Nursing Considerations for Clofarabine in the Treatment of Acute Lymphoblastic Leukemia in Children

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Each year, almost 3,500 children are diagnosed with leukemia, representing approximately 30% of pediatric cancer cases. Acute lymphoblastic leukemia is the most common form of pediatric leukemia, accounting for approximately 80% of cases. A significant number of children fail to respond to existing chemotherapies or are unable to maintain remission. Their prognosis is poor, with little hope for long-term survival.

Clofarabine is a next-generation purine nucleoside analog (NA) approved by the U.S. Food and Drug Administration for use in children with relapsed or refractory acute lymphoblastic leukemia (ALL). In clinical trials, clofarabine induced remission in heavily pretreated patients with limited therapy options. Most treatment-related side effects have been manageable and reversible with appropriate therapeutic interventions. Side effects associated with clofarabine are similar to other chemotherapeutic agents and are manageable with proper treatment.

As knowledgeable participants in the management of patients with complex, life-threatening diseases, nurses can facilitate a successful outcome through educating patients and their families and by actively intervening to prevent or reduce side effects.

Current Treatment of Pediatric Acute Lymphoblastic Leukemias

Initial Disease

The key to securing long-term survival in children diagnosed with ALL is to achieve a complete and durable remission through aggressive induction chemotherapy followed by delayed intensification and maintenance therapy. Most protocols recommend less toxic regimens for low- or standard-risk patients and more aggressive regimens for patients at higher risk. The presence of certain characteristics at initial diagnosis appears to be associated with more favorable prognoses. Factors such as age (1–10 years) and initial low white blood cell counts (less than 50,000/mcl) (see Figure 1) appear to signify a more positive outcome. Conversely, patients who are older than 10 years, with higher initial white blood cell counts (more than 50,000/mcl) or who also have certain chromosomal abnormalities, have less favorable prognoses (Bleyer, 1997; Weinstein & Tarbell, 2001). Immunophenotype is another prognostic factor. Patients with pre–B-cell leukemia are considered to have standard risk, whereas patients with T-cell

At a Glance

✦ Clofarabine is a nucleoside analog approved for treatment of relapsed or refractory acute lymphoblastic leukemia in pediatric patients.

✦ The recommended dose of clofarabine in children is 52 mg/m² per day for five consecutive days.

✦ Side effects of clofarabine are similar to those seen with other chemotherapeutic agents and are manageable with timely and appropriate nursing interventions.
leukemia historically have had poorer prognoses, with shorter remission duration and decreased overall survival (Margolin, Steuber, & Poplack, 2002). More aggressive and potentially more toxic regimens have been used for patients considered at higher risk.

A standard four-week induction regimen in low-risk patients with ALL includes vincristine, a steroid (prednisone or dexamethasone), and L-asparaginase. In higher-risk patients, anthracycline (daunorubicin or doxorubicin) or cyclophosphamide is added to the regimen (Rubnitz & Pui, 2003; Uderzo et al., 2001; Vora, 2002; Weinstein & Tarbell, 2001). Most patients receive some form of delayed intensification therapy in which the drugs used during induction are repeated, followed by at least two years of maintenance or continuation therapy (e.g., daily 6-mercaptopurine plus intermittent low-dose methotrexate with intermittent monthly pulses of vincristine and steroids) and central nervous system (CNS) disease prophylaxis (Rubnitz & Pui; Weinstein & Tarbell). The rationale behind periodically intensifying treatment has been that drug-resistant strains are less likely to develop with episodic use of high-dose drugs and that toxicity may be reduced by using the drugs for brief, intense periods. In addition, the CNS has been a frequent site of disease relapse because it can serve as a reservoir for leukemia cells and most systemically administered chemotherapy does not effectively cross the blood-brain barrier (Westlake & Bertolone, 2002). Therefore, the standard of care for pediatric ALL involves some form of intrathecally administered CNS prophylaxis. These measures have yielded overall long-term survival rates now approaching 80% (Margolin et al., 2002).

**Refractory and Relapsed Disease**

Despite the dramatic improvements offered by induction regimens, approximately 5% of children with ALL do not respond to the first induction attempt and as many as 20%-25% do not maintain remission (Gaynon et al., 2000; Leukemia and Lymphoma Society, 2003). Upon relapse, key prognostic factors are the (a) duration of initial remission, with a much higher likelihood of survival in patients with late relapse, and (b) site of relapse, with poorer prognosis in bone marrow relapse versus extramedullary disease (Boulad et al., 1999; Buchanan et al., 2000; McCarthy, Pitcher, Hann, & Oakhill, 1999). In general, patients with a longer duration of remission have a better prognosis than patients who relapse early in treatment. Patients who relapse within three years of achieving remission may be considered “early,” with a poorer chance of survival (Weinstein & Tarbell, 2001).

For first relapse in patients with ALL, reinduction therapies may be similar to prior induction regimens but with increased intensity, especially for patients who experience late relapses. The majority (approximately 80%) of children will achieve second remission; however, remission is less likely to be sustained without a hematopoietic stem cell transplant (HSCT) (Boulad et al., 1999; Buchanan et al., 2000). In patients who achieve remission, allogeneic HSCT is considered, especially in early relapse patients and those with human leukocyte antigen–matched related donors (Boulad et al.). Treatment of a second or third relapse is more difficult because of a greater likelihood of drug resistance and accumulated toxicities from prior regimens.

**Clofarabine Overview**

Clofarabine (Clofarabine, Genzyme Corporation, Cambridge, MA) is a chemotherapy agent approved in December 2004 for pediatric patients with refractory or relapsed ALL aged 1–21 years who have failed two prior regimens. Clofarabine offers an important new treatment alternative for patients with relapsed or refractory ALL who have few viable therapeutic options.

Clofarabine is a next-generation purine NA, which is a broad class of agents that slow or prevent reproduction of malignant cells by interfering with DNA synthesis (Galmarini, 2002). Older NAs, such as fludarabine or cladribine, have been associated with potentially severe neurologic effects. Adverse events associated with neurologic toxicity such as agitation, confusion, visual disturbances, and coma have been reported in a small percentage of patients taking fludarabine at the recommended dose for chronic lymphocytic leukemia (Berlex Laboratories, Inc., 2003; Ortho Biotech Products, LP, 2002). Clofarabine and fludarabine have similar structures and modes of action, but the degree of neurologic toxicity has not been observed with clofarabine. Although the possibility of severe neurologic effects of clofarabine cannot be ruled out, clofarabine appears to have limited ability to penetrate the CNS. Additional monitoring for these types of toxicity is ongoing.

**Mechanism of Action**

Clofarabine was designed to improve the efficacy of the purine NAs in acute leukemia by combining the most favorable cytotoxic properties of fludarabine and cladribine (Gandhi et al., 2003) while attempting to reduce the likelihood of serious adverse events. Clofarabine appears to have a dual mechanism of action (Gandhi et al.). First, it slows or halts the reproduction of leukemic cells by interfering with DNA replication. Like fludarabine, the active form of clofarabine inhibits the activity of DNA polymerase, which, in turn, terminates elongation of
the DNA chain or limits a cell’s ability to repair chain breaks. Like cladribine, it inhibits ribonucleotide reductase, which also interferes with DNA synthesis and cell reproduction. Second, clofarabine directly promotes programmed death of leukemic cells by disrupting the membrane of the mitochondria in the nucleus of the leukemia cell leading to the release of cytochrome C and other factors that cause apoptosis, including caspase 3 (Genini et al., 2000).

Pharmacokinetics

The pharmacokinetic properties of clofarabine in different patient populations still are under investigation but have been shown to be weight dependent. In a 40 kg pediatric patient, the half-life of clofarabine is relatively short (6.4 hours), with total systemic clearance of 32.8 L per hour (27% between-subject variability) and a volume of distribution at a steady state of 210 L (72% between-subject variability) (Bonate et al., 2004). Clearance is balanced, with approximately 50% of the drug excreted renally. Following this model, clofarabine would have a shorter half-life in smaller patients; therefore, a 10 kg patient would have a clofarabine half-life of approximately four to five hours (Bonate et al.).

Clinical Studies

The rationale for clinical studies of clofarabine was provided by in vitro studies that demonstrated its potent cytotoxic activity in hematologic malignancies and solid tumors (i.e., leukemia; melanoma; and non-small cell lung, colon, ovarian, renal, prostate, and breast cancer lines). Clofarabine has shown therapeutic activity in leukemia, colon, and mammary malignancies in animal and xenograft tumor models. In addition, clofarabine has proven activity against a wide range of human tumor models of hematologic and solid tumor types, both in vivo and in vitro (ILEX Products, Inc., and Genzyme Corporation, 2004c).

Phase I clinical studies of clofarabine in children and adults were initiated by the University of Texas M.D. Anderson Cancer Center in 1999. The studies established the maximum tolerated dose of clofarabine and demonstrated promising antileukemic activity in children and adults. The maximum tolerated dose in children was 52 mg/m² per day for five days, which was higher than the 40 mg/m² per day determined for adults. The dose-limiting toxicities were reversible skin rash and liver toxicity (Jeha et al., 2004; Kantarjian et al., 2003). In general, children are thought to tolerate higher doses of clofarabine because of less end-organ toxicity and faster clearance of drug compared to adult patients.

Following phase I trials, two multicenter phase II trials for pediatric patients with refractory or relapsed ALL and acute myeloid leukemia (AML) were conducted. Enrolled patients were aged 1–21 years at diagnosis, had a poor prognosis, and were heavily pretreated. All patients had undergone two to six prior regimens (median number of prior regimens was three), and 35 were refractory to one or more prior regimens. Thirty percent of patients with ALL (18 of 61) and 43% of patients with AML (18 of 42) had failed previous HSCT. Key efficacy results are summarized in Table 1. In the ALL study, of the 61 children evaluated, the response rate was 30% with

### Table 1. Clofarabine Efficacy in Acute Pediatric Leukemia in Phase II Clinical Trials

<table>
<thead>
<tr>
<th>END POINT</th>
<th>ALL STUDY (N = 61)</th>
<th>AML STUDY (N = 42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>12% (7 patients)</td>
<td>–</td>
</tr>
<tr>
<td>CRp</td>
<td>8% (5 patients)</td>
<td>2% (1 patient)</td>
</tr>
<tr>
<td>Partial response</td>
<td>10% (6 patients)</td>
<td>24% (10 patients)</td>
</tr>
<tr>
<td>Median survival</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Responders</td>
<td>53.7 weeks</td>
<td>35.6 weeks</td>
</tr>
<tr>
<td>Nonresponders</td>
<td>7.6 weeks</td>
<td>14.4 weeks</td>
</tr>
<tr>
<td>Median duration of remission</td>
<td>Responders (CR + CRp)</td>
<td>28.6 weeks</td>
</tr>
<tr>
<td></td>
<td>12.4 weeks</td>
<td></td>
</tr>
</tbody>
</table>

All—acute lymphoblastic leukemia; AML—acute myeloid leukemia; CR—complete response; CRp—complete response without platelet recovery

### Table 2. Response Definitions

<table>
<thead>
<tr>
<th>RESPONSE CATEGORY</th>
<th>RESPONSE CRITERIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete response (CR)</td>
<td>No evidence of circulating blasts or extramedullary disease</td>
</tr>
<tr>
<td>M1 bone marrow (≤ 5% blasts) (for acute myeloid leukemia [AML] &lt; 5% blasts)</td>
<td></td>
</tr>
<tr>
<td>Recovery of peripheral counts (platelets ≥ 100 × 10⁹/L and absolute neutrophil count ≥ 1.0 × 10⁹/L)</td>
<td></td>
</tr>
<tr>
<td>CR without platelet recovery (CRp)</td>
<td>Meets all of the criteria for CR except platelet recovery to ≥ 100 × 10⁹/L</td>
</tr>
<tr>
<td>Partial response</td>
<td>Complete disappearance of circulating blasts</td>
</tr>
<tr>
<td>M2 bone marrow (&gt; 5% and ≤ 25% blasts) and appearance of normal progenitor cells (for AML ≤ 5% blasts)</td>
<td></td>
</tr>
<tr>
<td>M1 marrow that does not qualify for CR or CRp</td>
<td></td>
</tr>
<tr>
<td>Treatment failures</td>
<td>All other responses</td>
</tr>
</tbody>
</table>
Nursing Considerations for Clofarabine

Dosage

The recommended dose and schedule for clofarabine in children is 52 mg/m² per day by IV infusion over two hours daily for five consecutive days (Genzyme Corporation, 2005). Dosage is based on body surface area calculated using the actual height and weight before the start of each cycle. Patients weighing less than 10 kg or those younger than one year will be dosed based on mg/kg (1.7 mg/kg). However, no patients younger than one year were enrolled in either of the phase II studies with clofarabine. Treatment cycles are to be repeated every two to six weeks based on response and toxicity. Once the absolute neutrophil count has recovered or returned to baseline and toxicities have resolved, initiation of subsequent cycles can be considered (Genzyme Corporation). In patients with prolonged neutropenia or other serious toxicities, dose reduction for subsequent cycles or discontinuation of clofarabine should be considered.

Administration Guidelines

Based on clinical trials, clofarabine may be given safely on an outpatient basis; however, inpatient hospitalization for the first cycle of treatment should be considered. Once stabilized, patients can be discharged and administration of subsequent cycles in the outpatient setting can be considered.

As with most cytotoxic agents, premedication with antiemetics, such as 5-HT₃ antagonists, promethazine, or lorazepam, prior to each dose is recommended to prevent nausea and vomiting. The use of prophylactic steroids (e.g., 100 mg/m² hydrocortisone on days 1–3) may be of benefit in preventing signs or symptoms of systemic inflammatory response syndrome or capillary leak, which occurred in four pediatric patients treated during the phase II trials. Typically, systemic inflammatory response syndrome is manifested by the rapid development of tachypnea, tachycardia, hypotension, shock, and multiorgan failure. The release of cytokines may contribute to development of systemic inflammatory response syndrome or capillary leak syndrome (Ek, Jarfelt, Mellander, & Abrahamsen, 2001). Continuous IV fluids are encouraged throughout the first cycle (first five days of clofarabine infusion) to reduce the effects of tumor lysis and other adverse events, particularly in patients with comorbidities. In stable patients, IV fluids could be administered at home via ambulatory pump. Nephotoxic or hepatotoxic medications should be avoided during the five days of clofarabine administration. Because the kidneys are the primary route of clofarabine excretion, administration of clofarabine in patients with severe renal impairment (i.e., renal insufficiency or failure requiring dialysis) would not be recommended. In the event of increased creatinine, grade 3 or 4 creatinine, and/or decreased urine output, exercise caution and consider discontinuing drug until toxicities resolve. Clofarabine has been selected in patients with severe renal or hepatic dysfunction, and caution is advised in these populations (Genzyme Corporation, 2005).

Clofarabine is supplied in a 20 ml vial containing 20 mg of drug dissolved in 20 ml of 0.9% sodium chloride injection, U.S. Pharmacopeia (USP) (pH range = 4.5–7.5). The solution is clear, practically colorless, and free from foreign matter. Clofarabine should be filtered through a sterile 0.2 nm syringe filter and then further diluted with 5% dextrose injection USP or European Pharmacopeia (EP) or 0.9% sodium chloride injection (normal saline) USP or EP prior to IV infusion. The resulting mixture may be stored at room temperature but must be used within 24 hours of preparation (Genzyme Corporation, 2005).

In children, clofarabine appears to be best tolerated when infused over two hours, although a longer infusion time, over two to four hours, may be recommended in small children (less than 20 kg). Like adults, children were infused initially over a one-hour period. However, some children experienced irritability during infusion. Increasing the infusion time to two hours appeared to reduce this side effect (Faderl et al., 2005). To prevent drug incompatibilities, no other medications should be administered simultaneously through the same IV line. Clofarabine has not been shown to be a vesicant. Clofarabine has been given via a peripheral vein to some children and adolescents without causing venous irritation.

Table 3. Most Commonly Reported Grade 3 and 4 Adverse Events in Pediatric Trials

<table>
<thead>
<tr>
<th>ADVERSE EVENT</th>
<th>TOTAL n</th>
<th>%</th>
<th>GRADE 3 n</th>
<th>%</th>
<th>GRADE 4 n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>80</td>
<td>83</td>
<td>8</td>
<td>8</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Nausea</td>
<td>72</td>
<td>75</td>
<td>14</td>
<td>15</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Febrile neutropenia&lt;sup&gt;a&lt;/sup&gt;</td>
<td>55</td>
<td>57</td>
<td>51</td>
<td>53</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>51</td>
<td>53</td>
<td>10</td>
<td>10</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Pruritus</td>
<td>45</td>
<td>47</td>
<td>1</td>
<td>1</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Headache</td>
<td>44</td>
<td>46</td>
<td>4</td>
<td>4</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Dermatitis</td>
<td>39</td>
<td>41</td>
<td>7</td>
<td>7</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>39</td>
<td>41</td>
<td>15</td>
<td>16</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Rigos</td>
<td>36</td>
<td>38</td>
<td>3</td>
<td>3</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>35</td>
<td>36</td>
<td>7</td>
<td>7</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Fatigue</td>
<td>35</td>
<td>36</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>33</td>
<td>34</td>
<td>6</td>
<td>6</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Anorexia</td>
<td>30</td>
<td>31</td>
<td>5</td>
<td>5</td>
<td>7</td>
<td>7</td>
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<tr>
<td>Epistaxis</td>
<td>30</td>
<td>31</td>
<td>14</td>
<td>15</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Hypotension</td>
<td>28</td>
<td>29</td>
<td>12</td>
<td>13</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Pain in limb</td>
<td>28</td>
<td>29</td>
<td>5</td>
<td>5</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Petechiae</td>
<td>28</td>
<td>29</td>
<td>7</td>
<td>7</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

N = 96

Note. Events were reported in at least 10% of patients receiving 52 mg/m² per day for five days.

<sup>a</sup> See full prescribing information (Genzyme Corporation, 2005) for a list of all adverse events.

<sup>b</sup> Patients with more than one occurrence of an adverse event are counted only once (ILEX Products, Inc., and Genzyme Corporation, 2004a, 2004e).

<sup>c</sup> Colony-stimulating factors were not employed as standard supportive care.

Patient Monitoring and Management of Side Effects

Safety data were compiled across six studies for 96 heavily pretreated pediatric patients who received clofarabine at the recommended pediatric dose (52 mg/m² per day) (ILEX
### Table 4. Management of Side Effects Observed in Some Patients Treated With Clofarabine

<table>
<thead>
<tr>
<th>SIDE EFFECT</th>
<th>NURSING INTERVENTION</th>
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</table>
| — | Days 1–5: With each infusion of clofarabine  
Check vital signs before and after each infusion.  
Record daily weights.  
Strictly record intake and output.  
Perform daily nursing assessment. |
| Day 1  
Nausea or vomiting | Premedicate with antiemetics (5-HT₃ antagonists, promethazine, lorazepam).  
Continue antiemetics until 24 hours after last infusion.  
Encourage an increase in oral fluid intake.  
Encourage patients to eat a soft, bland diet on days of clofarabine administration; it may help to decrease nausea.  |
| Anxiety (usually during infusion) | Administer lorazepam (0.5–2 mg) or low-dose diphenhydramine (1 mg/kg; maximum dose is 50 mg).  
Consider premedication with 0.5 mg lorazepam prior to subsequent cycle(s).  
Use distraction techniques. Provide emotional support to patients or caregivers.  |
| Headache | Treat with acetaminophen or acetaminophen with codeine.  |
| Fever | Treat with acetaminophen.  
Obtain blood culture(s); consider prophylactic antibiotics.  |
| Tumor lysis syndrome (days 1–5) (Doane, 2002) | Begin aggressive hydration (2–3 L/m² per day).  
Treat with hyperuricemic agents (allopurinol, rasburicase).  
Monitor electrolytes and uric acid frequently (one to four times per day) days 1–5 or until risk for lysis resolved.  
Monitor fluid balance.  |
| Diarrhea | Days 1–28  
Avoid concomitant renal or hepatic toxic drugs until the levels return to baseline.  
Hold clofarabine administration until return to normal or baseline.  |
| Days 2–5  
Diarrhea | Treat with an antidiarrheal, and increase fluids.  |
| Lower-extremity pain (generalized aching and cramps in legs) | Treat with acetaminophen or acetaminophen with codeine.  
Apply massage or heat therapy.  |
| Hand-foot syndrome | Apply ice packs during infusion.  
Use Bag Balm® (Dairy Association Co., Inc., Lyndonville, VT) or unfragranced moisturizer to alleviate dryness.  
Consider dexamethasone 10 mg/m² via IV every day for 24 hours following the last dose of clofarabine.  
Syndrome generally resolves within a week to 10 days.  
Inform patients or caregivers of the potential for desquamation and steps to decrease the superimposed skin infection.  |
| Random rash (flat red; not puffy or edematous) or butterfly rash | For symptom relief, give diphenhydramine (1 mg/kg every four to six hours; maximum of 50 mg per dose) or hydroxyzine (0.5–1 mg/kg every four to six hours; maximum of 600 mg per 24 hours).  
To prevent progression, consider cetirizine (2.5 mg by mouth once daily for children aged two to five years; 5–10 mg by mouth once daily for children aged six years to adult) and hydrocortisone IV (1 mg/kg; maximum of 200 mg) once per day.  
Consider premedicating subsequent doses of clofarabine with cetirizine and hydrocortisone.  
Rash usually begins to resolve by week 2.  
Instruct patients or caregivers to contact a medical provider if the rash worsens.  |
| Days 6–28  
Myelosuppression | Anticipate a rapid drop in blood counts and the potential for blood product support.  
Follow standard myelosuppression recommendations (e.g., careful hand washing, avoiding crowds).  
Consider prophylactic antibiotic, antifungal, or antiviral coverage while neutropenic.  
Consider granulocyte–colony-stimulating factor for prolonged neutropenia (lasting more than six weeks).  |
| Febrile neutropenia | Initiate antibiotic therapy immediately. Anticipate hospital admission. Provide emotional support to patients or caregivers.  
Obtain blood cultures (central and peripheral per institution guidelines).  
Give acetaminophen 10–15 mg/kg for comfort when the temperature is higher than 101°F.  |
| Transaminase elevation | The condition is generally asymptomatic and reversible.  
Dose delay or suspension generally is not necessary or recommended.  
Avoid concomitant hepatotoxic drugs until return to baseline.  |
The overall tolerability profile of clofarabine is acceptable. The commonly reported side effects in this population are similar to those seen with most chemotherapeutic agents: myelosuppression, nausea, vomiting, diarrhea, fever, infection, chills, and headache (see Table 3). In addition, some less-frequent side effects have been observed in patients receiving clofarabine such as anxiety, early-onset fever or infection, and rash, including hand-foot syndrome. The development of significant hypotension (i.e., hypotension requiring pharmacologic support) has been observed in some patients. The cause of the hypotension is not clear and is being studied further. Nurses are advised to monitor patients closely for changes in blood pressure, prepare to provide additional fluids, and alert a physician if pharmacologic support is required to maintain blood pressure. Most of the side effects observed to date with clofarabine in heavily pretreated patients have been reversible, manageable, and noncumulative. Increases in liver function parameters, particularly elevations in transaminases (aspartate amino transferase [AST] and alanine amino transferase [ALT]), are expected and should be monitored closely. Although elevations in AST and ALT were transient and returned to baseline or less than or equal to grade 2 in several days, extended elevations and/or concurrent increases in bilirubin may require physicians to reduce or hold additional clofarabine doses (Genzyme Corporation, 2005). The increases in total bilirubin, which typically are reversible, may be slow to recover.

Timely and appropriate nursing intervention is crucial to effective management of side effects and improving the outcome of treatment. Clofarabine causes a rapid drop in white blood cell counts that should be anticipated in most patients. All patients should have a complete physical examination at baseline, and vital signs should be monitored before and after each infusion. In particular, nurses should monitor carefully for fever, hypotension, weight gain, and edema, which could be signs of possible tumor lysis syndrome, capillary leak syndrome, or sepsis (Tan, 2002). Required laboratory tests will depend on a patient’s clinical status during the cycle of therapy. For patients with elevated white blood cell counts at baseline, complete blood count, electrolytes, liver and renal function, and uric acid tests should be conducted at least once daily during the first cycle of treatment to monitor for the possibility of a rapid drop in counts necessitating blood product transfusions or other supportive care measures. During subsequent cycles, complete blood cell counts should be monitored closely, with the frequency dependent on patients’ clinical condition. Generally, peripheral counts recover in 21–28 days and may require longer recovery times with additional cycles of treatment. In patients with ALL, median time to recovery was 24 days following bone marrow suppression resulting from treatment with clofarabine (ILEX Products, Inc., and Genzyme Corporation, 2004a).

Clofarabine treatment-related side effects can be grouped into three categories: those most likely to be seen during the infusion or on the first day of treatment, those presenting during the next four days of treatment, and delayed effects that are observed between cycles. Table 4 summarizes the nursing interventions recommended for the side effects. The interventions have improved patients’ quality of life, increased their ability to stay on treatment, and may have contributed to the overall effectiveness of the treatment.

Conclusion

A significant challenge in the treatment of pediatric leukemia is the development of effective treatments in children refractory to existing therapies. Clofarabine represents a new addition to the therapeutic options available for treatment of pediatric acute leukemia. As a single agent, it has induced remission in a number of cases, extended survival, and improved quality of life for many heavily pretreated relapsed and refractory patients. The safety profile of clofarabine appears to be comparable to other NAs and may be preferable because of the absence of serious CNS and renal toxicities. Tolerability is similar to other chemotherapeutic agents, with the most commonly reported side effects being myelosuppression, nausea, vomiting, diarrhea, fever, infection, chills, headache, and pruritus. Most of the side effects observed with clofarabine were reversible and noncumulative and can be managed with skilled nursing interventions.

Nurses will play a critical role in ensuring that the therapeutic potential of clofarabine is realized in appropriate patients. Nurses will inform patients or family members regarding the possible side effects and can manage their expectations of efficacy and tolerability during clofarabine therapy. Nurses can encourage and assist patients and family members to become full partners in identifying treatment-related side effects. Given the potency of clofarabine and the possibility that complications may be associated with the expected rapid drop in white blood cells, administration of relevant prophylaxis and careful monitoring of patient condition may be critical to keeping patients on therapy, especially during the first cycle. Additional interventions have proven effective in relieving the symptoms of less serious side effects, such as anxiety, headache, and rash. Nurses experienced with clofarabine will play an important role in educating colleagues in the healthcare community about the scientific and medical aspects of this new chemotherapeutic agent.

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Nursing Considerations for Clofarabine


