HLA Typing, Donor Selection and Donor Registries

Dennis L. Confer, MD

Chief Medical Officer,
NMDP/Be The Match

Associate Scientific Director,
CIBMTR

Donor Registries for Unrelated Transplantation

- >29 million adult donors and 720,000 CBU are listed in Bone Marrow Donors Worldwide
- 98 Registries and 92 cord blood banks in 54 countries
- BMDW 4.0 is a service of WMDA
  - New User Interface
  - New predictive search algorithm
- NetCord is now merged with WMDA

High-resolution donor-recipient HLA matching contributes to the success of unrelated donor marrow transplantation

BLOOD (2007) 110: 4576-83

Stephanie J. Lee, John Klein, Michael Haagenson, Lee Ann Baxter-Lowe, Dennis L. Confer, Mary Eapen, Marcelo Fernandez-Vina, Neal Flomenberg, Mary Horowitz, Carolyn K. Hurley, Harriet Noreen, Machteld Oudshoorn, Effie Petersdorf, Michelle Setterholm, Stephen Spellman, Daniel Weisdorf, Thomas M. Williams and Claudio Anasetti

Any Single Locus Mismatch

9/10 associated with worse survival, DFS, TRM, acute GVHD

	n	RR (95% CI)	P-value
Survival	952	1.17 (1.06-1.329)	0.002
DFS	945	1.16 (1.05-1.28)	0.003
TRM	945	1.31 (1.16-1.47)	<0.0001
Relapse	945	0.90 (0.81-1.00)	0.04
Engraftment	956	OR 0.90 (0.80-1.01)	0.06
Acute GVHD	957	1.35 (1.19-1.56)	<0.0001
Chronic GVHD	910	0.96 (0.91-1.03)	0.25

HLA DQ Lacked Impact: As a Single Mismatch

	Survival		TRM		Acute GVHD	
	RR	p	RR	p	RR	p
10/10	1.00		1.00		1.00	
DQ MM	0.97	0.77	1.08	0.50	1.03	0.86

As a Second Mismatch

	8/10	9/10	RR (95% CI)	P-value
DQ MM	191	797	1.14 (0.94-1.38)	0.17

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Single Antigen vs Allele MM

	Antigen	Allele	P-value
Survival	1.16	1.19	0.69
DFS	1.16	1.17	0.92
TRM	1.34	1.32	0.86
Relapse	0.80	0.93	0.31
Engraftment	0.74	1.08	0.07
Acute GVHD	1.52	1.24	0.06
Chronic GVHD	0.95	0.97	0.84

No statistical difference if mismatched at antigen or allele level, except for C – Antigen worse than Allele

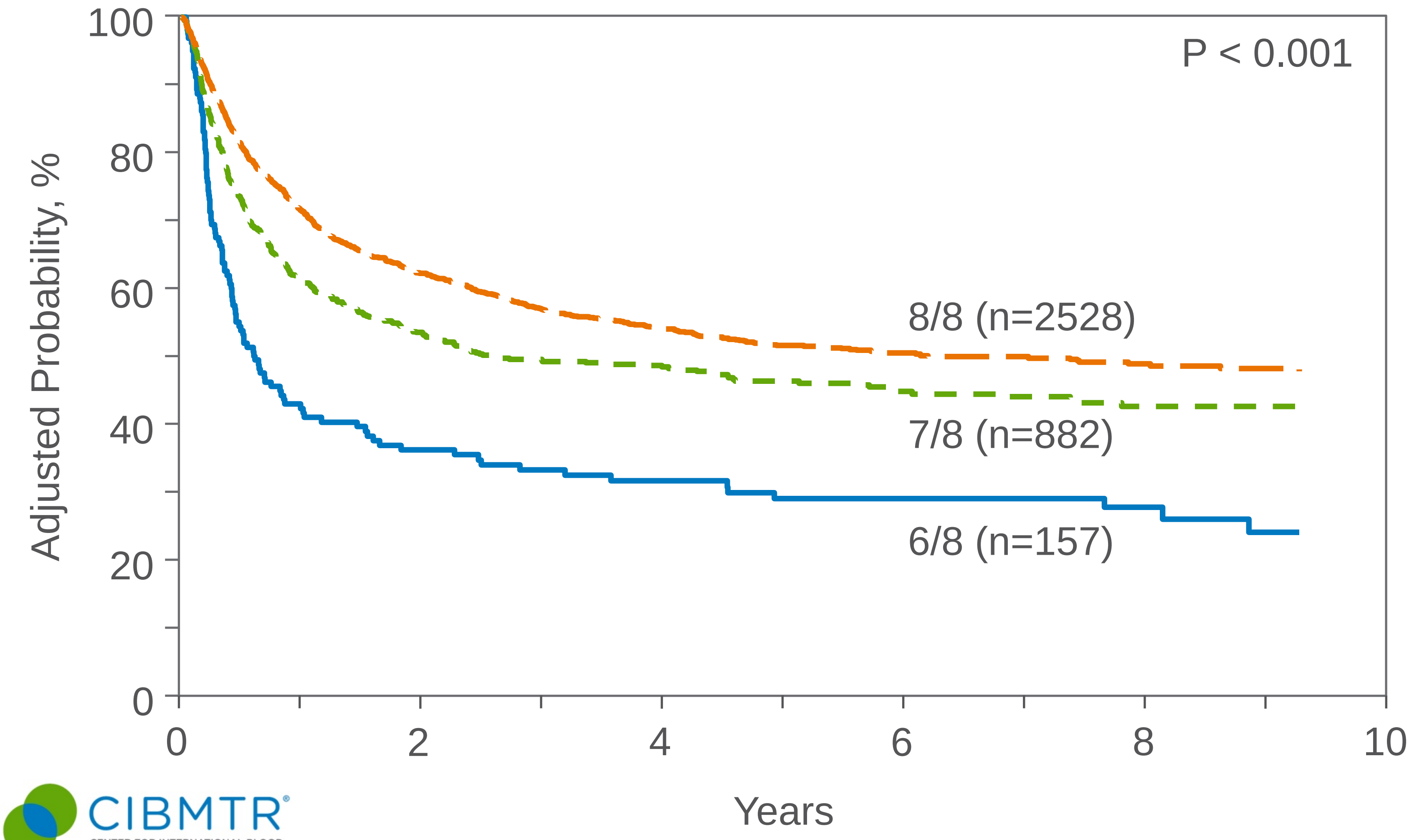
blood

2014 124: 2596-2606
doi:10.1182/blood-2014-05-576041 originally published
online August 26, 2014

Nonpermissive HLA-DPB1 mismatch increases mortality after myeloablative unrelated allogeneic hematopoietic cell transplantation

Joseph Pidala, Stephanie J. Lee, Kwang Woo Ahn, Stephen Spellman, Hai-Lin Wang, Mahmoud Aljurf, Medhat Askar, Jason Dehn, Marcelo Fernandez Viña, Alois Gratwohl, Vikas Gupta, Rabi Hanna, Mary M. Horowitz, Carolyn K. Hurley, Yoshihiro Inamoto, Adetola A. Kassim, Taiga Nishihori, Carlheinz Mueller, Machteld Oudshoorn, Effie W. Petersdorf, Vinod Prasad, James Robinson, Wael Saber, Kirk R. Schultz, Bronwen Shaw, Jan Storek, William A. Wood, Ann E. Woolfrey and Claudio Anasetti

Adjusted Overall Survival (Early disease stage)



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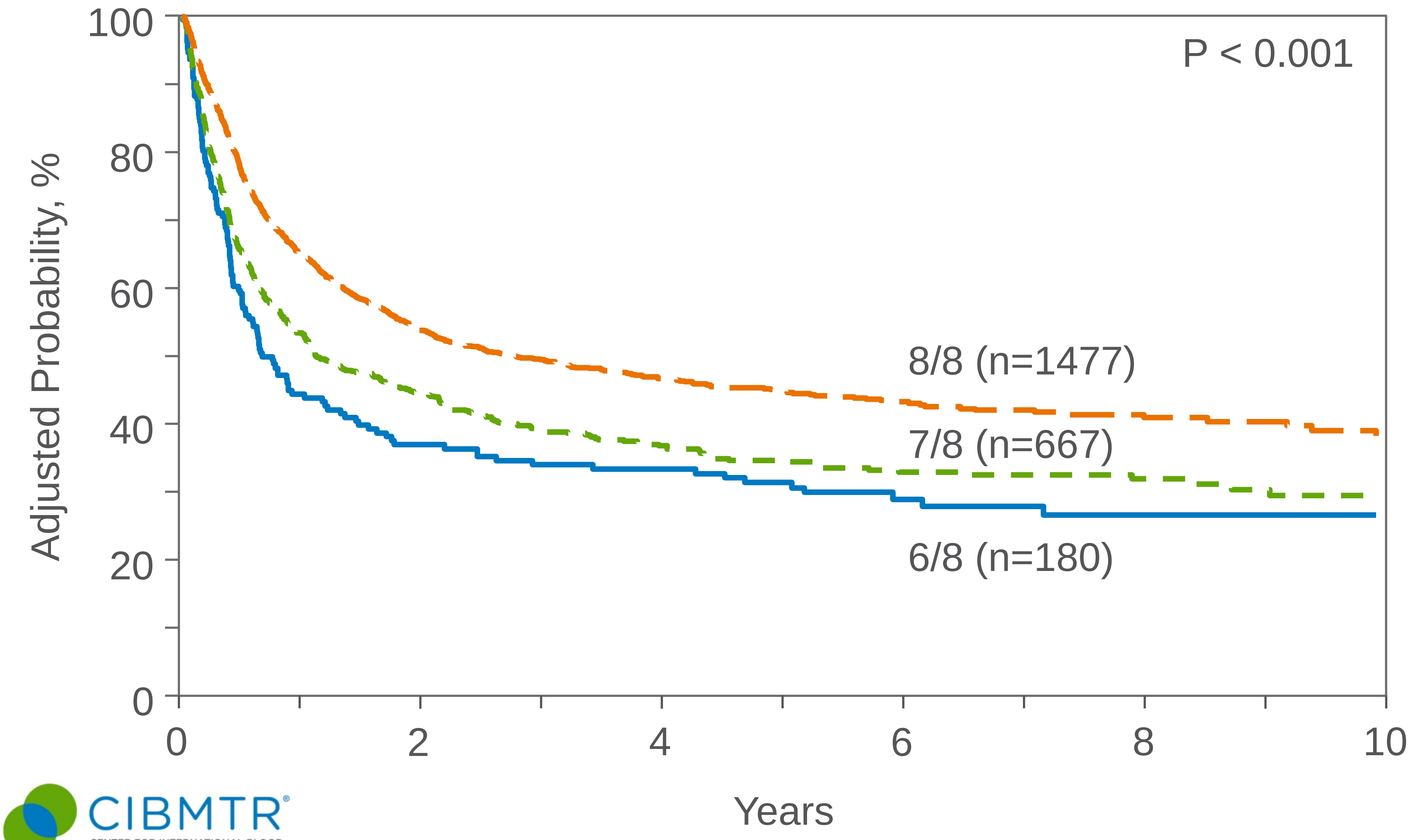
Adjusted Overall Survival (Intermediate disease stage)



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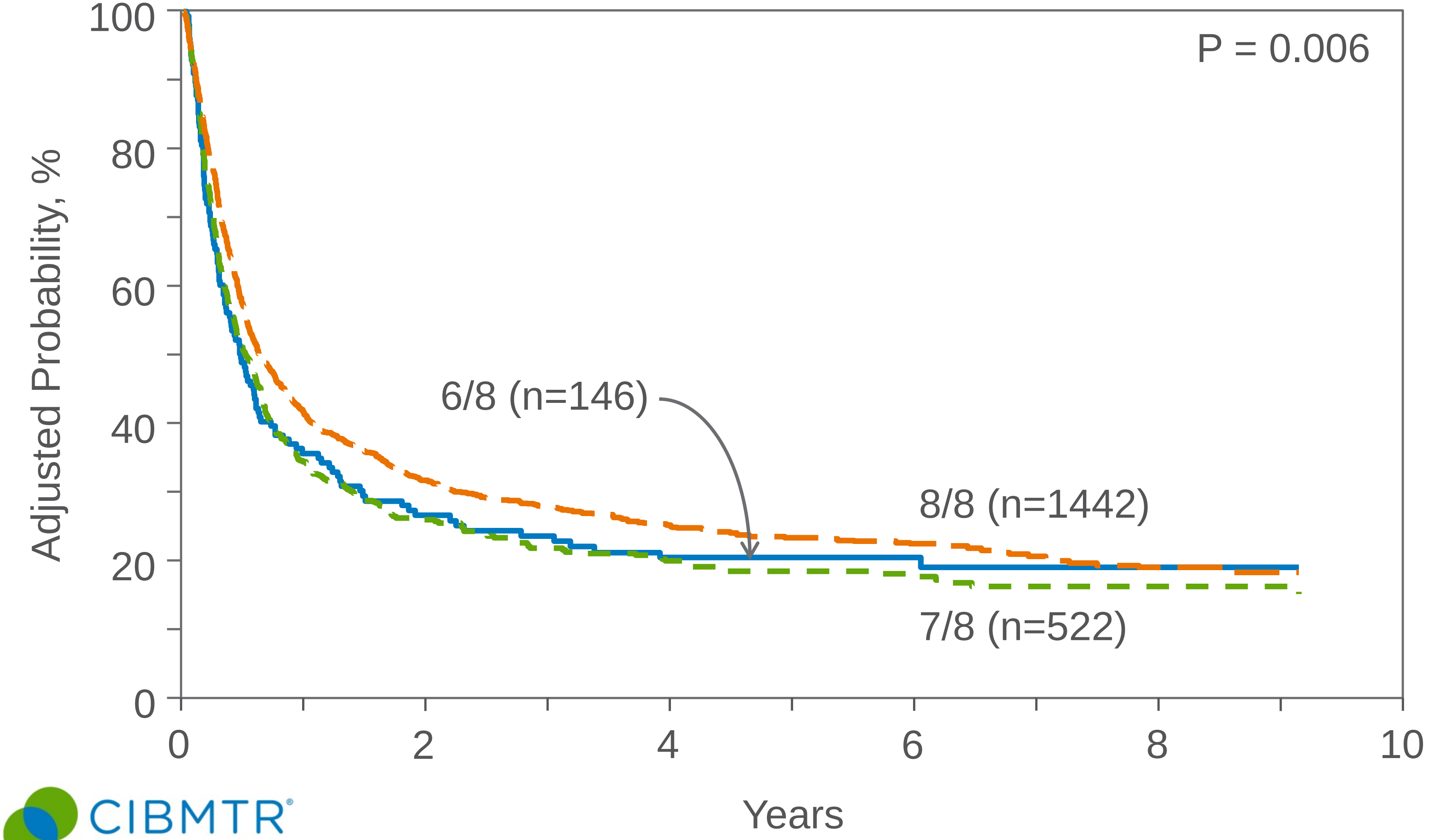
Adjusted Overall Survival (Advanced disease stage)



blood

2014 123: 1270-1278
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online January 9, 2014

Identification of a permissible HLA mismatch in hematopoietic stem cell transplantation

Marcelo A. Fernandez-Viña, Tao Wang, Stephanie J. Lee, Michael Haagenson, Mahmoud Aljurf, Medhat Askar, Minoo Battiwalla, Lee-Ann Baxter-Lowe, James Gajewski, Ann A. Jakubowski, Susana Marino, Machteld Oudshoorn, Steven G. E. Marsh, Effie W. Petersdorf, Kirk Schultz, E. Victoria Turner, Edmund K. Waller, Ann Woolfrey, John Umejiego, Stephen R. Spellman and Michelle Setterholm

On behalf of the CIBMTR Immunobiology Working Committee

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Introduction

- C*03:03 vs C*03:04 mismatch (MM) DOES NOT elicit CTL responses (Oudshoorn, Human Immunol 2002)

- C*03:03/03:04 is the predominant allele level MM in patients and donors with European ancestry
    - 69% of HLA-C MM were C*03:03/03:04

- Hypotheses:
    - C*03:03/03:04 MM is well tolerated in HCT
    - Other C-allele MM are as detrimental as C-antigen or HLA-A, B or DRB1 (other) MM

Overall Survival

Mismatch	n	RR	95% CI	p
8/8	4779	1.00		
C*03:03/03:04	134	**0.98**	0.78-1.23	0.85
C-allele	61	**1.43**	1.06-1.92	0.02
C-antigen	700	**1.37**	1.24-1.51	**<0.0001**
A, B or DRB1	959	**1.30**	1.19-1.43	**<0.0001**

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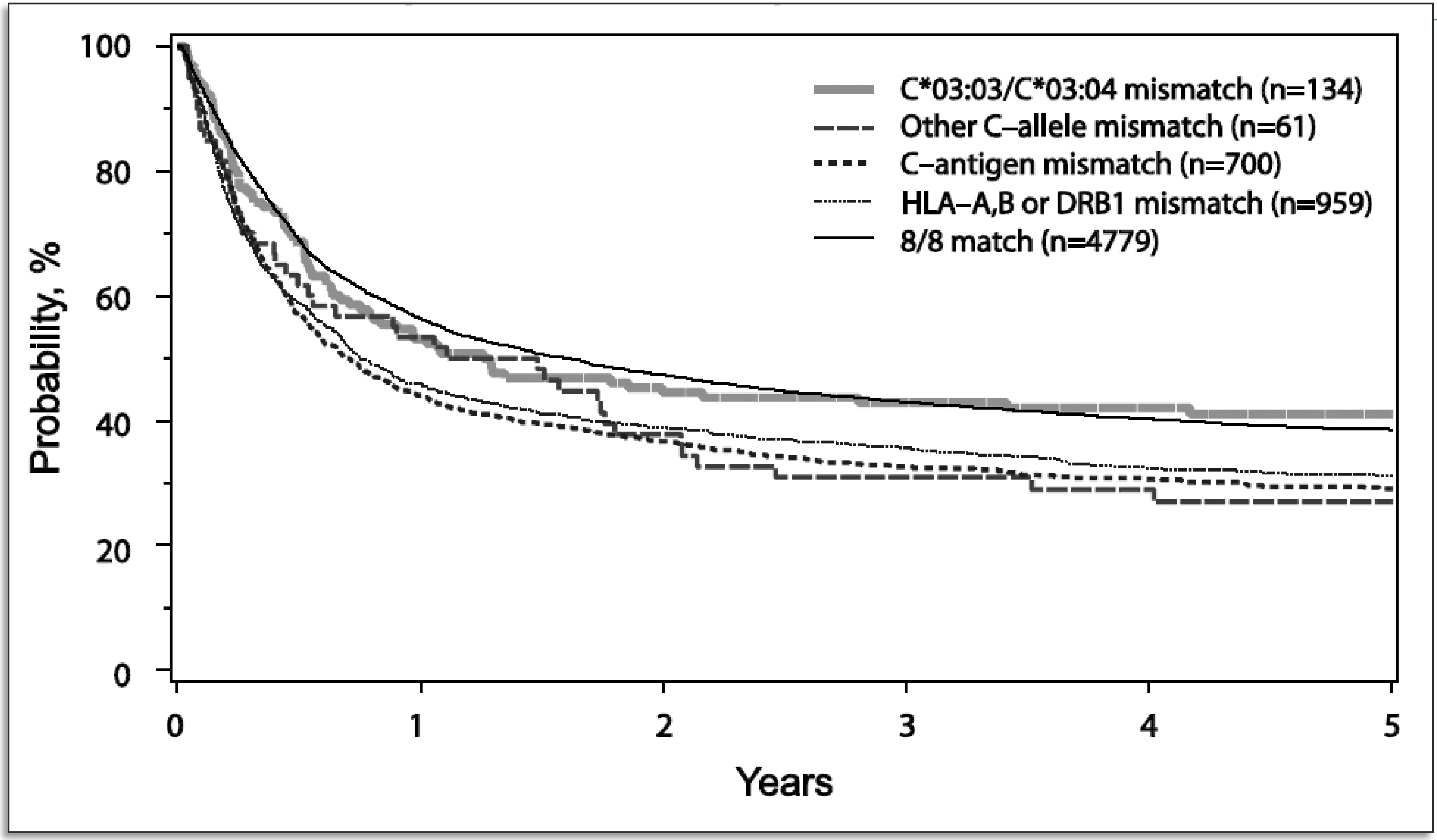
Overall survival



Summary of C*03:03/03:04 Story

- C*03:03/03:04 was the predominant HLA-C allele MM (69%)

- C*03:03/03:04 mismatch is better tolerated than other HLA mismatches

- Prioritize C*03:03/C*03:04 mismatch over other HLA-A, B, C and DRB1 mismatches
  - ~23% of 7/8 matched patients carried C*03:03 or C*03:04

Synthesis and Recommendations

- <u>8/8 match (HLA-A, B, C, DRB1)</u>

- Permissive – DPB1 mismatch (Fleischhauer. Lancet Oncol, 2012)
- Avoid donor-specific antibodies (DSA) against HLA DPB1 (Spellman. Blood 2010)

- <u>7/8 match</u>

- HLA-C*03:03/03:04 (Fernandez-Vina. Blood, 2014)
- Permissive – DPB1 mismatch (Fleischhauer. Lancet Oncol, 2012)
- LEL (DP, DQ, DRB3/4/5) (Fernandez-Vina. Blood, 2014)
- Non-permissive allele combinations, amino acid substitutions

(Kawase. Blood, 2007)
(Marino. BMT, 2012)
(Pidala. Blood, 2013)

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