PROCEEDINGS ARTICLE

Treating older patients with AML

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The treatment of older patients with acute myeloid leukemia is a difficult challenge. Older adults are more likely to have comorbidities that can limit treatment options, the disease tends to be more aggressive biologically and outcomes are worse than those in younger patients. Deciding which older patients would benefit from intensive chemotherapy is difficult, and efforts are underway to improve existing risk-assessment tools. Treatment should be individualized and may include standard chemotherapy for those patients who have none or at most one adverse factor, or investigational agents for those presenting with multiple poor-risk features. Low-intensity therapies are recommended for those patients who are deemed too frail to tolerate myelosuppressive regimens.

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Acute myeloid leukemia (AML), a disease affecting primarily older adults with a median age at presentation of approximately 68 years, continues to pose significant treatment challenges. Although there have been improvements in treatment outcomes for AML in recent years, these have primarily benefited younger patients under the age of 60 years. It is clear that high complete remission rates and improved survivals are achieved with intensification of treatment, possibly including allogeneic stem cell transplantation, in younger patients. In older patients, intensive chemotherapy, traditionally based on combinations of standard doses of anthracyclines and cytarabine, achieves lower remission rates (around 50–60%) and the risk of relapse is higher (>85%), resulting in a poorer long-term survival (<10%); in addition, comorbidities typically result in a higher treatment-related mortality. Some of the reasons why older patients do less well are widely known: inability to tolerate intensive chemotherapy owing to excess comorbidity and poor physiologic reserve, and inherent chemoresistance of the leukemic cells due to a high frequency of poor biological features, including adverse cytogenetics, expression of resistance proteins and associated myelodysplasia. Taken together, these factors may explain why only a minority of older patients are included in clinical trials. It is, in fact, the perception of many physicians that currently available intensive chemotherapy is not appropriate for a majority of older patients.¹

A variety of strategies have been explored to improve initial response and long-term outcome beyond that achieved with conventional chemotherapy, but optimal induction and post-remission regimen has yet to be determined. One option to improve outcome could be to incorporate allogeneic stem cell transplantation into treatment, with the aim of reducing the risk of relapse. Recent retrospective registry studies have shown that reduced-intensity allotransplantation is feasible in patients up to the age of 75–80 years, and may yield better outcomes than chemotherapy, thereby rekindling much interest in using allografting in such patients.²

Deciding which older patients would benefit from intensive chemotherapy is difficult, and efforts are underway to develop objective risk-assessment tools. In particular, the identification of

risk factors that predict a low response rate, a high early death rate and a low 1-year survival rate in patients treated with intensive chemotherapy has led to the development of prognostic risk scores (such as the Wheatley and the MD Anderson indices) able to predict the outcome for patients who may then be given the choice of intensive or alternative treatment strategies.^{3–4}

Treatment should be individualized and may include standard intensive therapy for those patients who are otherwise healthy and without adverse risk factors, or investigational agents for those presenting with multiple poor-risk features. The latter include monoclonal antibodies, hypomethylators, signal-transduction inhibitors, novel nucleoside analogs and cytotoxics. These agents are currently being investigated in clinical trials as monotherapy or in combination, with encouraging results. For patients who are deemed too frail for myelosuppressive therapy because of excess comorbidity, low-intensity therapies (such as low-dose cytarabine) appear to be superior to palliative care alone.⁵

In the future, it is expected that a better understanding of the pathophysiology of AML in the elderly will lead to newer treatment strategies that are more targeted and less toxic. Until that goal is achieved, all patients with AML over the age of 60 years should be encouraged to participate in clinical trials whenever possible.

CONFLICT OF INTEREST

The author declares no conflict of interest.

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