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What is the impact of hematopoietic cell transplantation (HCT) for older adults with acute myeloid leukemia (AML)?

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Acute myeloid leukemia (AML) patients over the age of 55 years are generally more difficult to treat than younger patients due to intrinsic drug resistance and diminished tolerance to treatment. The unfortunate result is that conventional chemotherapy is toxic and rarely curative. Recent studies suggest a better outcome for older AML patients treated with reduced-intensity conditioning (RIC) hematopoietic cell transplantation (HCT) than those treated with conventional chemotherapy. However, there are major limitations to RIC HCT. Some of these limitations may be able to be overcome, broadening the impact of allogeneic RIC HCT for older patients with AML. Ways to improve RIC HCT include making more patients eligible for RIC HCT by improving initial complete response rates using novel agents or combinations; finding a way to more rapidly identify alternative stem cell sources, such as by using donors that have already undergone HLA profiling or by using unrelated cord blood; eliminating the requirement for a complete response prior to transplant; and educating patients and physicians about the chances of survival after RIC HCT when compared to conventional chemotherapy.

Key words: reduced-intensity conditioning; hematopoietic cell transplantation; elderly; acute myeloid leukemia; cord blood.

INTRODUCTION

Acute myeloid leukemia (AML) in older adults is a very difficult disease to treat. Because of both intrinsic drug-resistance of the disease and diminished tolerance of

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the patient to treatment, chemotherapy is rarely curative, and less than 1 in 5 patients over age 55 or 60 (the age cut-off for older adults varies from study to study) can expect to be alive 3 years after diagnosis. Several small trials on the use of allogeneic reduced-intensity conditioning (RIC) hematopoietic cell transplantation (HCT) for AML in older adults have recently been published, reporting a 45%–74% survival rate at 3 years, an outcome seemingly better than might be expected with conventional chemotherapy. These results are obviously quite encouraging, but they also raise two important questions: how broadly can allogeneic RIC HCT be applied to older adults with AML, and, if the application is limited, what can be done to expand it?

ACUTE MYELOID LEUKEMIA IN THE OLDER ADULT

The nature of AML changes as the age of the patient increases. Compared to AML in younger patients, AML in patients over age 55 is more often associated with an antecedent hematological disorder (AHD), is less proliferative, presenting with a lower white count and a lower percent of marrow blasts, is more often associated with the expression of P-glycoprotein (P-gp) in the AML blasts, and is much more likely to have an unfavorable cytogenetic profile.[1] In virtually all studies, having an AHD, the presence of P-gp, and demonstration of unfavorable cytogenetics are each independently associated with a lower likelihood of achieving a complete remission and with diminished remission duration.[2–5] In addition to a more unfavorable disease profile, older patients more often have a diminished performance status and an increased number of co-morbidities, both of which further reduce the likelihood of a favorable response to chemotherapy.[1,6]

With conventional therapy including an anthracycline and cytarabine, complete response (CR) rates in patients over age 55 average ~40% in most studies. In patients aged between 55 and 70 years, the CR rate might be a bit higher, averaging around 45%, while in those over age 70, only approximately 25% of patients can be expected to achieve CR. The median duration of remission averages is 6 to 8 months in most studies, and survival at 3 years is less than 20% in virtually all studies. The survival curve from a typical study is shown in Figure 1.[7] In the Eastern Oncology Cooperative Group trial by Rowe et al, almost no patients were over age 75, and approximately

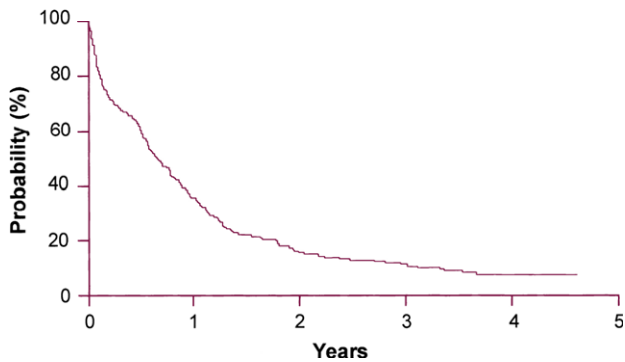

Figure 1. Overall survival among 348 patients aged older than 55 years with previously untreated AML entered onto a recent ECOG trial.[7]