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## Reduced-Intensity Allogeneic Hematopoietic Transplantation Should Be Considered a Standard of Care for Older Patients with Acute Myeloid Leukemia

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Acute myeloid leukemia (AML) is primarily a disease of older people with a median age greater than 65 years. The treatment of AML in elderly patients remains a major challenge. Older patients are more likely to have high-risk cytogenetic abnormalities, and age itself confers a poor prognosis. There has been little progress with standard forms of chemotherapy [1-3].

Allogeneic stem cell transplantation (SCT) were originally developed as a means of delivering high-dose myeloablative chemotherapy or radiation with the transplant to provide hematologic recovery after the myeloablative therapy [4]. This approach is associated with considerable toxicity, and could only be performed in relatively young patients in excellent general medical condition. We have come to appreciate that much of the benefit is derived from the graft-versus-leukemia effect mediated by donor immune cells [5,6]. This realization has supported the development of reduced-intensity or nonmyeloablative preparative regimens involving lower doses of chemotherapy and/or total-body radiation, which are sufficiently immunosuppressive to prevent rejection and allow development of the graft-versus-leukemia effect [7-10]. These reduced-intensity regimens allow treatment of older or medically infirm patients who were not previously eligible for allogeneic stem cell transplantation [11]. Reduced-intensity regimens may be associated with a higher risk of relapse compared with myeloablative conditioning, but leukemia-free survival is similar in most studies [12,13]. Patients up to age 75 years have been treated with this approach. Similar results are reported with matched related or unrelated donors [14,15].

A number of studies have shown promising results of reduced-intensity transplants in patients with AML. In this issue, Farag et al. [16] evaluate the results of treatment for patients age 60 to 70 years, comparing the results of reduced-intensity allogeneic transplantations reported to the Center for International Blood and Marrow Transplant Research with patients receiving standard chemotherapy on Cancer and Leukemia Group B protocols. The 2 groups had similar patients characteristics and prognostic factors. The transplant recipients were slightly younger than the chemotherapy group. Patients receiving allogeneic HCT had a significantly lower risk of relapse (32% versus 81% at 3 years;  $P < .001$ ), and longer leukemia-free survival (32% versus 15% at 3 years;  $P < .001$ ). Allogeneic

stem cell transplantation is a high-risk procedure, and as expected, there was a higher risk of nonrelapse mortality at 3 years (36% versus 4%;  $P < .001$ ). Overall survival was 37% versus 25% at 3 years ( $P = .08$ ).

One limitation of this type of analysis is the effect of patient selection. Older patients undergoing SCT are selected to be in good enough medical condition to undergo SCT and are a self-selected, highly motivated group of patients. Allogeneic SCT involves a major commitment on the part of the patient, requiring close medical monitoring for at least several months. It frequently requires patients and their caregivers to relocate temporarily to another city to be near the transplant center. Allogeneic hematopoietic transplantation is not a feasible or desirable choice for many elderly patients. These considerations make it almost impossible to conduct a prospective randomized study. However, this and other studies demonstrate that allogeneic SCT provides durable complete remission in a high fraction of older patients, and the reported results consistently compare favorably to those achieved with alternative conventional treatments [17]. Age alone should not be considered a contraindication to allogeneic SCT for AML [15]. Allogeneic hematopoietic transplantation using a reduced-intensity regimen should be considered an effective treatment option and an established standard of care for older patients with AML.

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