Advances in the Management of Acute Myeloid Leukemia in Older Adult Patients

Barbara B. Rogers, CRNP, MN, AOCN®, ANP-BC

Acute myeloid leukemia (AML) is a group of clonal hematopoietic stem cell disorders characterized by overproliferation of undifferentiated myeloid cells, known as myeloblasts. AML is the most common form of acute leukemia in adults, accounting for 25% of leukemias in this population in the Western world (Deschler & Lubbert, 2006). An estimated 12,810 new cases were diagnosed and 9,000 deaths recorded in the United States in 2009 (American Cancer Society, 2009). The incidence of AML is expected to increase as a result of the aging of the population, a rise in secondary cases from environmental exposures, and wider recognition that low blood counts may be indicative of a bone marrow disorder rather than a normal consequence of aging (Sekeres, 2006; Stone, 2002). Left untreated, AML ultimately is fatal from complications of bone marrow failure, typically occurring within one year of diagnosis (Estey, 2006).

Two systems have been used to classify hematopoietic malignancies (National Comprehensive Cancer Network [NCCN], 2009). The older French-American-British classification consists of eight AML subtypes based on cell morphology (Bennett et al., 1985). Using these criteria, AML is diagnosed when a bone marrow aspirate reveals the presence of 30% or more blasts. The World Health Organization (WHO) classification (Harris et al., 1999) includes newer prognostic factors, such as molecular markers, chromosome translocations, and evidence of dysplasia, which might predict responsiveness to treatment. Using the WHO criteria, AML is diagnosed if 20% or more blasts are present in the bone marrow.

Acute Myeloid Leukemia in Older Adult Patients

AML is considered to be a disease afflicting an older adult population, one with a median age of 67 years at

Purpose/Objectives: To update oncology nurses on new developments in the care of older adult patients with acute myeloid leukemia (AML).

Data Sources: Clinical trial data, published guidelines, review articles, and conference proceedings.

Data Synthesis: Therapies for older adult patients with AML include cytarabine-based intensive-induction chemotherapy, investigational therapy, and supportive care. Nonmyeloablative allogeneic hematopoietic stem cell transplantation may provide the best opportunity for cure following remission if a human leukocyte antigen–matched hematopoietic stem cell donor is available. Careful assessment of patient- and disease-related factors is critical in determining the appropriate treatment modality for individuals. Assessment tools and algorithms may identify patients likely to be intolerant of intensive therapies. Supportive care may improve treatment tolerance and quality of life.

Conclusions: Survival outcomes have not improved significantly for older adult patients with AML. Novel therapies, coupled with better understanding of prognostic factors, may allow more highly individualized care. Performance status or comorbidity score may provide insights regarding outcome, particularly when combined with age, cytogenetic risk, or molecular markers. Efforts to improve transplantation safety may increase use in the older adult patient population.

Implications for Nursing: Nurses provide disease and treatment information, manage adverse effects, and offer emotional support. Knowledge of the key management issues for older adult patients with AML is critical in fulfilling this role.

the time of diagnosis (National Cancer Institute [NCI], 2008b). Compared with their younger counterparts (patients younger than 60 years), older adult patients with AML have poorer survival outcomes (see Figure 1). Although patients younger than 45 experience a five-year overall survival of 38%, the rate declines to 8% in patients aged 60–69 years and abruptly falls to 0% for those 80 years or older (Farag et al., 2006; NCI, 2008b). Treatment responses also are inferior for older adult
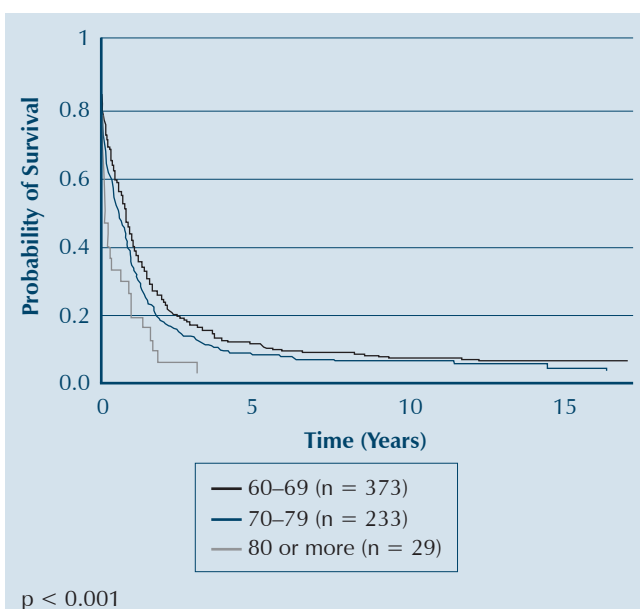
Figure 1. Overall Survival for Patients Older Than 60 Years With Acute Myeloid Leukemia Enrolled in Cancer and Leukemia Group B

Note. From "Pretreatment Cytogenics Add to Other Prognostic Factors Predicting Complete Remission and Long-Term Outcome in Patients 60 Years of Age or Older With Acute Myeloid Leukemia: Results From Cancer and Leukemia Group B 8461," by S.S. Farag, K.J. Archer, K. Mrozek, A.S. Ruppert, A.J. Carroll, J.W. Cardiman . . . C.D. Bloomfield, 2006, *Blood, 108,* p. 68. Copyright 2008 by American Society of Hematology. Reprinted with permission.

patients. An analysis of 968 patients entered in age group–restricted trials from the Southwest Oncology Group who were treated with aggressive induction regimens found that the proportion of patients achieving a complete response (CR) declined from 64% in those younger than 56 years to 33% in those older than 75 years (Appelbaum et al., 2006). Over the same age ranges, the incidence of treatment-resistant disease increased from 27% to 36%, median disease-free survival declined from 22 to 9 months, and overall survival declined from 19 to 4 months (Appelbaum et al., 2006).

Poorer outcomes in this age group are likely related to characteristics of both the older adult patient and the disease. Older adult patients are more likely to have comorbidities that can reduce tolerance to therapy. In addition, these patients are more likely to have unfavorable cytogenetics, which reduce their responsiveness to treatment (see Table 1). In a study of patients aged 65 years or older who were treated with intensive chemotherapy, Kantarjian et al. (2006) identified several factors associated with poor outcomes, including being aged 75 years or older, unfavorable karyotypes (often complex), poor performance status (PS), longer duration of antecedent hematologic disorder, treatment outside the laminar airflow room, creatinine of more than 1.3 mg/dl, and abnormal organ function. According

to the data, patients with none or one poor prognostic factor represent about 20% of the older adult population with AML and have expected CR rates of greater than 60%, eight-week mortality rates of 10%, and one-year survival rates of 50% or higher. In contrast, patients with three or more factors have a less favorable prognosis, with expected CR rates of less than 20%, eight-week mortality exceeding 50%, and one-year survival of less than 10%. This latter group constitutes about 25%–30% of older adult patients with AML.

AML in older adult patients is generally more drug resistant, more likely to be preceded by myelodysplasia, and more often associated with unfavorable cytogenetic abnormalities (Appelbaum et al., 2006; Byrd et al., 2002; Farag et al., 2006). Multidrug resistance protein expression has been documented in a greater percentage of older versus younger patients with AML (about 71% versus 35%) (Leith et al., 1999).

In general, older adult patients may be less tolerant of the toxicities associated with standard cytarabine-based induction and consolidation chemotherapy, possibly because they typically present with comorbid conditions. By one estimate, more than 25% of patients with cancer aged 75 years or older have at least six comorbidities (Yancik, 1997). In addition, concomitant cognitive impairment may preclude the delivery of an intensive treatment regimen or prevent clinical trial enrollment (Pinto, Zagonel, & Ferrara, 2001).

Poor performance status is an important prognostic factor in older adult patients. Appelbaum et al. (2006) found that the frequency of early deaths (i.e., occurring within the first 30 days of remission induction) increased dramatically in patients with a baseline PS of 2 or higher as their age advanced. For example, among patients with a PS of 2, early mortality rates increased from 2% in patients younger than 56 years to 18%, 31%, and 50% in those aged 56–65 years, 66–75 years, and older than 75 years, respectively. Among patients with a PS of 3, corresponding mortality rates were 0%, 29%, 47%, and 82% (Appelbaum et al., 2006).

Cytogenetic abnormalities have been established as significant prognostic factors in AML (Byrd et al., 2002; Grimwade et al., 2001). These abnormalities are classified into three risk groups based on anticipated clinical outcomes: favorable, unfavorable, and intermediate (see Table 1). Among older adult patients, a markedly smaller proportion belongs to the favorable risk group. In one study, 16% of patients younger than 56 years had favorable cytogenetics compared with 4% in patients older than 75 years (Appelbaum et al., 2006). In these same age groups, unfavorable cytogenetics were observed in 33% and 50%, respectively. In another analysis, which involved patients aged 60 years or older with AML, those with complex karyotypes containing at least five abnormalities were distinguished as a particularly poor prognostic group (Farag et al., 2006). The five-year disease-free

survival rate for these patients was 0% compared to 9% for those with fewer than five aberrations. Gene mutations have been identified that may further characterize risk. One example is *FLT3* internal tandem duplication, the most common gene mutation in AML (Markovic,

Table 1. Risk Stratification Based on Cytogenetics and Molecular Mutations in Patients With AML

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MacKenzie, & Lock, 2005). This mutation has been associated with lower rates of complete remission, disease-free survival, event-free survival, and overall survival (Kottaridis et al., 2001). Similarly, the presence of the partial tandem duplication of the *MLL* gene in 5%–11% of cytogenetically normal patients with AML has been linked to shortened response duration and event-free survival (Döhner & Döhner, 2008; Mrozek, Marcucci, Paschka, Whitman, & Bloomfield, 2007) (see Figure 2).

Therapeutic Decisions in Older Patients With Acute Myeloid Leukemia

In addition to the prognostic factors discussed earlier, patient wishes regarding treatment may vary and should be considered in the decision-making process. Patients' families also may participate in this process and should be well informed. Some patients are willing to receive aggressive therapy that may extend overall survival, whereas others may prefer a gentler and potentially less toxic regimen. General practitioners and family practice physicians may be hesitant to refer older adult patients for standard induction chemotherapy given the perception of a relatively short survival time and high risk of treatment-related mortality (Pinto et al., 2001). However, in addition to the established standard treatments, novel therapeutic approaches are increasingly being developed which may offer improved outcomes to challenging patient populations (Stock, 2006).

An initial patient evaluation should assess the patient's educational level, advice from family practitioners, attitude toward the disease, family dynamics and support system, and economic limitations (Pinto et al., 2001). Emphasizing the need for effective communication during this critical time also is important. One patient survey revealed a significant disagreement between patients and physicians regarding expectations for outcome: 74% of patients estimated their chance of cure to be 50% or higher, whereas 89% of physicians predicted a 10% or less cure rate for the same patients (Sekeres et al., 2004). Similar discordances were observed for predictions of one-year survival and treatment-related mortality. In addition, most patients (68%) considered themselves to be a primary or equal decision maker with their physicians, whereas 66% of physicians identified themselves as the sole decision maker with or without input from patients.

Treatment Options

The main treatment options for older adult patients with AML include standard cytarabine-based induction chemotherapy, off-label therapies that are administered outside a clinical trial, investigational therapy in the setting of a clinical trial, and palliative care. Based on the current understanding of the impact of prognostic

factors, treatment may be initiated according to the algorithm illustrated in Figure 3. Relatively healthy patients 60 years of age or older without additional adverse prognostic factors may be offered standard induction therapy consisting of cytarabine 100 mg/m^2 by continuous IV infusion for seven days and an anthracycline (idarubicin, daunorubicin, or mitoxantrone) for three days ("7 + 3"). Induction is followed by consolidation therapy, with the goal of improving long-term disease-free survival. Although younger patients are known to benefit from one to four cycles of high-dose cytarabine (Mayer et al., 1994), a standard consolidation regimen in older adult patients has not been identified, although one to three courses of the induction regimen or intermediate-dose cytarabine may minimize the risk of relapse (Melchert, 2006). Although high-dose cytarabine during consolidation therapy is frequently avoided in older adult patients because of the increased incidence of neurologic toxicity, it may represent a useful strategy in patients with good PS and normal renal function (Stock, 2006). Additional intensive postremission therapy, maintenance therapy, or addition of other agents has not yet demonstrated therapeutic benefit (Sekeres, 2006). Recommended monitoring parameters during induction, after remission, and after consolidation are outlined in Table 2. Older adult

Figure 2. Overall Survival in Patients With Acute Myeloid Leukemia Categorized Into Favorable, Intermediatae, and Adverse Cytogenetic Risk Groups Using the Cancer and Leukemia Group B Criteria

Note. From "Pretreatment Cytogenetic Abnormalities Are Predictive of Induction Success, Cumulative Incidence of Relapse, and Overall Survival in Adult Patients With De Novo Acute Myeloid Leukemia: Results From Cancer and Leukemia Group B 8461" by J.C. Byrd, K. Mrozek, R.K. Dodge, A.J. Carroll, C.G. Edwards, D.C. Arthur . . . Cancer and Leukemia Group B, 2002, *Blood, 100,* p. 4334. Copyright 2002 by American Society of Hematology. Reprinted with permission.

patients with a good PS but poor-risk cytogenetics may be candidates for a nonmyeloablative transplantation or investigational therapy. Patients 70 years old or younger in first CR and with an available human leukocyte antigen–matched donor may undergo reduced-intensity conditioning followed by an allogeneic hematopoietic stem cell transplantation. The NCCN guidelines indicate that reduced-intensity allogeneic HSCT is considered an additional option for patients 60 years or older as a postremission therapy for patients achieving a complete response to induction therapy or for treatment of induction failure only in patients with low-volume disease (NCCN, 2009).

Clinical Trials

For relatively healthy patients 60 years of age or older without additional adverse prognostic factors, an alternative approach may be enrollment in a clinical trial assessing the efficacy of novel approaches alone or in combination with standard chemotherapy. Patients with 1 or higher adverse prognostic factor who are older than 80 years of age or have a poor PS may be offered participation in clinical trials with less toxic agents. Although most patients with AML are older, patients older than 60 years of age represent only 33% of patients in large, multicenter clinical studies (Buchner et al., 2005). Older adult patients also are less likely to be referred to treatment centers and are less likely to be treated aggressively (Appelbaum et al., 2006; Deschler & Lubbert, 2006). Therefore, clinical trial data may not necessarily be applicable to older adult patients, particularly with regard to clinical outcomes (achieving remission) or tolerance to therapy (early mortality). As of this writing, studies were being conducted that exclusively include the older population. Data regarding the response rates and tolerability of newer treatments for AML in the older adult population are necessary to determine the optimal treatment for this population, which frequently has increased risk factors and less tolerability of therapy.

Decitabine

Decitabine has been used off-label as an induction therapy for older adult patients with AML. Cashen, Schiller, Larsen, Cullen, and DiPersio (2006) reported a complete response rate of 29% with decitabine in older adult patients with AML. The NCCN (2009) panel on AML recommended the use of decitabine only in the context of clinical trials.

Additional Therapies

An improved understanding of the molecular and cytogenetic factors and signaling pathways in AML has revealed targets that may be exploited for therapeutic benefit. Over the next 10 years, new therapies may be tailored to several genetic subtypes of AML, including
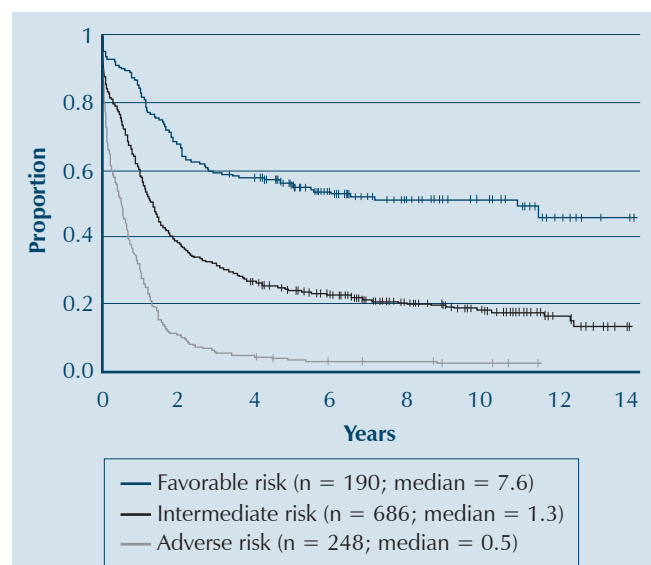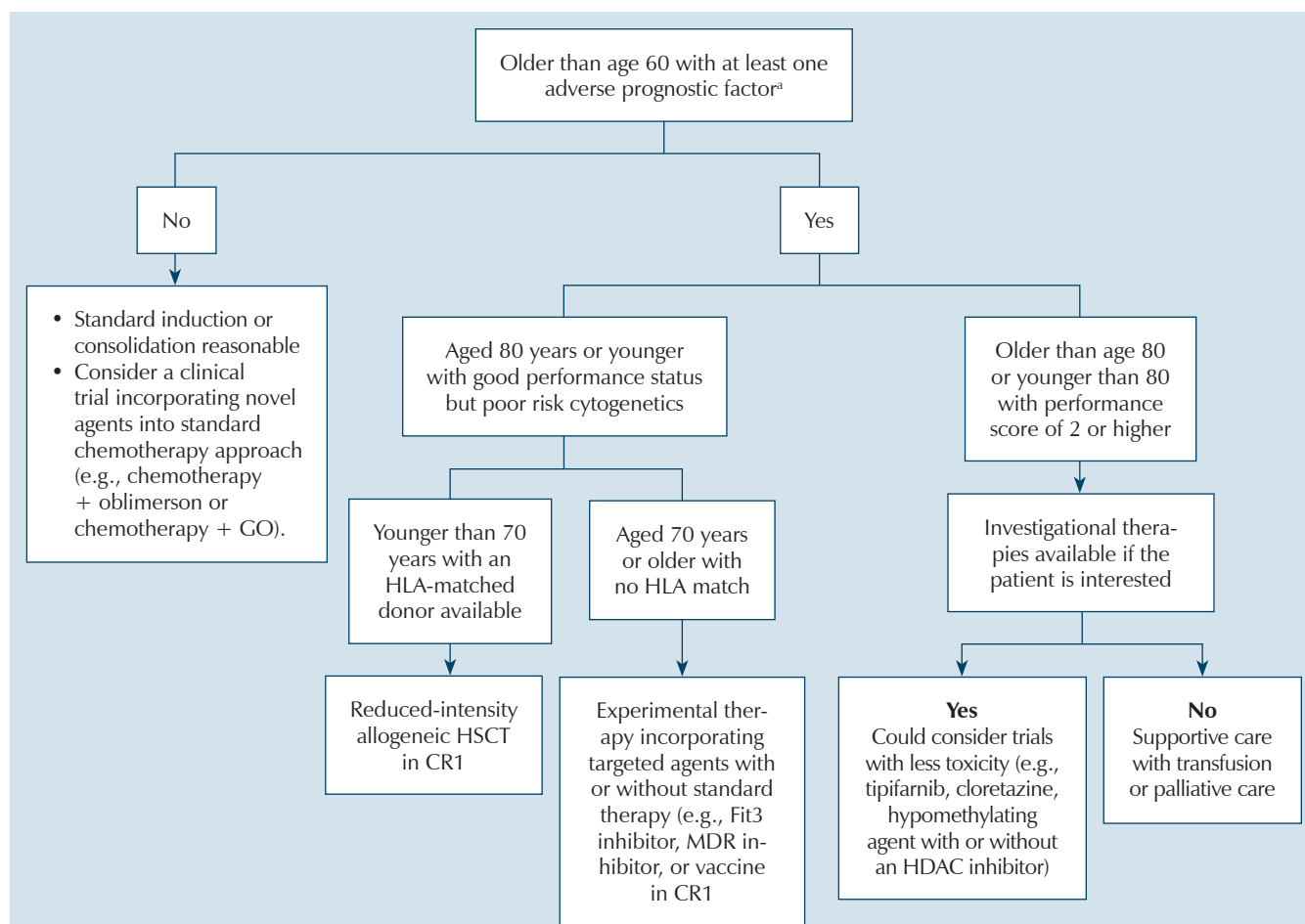
Older than age 60 with at least one adverse prognostic factor[a]

No →
- Standard induction or consolidation reasonable
- Consider a clinical trial incorporating novel agents into standard chemotherapy approach (e.g., chemotherapy + oblimerson or chemotherapy + GO).

Yes →

Aged 80 years or younger with good performance status but poor risk cytogenetics

Younger than 70 years with an HLA-matched donor available → Reduced-intensity allogeneic HSCT in CR1

Aged 70 years or older with no HLA match → Experimental therapy incorporating targeted agents with or without standard therapy (e.g., Fit3 inhibitor, MDR inhibitor, or vaccine in CR1

Older than age 80 or younger than 80 with performance score of 2 or higher

Investigational therapies available if the patient is interested

Yes Could consider trials with less toxicity (e.g., tipifarnib, cloretazine, hypomethylating agent with or without an HDAC inhibitor)

No Supportive care with transfusion or palliative care

[a]Adverse prognostic factors include increasing age (older than 75); t-AML, secondary AML; a performance status of 2 or higher; abnormal organ function; abnormal cytogenetics (other than t[8;21]); inv (16); and MDR1 expression *FLT3* mutation

AML—acute myeloid leukemia; CR1—clinical remission; GO—gemtuzumab ozogamicin; HDAC—histone deacetylase; HLA—human leucocyte antigen; HSCT—hematopoietic stem cell transplantation; MDR—multidrug resistance

Figure 3. Algorithm for Management of Older Patients With Acute Myeloid Leukemia

Note. From "Algorithm for Management of Older Patients With AML," by W. Stock, 2006, *Hematology,* p. 190. Copyright 2006 by American Society of Hematology. Adapted with permission.

acute promyelocytic leukemia (APL), CD33+ AML, AML with *FLT3* mutations, AML with c-KIT mutations, and AML with mixed-lineage leukemia partial tandem duplications. These agents include the *FLT3* tyrosine kinase inhibitors PKC-412 and CEP-701, the farnesyltransferase inhibitor tipifarnib, the apoptosis inhibitor oblimersen sodium, the deoxyadenosine analog clofarabine, and vaccines that promote anti-AML T cell activity (Greiner, Döhner, & Schmitt, 2006; King & Rowe, 2007). Although investigational therapies have not yet resulted in significant improvement in CR rates, they may prove to be useful in maintaining remission, rather than as induction therapy, and may enhance remission when used in combination with chemotherapy (Estey, 2007). Therapies under investigation are summarized in Table 3. Notably, clofarabine may be effective in older adult patients with relapsed or refractory disease, although myelosuppression is a concern (Burnett & Mohite, 2006).

Although cloretazine initially appeared promising, a phase III trial in relapsed AML patients was suspended pending a data safety monitoring board review of on-study mortality. Trials investigating the multidrug resistance inhibitor PSC833 have revealed no response in older adults (Sekeres & Stone, 2002). *FLT3* inhibitors, on the other hand, appear promising in early clinical studies (Burnett & Mohite, 2006). Decitabine and azacitidine are hypomethylating agents that have demonstrated efficacy and safety in older adults (Lubbert et al., 2007; Sudan et al., 2006). Decitabine and azacitidine have been used in older adults for whom the "7 + 3" regimen is thought to be too aggressive and for whom excessive toxicity has been a concern. It is hoped that novel agents specifically targeting key processes in the pathogenesis of AML will be associated with improved safety and efficacy profiles (Aribi, Ravandi, & Giles, 2006; Burnett & Mohite, 2006; Estey, 2006; Estey & Döhner, 2006).

Table 2. Monitoring Parameters for Patients With Acute Myeloid Leukemia

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Finally, patients with multiple risk factors and a high risk of treatment-related death should be considered for palliative care to diminish symptoms. Blood transfusions may be administered to minimize symptoms associated with significant anemia and thrombocytopenia. The use of hydroxyurea, thioguanine, etoposide, or low-dose cytarabine can be considered to reduce leukocytosis, although these therapies do not lengthen survival (Jackson & Taylor, 2002; Sekeres & Stone, 2002).

Hospice services may be arranged and guided by discussions between the medical team and the patient and his or her family.

Acute Promyelocytic Leukemia

APL, a subtype of AML accounting for 10%–15% of all cases, is managed differently from other types of AML. About 20% of patients with APL are older than 60 years, which is a poor prognostic factor during induction. Those

patients were more likely to die during induction therapy than patients 60 years or younger (de la Serna et al., 2008). Induction therapy should include the simultaneous administration of all-trans–retinoic acid (ATRA) and an anthracycline-based chemotherapy. Although the choice of anthracycline is still debated, idarubicin is frequently used as a single agent along with ATRA, whereas daunorubicin usually is used in combination with other agents such as cytarabine. Although single-agent ATRA therapy induces excellent CR rates in patients with APL, these CRs are short-lived, indicating the need for the addition of chemotherapy. Several randomized, clinical trials have established the combination of ATRA and an anthracycline-based chemotherapy as standard of care for APL induction. Molecular remission as determined by PCR is the goal of consolidation therapy in

Table 3. Investigational Agents for the Treatment of Acute Myeloid Leukemia

Class	Mechanism of Action	Phase
DNA transcription inhibitors	Decreases DNA synthesis and repair	
Clofarabine		I–III
Hypomethylating agents	Hypermethylation is associated with disease progression and poorer outcomes	
DNA methyltransferase inhibitors		I–III
Decitabine		III
Azacitidine		III
Histone deacetylase inhibitors		
Suberoylanilide hydroxamic acid, or vorinostat	Prevents gene transcription	I–II
Valproic acid		I–III
SB939		I
Alkylating agents		
Cloretazine	Damages DNA and/or impairs DNA replication	I–II
Signal transduction inhibitors		
CEP-701	*FLT-3* inhibitor	I–II
PKC-412	*FLT-3* inhibitor	III
Tipifarnib	Farnesyl transferase inhibitor	I–III
Bortezomib	Proteasome inhibitor	I
Immunotherapy	Induces T cell responses against acute myeloid leukemia	
PR1 peptide vaccine		III
WT1 peptide vaccine		II
GVAX allogeneic tumor cell vaccine		II
GRNVAC1 autologous dendritic cell vaccine		II
Autologous tumor cell vaccine		I

Note. Based on information from National Cancer Institute, 2008a.

APL. The standard therapeutic approach for consolidation in APL includes two to three cycles of postremission anthracycline-based therapy followed by maintenance therapy. ATRA maintenance after a CR has been shown to improve disease-free survival (NCCN, 2009; Sanz, Tallman, & Lo-Coco, 2005).

Treatment for Relapsed Acute Myeloid Leukemia

Clinical trial enrollment should be considered for patients who relapse early (less than six months following induction). Other options for these patients include palliative care or gemtuzumab ozogamicin therapy. Treatment options for patients who experience a late relapse (more than six months following induction therapy) include clinical trial enrollment, retreatment with the initial induction therapy, gemtuzumab ozogamicin, or palliative care (NCCN, 2009). Gemtuzumab ozogamicin, a monoclonal antibody conjugated to the antitumor toxin calicheamicin, is approved for the treatment of relapsed disease in older adult patients whose cells express the CD33 antigen. This agent received accelerated approval from the U.S. Food and Drug Administration in 2000. Although effective, postmarketing experience has identified a moderately high incidence of infusion-related reactions, hepatic dysfunction, and veno-occlusive disease for which patients should be closely monitored (Giles et al., 2001). Additional stud-

ies are under way with targeted agents such as those mentioned in the relapsed setting.

Although granulocyte colony-stimulating factors are administered after induction therapy once the marrow has been cleared of blast cells, the administration of colony-stimulating factors (CSFs) prior to or during induction therapy in AML is controversial. The premise for this intervention is that CSFs could be used to stimulate leukemic cell growth and increase the cytotoxicity of cell cycle-specific chemotherapeutic agents. However, four randomized trials (Lowenberg, Boogaerts, et al., 1997; Lowenberg, Suciu, et al., 1997; Ohno et al., 1994; Zittoun et al., 1996) have demonstrated no benefit in CR rate or survival associated with the CSF priming approach; therefore, this approach is not recommended outside of a clinical trial.

Supportive Care and Nursing Management

Expert nursing management and supportive care are vital during the treatment of older adult patients with AML. A complete geriatric assessment should be performed at baseline, including an evaluation of functional status, comorbid conditions, current medications, organ function, social support, and nutrition status (Simpson & Rosenzweig, 2002). Before treatment is initiated for

AML, the patient's other healthcare providers should be consulted to assist in managing comorbidities during therapy.

During induction therapy, patients with AML may be at risk for tumor lysis syndrome (TLS) caused by rapid tumor cell breakdown. TLS prophylaxis, which involves IV hydration with diuresis, urinary alkalinization, and allopurinol, should be initiated before chemotherapy is started (NCCN, 2009). If patients develop a rapid rise in serum uric acid or creatinine (indicating the development of TLS) or become intolerant of oral allopurinol, the administration of rasburicase should be considered (NCCN, 2009).

Patients receiving high-dose cytarabine should receive saline or steroid drops in both eyes during cytarabine therapy to diminish the risk of ocular toxicity. Eye drops should be applied every 4 hours until 48 hours following the last dose of chemotherapy (Higa, Gockerman, Hunt, Jones, & Horne, 1991). Exposure to high concentrations of cytarabine increases the vulnerability of older adult patients to cerebellar damage. Therefore, these patients should be evaluated for nystagmus, slurred speech, and dysmetria prior to each dose of cytarabine (NCCN, 2009).

Because chemotherapy often induces myelosuppression, patients should be carefully monitored and treated for anemia, thrombocytopenia, infection, and mucositis. A complete blood count and absolute neutrophil count should be assessed daily during induction. Blood products are administered frequently to manage anemia (hemoglobin < 8 gm/dl) and severe thrombocytopenia (platelets less than 10,000/mm³) (see Table 4). Blood products administered to patients with AML should be leukocyte-depleted to reduce the risk of alloimmunization (Jabbour, Estey, & Kantarjian, 2006). In addition, radiation of all blood products is advised to reduce the risk of graft-versus-host disease in patients who are immunosuppressed (NCCN, 2009).

The Putting Evidence Into Practice (PEP) guidelines published by the Oncology Nursing Society provide recommendations for evidence-based interventions for the prevention of infection (Zitella, Gobel, & O'Leary, 2009) (see Figure 4). CSFs have not been shown to be useful before or during induction chemotherapy to increase cytotoxicity; however, they may be effective in enhancing neutrophil recovery, diminishing the risk of infection, and prolonging survival in patients with neutropenia when used appropriately (Geller, 1996). Granulocyte-CSF is not usually initiated until the follow-up bone marrow demonstrates the ab-

Table 4. Blood Product Support

Blood Product	When to Transfuse	Comments
Red blood cells	Hgb of 8 g/dl or less Symptomatic anemia	Counsel patients regarding signs and symptoms of anemia (i.e., fatigue, shortness of breath, and pale skin).
Platelets	Platelets less than 10,000/mcl Signs of bleeding	Minimize invasive procedures. Educate patients about minimizing risks for falls and injury. Administer platelet transfusions as prescribed. Consider premedications. Post-transfusion platelet count Counsel patients on signs and symptoms of thrombocytopenia (i.e., swollen gums, slow-healing cuts, small red spots under the skin, prolonged bleeding from cuts, and bruises). For inadequate response, consider platelets from HLA-matched donors or siblings or IV immunoglobulin infusions.

Hgb—hemoglobin; HLA—human leucocyte antigen

sence of blast cells (around day 14 of induction cycle). Patients should be counseled to report all signs and symptoms of infection (e.g., fever, chills, cough, sore throat, pain with urination, loose bowel movements). Among patients who have profound neutropenia, no other signs of infection may be present except for fever from the inability of the immune system to mount an inflammatory response.

Mucositis can affect all mucous membranes (Epstein & Schubert, 1999) and can adversely impact quality of life (Harris & Knobf, 2004). Careful oral assessment and treatment are imperative to prevent serious complications (Harris & Knobf, 2004). Numerous preventive measures and therapeutic agents have been studied; however, no standard of care currently exists for the management of mucositis. The PEP guidelines indicate that oral care protocols, including regular cleansing of the teeth and mucosal tissue, coupled with patient education, significantly reduce the severity of chemotherapy-induced mucositis (Harris, Eilers, Harriman, Cashavelly, & Maxwell, 2008). The regular use of commercial mouthwash is discouraged because of the high alcohol content that may irritate the oral mucous membrane. Two commonly used mouthwashes include a simple saline mouthwash (1 tsp each of salt and sodium bicarbonate per pint of water) and "magic mouthwash" (equal parts viscous lidocaine, Maalox® [Novartis Consumer Health, Inc.], and injectable diphenhydramine liquid), which may be swished (1 tsp) and spit out as often as every four hours. The salt and soda mouthwash is primarily used for cleansing, and the magic mouthwash is used to relieve discomfort. Educating patients about the potential loss of the gag reflex related to viscous lidocaine is important. For patients experiencing diarrhea, the Maalox component of the magic mouthwash may be replaced with aluminum hydroxide. Oral

diphenhydramine liquid should not be used because of its alcohol content and associated drying effects on the oral mucosa. Patients experiencing severe mucositis and pain may require parenteral analgesics.

Several additional clinical practices are employed in the care of patients with AML, although many lack supportive data. Examples of practices with little data to support their use include the avoidance of crowds and use of masks during significant myelosuppression, as well as the avoidance of fresh fruits and vegetables to reduce the risk of infection (Estey, 2007). Unpublished results from a trial at the University of Texas M.D. Anderson Cancer Center suggest that infection rates are comparable whether patients eat fresh fruits and vegetables or avoid these foods (Estey, 2007).

Quality of Life and Psychosocial Support

An AML diagnosis may significantly impact the quality of life of affected individuals, which is underscored by the fact that 97% of patients older than 60 years with AML report that quality of life is more important than length of life (Sekeres et al., 2004). Physical, psychological, and emotional well-being and sexual function domains are most affected by AML (Redaelli, Stephens, Brandt, Botteman, & Pashos, 2004). The impact is most noticeable during the initial months following diagnosis and improves over time. The quality of life in long-term survivors is generally normal (Redaelli et al., 2004) or comparable to the life of someone who did not have the disease.

Psychosocial support is critical during the period following diagnosis when decisions regarding treatment are made. The condition of patients with AML can decline quickly; therefore, treatment decisions should be made in a timely manner to allow rapid initiation of therapy. Because older adult patients with AML face poorer outcomes compared to younger patients, such decisions may be quite difficult (Sekeres et al., 2004). Nurses can assist patients and their families by providing accurate information and psychosocial support during this time. In addition, the nurse may need to serve as the patient's advocate to assist the patient in voicing a desire for the type of treatment he or she wishes to receive. Because the standard induction regimens can be significantly toxic to older individuals, patients may decide to undergo less aggressive therapy. The nurse should assist the patient in verbalizing desire for aggressive treatment versus less aggressive therapy or palliative care.

Nurses should be prepared for numerous questions from patients and their families. Nurses may need to help clarify information about treatment options. Knowledge about potential treatments and the impact of prognostic factors is valuable in the decision-making process (Pinto et al., 2001). The effect of treatment on the patient's comorbid conditions also will need to be explained. For example, anthracycline therapy may fur-

ther impair cardiac function in a patient with significant heart disease. Also, infection associated with significant myelosuppression can induce additional stress and increase the risk for cardiac failure.

The emotional needs of patients and their family members must be considered. Patients are likely to experience feelings of denial, depression, hopelessness, and fear. Because treatment often starts soon after the AML diagnosis is confirmed, many of these feelings may not be expressed until recovery from induction therapy begins. Nurses may provide emotional support throughout each phase of treatment by ensuring that patients and families understand the usual course of treatment, its potential complications, and the significance of milestones during treatment (such as the expected results of follow-up bone marrow biopsies). Frequent evaluation of a patient's support system (e.g., ability of caregivers to perform technical tasks, transportation, spousal support, financial resources) is critical, and referral to a social worker within the institution providing care is recommended (Simpson & Rosenzweig, 2002).

Once induction therapy is completed, patients may need additional support to cope with an AML diagnosis. Continued follow-up with a social worker or referral to a psychologist knowledgeable in the care of individuals

- Hand hygiene using soap and water or an antiseptic alcohol-based hand rub for all patients and their caregivers
- Colony-stimulating factors for patients undergoing chemotherapy with a greater than 20% risk of febrile neutropenia[a]
- Antifungal prophylaxis for severely neutropenic afebrile patients (absolute neutrophil count of less than 1,000 for more than one week)
  - Fluconazole
  - Itraconazole oral suspension 400 mg
  - Itraconazole 20 mg IV
  - IV amphotericin B
- Antibacterial prophylaxis with quinolones for high-risk afebrile neutropenic patients undergoing chemotherapy
  - Ciprofloxacin 500–750 mg twice daily for seven days
  - Levofloxacin 500 mg daily for seven days
- Herpes viral prophylaxis for selected seropositive patients
  - Acyclovir
  - Valacyclovir
- Do not allow visitors with symptoms of infections.
- Avoid fresh or dried flowers or plants.
- Avoid animal encounters.
- Advise patients to avoid contact with animal feces, saliva, urine, or solid litter box material.
- Promptly clean and treat scratches, bites, or other wounds that break the skin.
- Advise patients to avoid direct or indirect contact with reptiles.
- Practice hand hygiene after any animal contact.

[a] Refer to National Comprehensive Cancer Network (2009) for appropriate growth factor support in patients with acute myeloid leukemia.

Figure 4. Nursing Management Strategies for the Prevention of Infection

Note. Based on information from Zitella et al., 2009.

Table 5. Commonly Used Resources for Nurses and Patients

Organization	Web Site	Target Audience	Types of Information
American Cancer Society	www.cancer.org	Clinicians, patients, family members	Educational materials, treatment-decision tools, news updates, and support resources
Hartford Institute for Geriatric Nursing	www.hartfordign.org	Nurses	Resources focusing on older adult patients with cancer
Leukemia-Lymphoma Society	www.lls.org	Clinicians, patients	Patient call center, support group locator, discussion boards, and educational information
National Cancer Institute	http://cancer.gov	Clinicians, patients	Educational materials and clinical trial information
National Comprehensive Cancer Center	www.nccn.org	Clinicians, patients	Clinical trial information, treatment guidelines, physician locator, cancer resource links, genetic counseling or testing, and pediatric cooperative group information
Oncology Nursing Society	www.ons.org	Nurses	Links to additional resources, educational materials, and patient workbooks

with AML may be necessary. Some patients or family members may prefer to participate in local support groups. Major cancer organizations offer educational resources and links to a variety of support groups (see Table 5). Some also may provide financial support to patients undergoing therapy for AML.

Conclusions

AML in older adult patients represents a biologically and clinically distinct disease from AML in younger patients. Individual patient assessment is necessary, because treatment choices and outcomes depend on multiple factors. Historically, poor outcomes for older adult patients with AML highlight the need for new therapies and for increased understanding of the pathogenesis of AML in this population. Novel therapeutic approaches (e.g., hematopoietic stem cell transplantation) continue to be studied to increase overall survival in this patient population. Clinical trial enrollment is critical to accrue meaningful data. Nurses are important members of the patient care team, providing education and active support during treatment. New therapies coupled with improved understanding regarding prognostic variables offer hope for older adult patients with AML.

Barbara B. Rogers, CRNP, MN, AOCN®, ANP-BC, is an adult hematology-oncology nurse practitioner at Fox Chase Cancer Center in Philadelphia, PA. No financial relationships to disclose. Mention of specific products and opinions related to those products do not indicate or imply endorsement by the *Oncology Nursing Forum* or the Oncology Nursing Society. Rogers can be reached at barbara.rogers@fccc.edu, with copy to editor at ONFEditor@ons.org. (Submitted December 2008. Accepted for publication May 26, 2009.)

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