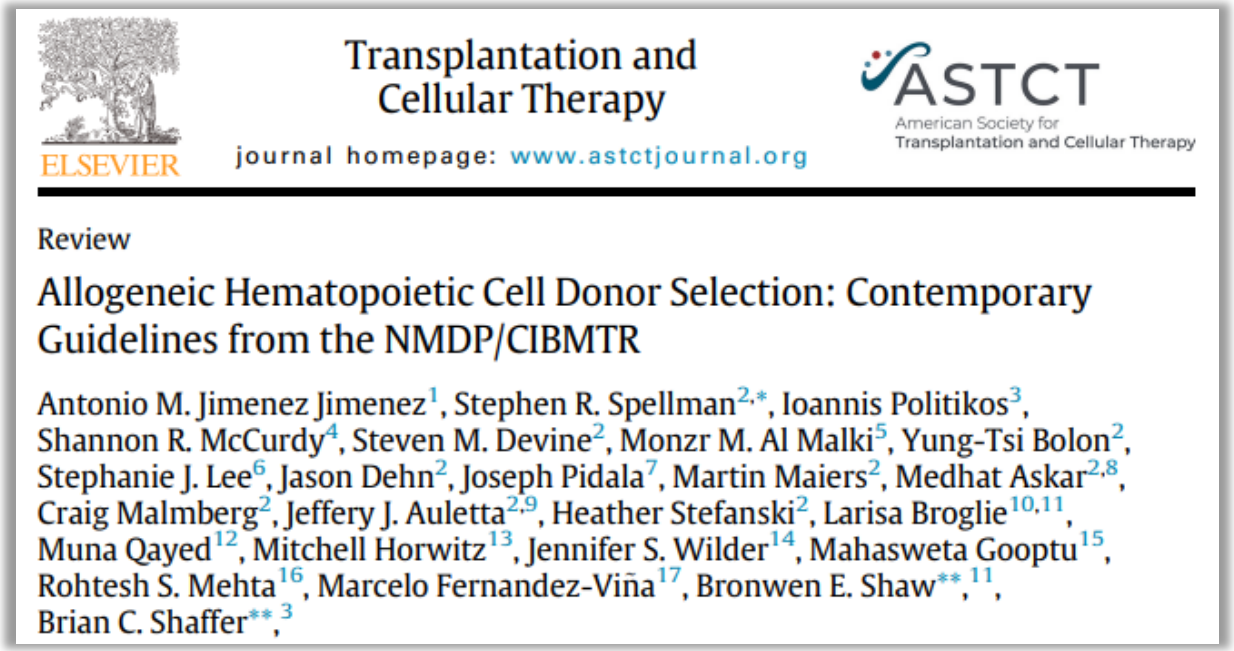
Allogeneic Donor Selection – Contemporary Guidelines from NMDP/CIBMTR

Stephen Spellman
VP, Research, NMDP
Sr. Scientific Director, CIBMTR

Art by Lola-Anne Davis

Outline

- Why update the guidelines?
- What remains the same?
- What has changed and why?



ELSEVIER

Transplantation and Cellular Therapy

journal homepage: www.astctjournal.org

ASTCT American Society for Transplantation and Cellular Therapy

Review

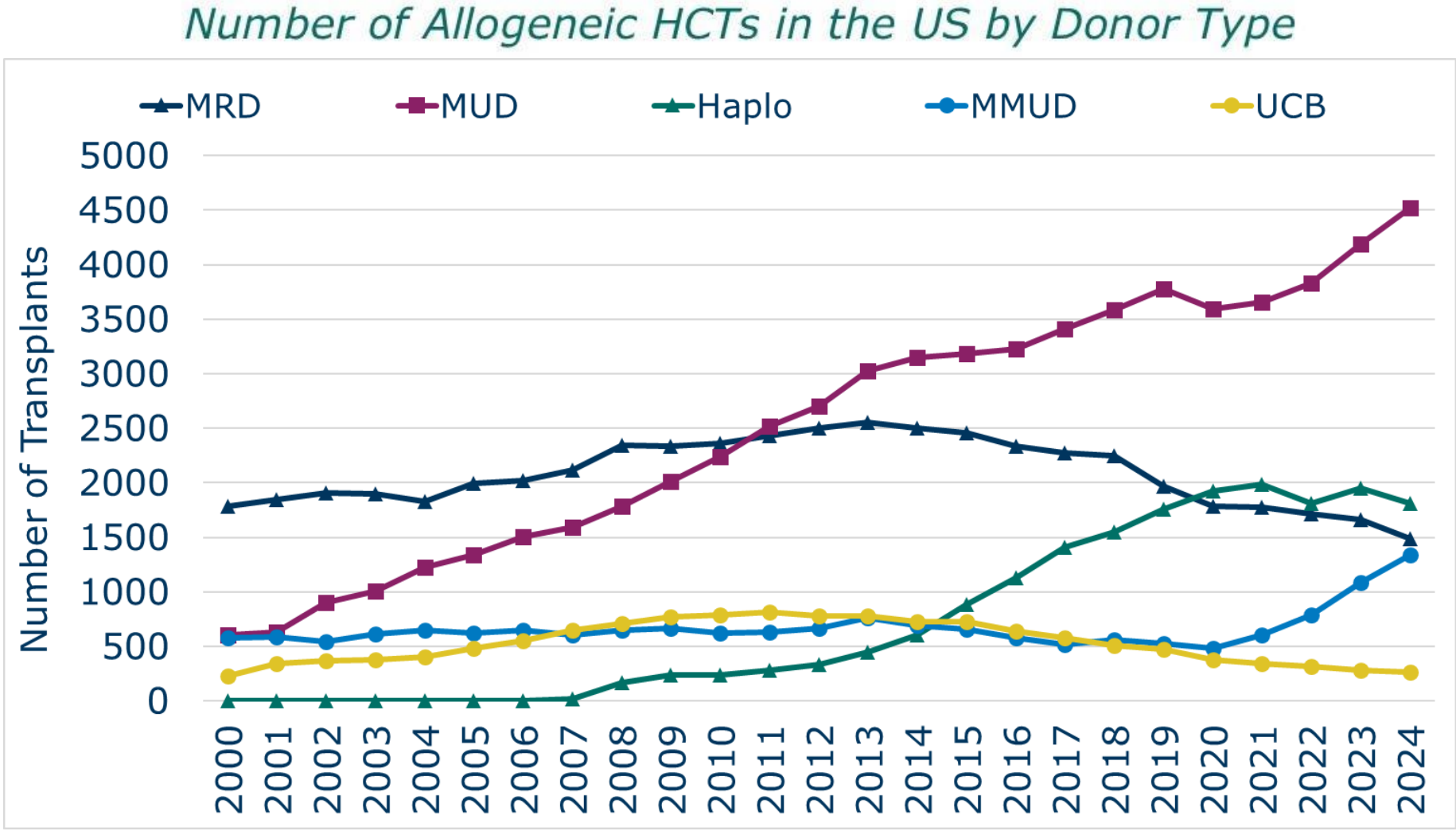
Allogeneic Hematopoietic Cell Donor Selection: Contemporary Guidelines from the NMDP/CIBMTR

Antonio M. Jimenez Jimenez[1], Stephen R. Spellman[2,*], Ioannis Politikos[3], Shannon R. McCurdy[4], Steven M. Devine[2], Monzr M. Al Malki[5], Yung-Tsi Bolon[2], Stephanie J. Lee[6], Jason Dehn[2], Joseph Pidala[7], Martin Maiers[2], Medhat Askar[2,8], Craig Malmberg[2], Jeffery J. Auletta[2,9], Heather Stefanski[2], Larisa Broglie[10,11], Muna Qayed[12], Mitchell Horwitz[13], Jennifer S. Wilder[14], Mahasweta Gooptu[15], Rohtesh S. Mehta[16], Marcelo Fernandez-Viña[17], Bronwen E. Shaw[**,11], Brian C. Shaffer[**,3]

CIBMTR® A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

Why update the guidelines?

Substantial growth in mismatched donor sources in recent years



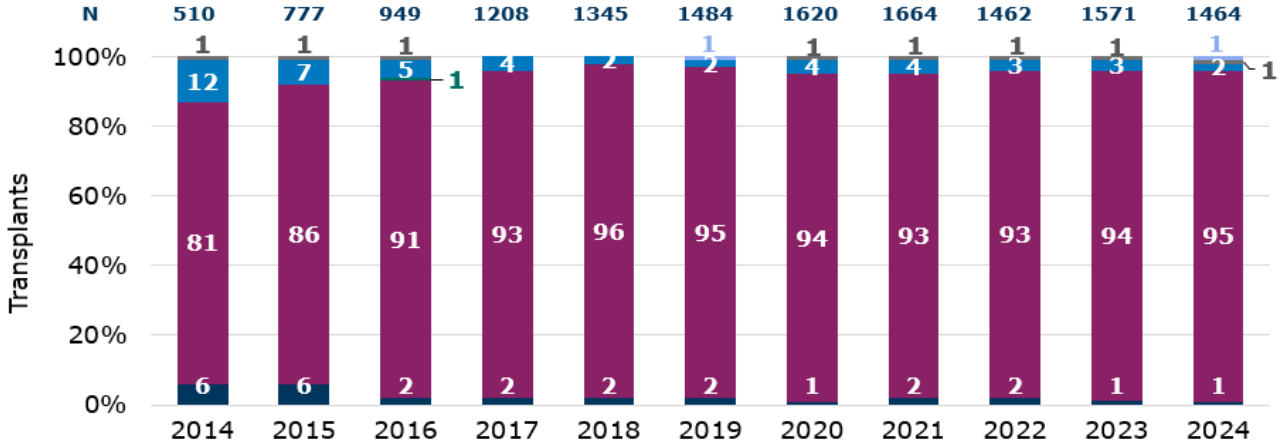
Broglie et al 2025 - https://cibmtr.org/CIBMTR/Resources/Summary-Slides-Reports

CIBMTR®
A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

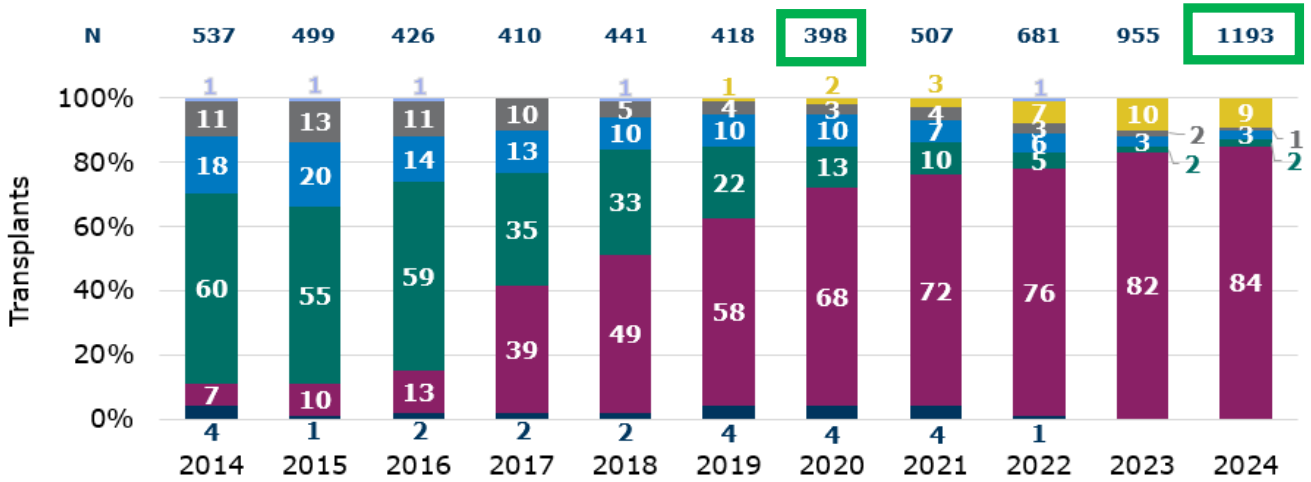
Driven by an increase in PTCy use

GVHD Prophylaxis in adult HCT in the U.S. 2014-2024

Haploidentical Related Donors



Mismatched Unrelated Donors



3x growth, since the nadir in 2020

Ex vivo and CD34 | PTCy | CNI+MTX | CNI+MMF | CNI ± others | Abatacept | Others

CIBMTR® A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

Broglie et al 2026 – manuscript in preparation

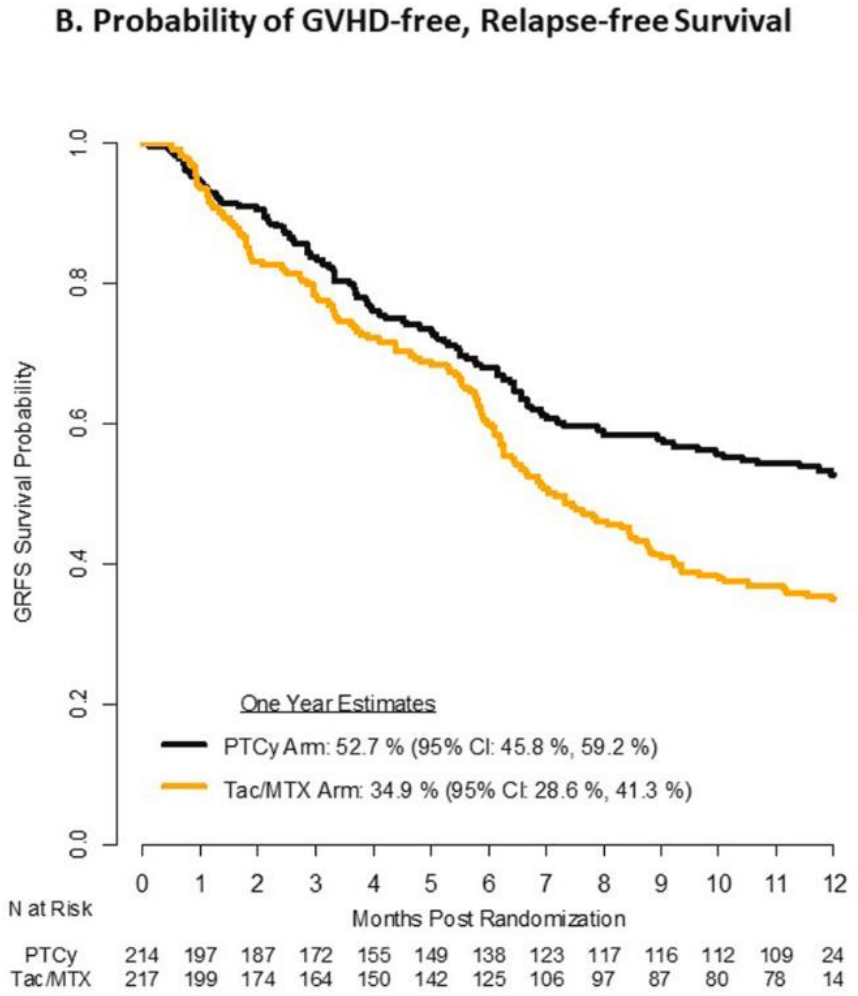
PTCy-based GVHD prophylaxis as the new standard in RIC HCT using HLA-matched donors

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Post-Transplantation Cyclophosphamide-Based Graft-versus-Host Disease Prophylaxis

J. Bolaños-Meade, M. Hamadani, J. Wu, M.M. Al Malki, M.J. Martens, L. Runaas, H. Elmariah, A.R. Rezvani, M. Gooptu, K.T. Larkin, B.C. Shaffer, N. El Jurdi, A.W. Loren, M. Solh, A.C. Hall, A.M. Alousi, O.H. Jamy, M.-A. Perales, J.M. Yao, K. Applegate, A.S. Bhatt, L.S. Kean, Y.A. Efebera, R. Reshef, W. Clark, N.L. DiFronzo, E. Leifer, M.M. Horowitz, R.J. Jones, and S.G. Holtan, for the BMT CTN 1703 Investigators*

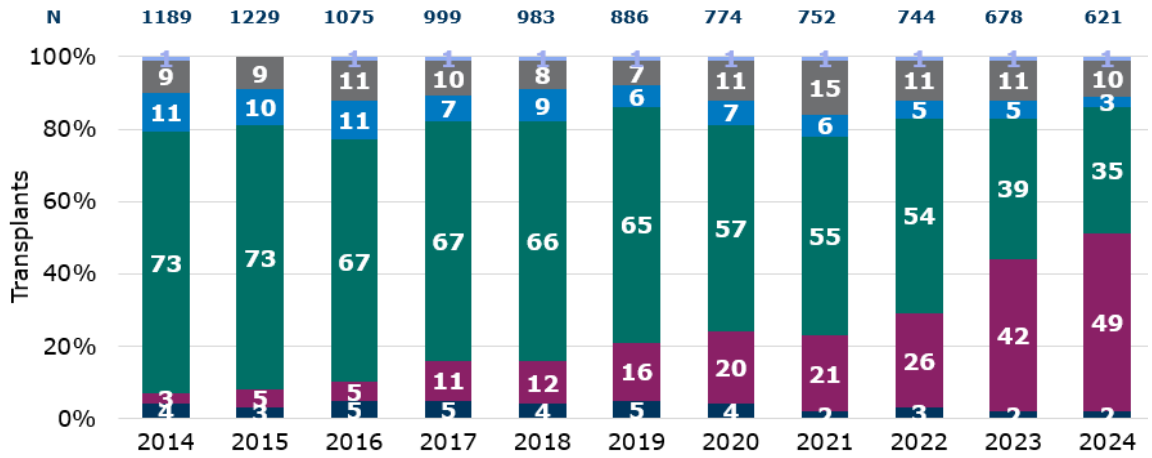


CIBMTR®
A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

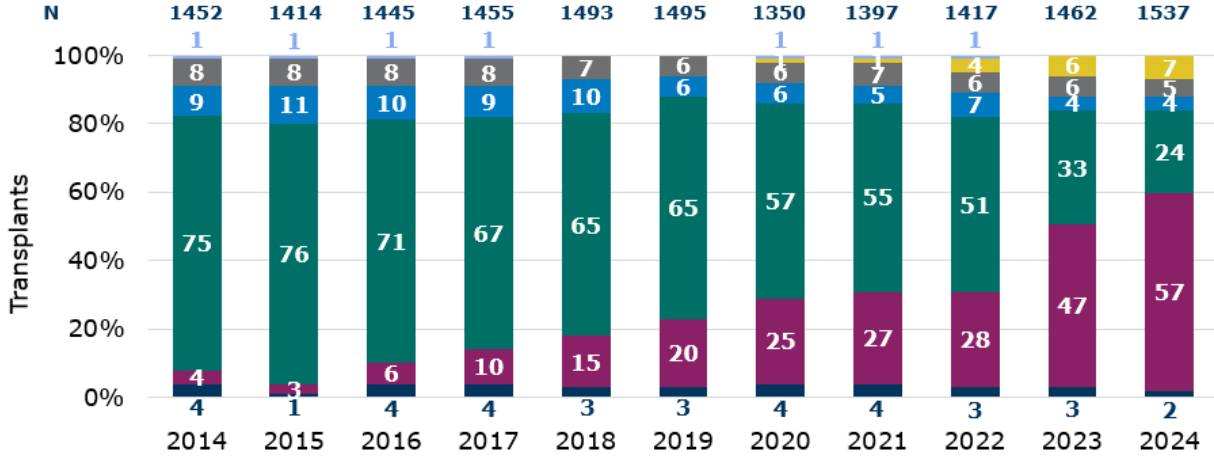
Bolanos-Meade et al, NEJM, 2023

Similar trends in matched donors

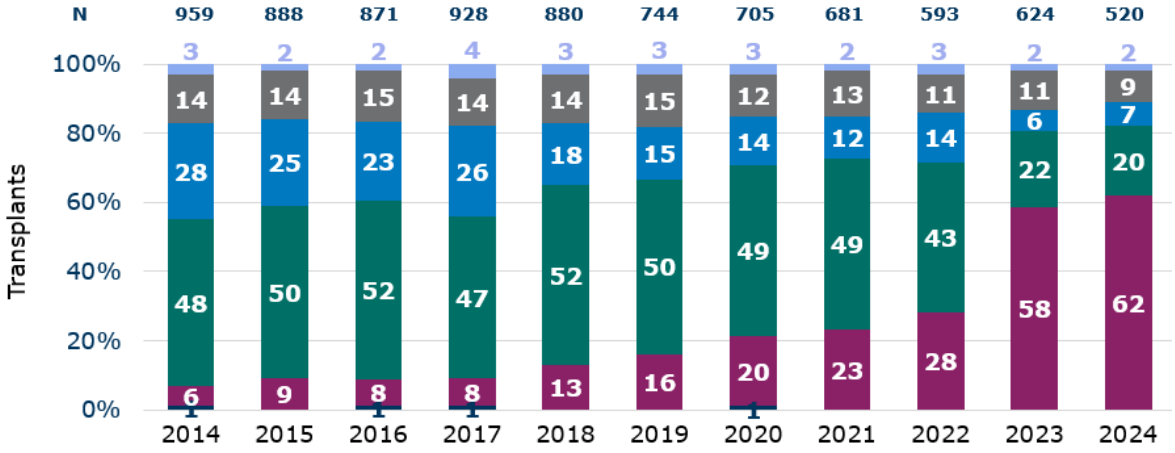
GVHD Prophylaxis of Matched Related Donor HCTs in the US, Adults, MAC



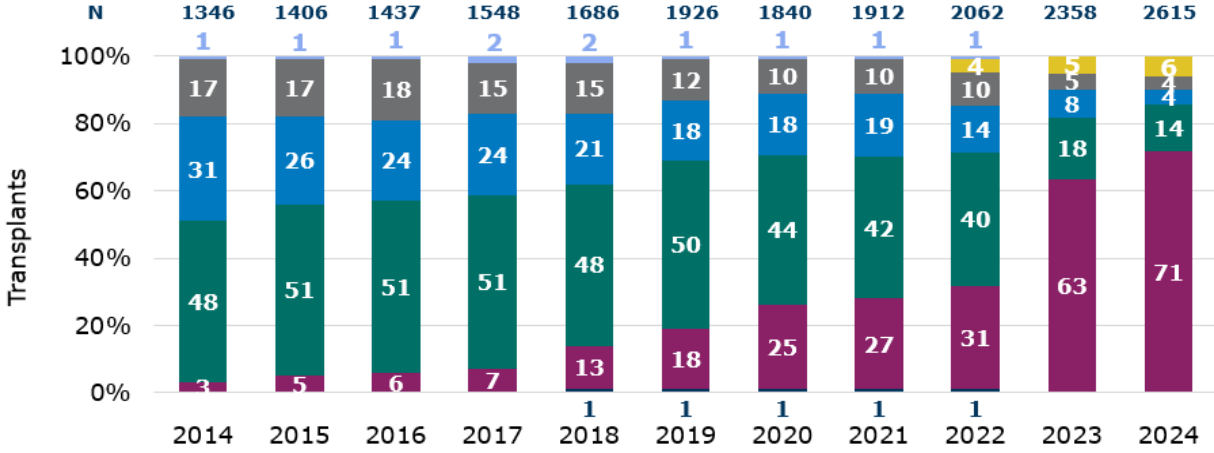
GVHD Prophylaxis of Matched Unrelated Donor HCTs in the US, Adults, MAC



GVHD Prophylaxis of Matched Related Donor HCTs in the US, Adults, RIC/NMA

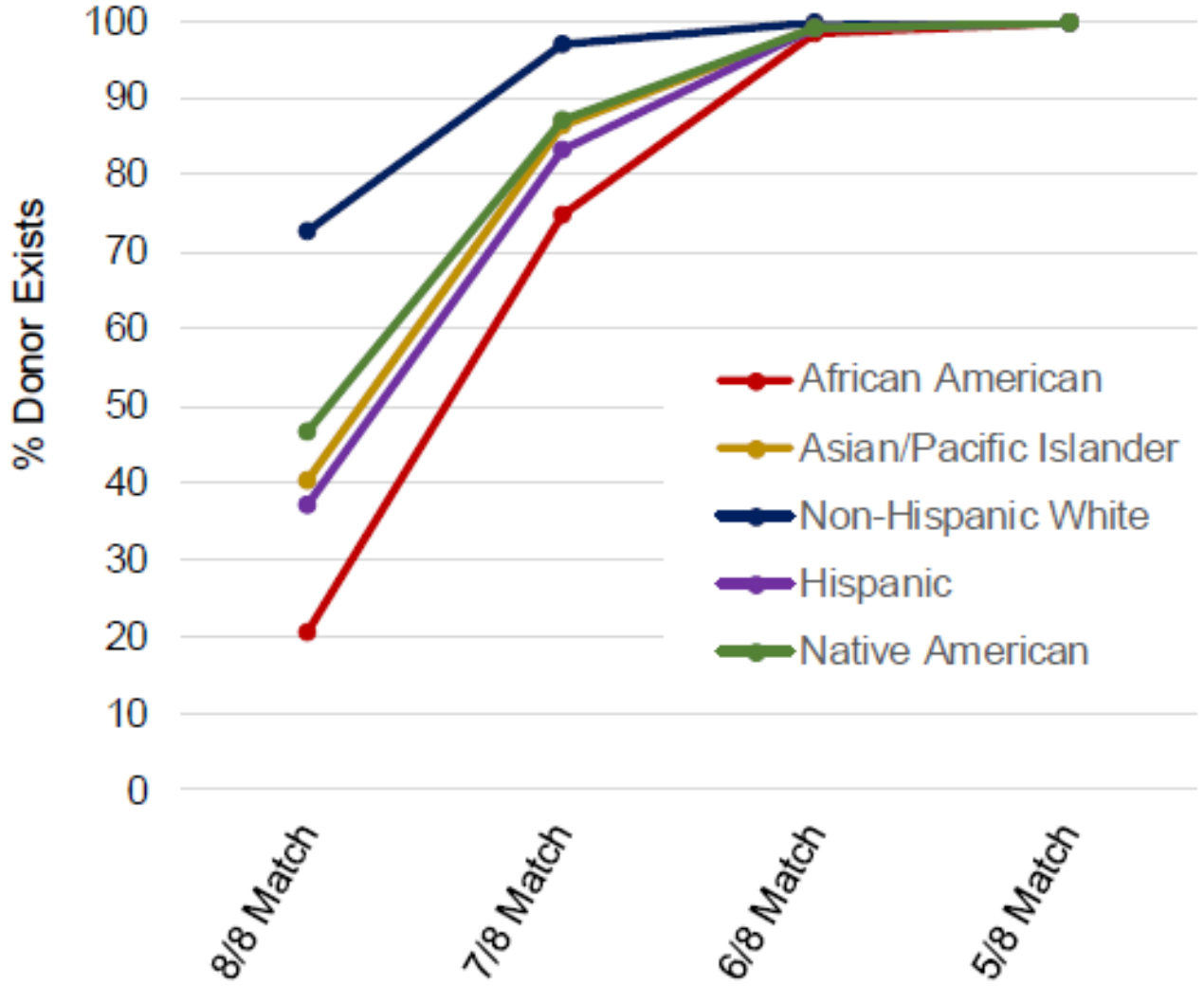


GVHD Prophylaxis of Matched Unrelated Donor HCTs in the US, Adults, RIC/NMA



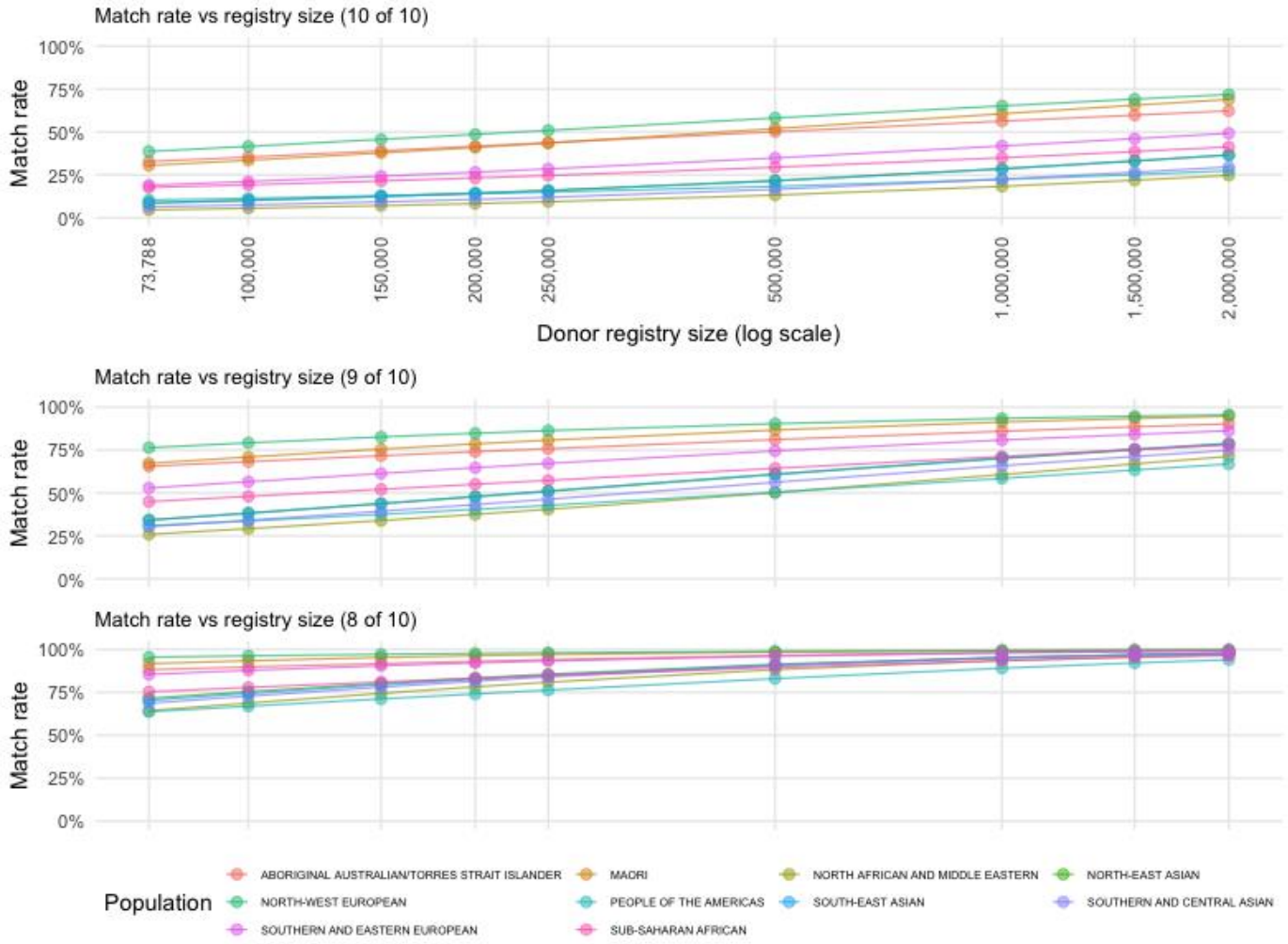
Broglie et al 2026 – manuscript in preparation

Unrelated donor match rates in U.S.



Jimenez-Jimenez et al JTCT 2025

Mismatched donors can reduce the existence gap in AUSNZ



O'Brien et al., BMT 2026

What remains the same?

CNI setting recommendations remain (mostly) the same

Consistent impact of HLA matching:

- BM and PBSC
- MAC and RIC
- Peds and Adult
- Malignant and non-malignant disease

blood Special Report

CME Article

Selection of unrelated donors and cord blood units for hematopoietic cell transplantation: guidelines from the NMDP/CIBMTR

Jason Dehn,[1] Stephen Spellman,[2] Carolyn K. Hurley,[3] Bronwen E. Shaw,[4] Juliet N. Barker,[5,6] Linda J. Burns,[1,2] Dennis L. Confer,[1,2] Mary Eapen,[4] Marcelo Fernandez-Vina,[7] Robert Hartzman,[8] Martin Maiers,[2] Susana R. Marino,[9] Carlheinz Mueller,[10] Miguel-Angel Perales,[5,6] Raja Rajalingam,[11] and Joseph Pidala[12]

Table 1. Guidelines for unrelated donor selection

	Multiple HLA-A, HLA-B, HLA-C, and HLA-DRB1 (8/8) HLA matched unrelated donors available	8/8 match unavailable; multiple 7/8 unrelated donors available
1. Resolution of typing HLA-A, HLA-B, HLA-C, and HLA-DRB1	High-resolution, matches for ARDs	High-resolution matches for ARDs for 7 matched alleles;
		Select HLA-C*03:03 vs C*03:04 mismatch, if present;
		No other preference for mismatched loci (HLA-A/B/C/DRB1) or other allele combinations
2. Donor age	Prioritize donors 18-30 years old	
3. Permissive mismatching HLA-DPB1	Select matched/permissive DPB1 mismatch based on the algorithm developed by Crivello et al[68,70] (http://www.ebi.ac.uk/cgi-bin/ipd/imgt/hla/dpb_v2.cgi)	Select matched/permissive DPB1 mismatch based on the algorithm developed by Crivello et al[68,70] (http://www.ebi.ac.uk/cgi-bin/ipd/imgt/hla/dpb_v2.cgi)
4. Matching HLA-DRB3/4/5 and HLA-DQB1	Minimize mismatches	Minimize mismatches
5. Vector of mismatch	N/A	Select donor with single allele mismatched at patient's homozygous locus (HLA-A/B/C/DRB1), if applicable
6. DSA in patient	Avoid mismatches of allotypes targeted by DSAs, including DQA1 and DPA1	Avoid mismatches of allotypes targeted by DSAs, including DQA1 and DPA1
7. Transplant center practice may differ in additional considerations to use in the selection among multiple donors equivalent for the characteristics above		

What has changed and why?

Donor Search Strategy and clinical trial participation

Recommendation	Evidence Level	References
Searching for all donor types should be performed concurrently	+++	Dehn et al 2024 Lee et al 2024 Nath et al 2025 Fingerson et al 2024
Search prognosis tools based on patient HLA and ancestry can identify patients who may benefit from early consideration of an alternative donor source (Haplo, MMUD or cord blood).	+++	Dehn et al 2024 Lee et al 2024
Enrolling patients in clinical trials should always be considered	+++	Kaur et al 2024 Nipp et al 2019

Biologic Assignment with ITT

n = 1756

MUD Very Likely
>2 potential MUDs
>90% likelihood of MUD

Go to Tx with 8/8 MUD

93% MUD

Expected:
>90% MUD
Alt donors: <10%

MUD Less Likely
1-2 potential MUDs
26% likelihood of MUD

Usual Center Practice

Observational Study of Search and Transplant Practice

64% alternative donors

MUD Very Unlikely
0 potentials
<10% likelihood of MUD

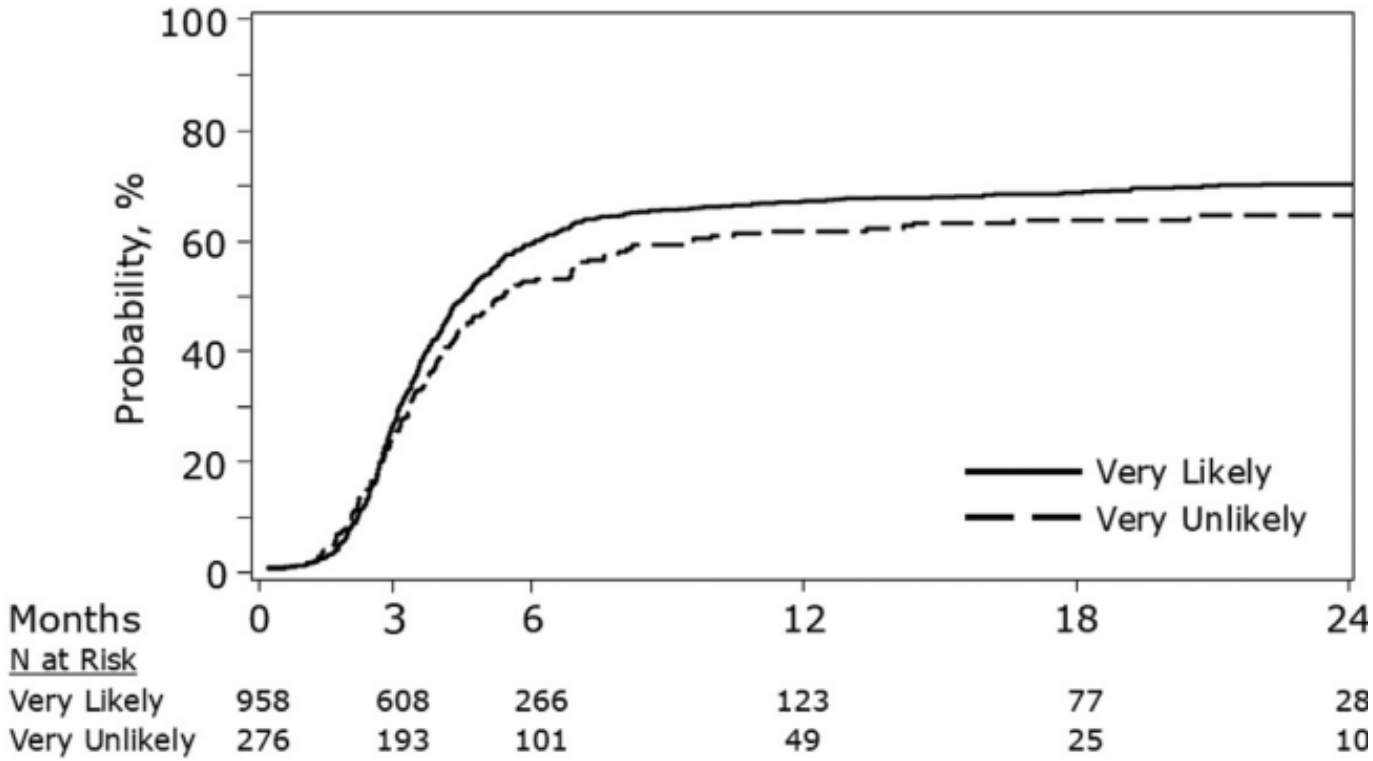
Proceed directly to center's preferred alternative donor (declared for each patient); No prolonged MUD search

Expected:
<10% MUD availa
(Alt: 70% HAPLO; 15%
15% MMUD)

89% alternative donors

Dehn et al JTCT 2025

Adjusted cumulative incidence of HCT

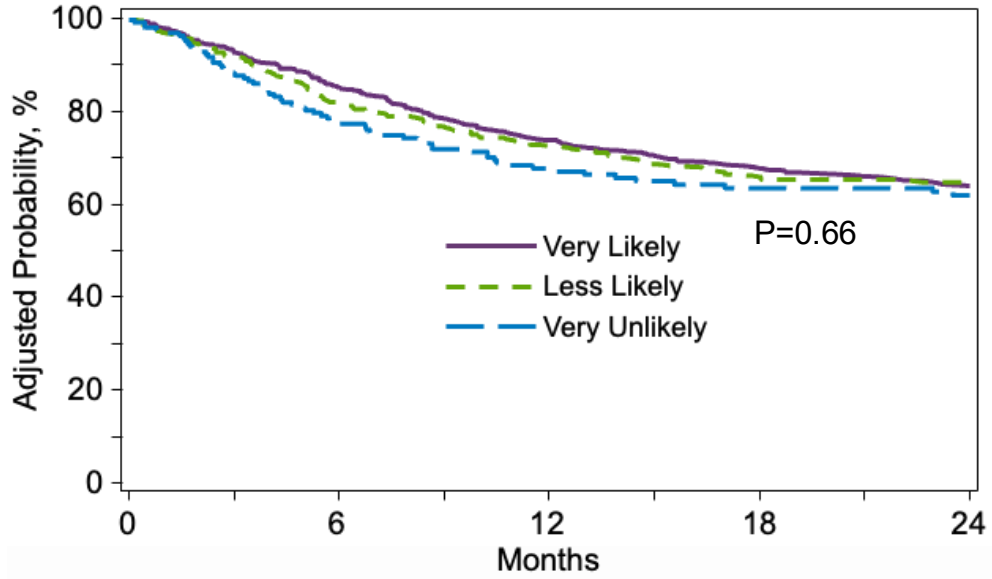


	Very likely		Very unlikely		
Outcomes	**N**	**Prob (95% CI)**	**N**	**Prob (95% CI)**	**P Value**
Transplant	958		276		0.113
6 months		59.8% (56.7–62.8)		52.3% (46.1-58.5)	
1-year		67.0% (64.0-70.0)		61.4% (55.3-67.5)	
2-year		70.1% (67.0-73.2)		64.2% (57.9-70.6)	

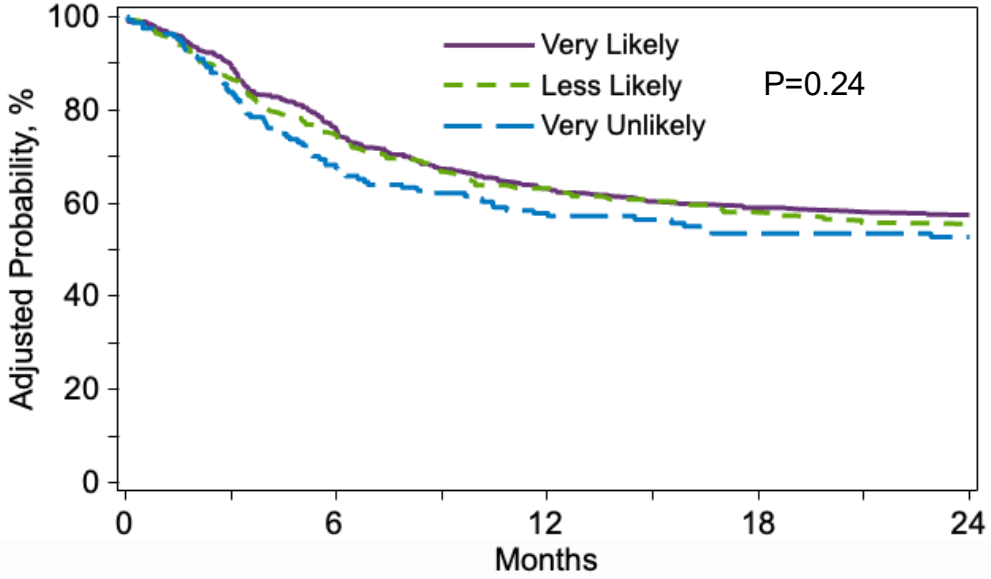
***covariates adjusted: age, gender, KPS, race/ethnicity, disease, disease status, interval from consent to evaluability**

Dehn et al JTCT 2025

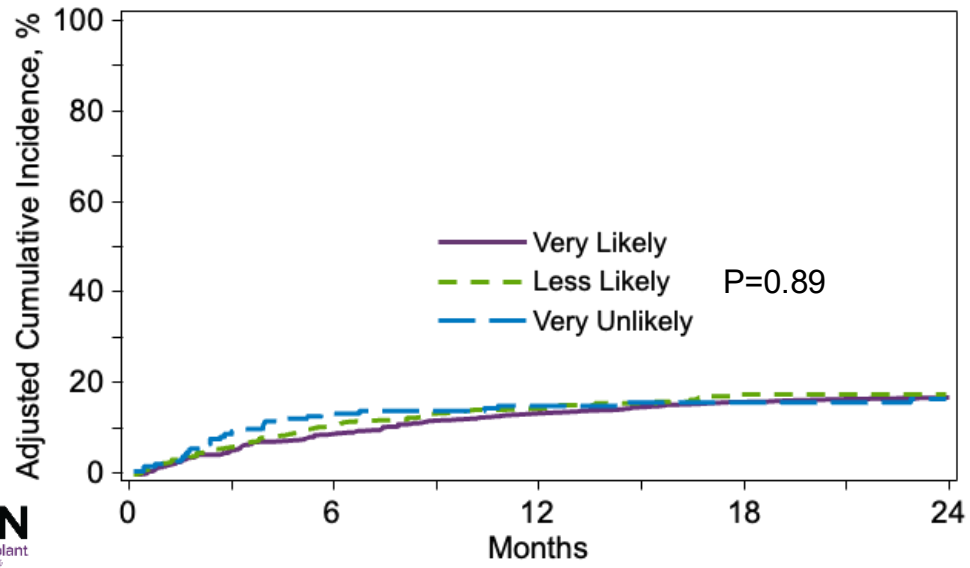
Overall survival from HCT by Donor Search Prognosis



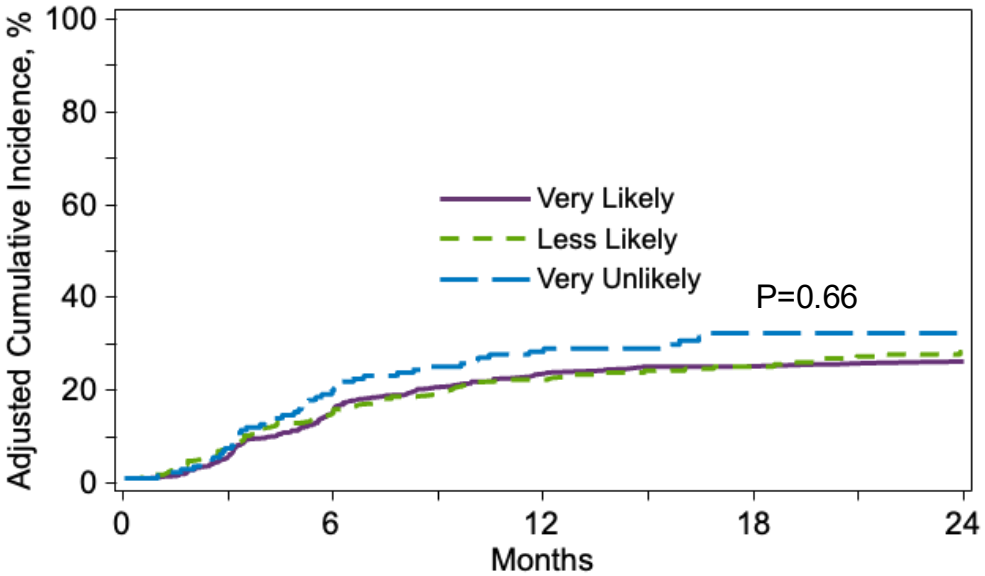
DFS from HCT by Donor Search Prognosis



NRM from HCT by Donor Search Prognosis



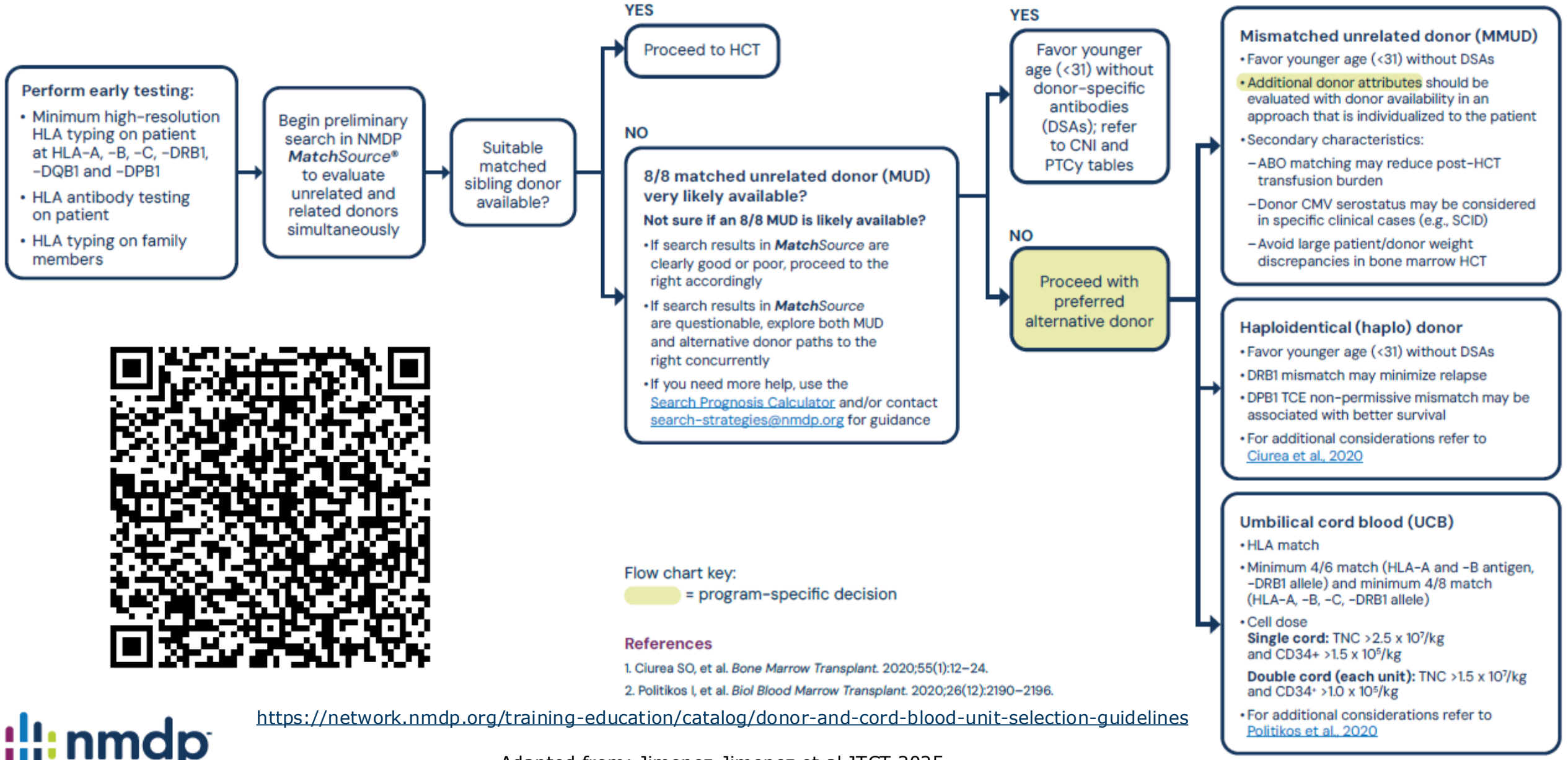
Relapse from HCT by Donor Search Prognosis



BMT CTN
Blood & Marrow Transplant Clinical Trials Network®

Lee et al JCO 2025

Allogeneic HCT donor search strategy



References

1. Ciurea SO, et al. *Bone Marrow Transplant.* 2020;55(1):12–24.
2. Politikos I, et al. *Biol Blood Marrow Transplant.* 2020;26(12):2190–2196.

https://network.nmdp.org/training-education/catalog/donor-and-cord-blood-unit-selection-guidelines

Adapted from: Jimenez-Jimenez et al JTCT 2025

Prioritizing available donor types

Recommendation	Evidence Level	References
A suitable matched sibling donor (MSD) is generally the first choice	++	Nath et al 2025 Sanz et al 2024 Piemontese et al 2024
Matched unrelated donors (MUD) are generally the second choice	+++	Dehn et al 2024 Nath et al 2025 Shaffer et al 2024 Gooptu et al 2021
Haploidentical and mismatched unrelated donors (MMUD) have similar outcomes using PTCy and these sources should be considered upfront in a patient with a very unlikely search prognosis score*.	+++	Dehn et al 2024 Lee et al 2024 Nath et al 2025 Devine et al 2025
Donors with a high titer DSA target should not be used.	+++	Gladstone et al 2013 Ciurea et al 2009

*Factors to consider in selection between these donor sources include prioritizing younger donor, avoiding DSA, logistic concerns, and available clinical trials

Do 2 year post-transplant patient outcomes differ by donor type using contemporary graft vs host disease prophylaxis?

Steven M. Devine[1], *Igor Litvinovich*[1], *Varuna Astha*[1], *Kwang Woo Ahn*[2], *Caitrin Bupp*[1], *Rajat Banjal*[3], *Javier Bolanos-Meade*[4], *Aleksandr Lazaryan*[5], *Mahasweta Gooptu*[6], *Bronwen E. Shaw*[2], *Heather E. Stefanski*[1], *Stephen R. Spellman*[1], *Jeffery J. Auletta*[1]

[1]CIBMTR® (Center for International Blood and Marrow Transplant Research), NMDP, Minneapolis, MN, USA, [2]CIBMTR® (Center for International Blood and Marrow Transplant Research) MCW, Milwaukee, WI, USA, [3]The University of Kansas Cancer Center, Kansas City, USA, [4]The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, USA, [5]Moffitt Cancer Center, Tampa, USA, [6]Dana Farber Cancer Institute, Boston, USA

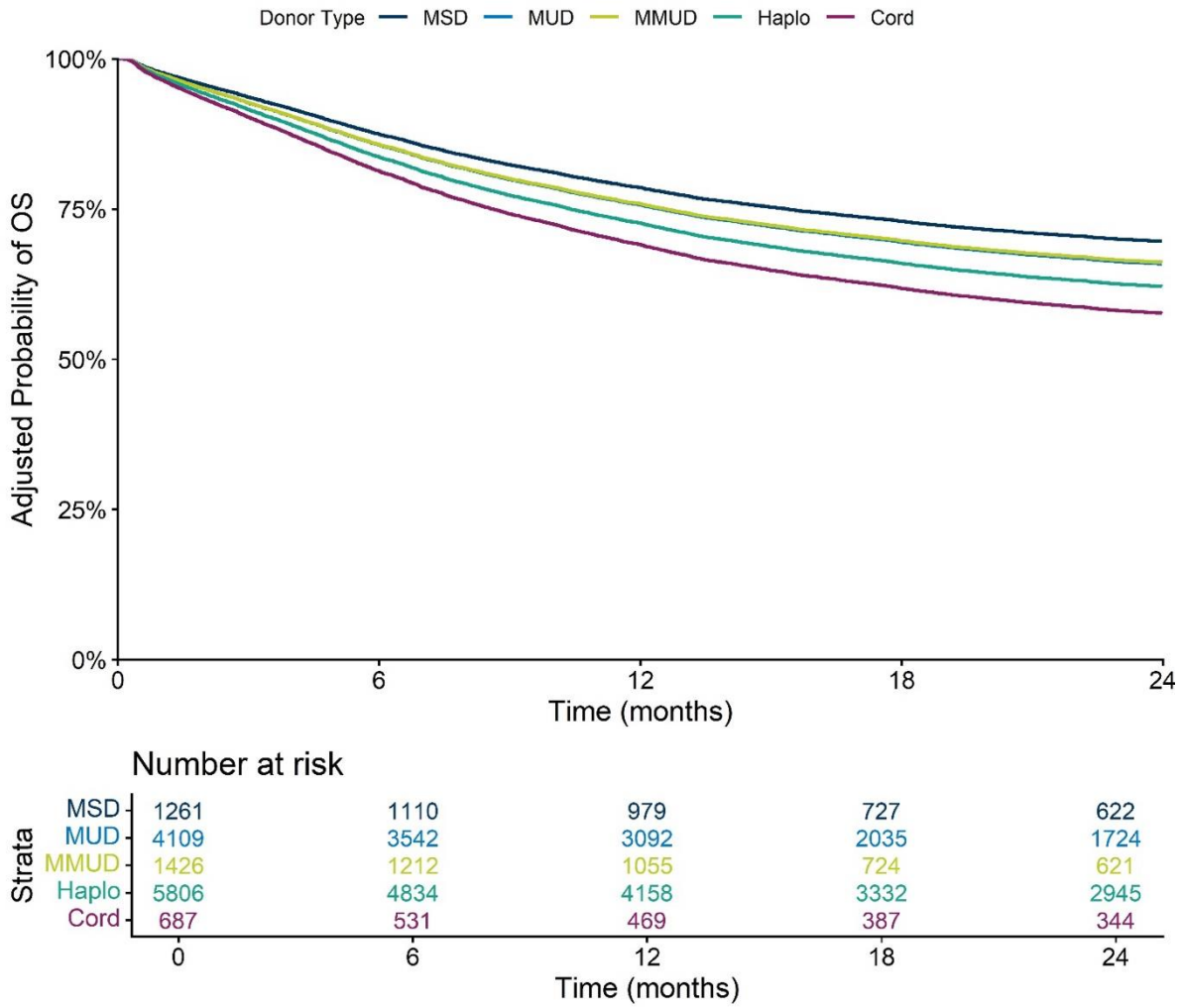
52nd Annual Meeting

Patient Cohort

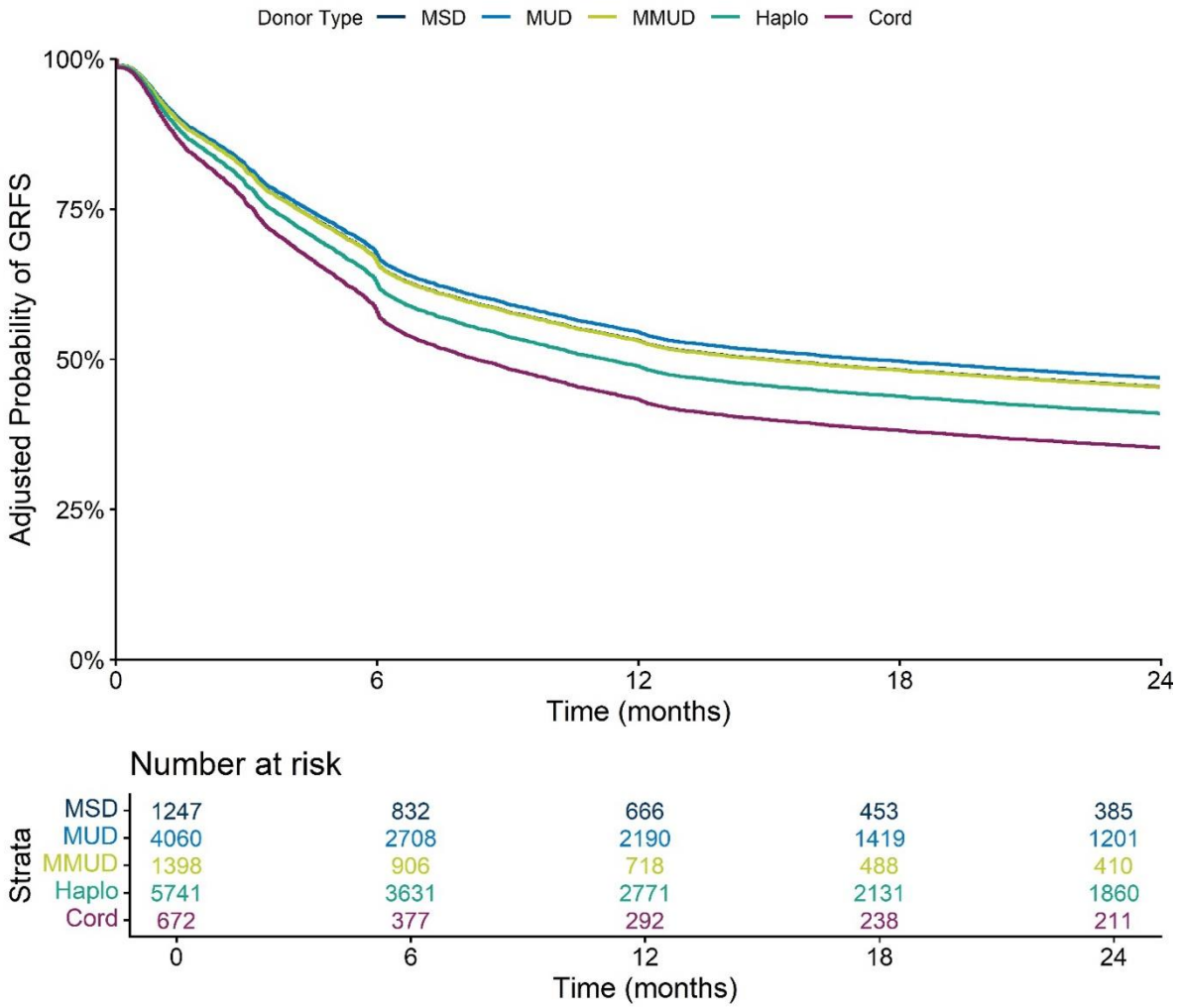
- **Patient population:**
  - Adults (≥18y) with acute leukemia (ALL/AML) or myelodysplastic syndrome (MDS) receiving first allogeneic HCT in U.S. between 2017-2023
- **Donor types:**
  - Matched related donor (MRD) – n=1263
  - Matched unrelated donor (MUD) – n=4117
  - Mismatched related donor (Haplo) – n=5811
  - Mismatched unrelated donor (MMUD) – n=1426
  - Cord blood (UCB) - n=719
- **GvHD prophylaxis:**
  - PTCy-based for marrow and PB allografts (standard of care)
  - CNI-based for UCB allografts (standard of care)
  - No ATG

Primary outcomes – All donor types

Overall Survival



GRFS



CIBMTR
A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

Aljawai et al., submitted

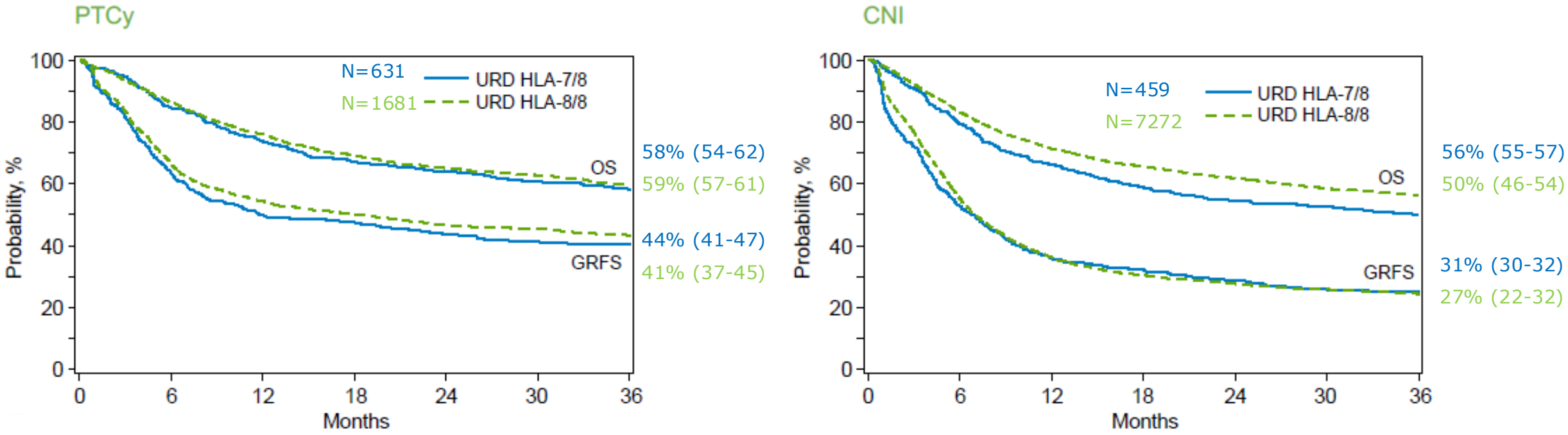
HLA matching considerations

Recommendation	Evidence Level	References
In the CNI setting: Avoid HLA-DPB1 non-permissive mismatches in MUD.	++	Lee et al 2007 Pidala et al 2014 Fleischhauer et al 2012 Crivello et al 2023
In the PTCy setting: • HLA-DRB1 mismatched **haplos** may be protective against relapse • HLA-DPB1 TCE non-permissive mismatching may be associated with better survival in **haplo** • **MUD** and **7/8 MMUD** outcomes are similar • There is insufficient evidence to recommend prioritization of specific HLA mismatches between **MMUDs** • Highly **MMUDs** (4-6/8) can be considered	 + + + ++ ++	Shaffer et al 2024 Shaw et al 2023 Fuchs et al 2022 Sanz et al 2024 Arrieta-Bolaños et al 2024
Donors with a high titer DSA target should not be Used*	+++	Gladstone et al 2013 Ciurea et al 2009

*There is ongoing debate regarding the MFI threshold for clinical significance, though a threshold of >10,000 is broadly accepted.

PTCy associates with similar OS, but improved 3y GRFS versus CNI-based GvHD following URD HCT

First allogeneic HCT in adults with ALL, AML or MDS using PTCy vs. CNI GvHD prophylaxis (Jan 2017-Jun 2021)



Adjusted for:
Age at HCT, HCT-CI, Refined Disk Risk Index, Race, Donor Age, Graft Source, Year of HCT, Donor/recipient CMV status (OS only)

CIBMTR®
A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

Shaffer et al, J Clin Oncol 2024

CIBMTR®
A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

Influence of the HLA Mismatched Locus on Outcomes in Mismatched Unrelated Donor Hematopoietic Cell Transplantation Using Post-Transplant Cyclophosphamide GVHD Prophylaxis: A CIBMTR Retrospective Analysis

Stephen R. Spellman, Varuna Astha, Kwang Woo Ahn, Caitrin Bupp, Antonio Jimenez Jimenez, Shannon McCurdy, Brian Shaffer, Bronwen Shaw, Heather Stefanski, Jeffery Auletta, Steven M. Devine

Poster Presentation at EBMT 2026

Results

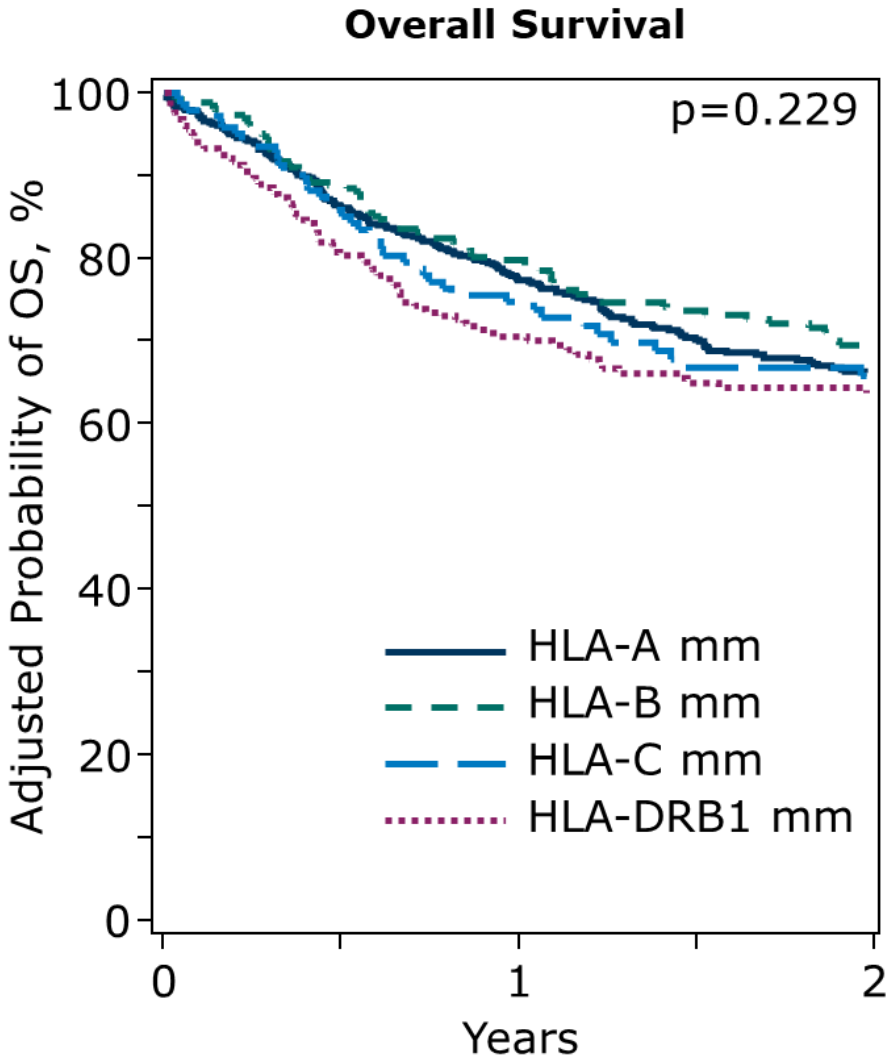
Study population:

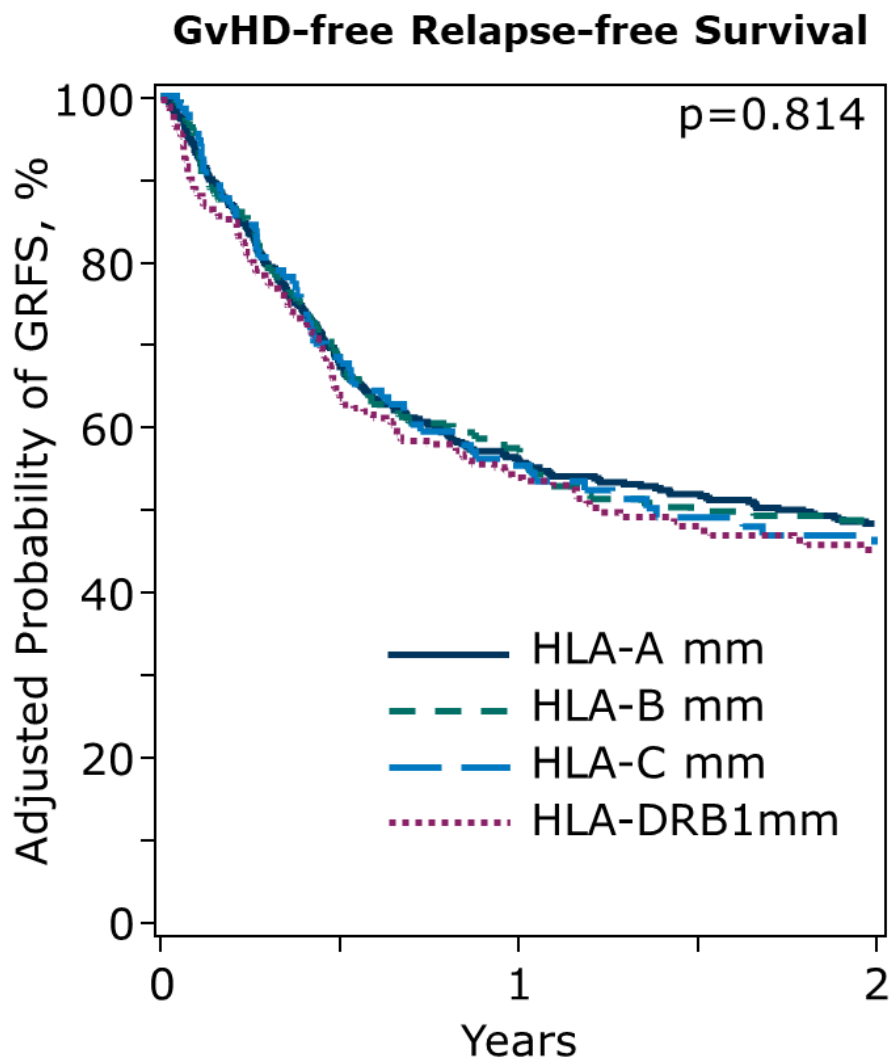
- 1,255 patients from 114 centers
- AML (n=692), ALL (n=235) and MDS (n=328).
- Median (range) recipient and donor age was 59.4 (18.7-78.4) and 27.7 years (18.4-61.2), respectively.
- 52% of recipients were female
- 32% were ethnically diverse
- 93% received PBSC grafts

HLA mismatching:

- HLA-A (n=591), HLA-B (n=279), HLA-C (n=128) and HLA-DRB1(n=257)
- DQB1 mismatches were more common among DRB1 mismatched pairs (49%) versus HLA-A (6%), -B (8%) and -C (7%) MMUD.
- HLA-DPB1 TCE matching was similar across groups (20-27% non-permissive)
- **Neither DQB1 MM nor DPB1 TCE status was associated with any outcomes in MVA models**

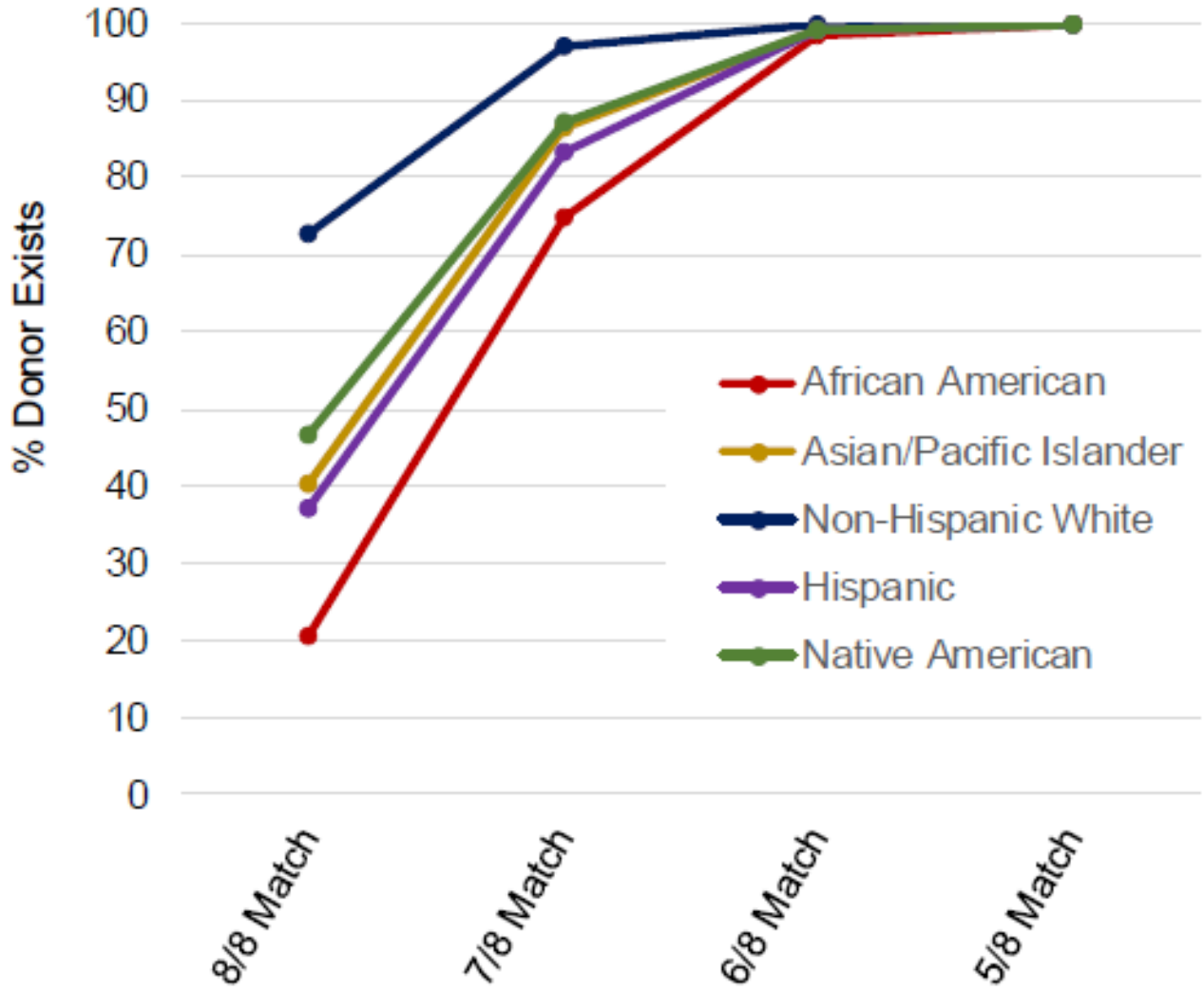
Results: Primary Outcomes





Using the largest group (HLA-A) as the reference MM locus, no significant differences were observed in OS or GRFS

7/8 does not close the existence gap



Jimenez-Jimenez et al JTCT 2025

CIBMTR®
A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

Outcomes after 7/8 and <7/8 mismatched unrelated donor PBSC transplantation with PTCy: results from the ACCESS trial

Antonio Martin Jimenez Jimenez, Joseph Stanek, Brent R Logan, Erin Leckrone, Heather E. Stefanski, Jeffery J. Auletta, Stephen R. Spellman, Craig Malmberg, Medhat Askar, Rachel N. Cusatis, Brian C. Shaffer, Dipenkumar Modi, Farhad Khimani, Mahasweta Gooptu, Mehdi Hamadani, Martin Maiers, Stephanie Bo-Subait, Javier Bolaños-Meade, Uttam Rao, Jordan Milner, Ramzi Abboud, Katarzyna Joanna Jamieson, George Carrum, Bhagirathbhai Dholaria, William J. Hogan, Ran Reshef, Satyajit Kosuri, Rachel J. Cook, Karen Ballen, Alison W. Loren, Karilyn Larkin, Sally Arai, Muna Qayed, Sung Won Choi, Larisa Broglie, Bronwen E. Shaw, Steven M. Devine, Monzr M. Al Malki

Study Sponsored by:

nmdp
FIND CURES. SAVE LIVES.

NCT04904588

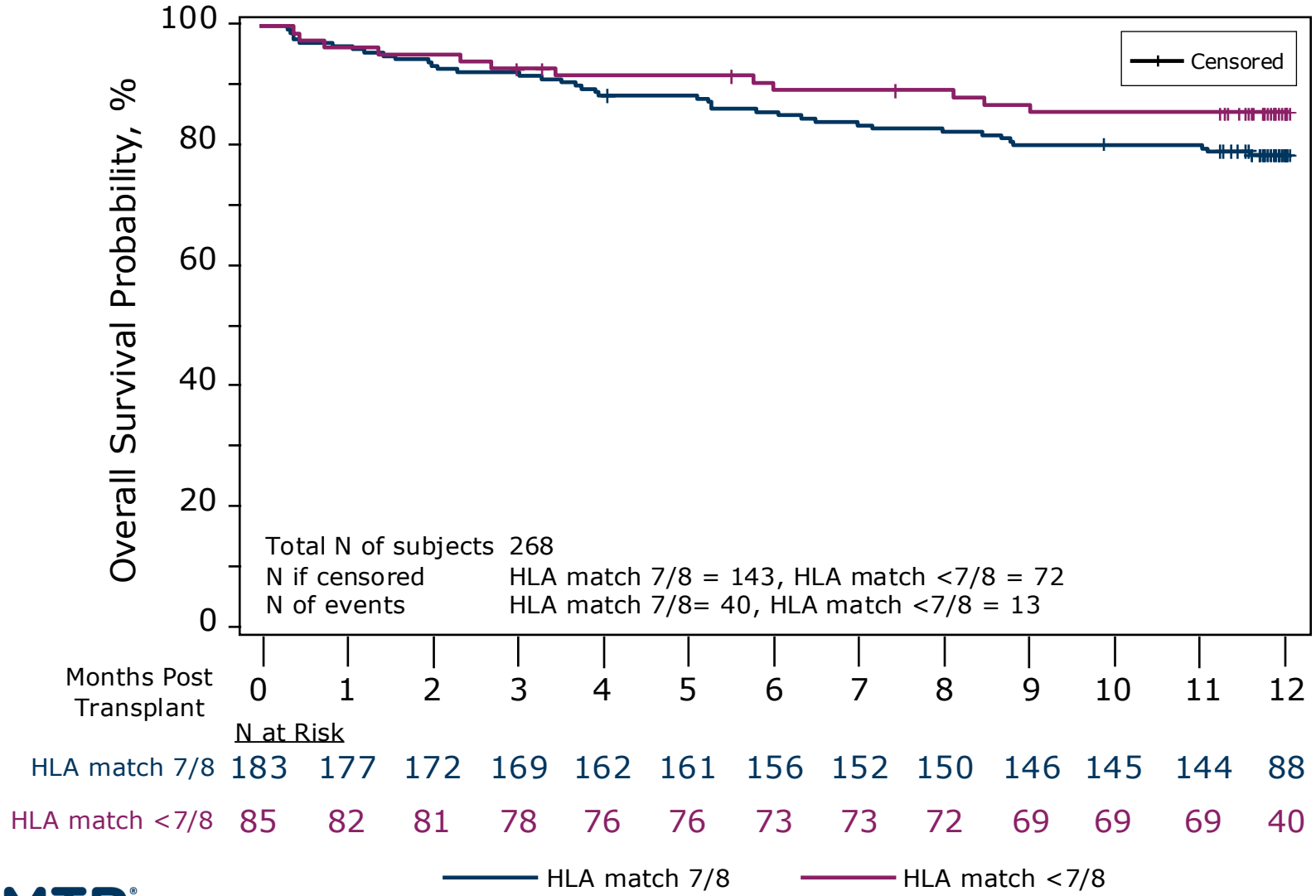
Patient Demographics

Characteristic	7/8 n (%)	<7/8 n (%)
No. of patients	183	85
No. of centers	30	21
Age at HCT (y)		
Median (min-max)	**63.3** (20.4-78.9)	**57.4** (24.3-77.9)
Sex		
Male	95 (51.9)	42 (49.4)
Female	88 (48.1)	43 (50.6)
Cryopreservation		
Cryopreserved	117 (60.6)	58 (77.3)
Fresh	76 (39.4)	27 (22.7)

Characteristic	7/8 n (%)	<7/8 n (%)
Patient Race/Ethnicity		
Non-Hispanic White (NHW)	98 (53.6)	30 (35.3)
Hispanic	45 (24.6)	21 (24.7)
Black/African-American	15 (8.2)	20 (23.5)
Asian or Pacific Islander	15 (8.2)	7 (8.2)
Native American	2 (1.1)	1 (1.2)
Multiple/Unknown	8 (4.3)	6 (7.1)

CIBMTR®
A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

Results – Primary Endpoint



1-year OS (95% CI)

<7/8=85.6% (76.0-91.5%)

7/8=78.6% (71.9-83.9%)

Exploratory multivariable analysis comparing <7/8 vs 7/8:

HR:0.70 (0.38-1.32), p=0.27

Variables considered: age, sex, race/ethnicity, Karnofsky performance score, HCT-CI, disease, disease status, conditioning intensity, cryopreserved product vs fresh, recipient CMV status.

No covariates remained in the models after stepwise selection using p=0.05

CIBMTR®
A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

Jimenez-Jimenez et al., Blood Advances 2026

CIBMTR.org

Results – Secondary Endpoints

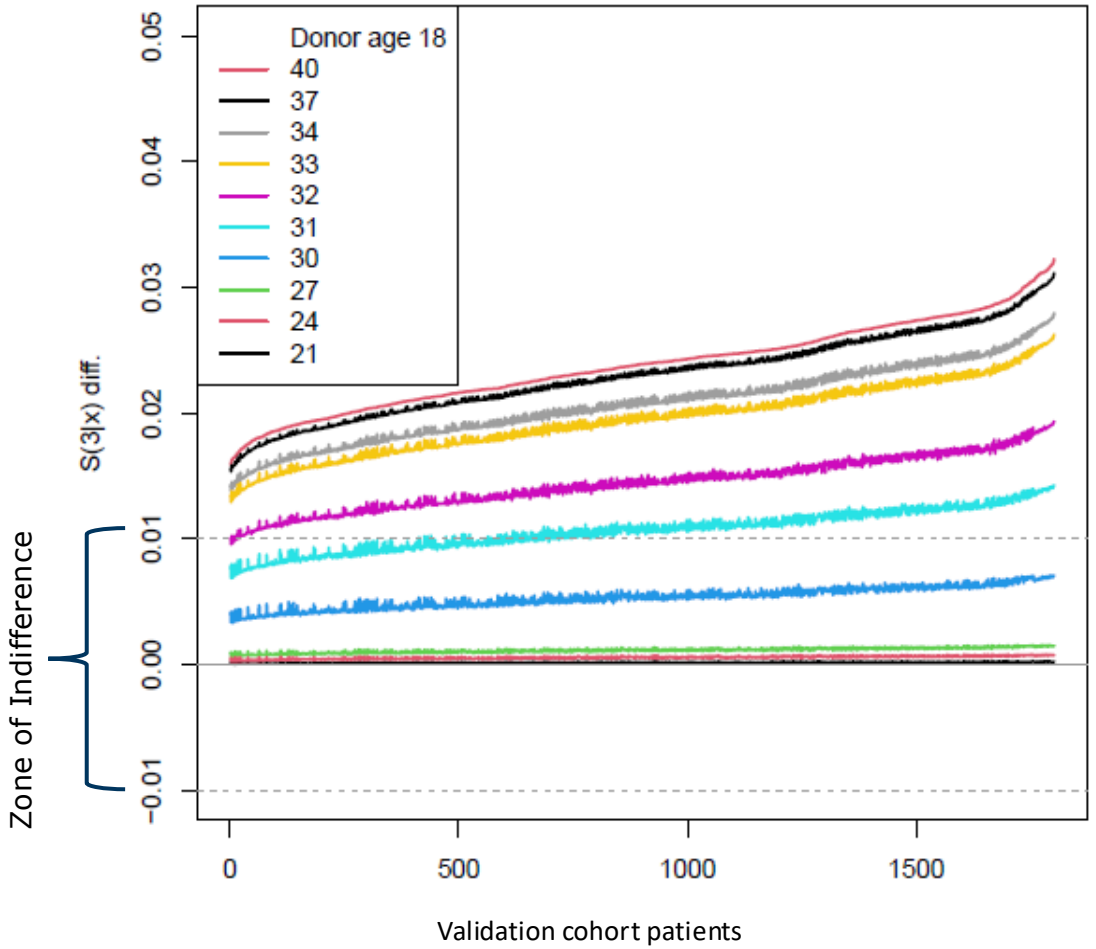
Clinical Endpoint	7/8 Match (n=183)	<7/8 Match (n=85)
	1yr est. (95% CI)	**1yr est. (95% CI)**
GVHD-free, Relapse-free survival (GRFS)	**51.1%** (43.5-58.2%)	**53.0%** (41.2-63.6%)
Acute GVHD grade II-IV (6 month)	**38.8%** (31.7-45.8%)	**34.3%** (24.3-44.4%)
Acute GVHD grade III-IV (6 month)	**8.2%** (4.8-12.8%)	**7.1%** (2.9-14.0%)
NIH moderate/severe chronic GVHD	**11.3%** (7.1-16.4%)	**7.7%** (3.1-15.1%)
Primary graft failure by Day 28	**3.1%** (0.8-7.6%)	**6.5%** (1.8-15.7%)
Non-relapse mortality (NRM)	**13.7**% (9.2-19.1%)	**8.4**% (3.7-15.6%)
Relapse	**17.1%** (12.0-22.9%)	**22.8%** (14.1-32.8%)

Secondary Characteristic Considerations

Recommendation	Evidence Level	References
Donor age: • Donors ≤ 30 years old should be prioritized to maximize OS.	+++	Dehn et al 2024 Ciurea et al 2020 Kollman et al 2016 Spellman et al 2024
Donor CMV, ABO, and sex: • Donor/recipient ABO matching may reduce post HCT transfusion burden. • Major ABO mismatches should be avoided in haplo and when using BM grafts. • Donor CMV serostatus may be considered in specific clinical cases (e.g., SCID)	 ++ ++ +	Mehta et al 2023 Anthias et al 2016 Sanz et al 2024 Murthy et al 2022
Donor weight: • A large patient-donor weight discrepancy should be avoided in the setting of BM HCT.	+++	

Impact of Donor Age on Overall Survival

- Waterfall plot of predicted OS differences at 3 years post-transplant for an 18-year-old vs. an older donor from the validation cohort.
- Compared to donors ≥31, an 18-year-old is associated with a substantial increase in OS where all recipient OS differentials >0.01
- Compared to donors **19 to 30, an 18-year-old choice produces benefits that are negligible and fall within the Zone of Indifference.**



Spellman, Blood Advances 2024

CIBMTR
A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

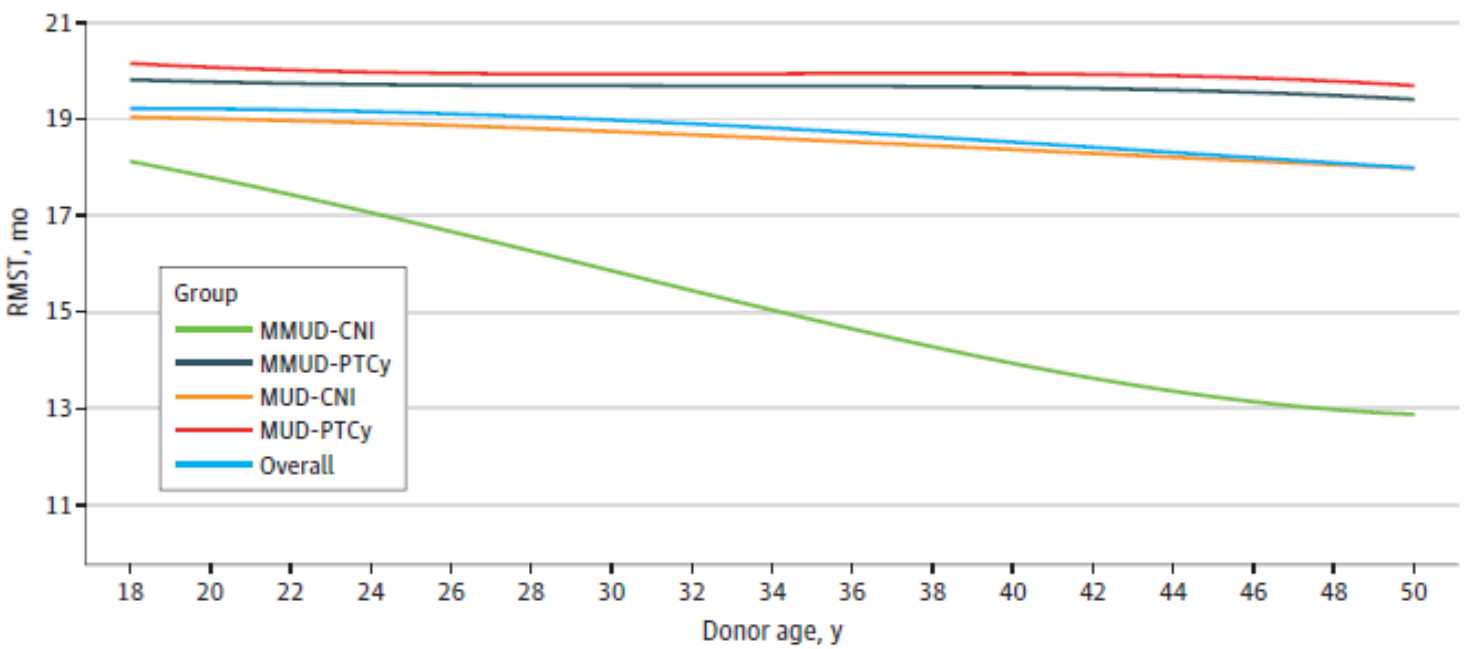
JAMA Oncology | Original Investigation

Unrelated Donor Age and Recipient Outcomes After Posttransplant Cyclophosphamide vs Conventional Prophylaxis

Rohtesh S. Mehta, MD, MPH, MS; Rodney A. Sparapani, PhD; Christopher G. Kanakry, MD; Shannon R. McCurdy, MD; Jennifer Saultz, MD; Aleksandr Lazaryan, MD; Filippo Milano, MD, PhD; Stephanie J. Lee, MD, MPH

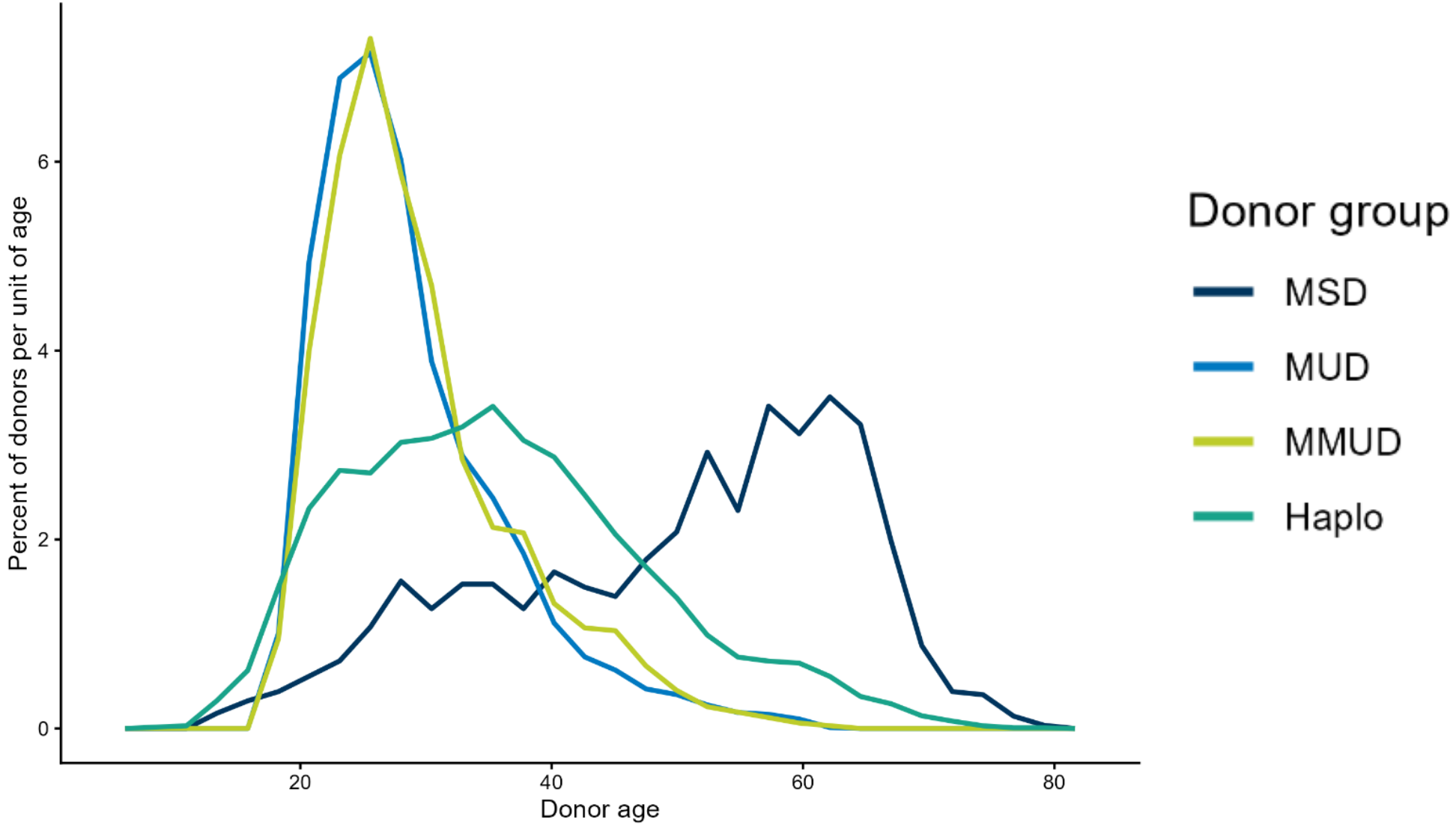
- Re-analysis of Shaffer et al., JCO 2024 *PTCy-Based Graft-Versus-Host Disease Prophylaxis Attenuates Disparity in Outcomes Between Use of MUD or MMUD*
- MUD/MMUD PTCy – little to no impact of increasing donor age
- MUD/MMUD CNI – decline in OS with increasing donor age

Figure 2. Model-Predicted 24-Month Restricted Mean Survival Time (RMST) as a Function of Donor Age



CIBMTR®
A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

Distribution of donor age by donor type

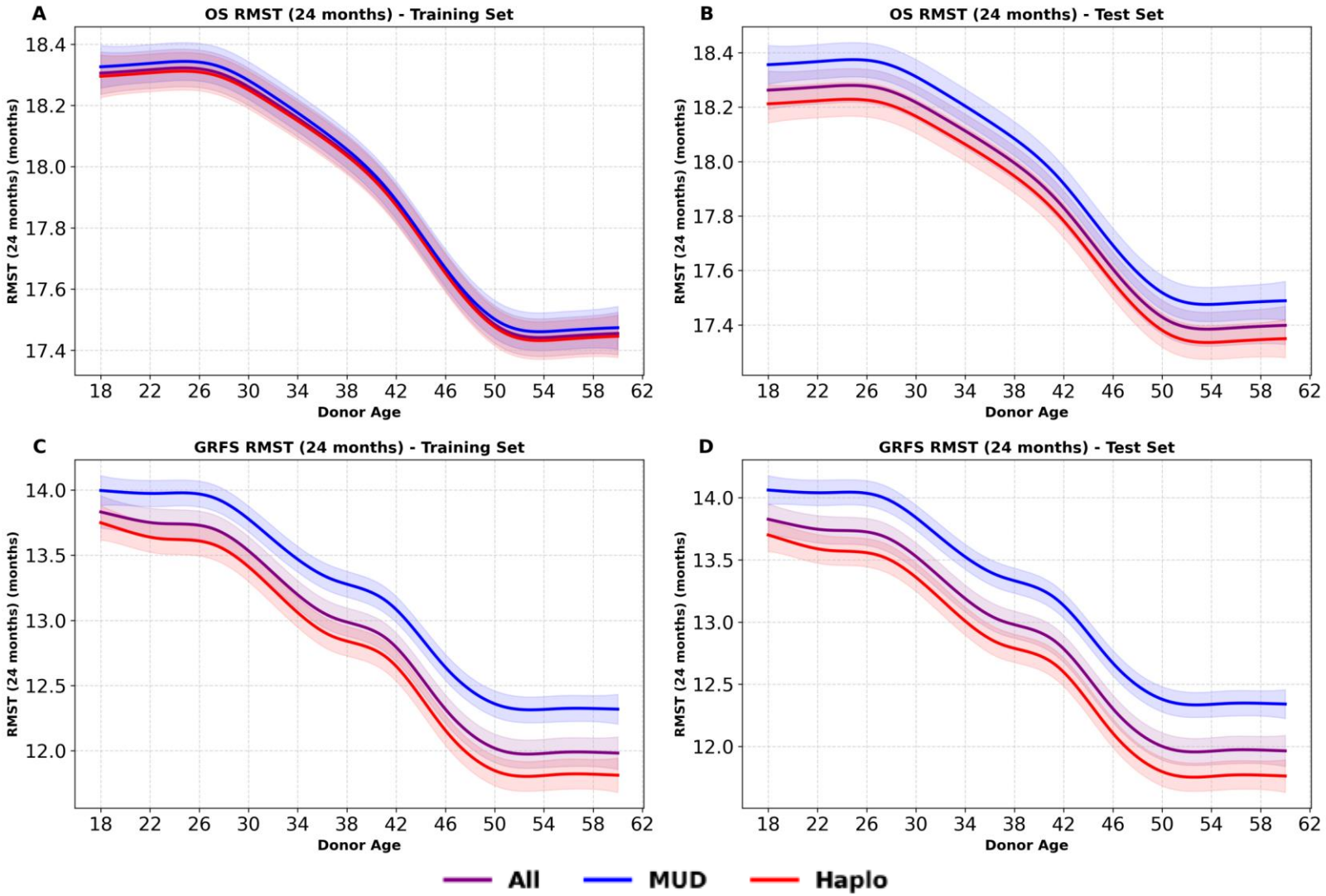


Aljawai et al submitted

CIBMTR®
A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

Impact of MUD/Haplo age – OS and GRFS

- Re-analysis of Modi et al., Blood Advances 2025 *Matched unrelated vs haploidentical donor hematopoietic cell transplantation using PTCy*
- OS - MUD and Haplo PTCy – OS declines with increasing age, shifted to later 30s
- GRFS – declines at >30 yo

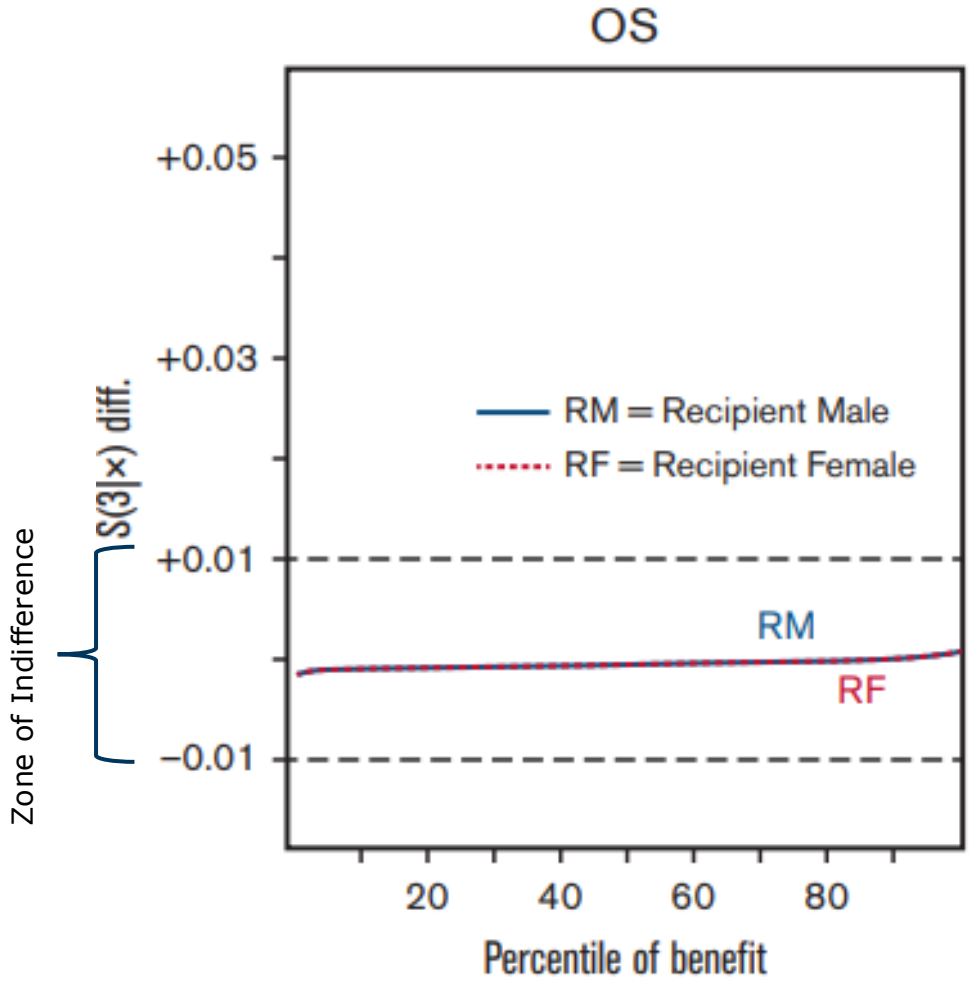


CIBMTR®
A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

Xie et al submitted

Impact of Donor Sex on Overall Survival

- Waterfall plot of predicted OS differences at 3 years post-transplant for male and female recipients based on predictions in the validation cohort
- Donor sex had no impact on OS in either male or female recipients
- When multiple equivalently aged male and female donors are available, selecting for the donor that meets the patient's timeline for transplant should be prioritized over donor sex



Spellman, Blood Advances 2024

CIBMTR
A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

Conclusions

- HLA is important when selecting donors
  - No change in recommendations in CNI-prophylaxis setting
  - We are still learning in the PTCy and MMUD setting
- Consider donor types simultaneously not consecutively
- Other factors may be equally (or even more) important
  - Donors 18-30 years old may be optimal
- Enroll on a clinical trial, if available
- Leverage the power of large registries
  - Combine data from trials and perform follow-up
  - ML/AI; sample collection; secondary analysis

Acknowledgments

- Transplant centers who support the mission of the CIBMTR by providing data
- Patients who enable us to learn from their transplant journeys
- Funding
  - **U24CA076518**
  - **75R60222C00011**
  - **N00014-24-1-2057** and **N00014-25-1-2146**

Questions?