ongoing ophthalmologic health. If DD-treated patients report symptoms consistent with loss of visual acuity or color vision, a complete patient evaluation and ophthalmologic examination is recommended to identify the potential causes of the symptoms (Ruddle et al., 2006).

Rash

Drug-related rash occurred in about 20% of patients in the phase III clinical trials of DD (Eisai Inc., 2010). Multiple descriptions of the DD rash were reported, including generalized maculopapular, petechial, vesicular, bullous, urticarial, and/or eczematous. Distinguishing DD-associated reaction from underlying CTCL lesions is important to employ appropriate management strategies. Several proactive measures carried out by patients can help maintain skin integrity during DD treatment, including adequate hydration (1–3 L of fluid per day), use of tepid water when bathing, and liberal use of moisturizing lotions. New non-CTCL rash that develops following DD administration can be treated with antihistamines, topical or oral steroids, and/or emollients (Olsen et al., 2001). In the authors’ experience, appropriate pretreatment of patients with oral steroids and antihistamines prior to DD therapy considerably decreases the incidence of rashes.

Conclusion

As with any antineoplastic agent, consistent therapy compliance is crucial for achieving optimal clinical outcomes. As such, management of adverse effects associated with therapy is key to ensuring that the recommended dose of treatment is consistent and continuously administered. Centers treating patients with CTCL need to have an established multidisciplinary model of care between oncologists and dermatologists to appropriately treat the disease and to care for the range of symptoms associated with CTCL and its treatment with DD or other agents.

The overall clinical experience with DD demonstrates that the agent is generally well tolerated with careful patient assessment and monitoring, with most side effects being mild to moderate in severity. Most associated adverse effects are manageable and often are transient or self-limiting. Judicious management of anticipated adverse effects can successfully see many patients through therapy.

Of critical importance in the success of DD therapy is the oncology nurse’s role in educating the patient about DD and its expected side effects and supporting the patient in all aspects of care.
clinical care. Patient education to promote understanding is best done with a face-to-face review of the adverse effects associated with therapy, providing printed teaching materials that outline the adverse effects along with contact information for the oncology nurses, mid-level providers, and physicians. Weekly follow-up calls by the oncology nurse to monitor and assess possible side effects related to therapy also are critical to successful outcomes. In addition, patients should be instructed to contact their physician or report to the emergency room should any major problems or signs or symptoms of infection emerge. Such strategies will help to ensure optimal patient care, including the best possible chance of success with DD therapy.

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