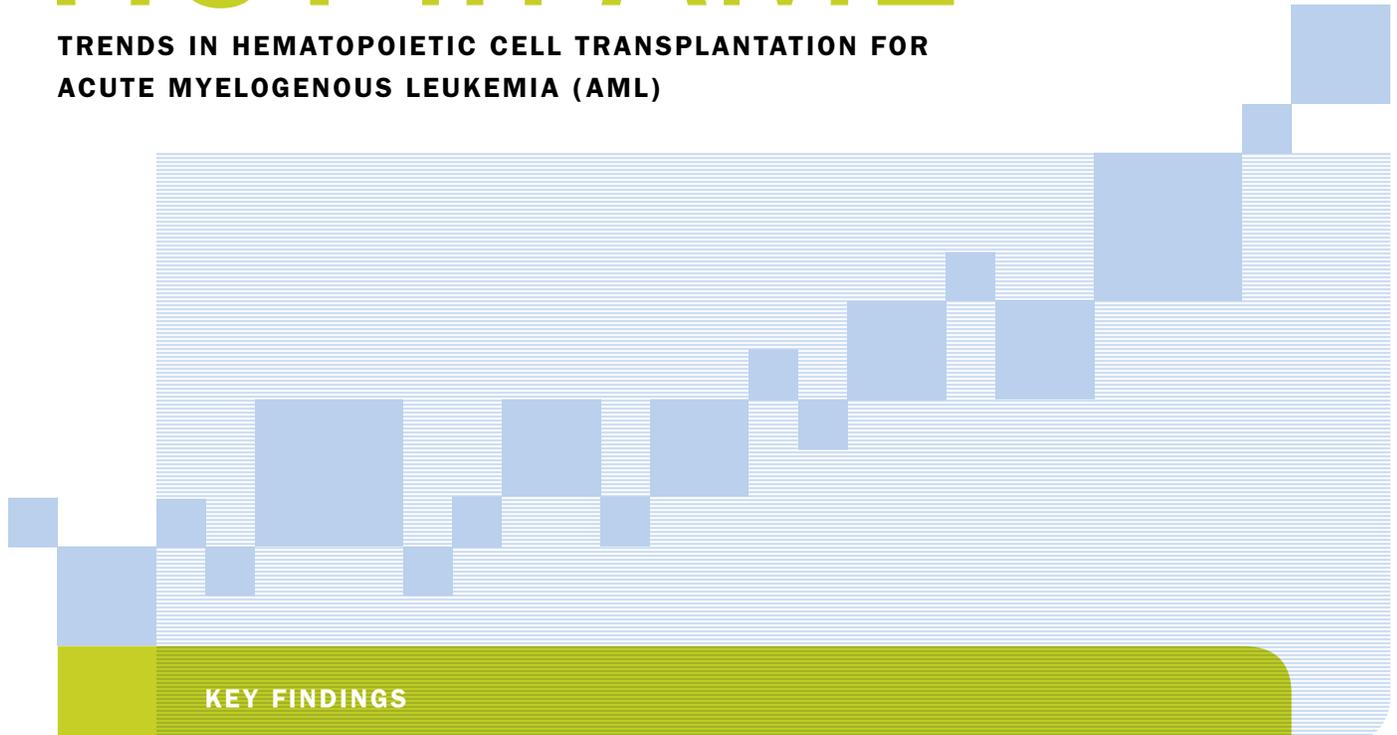


HCT in AML

TRENDS IN HEMATOPOIETIC CELL TRANSPLANTATION FOR ACUTE MYELOGENOUS LEUKEMIA (AML)



KEY FINDINGS

1

Molecular markers influence therapy choices.

New classifications based on cytogenetic and molecular abnormalities in AML allow physicians to better stratify patients into risk groups and select appropriate therapies.

2

Patient eligibility is expanding.

Improved outcomes now allow for more patients to be considered for transplant, resulting in growth in transplants for older patients and those in first complete remission (CR1).

3

Survival is improving.

Allogeneic transplant outcomes have improved due to advances in clinical practice and human leukocyte antigen (HLA) typing and matching.

Advances in Research Guide Clinical Practice

This summary provides clinicians with an overview of recent trends in allogeneic transplantation for acute myelogenous leukemia (AML) in adults and how the latest research affects clinical decision-making. Worldwide, more than 6,000 allogeneic hematopoietic cell transplants (HCT) are performed annually

for AML, making it the most common and fastest growing indication for allogeneic transplantation. Several factors have led to new applications of HCT to treat AML, including improved outcomes, expanded patient selection and refined risk stratification.

Refined Patient Selection

Molecular Markers Influence Therapy Choices

In 2008, the World Health Organization (WHO) re-classified AML into eight distinct categories with 25 sub-classifications based on the underlying cytogenetic and molecular genetic abnormalities that characterize AML.¹

Based on these WHO classifications, clinicians are now better able to refine risk stratification of patients with AML into prognostic risk groups and selecting those patients most likely to benefit from allogeneic HCT.²

Survival Benefit of HCT in Intermediate-Risk AML in CR1

A 2009 meta-analysis demonstrated the survival benefit of allogeneic HCT for intermediate-risk AML in first complete remission (CR1) over chemotherapy and autologous transplantation (see Table 1). Based on this research, transplant consultation guidelines have recently been updated (see Table 2).

Relapse-Free Survival Benefit of Allogeneic Transplant in Patients with AML				
CYTOGENETIC RISK	# OF TRIALS	HAZARD RATIO (95% CI)	P-VALUE	ALLOGENEIC BENEFIT
Good-risk	10	1.06 (0.80–1.42)	0.68	No
Intermediate-risk	14	0.76 (0.68–0.85)	<0.01	Yes
Poor-risk	14	0.69 (0.57–0.84)	<0.01	Yes

Table 1. Allogeneic HCT in patients with intermediate- and poor-risk AML in CR1 have significantly better relapse-free survival compared to consolidation chemotherapy and autologous transplantation.³

Transplant Guidelines Updated

Based on the new research, transplant consultation guidelines from the National Marrow Donor Program (NMDP) and the American Society for Blood and Marrow Transplantation (ASBMT) were updated to recommend that intermediate-risk AML patients in CR1 be referred for transplant consultation (see Table 2).

The intent of these guidelines, based on evidence-based reviews, is to identify patients at risk of disease progression and, therefore, which patients should be evaluated for transplantation.⁴

Recommended Timing for Transplant Consultation
ADULT ACUTE MYELOGENOUS LEUKEMIA
High-risk AML including:
• Antecedent hematological disease (e.g., myelodysplasia (MDS))
• Treatment-related leukemia
• Induction failure
CR1 with intermediate- or poor-risk cytogenetics or molecular markers
CR2 and beyond

Table 2. Excerpt from NMDP/ASBMT guidelines, which recommend transplant consultation for adult AML patients with: 1) high-risk disease, 2) CR1 with intermediate or poor-risk cytogenetics or molecular markers, and 3) CR2 and beyond.⁴



Increased Use in Older Patients

Reduced-Intensity HCT Expands Eligibility

Reduced-intensity conditioning regimens have expanded HCT to older patients and those with comorbidities unable to undergo myeloablative HCT. Studies show that reduced-intensity HCT can have comparable outcomes to myeloablative transplants using both related and unrelated donors.^{5,6,7,8}

Effect of Age on Survival

A multicenter study of 545 adults age 40–79 years with AML undergoing reduced-intensity transplantation did not identify age as a significant factor affecting overall survival.⁹ Other clinical studies have also shown that HCT can be appropriate therapy for older patients with AML.^{5,8}

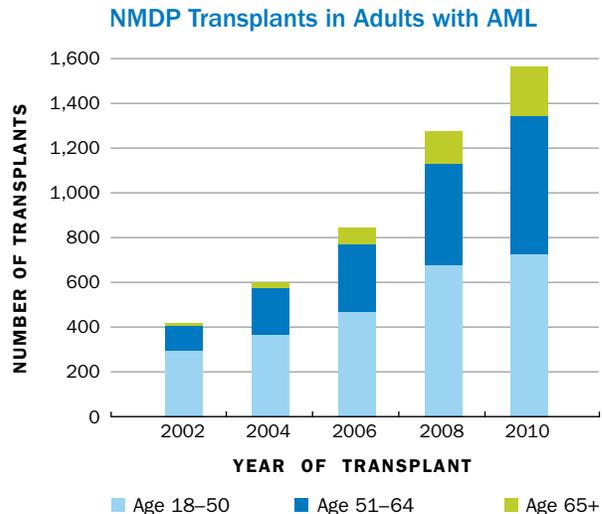


Figure 1. Distribution of unrelated donor transplants, by age, 2002–2010 for AML facilitated by the NMDP.¹⁰

Improved Survival

Several factors have led to the steady improvement in overall survival after HCT, including:

Clinical Practice Advances

- Improved ability to manage post-transplant complications¹¹
- Preparative regimens, such as reduced-intensity conditioning, tailored to the patient’s disease and condition⁵

HLA Matching Advances

- DNA-based patient and donor tissue typing^{12,13}
- Identification of which HLA loci are most significant to outcomes^{12–14}

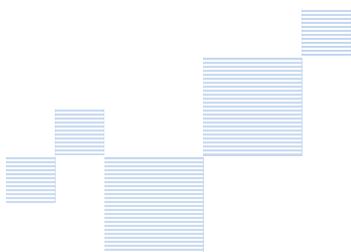
Several recently published studies show that unrelated donor transplant outcomes in AML are now comparable to related donor transplant results.^{6,15–17} Table 3 shows the improvement over time for unrelated transplants facilitated by the NMDP.¹⁸ These improved outcomes have been achieved even as a greater number of older patients are being transplanted.

Improved Survival Over Time—AML		
YEAR OF HCT	NUMBER OF CASES	ONE-YEAR SURVIVAL
2006–2008	2,061	55%
2003–2005	1,365	47%
1999–2002	863	41%
1987–1998	833	26%

Table 3. One-year survival of adults with AML after unrelated HCT is significantly better for patients transplanted during 2003–2005 and 2006–2008 compared to patients transplanted during 1987–1998 and 1999–2002 ($p < 0.001$).¹⁹

ACCESS AML RESOURCES

- Educational program and slides: *Decision-Making in AML and MDS*
marrow.org/md-CME
- NMDP/ASBMT Recommended *Timing for Transplant Consultation*
marrow.org/md-guidelines



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TRENDS IN HEMATOPOIETIC CELL TRANSPLANTATION FOR ACUTE MYELOGENOUS LEUKEMIA (AML)

CLINICAL ACTION POINTS

1

Use molecular markers to stratify patients with AML into prognostic risk groups and identify those most likely to benefit from allogeneic HCT.

2

Recommend transplant consultation for patients in CR1 with intermediate- or poor-risk AML.

3

Review current protocols and consider HCT as a treatment option for older patients with AML.

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