

ASBMT POSITION STATEMENT

The Role of Cytotoxic Therapy With Hematopoietic Stem Cell Transplantation in the Therapy of Acute Myeloid Leukemia in Children

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

- Define commonly accepted medical practice
- Develop standards of medical care for autologous and allogeneic transplants
- Provide recommendations and guidelines for the role of transplantation as a therapeutic approach for reimbursement by third party payers.

To this end, in 1999, the Society began the development of 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 diseases will be the subject of 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
- Make treatment recommendations based on the available evidence
- Identify discrepancies in study design or methodology among published studies that may have an 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 acute myelogenous leukemia (AML) in children, and are based on consensus reached by an expert panel¹ following an evidence-based review of the literature:²

Transplantation versus Chemotherapy

1. Autologous SCT and chemotherapy in the first complete remission are equivalent in outcomes. The lack of data on quality of life, secondary malignancies, and other late effects of treatment pre-

vent a recommendation of one treatment over the other.

2. Allogeneic SCT shows superior overall survival (OS) and leukemia-free survival when compared to chemotherapy for patients in the first complete remission (CR1). Thus, allogeneic SCT is recommended in the first complete remission. Additional prospective data regarding risk subgroups may subsequently alter this recommendation.
3. In allogeneic SCT versus chemotherapy in the second CR, the expert panel acknowledges a lack of evidence comparing matched related allogeneic donors (MRD) versus chemotherapy. Nonetheless, the expert panel consensus recommends the use of any suitable allogeneic MRD if one is available. A matched unrelated donor (MUD) or other alternative donor SCT is recommended in the context of a clinical trial.

Transplantation Techniques

1. MRD allogeneic SCT has superior survival outcomes compared to autologous SCT in the CR1. Additional prospective data regarding risk sub-

¹Expert panel members and authors of the review are: Denise Oliansky, Roswell Park Cancer Institute (RPCI), Buffalo, NY; J. Douglas Rizzo, Medical College of Wisconsin, Milwaukee, WI; Peter D. Aplan, National Institutes of Health, National Cancer Institute, Genetics Branch, Bethesda, MD; Robert J. Arceci, Kimmel Comprehensive Cancer Center, Baltimore, MD; Louis Leone, Children's Oncology Group, Arcadia, CA; Yaddanapudi Ravindranath, Children's Hospital of Michigan and Wayne State University School of Medicine, Detroit, MI; Jean E. Sanders, Fred Hutchinson Cancer Research Center, University of Washington, Seattle, WA; Franklin O. Smith III, Cincinnati Children's Hospital and Medical Center and University of Cincinnati College of Medicine, Cincinnati, OH; Fiona Wilmot, Blue Shield of California, San Francisco, CA; Philip L. McCarthy, Jr., RPCI; Theresa Hahn, RPCI.

²Reference: Oliansky D, Rizzo JD, Aplan PT, et al. Role of cytotoxic therapy with hematopoietic stem cell transplantation in the therapy of acute myeloid leukemia in children: an evidence-based review. *Biol Blood Marrow Transplant.* 2007;13(1):1-25.

groups may alter this recommendation. The consensus recommendation of the expert panel is to use bone marrow as the stem cell source in the MRD allogeneic SCT setting based on scientific, ethical, regulatory, and practical issues.

2. In the second CR, the consensus recommendation is to use any suitable MRD or MUD over autologous SCT. There is, however, a lack of evidence that one has better outcomes than the other.
3. Although the current practice is to use peripheral blood SCT (PBSCT), there are very few patients in the studies that fulfilled the inclusion criteria for the review. A randomized trial of autologous BMT versus PBSCT is not feasible because of the infrequent use of autologous SCT for pediatric patients with AML.
4. There is a preference for using MUD or other alternative donors over autologous SCT if an MRD is not available.
5. No effective purging agents are currently available. If one were available, it would increase interest in a clinical trial of purged versus unpurged autologous SCT.
2. MRD allogeneic SCT is preferred in the first or second CR. In the second remission, alternative donors could be considered if MRD is not available.
3. Based on a lack of evidence, no recommendation can be made for a preferred technique for unrelated allogeneic SCT (eg, T cell depletion, cord blood versus PBSCT versus BMT, and so on).
4. No difference or preference for one myeloablative condition regimen over another can be recommended with respect to OS, leukemia-free survival, or late effects of SCT.
5. There is no evidence of a benefit of SCT for acute promyelocytic leukemia (APL) in the first remission, and it is not recommended.
6. For APL in the second complete remission, the preferred practice is to use allogeneic SCT. Autologous SCT is recommended if there is no suitable MUD, MRD, or other alternative donor. An alternative would be a clinical trial comparing haploidentical allogeneic versus autologous SCT.

Indications for SCT

1. There are no data to recommend using related versus unrelated allogeneic SCT. Although there are differences among institutions with regard to transplant techniques, there are no apparent differences in outcomes.

*Adopted by the ASBMT Executive Committee
on January 18, 2007*

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