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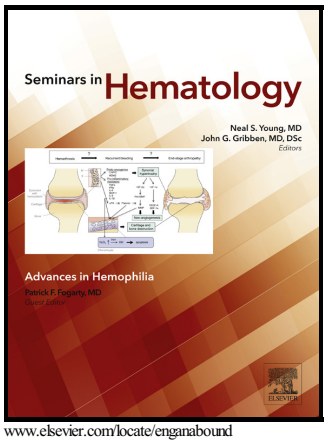

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Maximizing the benefit of allogeneic stem cell transplantation in MDS

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Abstract

Allogeneic stem cell transplantation (AHSCT) is an evolving field in the treatment of patients with myelodysplastic syndrome (MDS) and has become the third most frequent indication for AHSCT worldwide. Less toxic conditioning regimen as well as extension of the donor pool including haplo-identical donors have led to a broader utility of AHSCT, especially in older patients with MDS. While disease-specific scoring systems such as IPSS, IPSS-revised or WPSS have been used to select patients for AHSCT, new transplant-specific scoring systems have been developed to determine outcome after AHSCT, which include also transplant- and patient-related factors which determine more precisely outcome and allows to balance more properly the risk of relapse and non-relapse mortality. More recent studies suggested beside cytogenetics also a major impact of molecular genetics on outcome after AHSCT, mainly for p53 and RAS pathway mutations which are currently not included in any available risk score. The risk of clonal evolution and the known poor outcome of worse cytogenetics and molecular mutations argue to perform AHSCT at an earlier stage of the disease which is supported by an IPSS-revised based multistate model which recommends AHSCT at IPSS-r intermediate risk stage.

Introduction

Myelodysplastic syndromes (MDS) summarize a heterogeneous group of myeloid malignancies characterized by dysplastic features and cytopenias which have a high variable clinical course leading either to rapid transformation to acute leukemia or remain stable for many months or even years.[1,2] Despite growing insight into biology and molecular pathogenesis of the disease the treatment options for patients with MDS are still limited and mostly symptomatic or with only modest prolongation of survival.[2,3,4] Allogeneic hematopoietic stem cell transplantation is a curative treatment option and despite its inherent risk of transplant-related mortality and because of the lack of effective non-transplant options this procedure is increasingly used and has become the third most frequent indication for allogeneic stem cell transplantation.[5] Taking all MDS patients who received an allogeneic stem cell transplantation into account only less than half of them will be cured while in the majority of the patients the treatment will fail either because of therapy-related mortality or because of recurrence of the disease. While major improvement in reducing therapy-related mortality has been achieved in the last 20 years less progress has been made in reducing the risk of relapse which is nowadays the major cause of treatment failure after allogeneic stem cell