ASTCT treatment recommendations for patients with MDS

Indication for transplantation	
Should allo-HSCT routinely be offered early for advanced (intermediate- 2/ high-risk) *de novo* MDS?	Yes
Should allo-HSCT routinely be offered early for lower-risk (low/intermediate-1) *de novo* MDS?	No, most patients should be treated with non-transplantation approaches, and undergo allo-HSCT only if the disease progresses to high risk or fails to improve.
When should patients with MDS be referred for HSCT evaluation?	All patients with MDS should be referred to HSCT. Patients with HR-MDS should be referred at diagnosis or early in the disease course. For patients with LR-MDS, referral is less urgent.
Patient-specific considerations	
Should eligibility for allo-HSCT be limited by age?	No, although age should be considered in the decision-making process, allo-HSCT eligibility should not be restricted by it.
Should eligibility for allo-HSCT be limited by comorbidity?	Both comorbidities and performance status are relevant to allo-HSCT outcomes and should be carefully assessed in all patients. However, the comorbidity threshold for allo-HSCT eligibility is unclear.
Disease-specific considerations	
Should allo-HSCT be offered to patients with therapy-related MDS?	Yes, allo-HSCT should be offered early to these patients; although it has not demonstrated superiority over transplantation strategies.
How should germline variants be considered?	• The presence of an inherited bone marrow failure syndrome should be excluded. • In the presence of germline mutation, potential related donors should be counseled and offered targeted testing to screen for mutations. • If predisposition to germline MDS is suspected, attempts to find a MUD should be made to avoid risk of transplanting causative mutation.
Should patients be assessed for chromosomal aberrations and somatic mutations prior to allo-HSCT?	Yes, as cytogenetic and molecular disease profiles impact outcomes, they should be evaluated pre-allo-HSCT. Although high-risk disease features are associated with poor survival and high rates of relapse, allo-HSCT should be offered but on an individualized basis.
Treatment-specific considerations	
Should pretransplantation systemic therapy be offered for MDS?	Yes, patients with MDS may receive systemic therapy pre-allo-HSCT; although the value is uncertain.
How should transfusion iron overload be managed?	If feasible, iron chelation and therapeutic phlebotomy should be initiated and continued until serum ferritin level or liver/cardiac iron concentration by MRI have normalized.
Conditioning regimens	
Are RIC regimens a suitable alternative for adults considered unfit for MAC regimen?	Both MAC and RIC can be considered in patients with MDS undergoing allo-HSCT.
Should MAC be the preferred conditioning intensity in fit patients?	Whilst it is unclear whether MAC should be preferred, the low relapse rate, making it a favored option in patients at lower risk for NRM, is acknowledged.
Alternative donors	
Can haploidentical relatives, MMUDs, and umbilical cord blood be considered as alternative donor options?	Yes, in patients with no availability of HLA-matched related or unrelated donors, haploidentical donors and MMUDs should be considered.
Posttransplantation	
Should patients with MDS receive maintenance therapy after HSCT?	The clinical benefit of maintenance therapy post-allo-HSCT is currently unknown.
Is there a preferred treatment for relapsed disease after HSCT?	Chemotherapy, DLI, and/or second allo-HSCT should be considered for selected patients.

allo-HSCT, allogeneic hematopoietic stem cell transplantation; ASTCT, American Society for Transplantation and Cellular Therapy; DLI, donor lymphocyte infusion; HR, higher-risk; LR, lower-risk; HLA, human leukocyte antigen; MAC, myeloablative conditioning; MDS, myelodysplastic syndromes; MUD, matched unrelated donor; MMUD, mismatched unrelated donor; MRI, magnetic resonance imaging; NRM, non-relapse mortality; RIC, reduced intensity conditioning.

Adapted from DeFilipp, *et al.*[1]

This educational resource is supported through funds from pharmaceutical companies—a full list of our supporters can be found at https://mds-hub.com/. All content is developed independently by SES in collaboration with the faculty. The funders are allowed no influence on the content of this resource.

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