

ASBMT POSITION STATEMENT

The Role of Cytotoxic Therapy with Hematopoietic Stem Cell Transplantation in the Treatment of Acute Lymphoblastic Leukemia in Adults*

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 about 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 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 evidence regarding the role of cytotoxic therapy with hematopoietic stem cell transplantation related to the disease and the questions to be addressed in each review
 - Make treatment recommendations based on the available evidence
 - Identify discrepancies in study design or methodology among published studies that may impact the quality of the evidence
 - Identify needed areas of additional study

Guidelines

The following guidelines are offered for the role of stem cell transplantation (SCT) as therapy for acute lymphoblastic leukemia (ALL) in adults and are based on consensus reached by an expert panel¹ following an evidence-based review of the literature²:

1. In first complete remission (CR1), SCT yields outcomes similar to chemotherapy and is not recommended as first-choice therapy. For high-risk patients, there are no direct comparisons but some data suggest an advantage for SCT.
2. In second complete remission (CR2), SCT is recommended over chemotherapy as a sizeable fraction of patients achieve extended leukemia-free survival compared to chemotherapy alone.
3. Autologous purged SCT and autologous unpurged SCT produce leukemia-free survival comparable to chemotherapy.
4. Although there are no direct comparisons, there appears to be a survival advantage for related allogeneic SCT compared to chemotherapy in Ph+ adult ALL patients in CR1 or subsequent remissions.

*A separate evidence-based review and position statement are available for the role of SCT in pediatric ALL patients.^{3,4}

¹Expert panel members and authors of the review are: Theresa Hahn, PhD, Roswell Park Cancer Institute, Buffalo, NY; Donna Wall, MD, Texas Transplant Institute, San Antonio, TX; Bruce Camitta, MD, Midwest Children's Center, Medical College of Wisconsin and Children's Hospital of Wisconsin, Milwaukee, WI; Stella Davies, MD, PhD, Cincinnati Children's Hospital and Medical Center, Cincinnati, OH; Hildy Dillon, MPH, The Leukemia and Lymphoma Society, White Plains, NY; Paul Gaynon, MD, Children's Hospital of Los Angeles, Los Angeles, CA; Richard A. Larson, MD, University of Chicago, Chicago, IL; Susan Parsons, MD, Dana-Farber Cancer Institute/Harvard Medical School, and Tufts New England Medical Center/Tufts University School of Medicine, Boston, MA; Jerome Seidenfeld, Blue Cross and Blue Shield Association Technology Evaluation Center, Chicago, IL; Daniel Weisdorf, MD, University of Minnesota, Minneapolis, MN; Philip L. McCarthy, Jr., MD, Roswell Park Cancer Institute, Buffalo, NY.

²Reference: Hahn T, Wall D, Camitta B, et al. The role of cytotoxic therapy with hematopoietic stem cell transplantation in the therapy of acute lymphoblastic leukemia in adults: an evidence-based review. *Biol Blood Marrow Transplant.* 2006;12:1-30.

³Reference: Hahn T, Wall D, Camitta B, et al. The role of cytotoxic therapy with hematopoietic stem cell transplantation in the therapy of acute lymphoblastic leukemia in children: an evidence-based review. *Biol Blood Marrow Transplant.* 2005;11: 823-861.

⁴Reference: ASBMT Position Statement: The role of cytotoxic therapy with hematopoietic stem cell transplantation in the treatment of acute lymphoblastic leukemia in children. *Biol Blood Marrow Transplant.* 2006;12:370-371.

5. Unrelated allogeneic SCT produces extended leukemia-free survival in some patients. Although there are no direct comparisons, there is a possible benefit of unrelated allogeneic SCT over chemotherapy in Ph+ adult ALL patients. Higher treatment-related mortality, however, may compromise the potential anti-tumor advantage of unrelated allogeneic SCT.
6. There are not enough data to recommend one conditioning regimen over another, although there appears to be an advantage to TBI-containing compared to non-TBI-containing regimens.
7. There are not enough data evaluating nonmyeloablative conditioning regimens to determine the effect on treatment-related mortality and leukemia-free survival. No recommendation can be made.
8. A preponderance of evidence supports a recommendation of allogeneic over autologous SCT. There is insufficient evidence, however, to determine if this effect is more apparent in specific risk subgroups, including Ph+ adult ALL.
9. The following are recommended as the most important areas of needed research:
 - Monitoring of minimal residual disease and disease control before SCT
 - Comparison of non-family (unrelated bone marrow or cord blood) donor vs. autologous SCT
 - Definition of high risk groups, beyond Ph+ status, in CR1 with formal testing of SCT vs. other treatments
 - Analysis of the graft-versus-leukemia effect in reduced intensity vs. myeloablative conditioning regimens
 - Outcomes data for SCT in older (>50 years) patients with ALL
 - Evaluation of the impact of imatinib and other tyrosine kinase inhibitors on SCT for Ph+ ALL

*—Adopted by the ASBMT Executive Committee
on September 29, 2005*

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