

The Role of Cytotoxic Therapy with Hematopoietic Stem Cell Transplantation in the Therapy of Myelodysplastic Syndromes

Among the primary objectives of the American Society for Blood and Marrow Transplantation are to:

- Define commonly accepted medical and evidence-based practice
- Develop standards of medical care for autologous and allogeneic transplants
- Provide recommendations and guidelines for physicians, patients, and third-party payers on the role of transplantation as a therapeutic approach.

Toward this end, in 1999 the Society began sponsoring evidence-based reviews of the scientific and medical literature to document when blood and marrow transplantation is indicated in the treatment of selected diseases.

GOALS

The goals of the evidence-based reviews are to:

- Determine which disease will be the subject of each review, establish the focus for each review, and develop a list of questions to be addressed
- Assemble and critically evaluate all the valid, peer-reviewed evidence regarding the role of cytotoxic therapy with hematopoietic stem cell transplantation related to the disease
- Provide treatment recommendations based on the available evidence
- Identify discrepancies in study design or methodology among published studies that may impact on the quality of the evidence
- Identify needed areas of additional research.

GUIDELINES

The following guidelines are offered for the role of stem cell transplantation (SCT) as therapy for myelodysplastic syndromes (MDS), and are based on consensus reached by an expert panel¹ following an evidence-based review of the literature.²

TIMING OF TRANSPLANTATION

Early SCT is recommended for patients with an International Prognostic Scoring System (IPSS) score of INT-2, considered high risk, at diagnosis who have a suitable donor and meet the transplant center's eligibility criteria, and for selected patients at low risk (IPSS score of INT-1) at diagnosis who have poor prognostic features not included in the IPSS (e.g., older age, refractory cytopenias).

PRE-SCT INDUCTION CHEMOTHERAPY

In the absence of randomized controlled trials, insufficient data are available to make a treatment recommendation for or against pre-SCT induction chemotherapy. The decision to use pre-SCT induction therapy should be made on an individual basis.

DONOR SELECTION

1. There is no evidence of a survival advantage based on donor relation in allogeneic SCT. In clinical practice, matched related donor allogeneic SCT is recommended if available. If not, unrelated donor allogeneic SCT may provide equivalent outcomes.
2. There are sufficient data demonstrating a long-term curative outcome for related and unrelated allogeneic SCT.
3. Based on data and expert opinion, an HLA-matched allogeneic donor (sibling, other family member, unrelated individual, or cord blood) SCT is recommended if an appropriate donor is available. If an allogeneic donor is not available, and complete remission is achieved with induction therapy, then an autologous SCT can be considered in the context of a clinical trial.

TRANSPLANTATION TECHNIQUES

1. Bone marrow transplant (BMT) versus peripheral blood stem cell transplant (PBSCT):

- For low-risk disease, allogeneic BMT and PBSCT from *related* donors have equivalent outcomes.
 - Patients with high-risk disease may have a survival advantage with related donor allogeneic PBSCT.
 - There is insufficient evidence to recommend BMT versus PBSCT for *unrelated* donor allogeneic SCT.
 - There is no evidence of a survival advantage based on stem cell source for autologous BMT versus PBSCT.
2. Conditioning regimen comparisons:
 - There are insufficient data to make a recommendation for an optimal conditioning regimen intensity. A range of dose intensities is currently under investigation, and the optimal approach likely will depend on disease and patient characteristics, such as age and comorbidities.
 - There are insufficient data to make a recommendation for any one high-dose conditioning regimen over another.

AREAS OF NEEDED RESEARCH

The expert panel identified the following important areas of needed research in MDS:

1. The benefit of using alternative donor sources (e.g., cord blood; haploidentical family donors) for patients without matched sibling or unrelated donors

2. The role and appropriate timing of allogeneic SCT in combination with hypomethylating and immunomodulatory treatment regimens
3. Randomized trials comparing the safety and efficacy of various novel agents for treating MDS
4. The influence of the various MDS treatment modalities on patient-reported quality of life outcomes.

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