Transplants in Myelodysplastic Syndromes

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KEYWORDS

• MDS • Allogeneic HSCT • Relapse • Conditioning • Azacitidine

KEY POINTS

- Transplantation can be a potential curative option in elderly patients with myelodysplastic syndromes within prospective trials investigating the success of allogeneic stem cell transplantation (SCT) compared with other treatment options.
- In the absence of prospective trials, a careful individual selection should be done and patients should be stratified according to comorbidities, performance status, and disease risk.
- Chronic graft-versus-host disease (GVHD) and relapse are still the major challenges after SCT.
- Special attention should be paid to posttransplant care in terms of GVHD management, minimal residual disease (MRD) monitoring, and prevention of relapse.

INTRODUCTION

Because of the great variability of biology and presentation of the disease, the therapeutic management of patients with myelodysplastic syndromes (MDS) is challenging. Over the last decade, there has been a remarkable increase in scientific research on the pathogenesis and therapeutic approaches in MDS. However, despite a rapidly expanding therapeutic drug arsenal, allogeneic hematopoietic stem cell transplantation (SCT) remains the only potentially curative treatment. Only a minority of patients are considered for this treatment modality because cumulative mortality rates after SCT can exceed 30% and also because graft-versus-host disease (GVHD) as well as relapse remain major clinical challenges following transplantation. Because of the heterogeneous nature of MDS, ranging from low-risk patients with a life expectancy of 10 years with best supportive care only to high-risk patients with MDS with a median survival of 5 months with the very best standard treatment, not every patient

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with MDS will benefit from this potential curative but risky treatment procedure. In fact, physicians who treat patients with MDS are faced primarily with an older patient population (median age of 70 years at diagnosis) with significant comorbidities and reduced biological ability to regenerate. In these patients, the potential high treatment-related mortality (TRM) of standard conditioning would limit the benefit of this procedure. With the introduction of reduced-intensity conditioning (RIC), early TRM could be reduced, allowing a potentially curative treatment approach even for patients in the seventh decade of life. On the other hand, the use of RIC is accompanied by a higher risk of relapse, especially in patients with higher-risk disease.[1] Defining patients who should be referred to allogeneic SCT and the best time point within the treatment course of MDS is, therefore, essential. In fact, prospective randomized trials supporting these decisions are still not available. This review highlights the current selection process and therapeutic strategies before and after allogeneic SCT to potentially improve the outcome of patients with MDS undergoing this procedure.

PATIENT EVALUATION OVERVIEW

Diagnostic and Prognosis

According to the recently published guidelines from the European LeukemiaNet (ELN) (**Table 1**), every patient should receive a complete blood count, a peripheral blood (PB) smear with differential leukocyte count, a bone marrow (BM) aspiration for morphologic evaluation, as well as a BM biopsy to assess marrow fibrosis. Furthermore, cytogenetic analysis of BM should be undertaken in all cases of suspected MDS. At least 20 metaphases have to be analyzed; if less than 20 metaphases are

Table 1
Diagnostic tools for MDS in adults, recommendations from the ELN (modified)

Diagnostic Tool	Diagnostic Value	
1. Peripheral blood smear	Evaluation of dysplasia and blast count	Mandatory
2. Bone marrow aspirate	Evaluation of dysplasia and blast count, Quantification of ring sideroblasts	
3. Bone marrow biopsy	Assessment of cellularity, CD34+ count and fibrosis	
4. Cytogenetic analysis	Detection of clonal chromosomal abnormalities for conclusive diagnosis/prognostic assessment	
5. FISH	Detection of targeted chromosomal abnormalities in interphase nuclei following repeated failure of standard G banding	Recommended
6. Immunophenotyping	Detection of abnormalities in erythroid, myeloid, and lymphoid compartment	
7. SNP-array	Detection of chromosomal defects at a high resolution in combination with metaphase cytogenetic	Suggested
8. Mutation analysis of candidates genes	Detection of somatic mutations that can allow a conclusive diagnosis and also reliable for prognostic evaluation	

Abbreviations: FISH, fluorescence in situ hybridization; SNP, single-nucleotide polymorphism.

Adapted from Malcovati L, Hellstrom-Lindberg E, Bowen D, et al. Diagnosis and treatment of primary myelodysplastic syndromes in adults: recommendations from the European LeukemiaNet. Blood 2013;122(17):2943–64; with permission.