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## Significant Improvement in Survival after Unrelated Donor Hematopoietic Cell Transplantation in the Recent Era



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#### ABSTRACT

Patients and physicians may defer unrelated donor hematopoietic cell transplantation (HCT) as curative therapy because of the mortality risk associated with the procedure. Therefore, it is important for physicians to know the current outcomes data when counseling potential candidates. To provide this information, we evaluated 15,059 unrelated donor hematopoietic cell transplant recipients between 2000 and 2009. We compared outcomes before and after 2005 for 4 cohorts: age <18 years with malignant diseases (n = 1920), ages 18 to 59 years with malignant diseases (n = 9575), ages  $\geq$  60 years with malignant diseases (n = 2194), and nonmalignant diseases (n = 1370). Three-year overall survival in 2005 to 2009 was significantly better in all 4 cohorts (<18 years: 55% versus 45%, 18 to 59 years: 42% versus 35%,  $\geq$ 60 years: 35% versus 25%, nonmalignant diseases: 69% versus 60%; *P* < .001 for all comparisons). Multivariate analyses in leukemia patients receiving HLA 7/8 to 8/8–matched transplants showed significant reduction in overall and non-relapse mortality in the first year after HCT among patients who underwent transplantation in 2005 to 2009; however, risks for relapse did not change over time. Significant survival improvements after unrelated donor HCT have occurred over the recent decade and can be partly explained by better patient selection (eg, HCT earlier in the disease course and lower disease risk), improved donor selection (eg, more precise allele-level matched unrelated donors) and changes in transplantation practices.

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#### INTRODUCTION

Allogeneic hematopoietic cell transplantation (HCT) using an unrelated donor is curative therapy for patients with high-risk hematologic diseases who need a transplant but lack a human leukocyte antigen (HLA)—identical sibling

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donor. Survival after unrelated donor HCT has nearly doubled since the first unrelated donor transplantations in the late 1980s [1,2]. Currently, 1-year survival of 60% to 70% can be expected for patients with high-risk acute leukemia who receive an unrelated donor HCT relatively early in their disease course [3,4]. For some diseases, survival after HLAmatched unrelated donor transplantation has been shown to be comparable to HCT using HLA-identical sibling donors [5-10]. However, patient and physician perceptions of the risks and efficacy of unrelated donor transplantation may prevent some patients from being referred for this

### Table 1

Demographic Characteristics by Age, Diagnosis, and Time Period

2000-2004Recipients, n904Centers, n97Follow-up, median (range), mo91 (3-147)Recipient gender562 (40)Male362 (40)Male632 (70)Hispanic137 (15)Black/African American85 (9)Asian/Pacific Islander29 (3)American Indian/Alaska Native4 (<1)Other/multiple race10 (1)Declined/unknown7 (1)Karnofsky/Lansky score at HCT90 to 10090 to 100691 (76)10 to 80115 (13)Unknown98 (11)Recipient CMV statusNegativeNegative504 (56)Positive395 (44)Unknown5 (1)Coexisting disease at HCT269 (30)Diagnosis383 (42)AML279 (31)ALL383 (42)CML85 (9)Other leukemia26 (3)MDS57 (6)Myeloproliferative diseases39 (4)NHL30 (3)Hodgkin lymphoma1 (<1)Plasma cell disorders-Other malignant diseases4 (<1)SAA-Inherited erythrocyte disorders-Inherited disorders-Inherited disorders-Inherited disorders-Inherited disorders-Inherited disorders-Inherited disorders-Inherited disorders-Inherited disorders-Inherited platelet di	2005-2009 1016 103 47 (4-78) 410 (40) 606 (60) 694 (68) 178 (18) 65 (6) 39 (4) 7 (1) 22 (2) 11 (1) 822 (81) 126 (12) 68 (7) 500 (49)	P Value <sup>*</sup> <.001 .90 .06 .005	$\begin{array}{r} \hline 2000-2004 \\ \hline 3827 \\ \hline 138 \\ 95 (3-145) \\ \hline 1618 (42) \\ 2209 (58) \\ \hline 3324 (87) \\ 220 (6) \\ \hline 167 (4) \\ 64 (2) \\ 6 (<1) \\ 22 (1) \\ 24 (1) \\ \hline 2313 (60) \\ 1098 (29) \\ \hline \end{array}$	2005-2009 5748 152 42 (3-84) 2557 (44) 3191 (56) 4896 (85) 356 (6) 255 (4) 104 (2) 23 (<1) 31 (1) 83 (1)	P Value <sup>*</sup>	$\begin{array}{c} \hline 2000-2004 \\ \hline 410 \\ 76 \\ 76 (9-121) \\ 125 (30) \\ 285 (70) \\ \hline 391 (95) \\ 8 (2) \\ 6 (1) \\ 1 (<1) \\ 0 \\ 1 (<1) \\ \end{array}$	2005-2009 1784 115 36 (3-82) 628 (35) 1156 (65) 1671 (94) 41 (2) 31 (2) 17 (1) 1 (<1)	P Value <sup>*</sup> <.001 .07 .80	2000-2004 477 83 82 (4-147) 197 (41) 280 (59) 328 (68) 70 (15) 41 (9) 28 (6)	2005-2009 893 133 39 (2-85) 337 (38) 556 (62) 599 (67) 131 (15) 79 (9)	P Value <.001 .20 .58
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Coexisting disease at HCT269 (30)Diagnosis	507 (50)		2097 (55)	3300 (57)		269 (66)	1127 (63)		246 (52)	488 (55)	
DiagnosisAML279 (31)ALL383 (42)CML85 (9)Other leukemia26 (3)MDS57 (6)Myeloproliferative diseases39 (4)NHL30 (3)Hodgkin lymphoma1 (<1)	9(1)		32 (1)	65 (1)		4(1)	24(1)		11 (2)	10(1)	
AML $279 (31)$ $ALL$ $383 (42)$ $CML$ $85 (9)$ $Other leukemia$ $26 (3)$ $MDS$ $57 (6)$ $Myeloproliferative diseases$ $39 (4)$ $NHL$ $30 (3)$ $Hodgkin lymphoma$ $1 (<1)$ $Plasma cell disorders$ - $Other malignant diseases$ $4 (<1)$ $SAA$ - $Inherited erythrocyte disorders$ - $Inherited immune system disorders$ - $Inherited disorders of metabolism$ - $Histiocytic disorders$ - $Inherited platelet disorders$ -	376 (37)	<.001	1858 (49)	3644 (63)	<.001	296 (72)	1398 (78)	.02	196 (41)	443 (50)	.008
ALL383 (42)CML85 (9)Other leukemia26 (3)MDS57 (6)Myeloproliferative diseases39 (4)NHL30 (3)Hodgkin lymphoma1 (<1)		<.001			<.001			.002			<.001
CML $85 (9)$ Other leukemia $26 (3)$ MDS $57 (6)$ Myeloproliferative diseases $39 (4)$ NHL $30 (3)$ Hodgkin lymphoma $1 (<1)$ Plasma cell disorders-Other malignant diseases $4 (<1)$ SAA-Inherited erythrocyte disorders-Inherited immune system disorders-Inherited disorders of metabolism-Histiocytic disorders-Inherited platelet disorders-	290 (29)		1409 (37)	2412 (42)		202 (49)	884 (50)		-	-	
Other leukemia26 (3)MDS57 (6)Myeloproliferative diseases39 (4)NHL30 (3)Hodgkin lymphoma1 (<1)	462 (45)		667 (17)	973 (17)		18 (4)	65 (4)		-	-	
MDS     57 (6)       Myeloproliferative diseases     39 (4)       NHL     30 (3)       Hodgkin lymphoma     1 (<1)	44 (4)		620 (16)	421 (7)		20 (5)	32 (2)		-	-	
Myeloproliferative diseases39 (4)NHL30 (3)Hodgkin lymphoma1 (<1)	32 (3)		230 (6)	381 (7)		38 (9)	193 (11)		-	-	
NHL     30 (3)       Hodgkin lymphoma     1 (<1)	99 (10)		355 (9)	634 (11)		59 (14)	293 (16)		-	-	
Hodgkin lymphoma1 (<1)Plasma cell disorders-Other malignant diseases4 (<1)	44 (4)		98 (3)	210 (4)		20 (5)	93 (5)		-	-	
Plasma cell disorders       -         Other malignant diseases       4 (<1)	38 (4)		352 (9)	622 (11)		46 (11)	211 (12)		-	-	
Other malignant diseases4 (<1)SAA-Inherited erythrocyte disorders-Inherited immune system disorders-Inherited disorders of metabolism-Histiocytic disorders-Inherited platelet disorders-	3 (<1)		24 (1)	48 (1)		0	3 (<1)		-	-	
SAA - Inherited erythrocyte disorders - Inherited immune system disorders - Inherited disorders of metabolism - Histiocytic disorders - Inherited platelet disorders -	-		46 (1)	33 (1)		2 (<1)	7 (<1)		-	-	
SAA - Inherited erythrocyte disorders - Inherited immune system disorders - Inherited disorders of metabolism - Histiocytic disorders - Inherited platelet disorders -	4 (<1)		26(1)	14 (<1)		5(1)	3 (<1)		-	-	
Inherited immune system disorders-Inherited disorders of metabolism-Histiocytic disorders-Inherited platelet disorders-	-		-	-		-	-		186 (39)	402 (45)	
Inherited disorders of metabolism - Histiocytic disorders - Inherited platelet disorders -	-		-	-		-	-		95 (20)	137 (15)	
Histiocytic disorders - Inherited platelet disorders -	-		-	-		-	-		70 (15)	177 (20)	
Histiocytic disorders - Inherited platelet disorders -	-		-	-		-	-		71 (15)	59(7)	
Inherited platelet disorders -	-		-	-		-	-		43 (9)	96 (11)	
	-		-	-		-	-		10 (2)	8(1)	
Other nonmalignant diseases -	-		-	-		-	-		2 (<1)	14(2)	
Disease risk <sup>†</sup>		.03			<.001			.04	. ,	. ,	
Standard 546 (60)	644 (63)		1632 (43)	2810 (49)		141 (34)	700 (39)		-	-	
High 278 (31)	261 (26)		1740 (45)	2139 (37)		198 (49)	738 (41)		-	-	
Other 80 (9)	• •		455 (12)	799 (14)		71 (17)	346 (19)		-	-	
Time from diagnosis to HCT, mo		.03			<.001		5.0(10)	.003			
0 to 6 259 (29)	111 (11)		862 (23)	1779 (31)	2.001	84 (20)	519 (29)		-	-	
6 to 12 195 (22)			1076 (28)	1426 (25)		136 (33)	470 (26)		_	_	
12 to 24 178 (20)	360 (35)		878 (23)	1098 (19)		77 (19)	300 (17)		_	_	
12 to 24 178 (20)			010 (25)	1030 (13)		// (15)	500(17)		_	- (continued on	

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