

Outcomes

IN UNRELATED HEMATOPOIETIC CELL TRANSPLANTATION:

Applying New Data for Referral and Decision-Making

Key Findings

1

Survival is improving. Unrelated transplant outcomes have improved due to a number of factors including changes in clinical practice and a better understanding of human leukocyte antigen typing and matching.

2

Timing matters. Research shows that patients transplanted earlier in their disease stage have better outcomes than patients with advanced disease.

3

Patient selection is expanding. As outcomes improve and donor and cord blood registries grow, more patients become candidates for transplant – resulting in significant growth in the number of patients treated with unrelated transplant.

Improving Survival for Unrelated Transplantation

More than 10,000 allogeneic hematopoietic cell transplants (HCT) performed worldwide each year use unrelated donors or cord blood units, accounting for approximately half of all allogeneic transplants.

Recently published studies have found unrelated transplant survival outcomes comparable to related transplant results in several patient populations.¹⁻⁵ In some instances, unrelated transplant outcomes have even exceeded those obtained in related transplant.⁶

This summary provides clinicians with an overview of unrelated transplantation today and how the latest research results affect current clinical decision-making.

Why Outcomes are Improving

Several factors have led to better outcomes including:

1. Refined pre- and post-transplant clinical practices
2. Enhanced patient-donor matching
3. Better understanding of the optimal timing for referral and transplantation

1. Refined Clinical Practice

- Preparative regimens tailored to the patient's disease and condition and notable improvements in the ability to manage possible complications of HCT have led to a reduction in treatment-related mortality.⁷⁻⁹

2. Enhanced Patient-Donor Matching

- High-resolution human leukocyte antigen (HLA) typing in combination with knowledge about which HLA mismatches are important has improved survival.
- Use of cord blood as a stem cell source has increased the possibilities for patients to find a suitable match.
- Larger registries of donors and cord blood units enables a higher degree of match for more patients.

Improved Survival with Unrelated Transplantation

Report Year	Period	One-Year Survival
2003	1996-2001	42.2 %
2006	2000-2004	48.8 %
2007	2001-2005	51.5 %

Figure 1. One-year survival of unrelated transplant recipients at U.S. transplant centers has improved over recent years. NMDP-facilitated transplant analysis.

Reduction in Transplant-Related Mortality

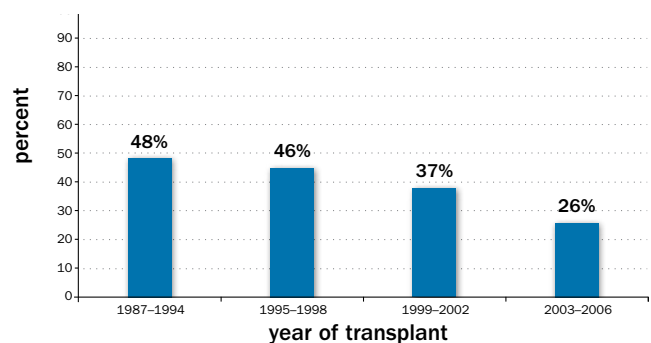


Figure 2. One-year transplant-related mortality for NMDP transplants for malignant diseases has steadily declined over time. NMDP-facilitated transplant analysis.

Outcomes

IN UNRELATED HEMATOPOIETIC CELL TRANSPLANTATION:

Applying New Data for Referral and Decision-Making

3. Better Understanding of Optimal Timing

- While having an optimally matched donor or cord blood unit is important, a 2007 study indicates that patients transplanted earlier in their disease have better outcomes than patients with advanced disease, regardless of the degree of the match.¹⁰
- Because disease stage at the time of transplant is the only factor under direct control of a physician, an **early referral is perhaps the single most important step that can affect survival.**

Probability of Overall Survival by HLA Matching:

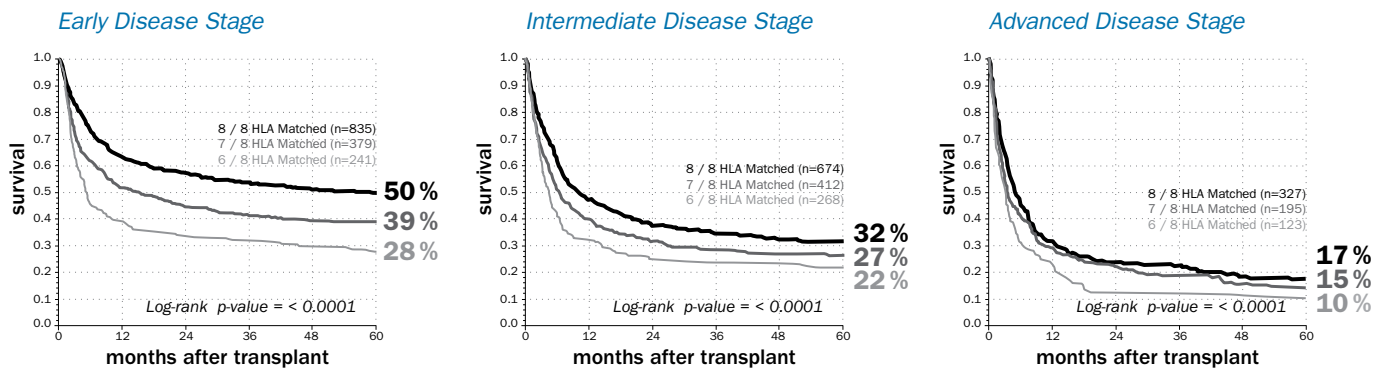


Figure 3. Overall survival of 3,857 U.S. transplant recipients from 1988–2003 with ALL, AML, CML and MDS using NMDP donors.



This research was originally published in Blood. Lee SJ, et al. High-resolution donor-recipient HLA matching contributes to the success of unrelated donor marrow transplantation. Blood. 2007; Vol 110: 4576-4583. (c) the American Society of Hematology.

Trends in Unrelated Transplantation

Several trends have led to the significant growth observed in unrelated transplantation:

1. **Increase in transplant for AML and MDS.** Unrelated transplantation is growing in nearly all diseases for which transplant is indicated; most dramatically in AML and MDS.
2. **Older patients eligible.**¹¹⁻¹³ Transplants for patients over age 50 now account for 35% of all NMDP-facilitated transplants.
3. **Cord blood expanding access.** Growing cord blood and adult donor registries are allowing more patients to find a suitable match, especially minorities using cord blood.

Overall Growth in NMDP-Facilitated Transplants by fiscal year 1987–2007

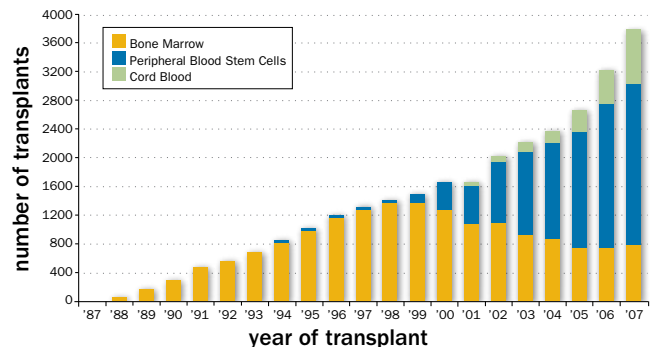


Figure 4. Number of NMDP-facilitated transplants has surpassed 30,000 transplants, with a 14% increase between 2006 and 2007.

Learn More: Trends

To learn more about trends in allogeneic transplantation, visit marrow.org/md-trends

PHYSICIANS' RESOURCE CENTER

Outcomes

IN UNRELATED HEMATOPOIETIC CELL TRANSPLANTATION:

Applying New Data for Referral and Decision-Making

Clinical Action Points

1

Requesting a transplant consultation earlier ensures that disease progression doesn't compromise outcomes.

2

Whether a related donor is available or an unrelated donor is needed, timing of transplant consultation should be the same. Early consultation ensures plans are in place to move forward if or when transplantation is warranted.

3

Clinicians treating older patients should review current protocols and consider transplant as a treatment option.

Learn More: Online Education

To access a one-hour webinar on the application of unrelated transplantation and receive CME credit, visit marrow.org/md-newdata

PHYSICIANS' RESOURCE CENTER

References

1. Nakamura R, Rodríguez R, Palmer J, et al. Reduced-intensity conditioning for allogeneic hematopoietic stem cell transplantation with fludarabine and melphalan is associated with durable disease control in myelodysplastic syndrome. *Bone Marrow Transplant.* 2007; 40(9):843–850.
2. Moore J, Nivison-Smith I, Goh K, et al. Equivalent survival for sibling and unrelated donor allogeneic stem cell transplantation for acute myelogenous leukemia. *Biol Blood Marrow Transplant.* 2007; 13(5):601-607.
3. Gassas A, Sung L, Saunders EF, Doyle J. Graft-versus-leukemia effect in hematopoietic stem cell transplantation for pediatric acute lymphoblastic leukemia: significantly lower relapse rate in unrelated transplantations. *Bone Marrow Transplant.* 2007; 40(10):951–955.
4. Maury S, Balère-Appert ML, Chir Z, et al. Unrelated stem cell transplantation for severe acquired aplastic anemia: improved outcome in the era of high-resolution HLA matching between donor and recipient. *Haematologica.* 2007; 92(5):589-596.
5. Weisdorf DJ, Anasetti C, Antin JH, et al. Allogeneic bone marrow transplantation for chronic myelogenous leukemia: comparative analysis of unrelated versus matched sibling donor transplantation. *Blood.* 2002; 99(6):1971-1977.
6. Chang CK, Storer BE, Scott BL, et al. Hematopoietic cell transplantation in patients with myelodysplastic syndrome or acute myeloid leukemia arising from myelodysplastic syndrome: similar outcomes in patients with de novo disease and disease following prior therapy or antecedent hematologic disorders. *Blood.* 2007; 110(4):1379-1387.
7. Khouri IF, Saliba RM, Giralt SA, et al. Nonablative allogeneic hematopoietic transplantation as adoptive immunotherapy for indolent lymphoma: low incidence of toxicity, acute graft-versus-host disease, and treatment-related mortality. *Blood.* 2001; 98(13):3595-3599.
8. Chakraverty R, Peggs K, Chopra R, et al. Limiting transplantation-related mortality following unrelated donor stem cell transplantation by using a nonmyeloablative conditioning regimen. *Blood.* 2002; 99(3):1071-1078.
9. Horowitz MM. Uses and growth of hematopoietic cell transplantation. In: Blume KG, Forman SJ, Appelbaum FR, eds. *Thomas' Hematopoietic Cell Transplantation*, 3rd ed. Malden, Mass: Blackwell, 2004:9-15.
10. Lee SJ, Klein J, Michael Haagenson, et al. High-resolution donor-recipient HLA matching contributes to the success of unrelated donor marrow transplantation. *Blood.* 2007; 110(13):4576-4583.
11. Alyea EP, Kim HT, Ho VT, et al. Comparative outcome of nonmyeloablative and myeloablative allogeneic hematopoietic cell transplantation for patients older than fifty years of age. *Blood.* 2005; 105(4):1810-1814.
12. Mielcarek M, Storer BE, Sandmaier BM, et al. Comparable outcomes after nonmyeloablative hematopoietic cell transplantation with unrelated and related donors. *Biol Blood Marrow Transplant.* 2007; 13(2):1499-1507.
13. Oran B, Giralt S, Saliba R, et al. Allogeneic hematopoietic stem cell transplantation for the treatment of high-risk acute myelogenous leukemia and myelodysplastic syndrome using reduced-intensity conditioning with fludarabine and melphalan. *Biol Blood Marrow Transplant.* 2007; 13(4):454-462.

NATIONAL MARROW DONOR PROGRAM®

3001 Broadway St. N.E., Suite 100
Minneapolis, MN 55413

Physicians' Resource Center: marrow.org/md
1 (800) MARROW-2 (1-800-627-7692)

Entrusted to operate the C.W. Bill Young Cell Transplantation Program

The National Marrow Donor Program facilitates unrelated marrow, PBSC and cord blood transplants. Our passion for patients drives our commitment to the physicians who serve them. We provide physicians with resources, services and education to support clinical decision-making. To learn more, visit marrow.org/md.