בחירת תורם בהשתלות מח עצם אלוגנאיות

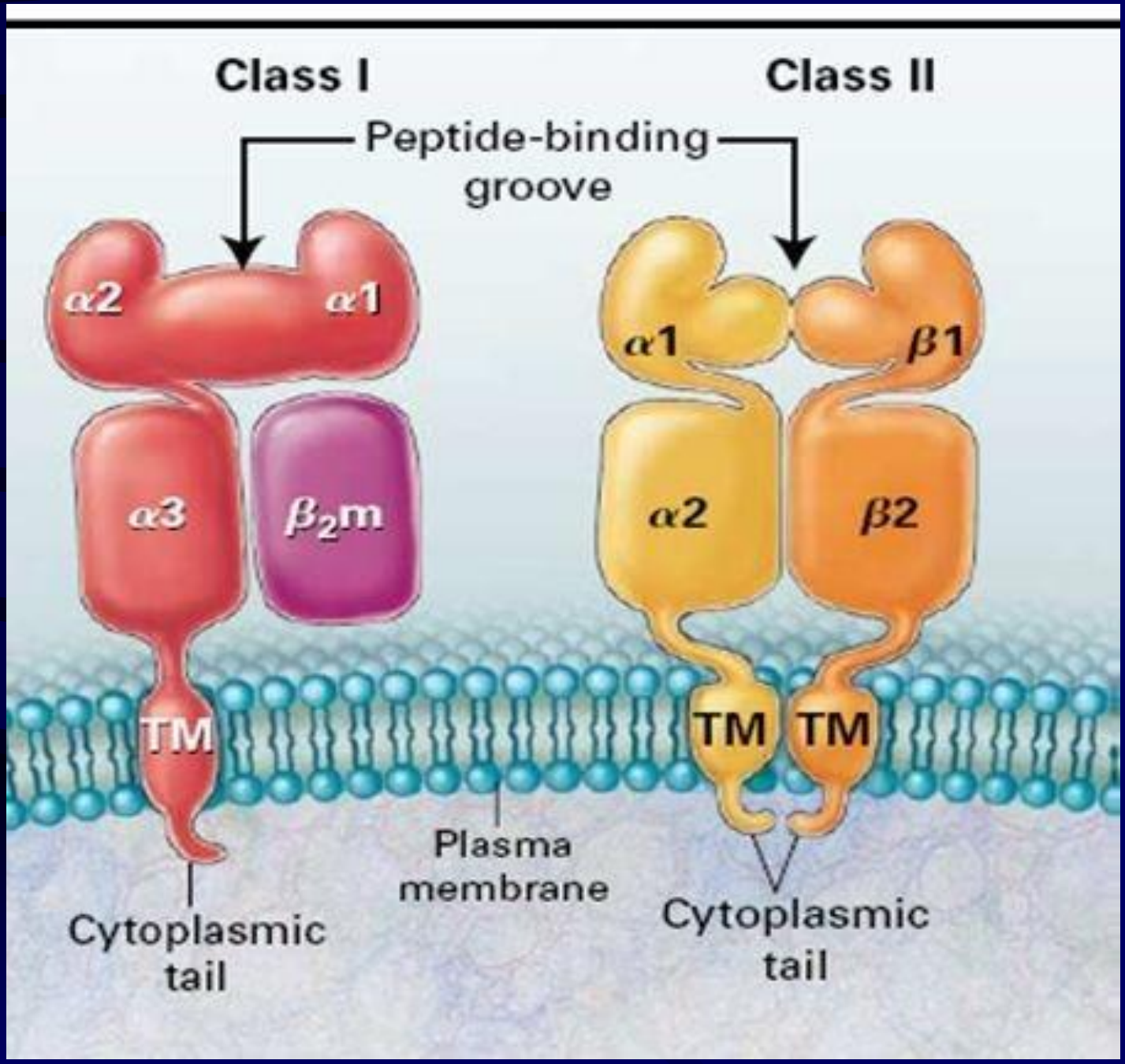
ד"ר ורד סתוי
המרכז הרפואי "סורוקה"

נושאים עיקריים

- הבסיס למציאת תורם - HLA
- מי הם התורמים האופציונלים?
- שיקולים נוספים בבחירת התורם
- תורם אלטרנטיבי בדגש על הפלו

Introduction

- Allogeneic stem cell transplantation is a curative therapy for a variety of hematological malignancies
- Donor T-cells recognize alloantigen on leukemia cells and can eradicate them (GVL effect)
- However, donor cells can also cause graft-versus-host disease.
- HLA matching of donor and recipient is crucial for optimal transplantation outcome.


Class I
Class II
Peptide-binding groove
α2
α1
α3
β2m
α1
β1
α2
β2
TM
TM
TM
Plasma membrane
Cytoplasmic tail
Cytoplasmic tail

Selective Expression of HLA

- Class I
- Nucleated cells
- Platelets

- *Higher expression levels on B cells than T cells*
- *Not on RBCs*

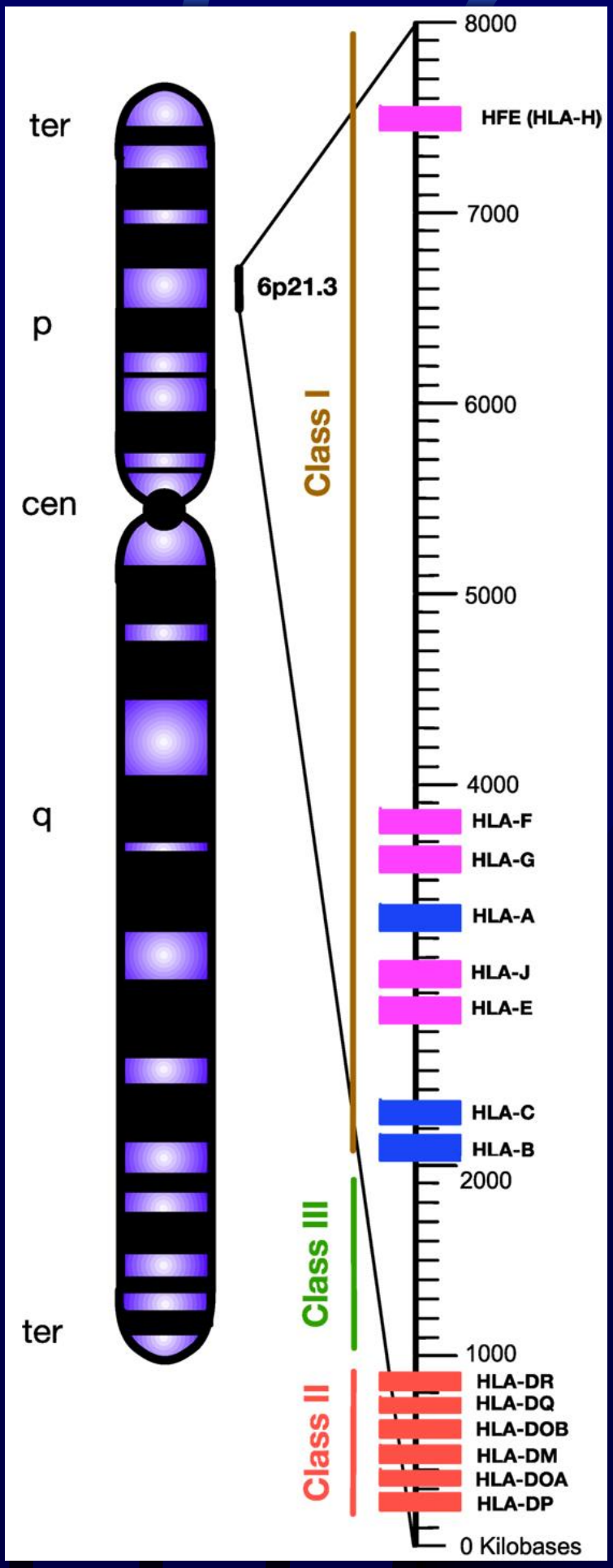
Class II

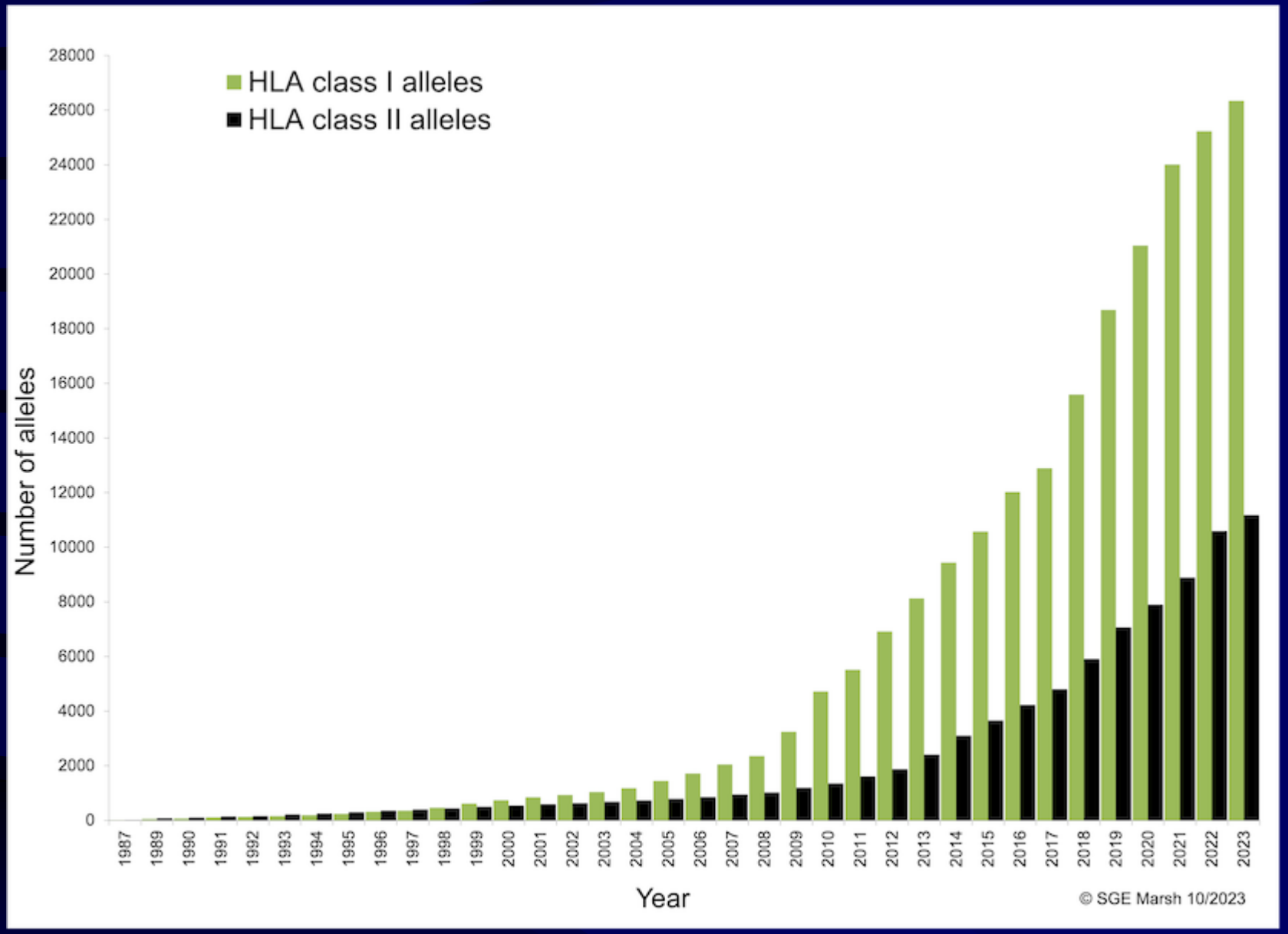
Constitutively on APCs:
B cells, Dendritic cells, langerhans cells

Myeloid cell lineages

Expression can be induced in other cell lineages

HLA A, B, C	HLA DR, DQ

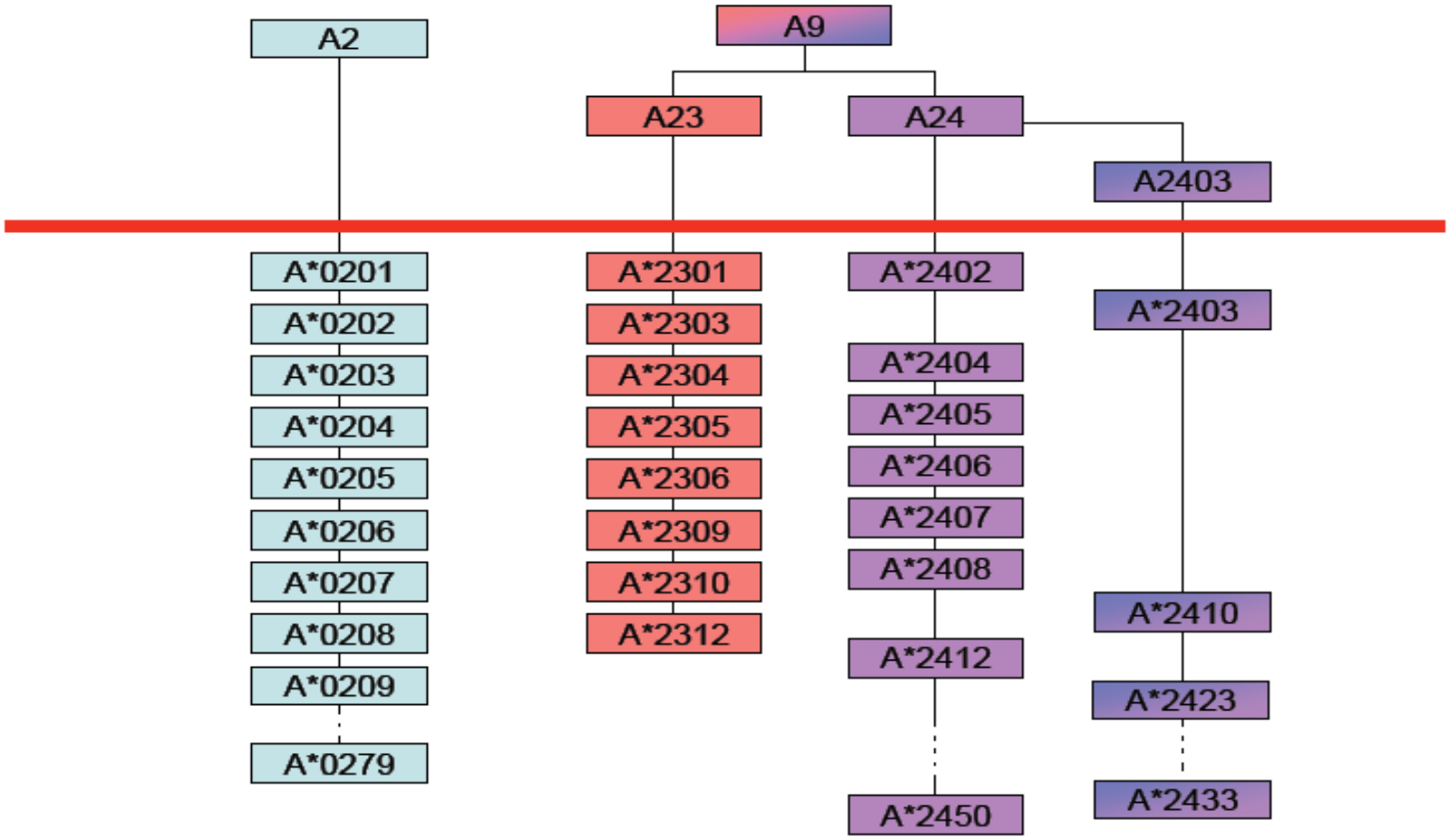

ter
p
cen
q
ter
6p21.3
Class I
Class III
Class II
8000
7000
6000
5000
4000
2000
1000
0 Kilobases
HFE (HLA-H)
HLA-F
HLA-G
HLA-A
HLA-J
HLA-E
HLA-C
HLA-B
HLA-DR
HLA-DQ
HLA-DOB
HLA-DM
HLA-DOA
HLA-DP

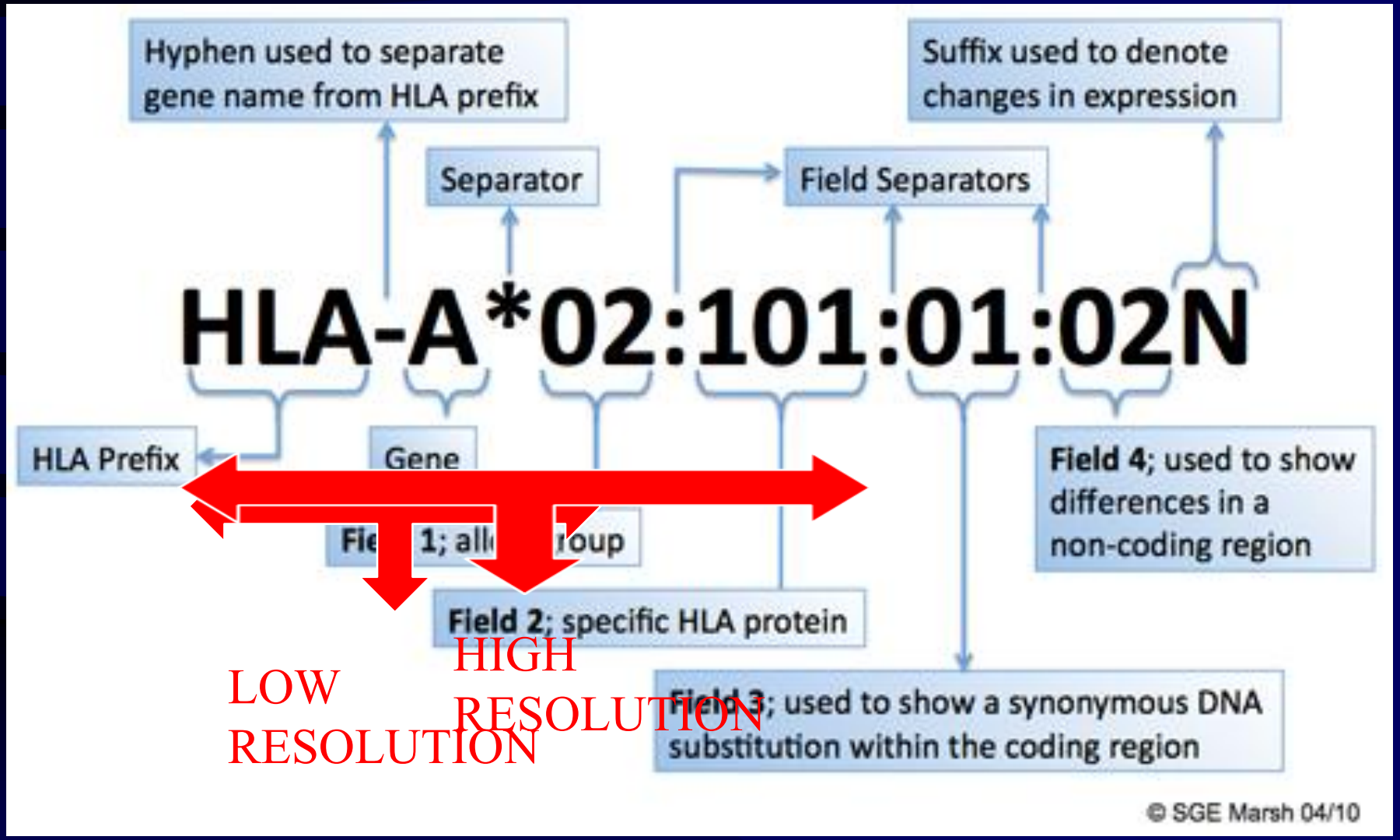


CLASS I	**25,844**
CLASS II	10,970

HLA-DPB1	HLA-DQB1	HLA-DRB1	HLA-C	HLA-B	HLA-A	
2393	2491	4530	7995	9573	8012	אלל
1399	1516	2983	4410	5694	4688	אנטיגן

Alleles versus Serology - ideal

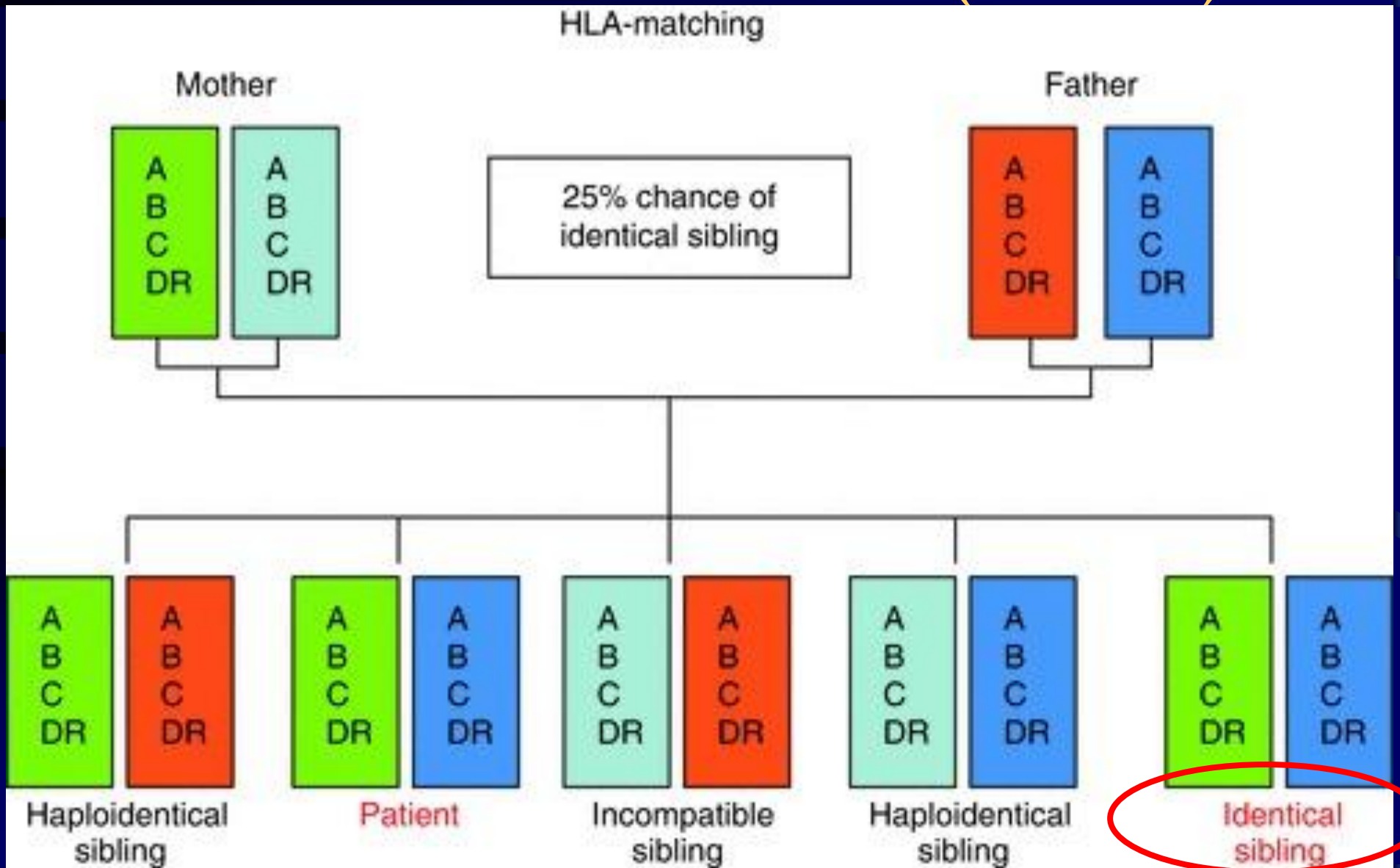



Hyphen used to separate gene name from HLA prefix
Suffix used to denote changes in expression
Separator
Field Separators
HLA-A*02:101:01:02N
HLA Prefix
Gene
Field 4; used to show differences in a non-coding region
Field 2; specific HLA protein
LOW RESOLUTION
HIGH RESOLUTION
Field 3; used to show a synonymous DNA substitution within the coding region
© SGE Marsh 04/10

נתוני נבדק:

A*	B*	C*	DRB1*	DQA1*	DQB1*	DPA1*	DPB1*
02:01	38:01	03:04	04:02	01:02	03:02	01:03	04:01
26:01	40:01	12:03	13:02	03:01	06:04	-	-

Matched sibling donor (MSD)\
Matched related donor(MRD)



Syngeneic donor

- Uses stem cells from an identical twin.
- Extremely low risk of GVHD due to complete genetic identity. However, syngeneic transplants lack the GVL effect, resulting in higher relapse rates compared to allogeneic transplants

1-antigen mismatching

- Recombination

  1-2% of families

Father a A1-B8-DR3 → a” A1-B8-DR15

b A31-B18-DR15

Mother c A2-B51-DR11

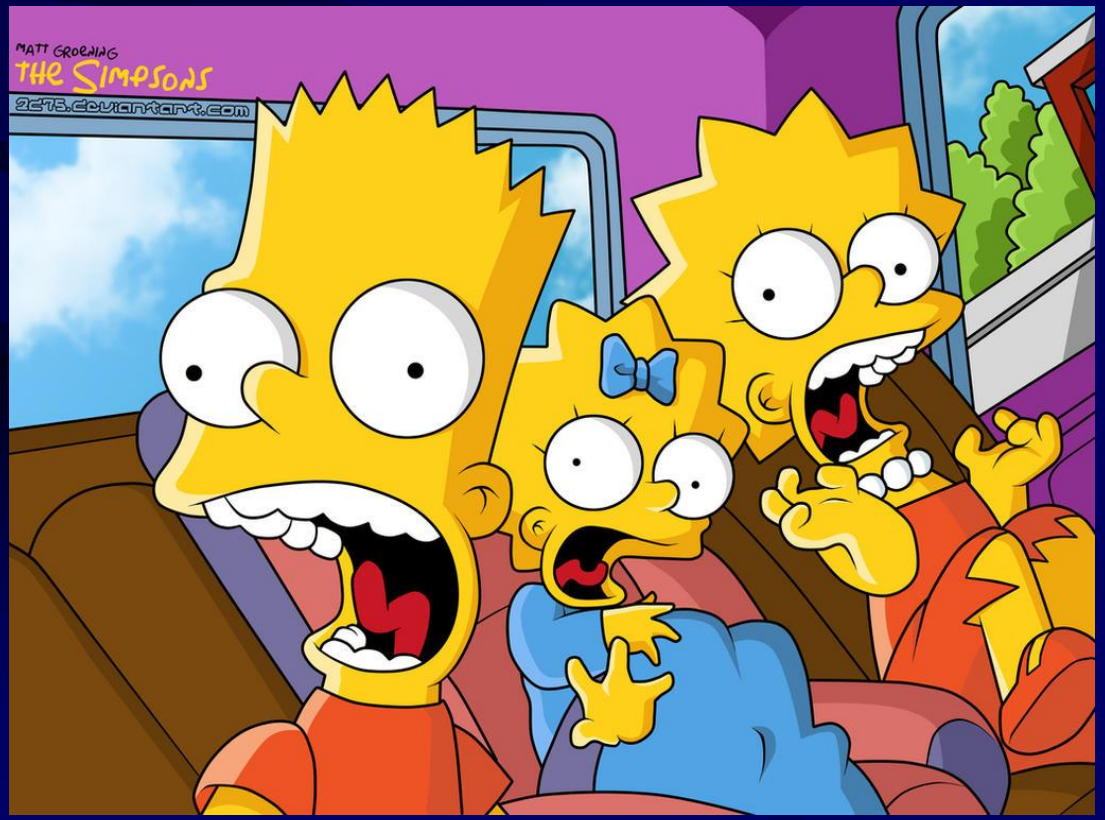
d A11-B27-DR2

Patient a A1-B8-DR3 Sibling a” A1-B8-DR15

c A2-B51-DR11 c A2-B51-DR11

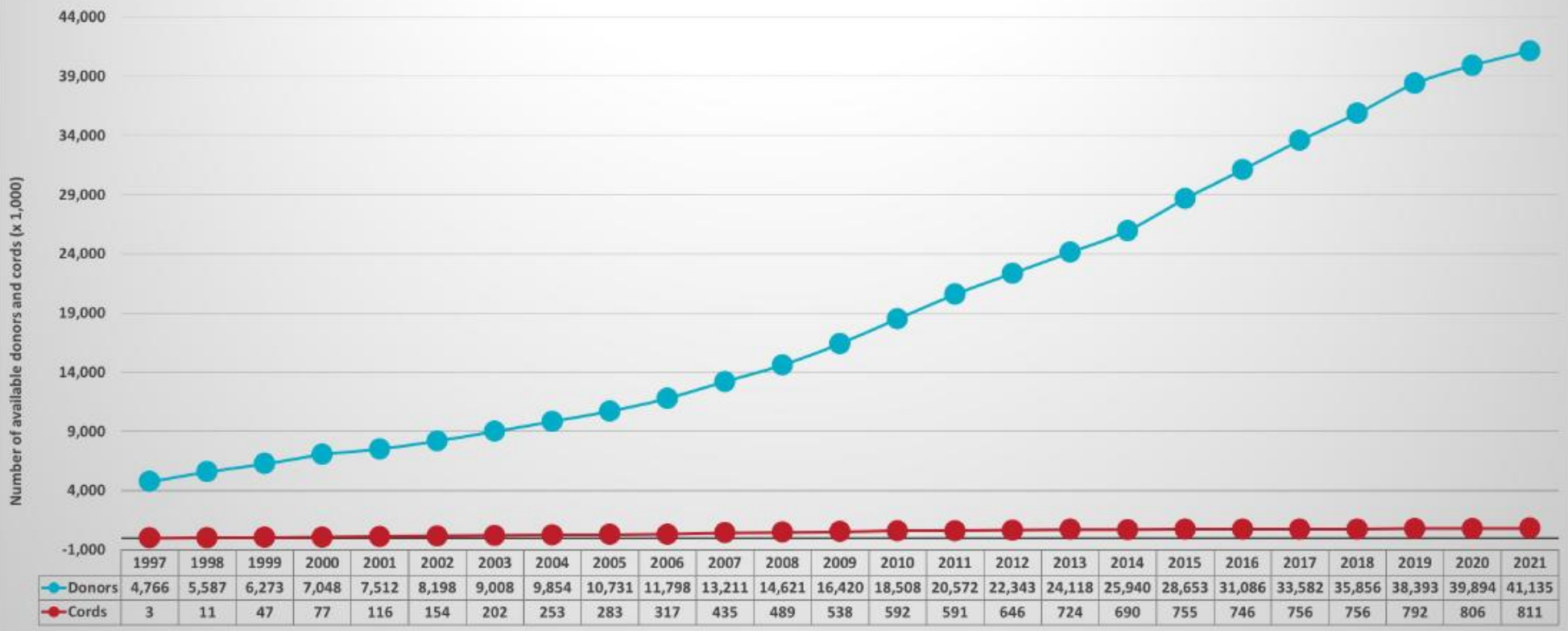
אז במי בוחרים?

הבחירה הראשונה תהיה ב MATCHED SIBLING DONOR (MSB)

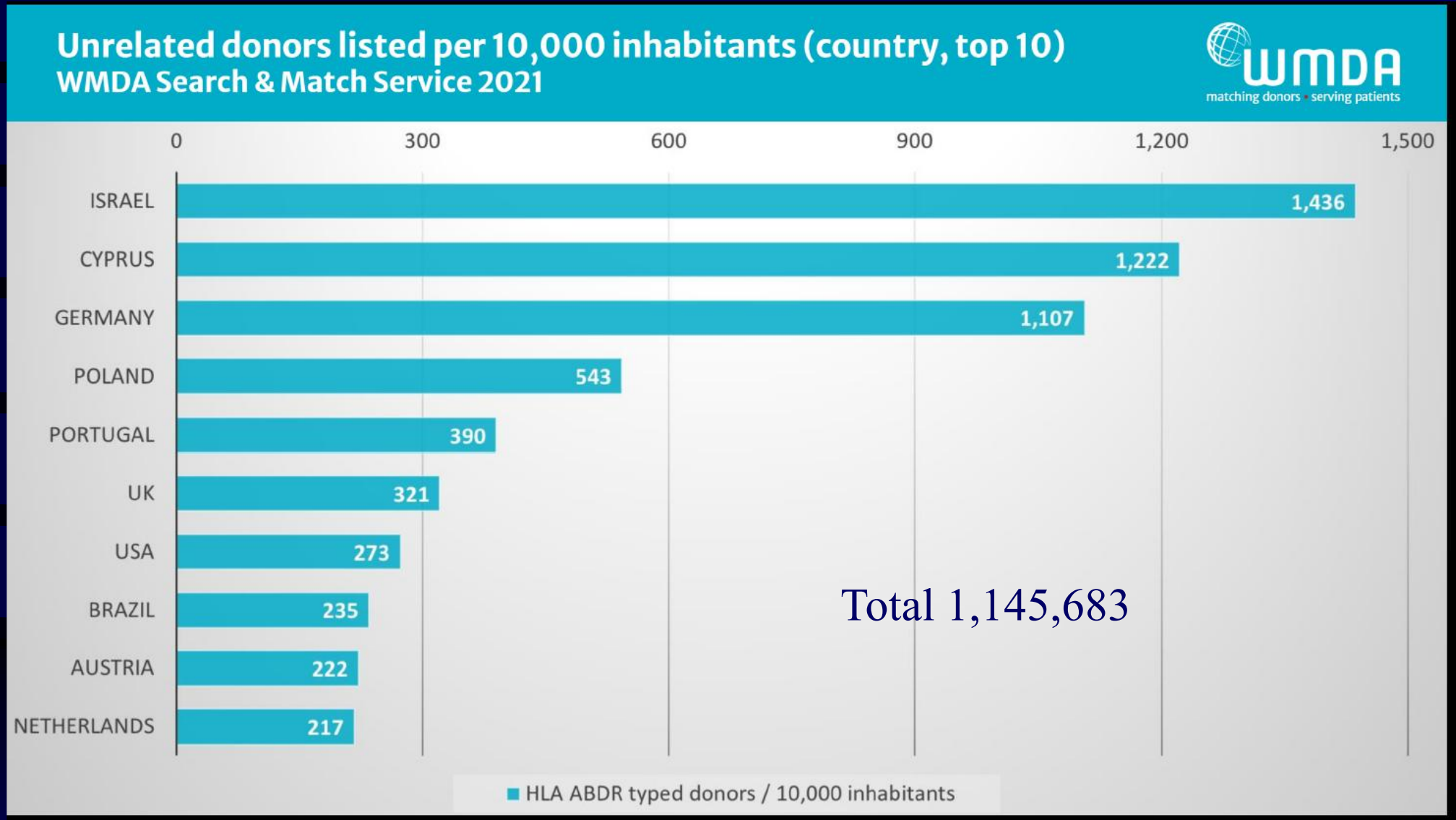


Number of unrelated blood stem cell donors and cord blood units available worldwide 1997–2021

WMDA
matching donors · serving patients

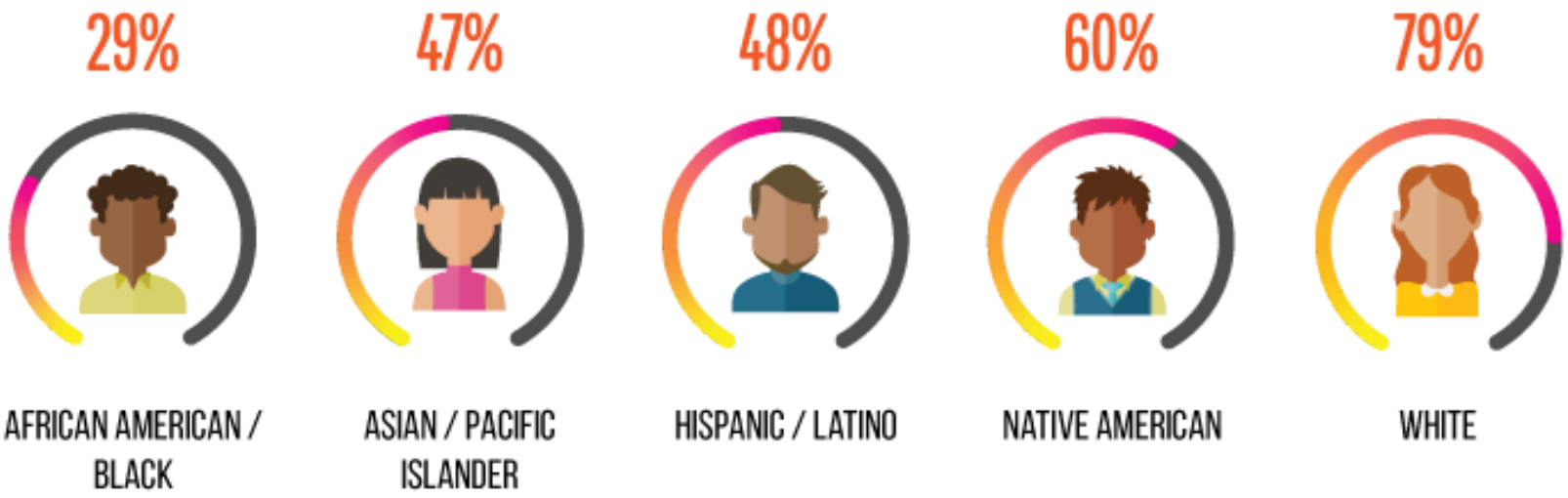


	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Donors	4,766	5,587	6,273	7,048	7,512	8,198	9,008	9,854	10,731	11,798	13,211	14,621	16,420	18,508	20,572	22,343	24,118	25,940	28,653	31,086	33,582	35,856	38,393	39,894	41,135
Cords	3	11	47	77	116	154	202	253	283	317	435	489	538	592	591	646	724	690	755	746	756	756	792	806	811


Unrelated donors listed per 10,000 inhabitants (country, top 10)
WMDA Search & Match Service 2021
WMDA
matching donors • serving patients
0
300
600
900
1,200
1,500
ISRAEL
1,436
CYPRUS
1,222
GERMANY
1,107
POLAND
543
PORTUGAL
390
UK
321
USA
273
BRAZIL
235
AUSTRIA
222
NETHERLANDS
217
Total 1,145,683
HLA ABDR typed donors / 10,000 inhabitants

DIVERSITY NEEDED

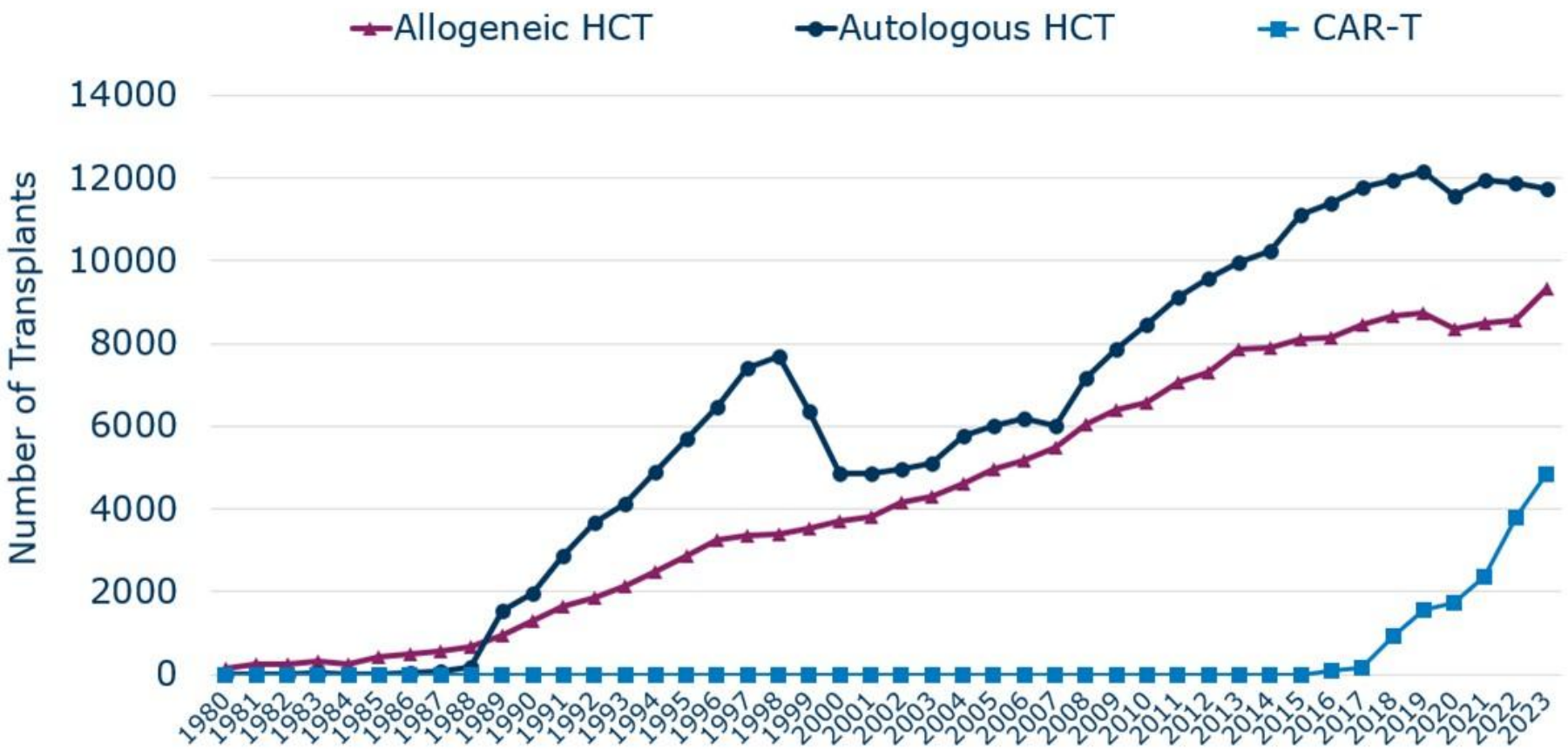
PERCENTAGE ABLE TO FIND A MATCHING DONOR



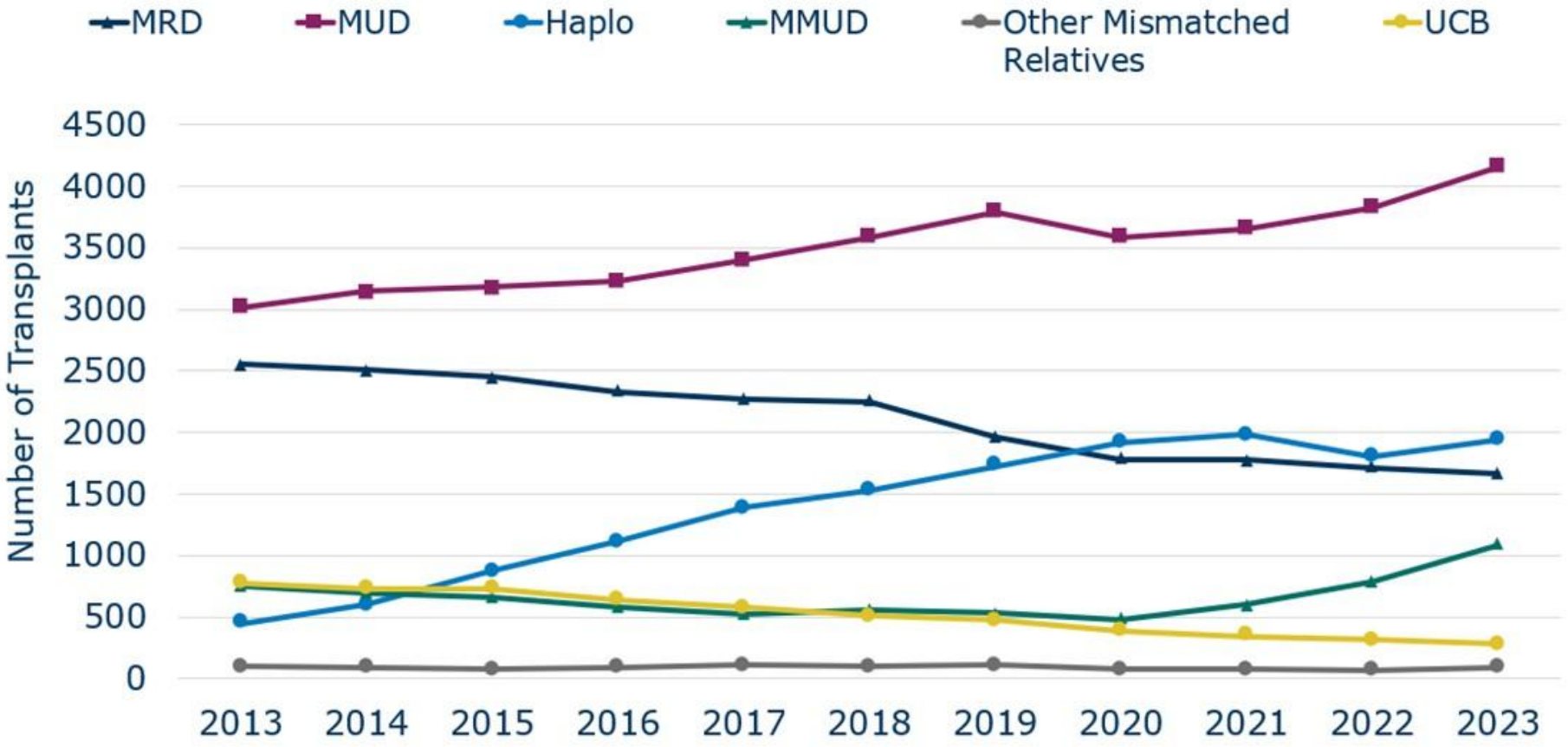
מיהו התורם האופציונלי?

Type	Major Histocompatibility Antigens	HLA A, B, C HLA DR, DQ, DP	Minor Histocompatibility Antigens
Conventional / preferred sources			
Matched sibling donor (MSD)\ Matched related donor (MRD)	matched	6/6, 8/8, 10/10, 12/12	Less disparity
Matched unrelated donor (MUD)	matched	6/6, 8/8, 10/10, 12/12	Random
"Alternative" donor sources			
Mismatched unrelated donor (MMUD)	Incompletely matched	≥1 mismatch major HLA	Random
Umbilical cord donation (UC)	More tolerant of m/m	4-6/6	Random
Haploidentical related donor (HRD)	50% unmatched	~3/6, 4/8, 5/10, 6/12	Less disparity

Number of 1st Cellular Therapies Reported to CIBMTR in the US



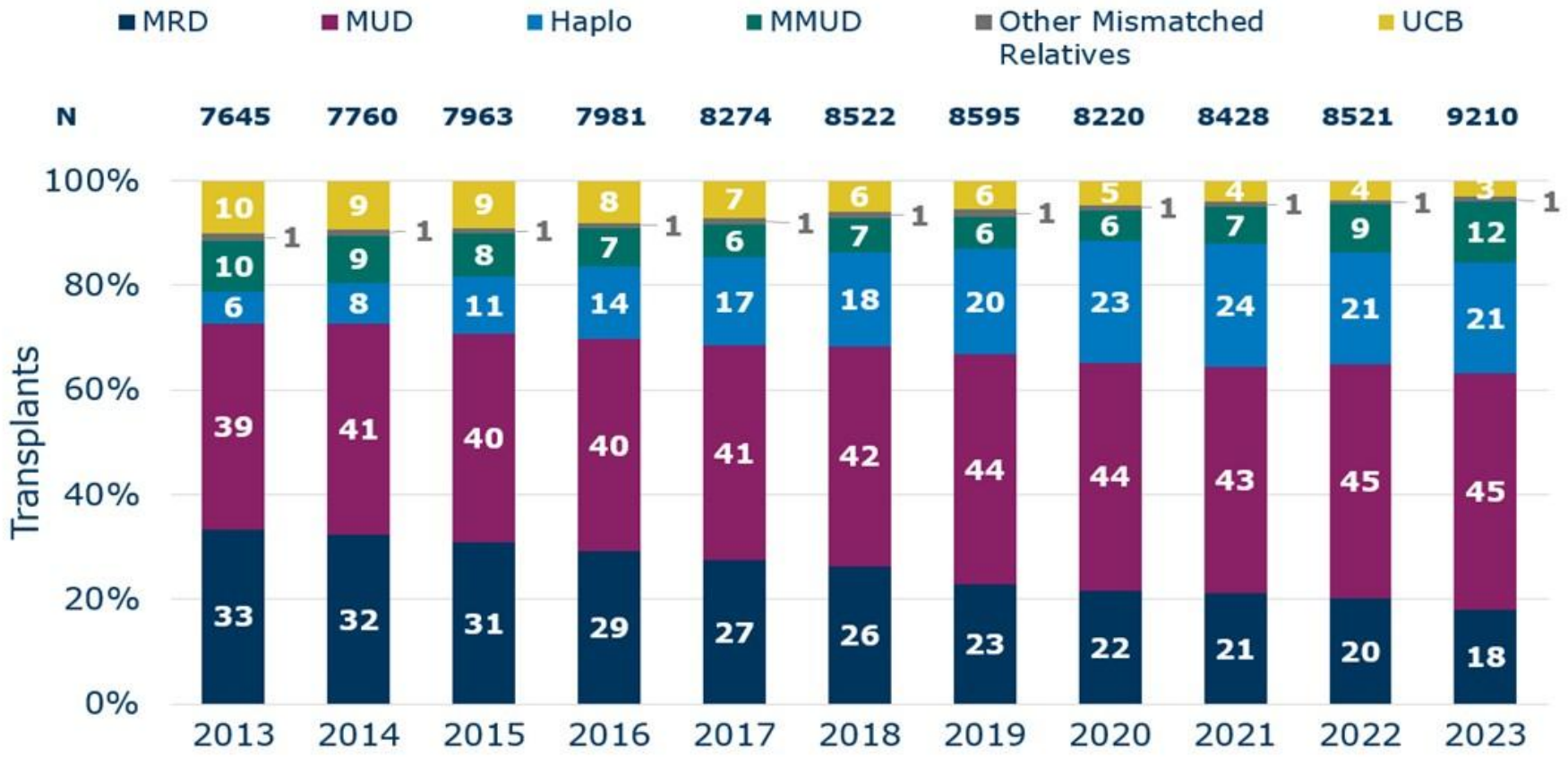
Number of Allogeneic HCTs in the US by Donor Type



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

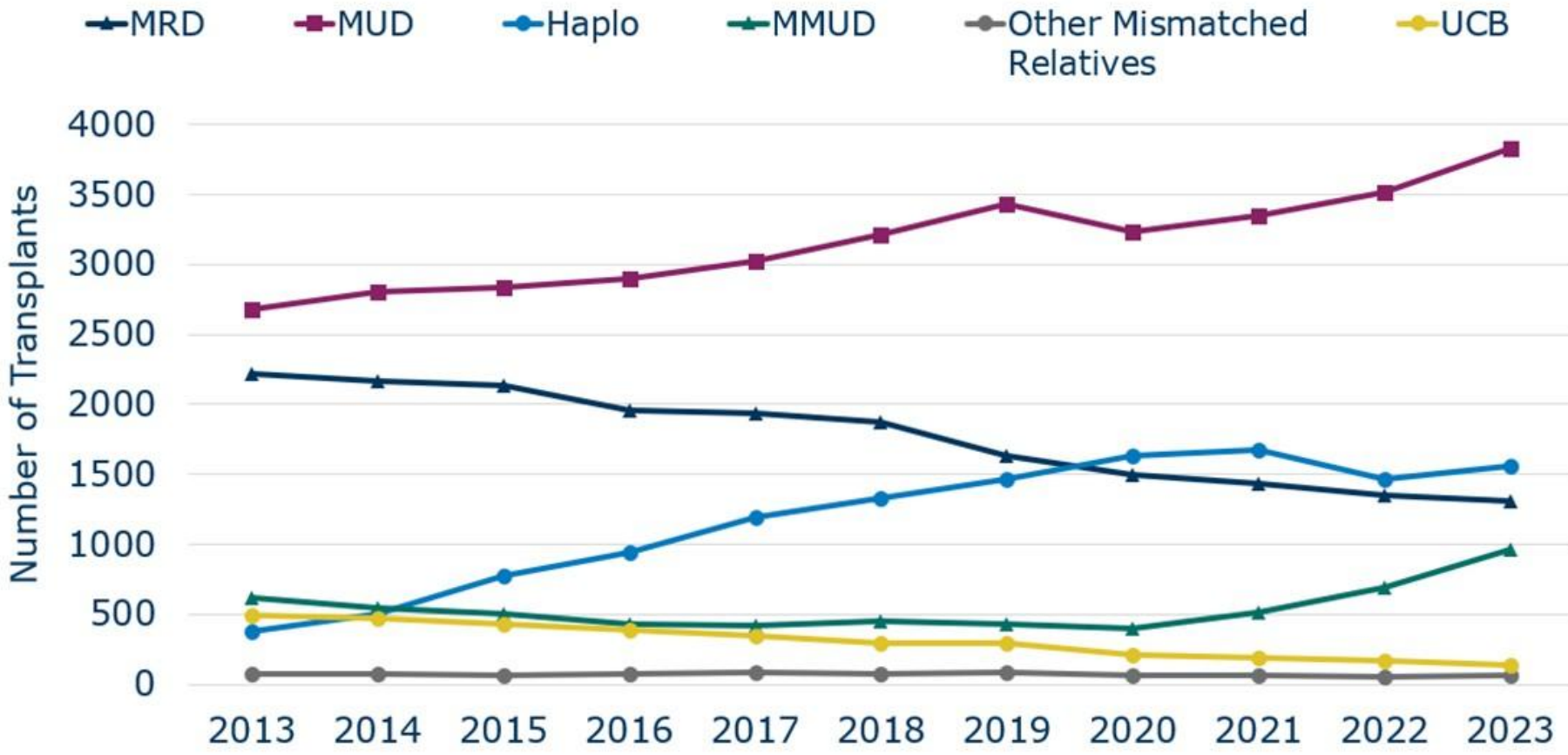
Abbreviations: MRD, matched related donor; MUD, matched unrelated donor; Haplo, ≥2 HLA antigen mismatch; MMUD, mismatched unrelated donor ≤ 7/8 HLA allele match; UCB, umbilical cord blood

Relative Proportion of Allogeneic HCTs in the US by Donor Type



Abbreviations: MRD, matched related donor; MUD, matched unrelated donor; Haplo, ≥ 2 HLA antigen mismatch; MMUD, mismatched unrelated donor ≤ 7/8 HLA allele match; UCB, umbilical cord blood

Number of Allogeneic HCTs in the US by Donor Type, Adults



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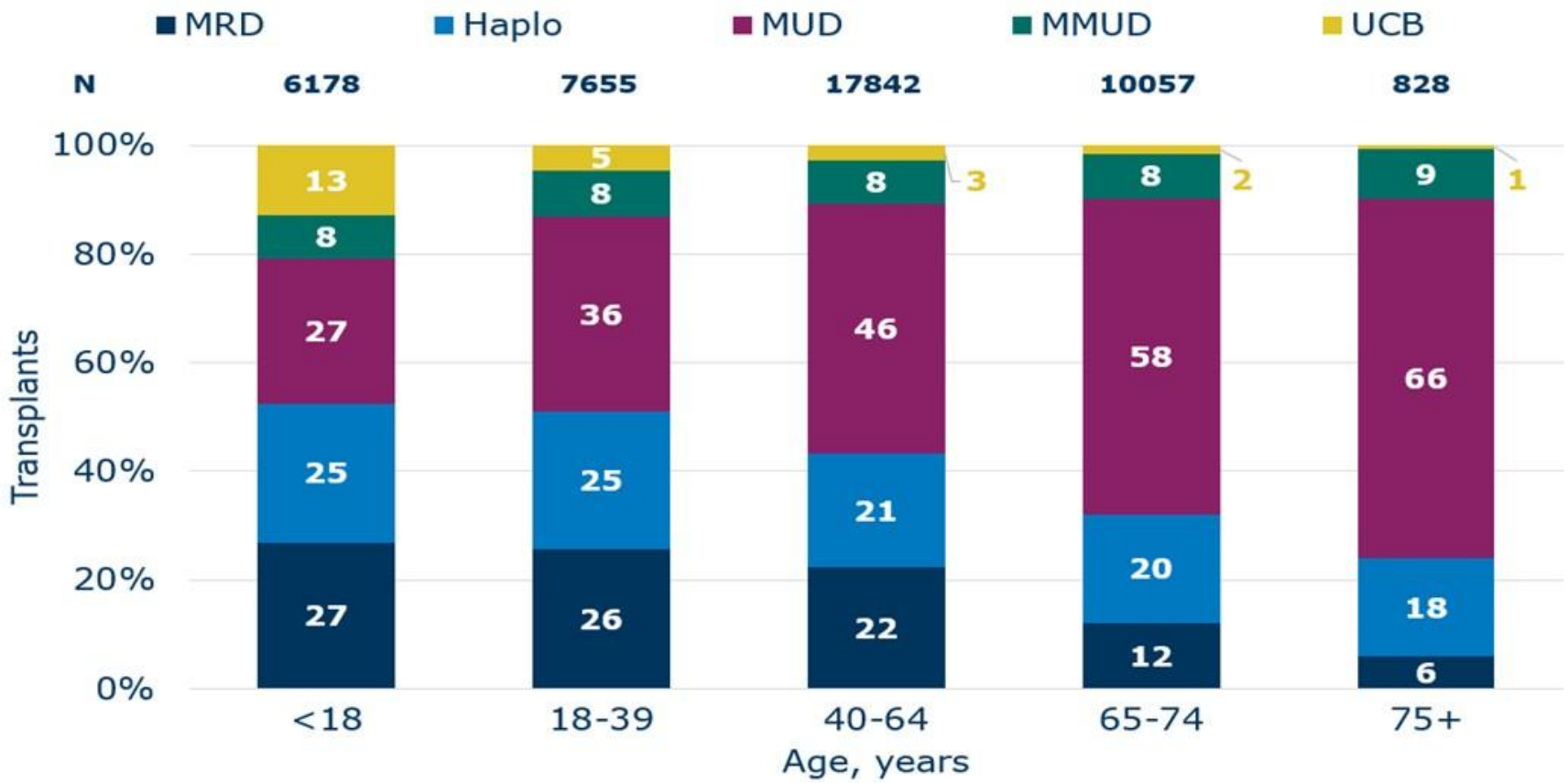
Relative Proportion of Allogeneic HCTs by Donor Types in the US by Recipient Age, 2019-2023



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A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

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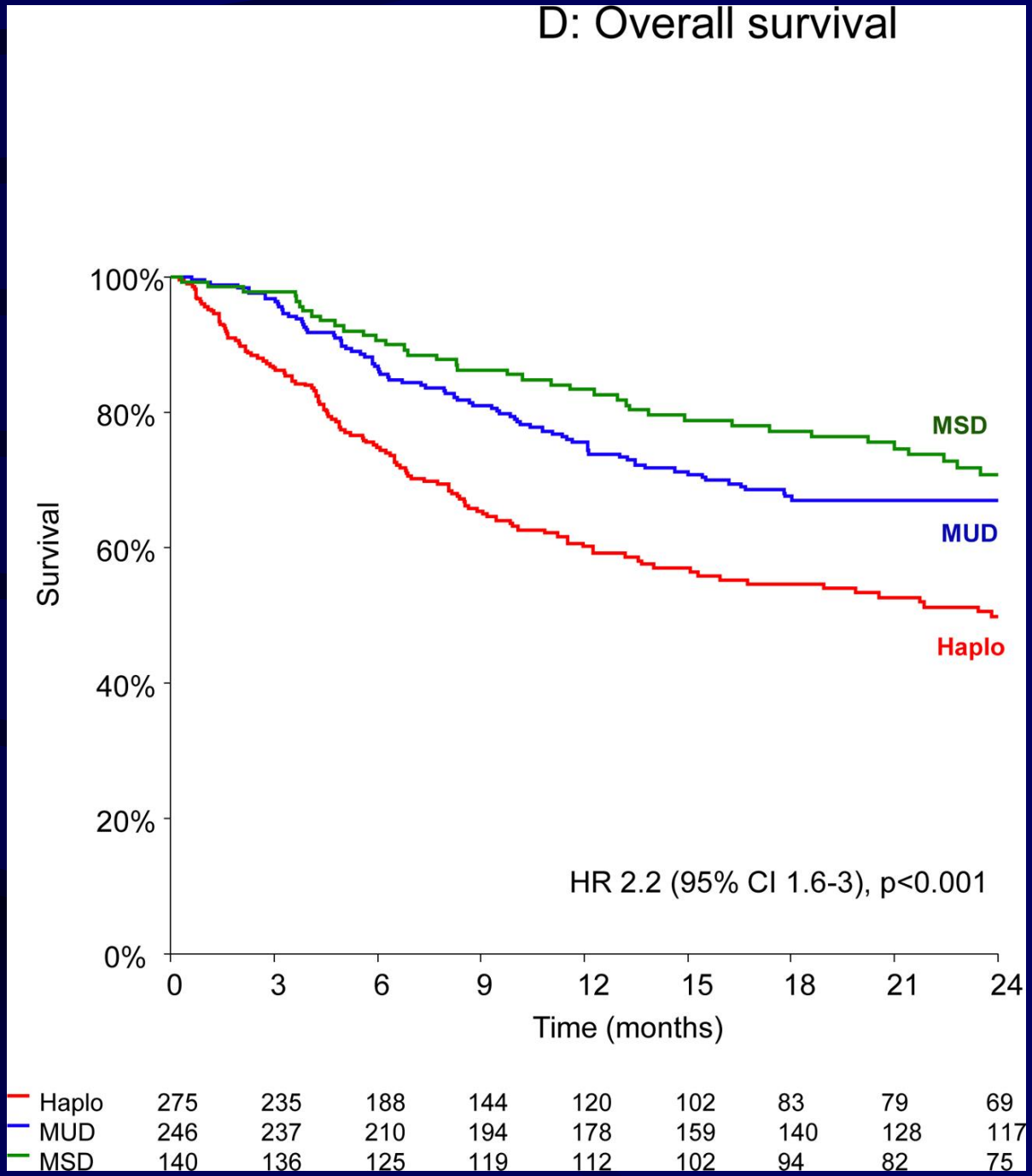
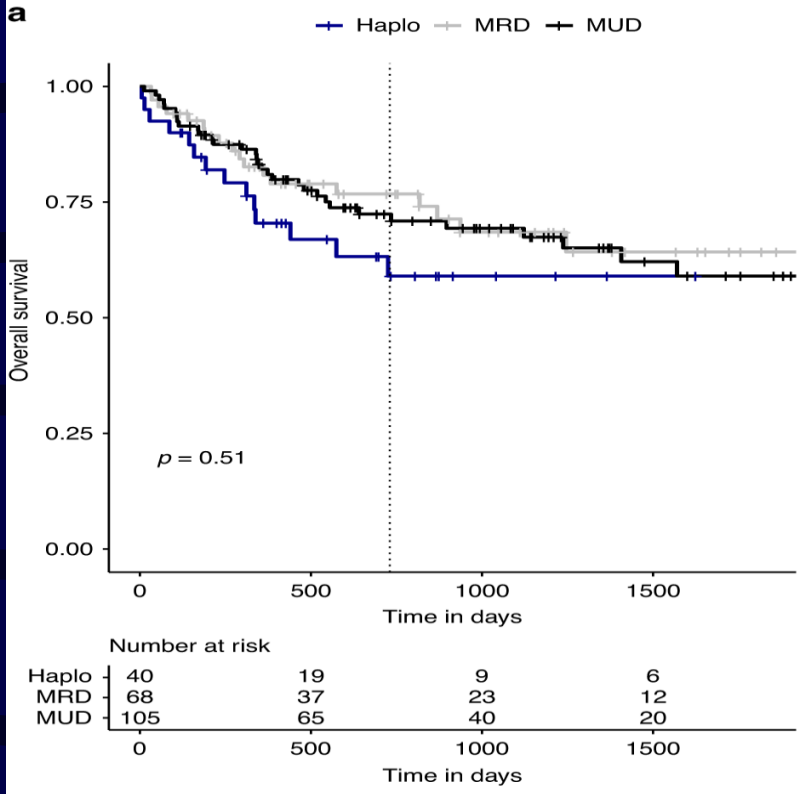
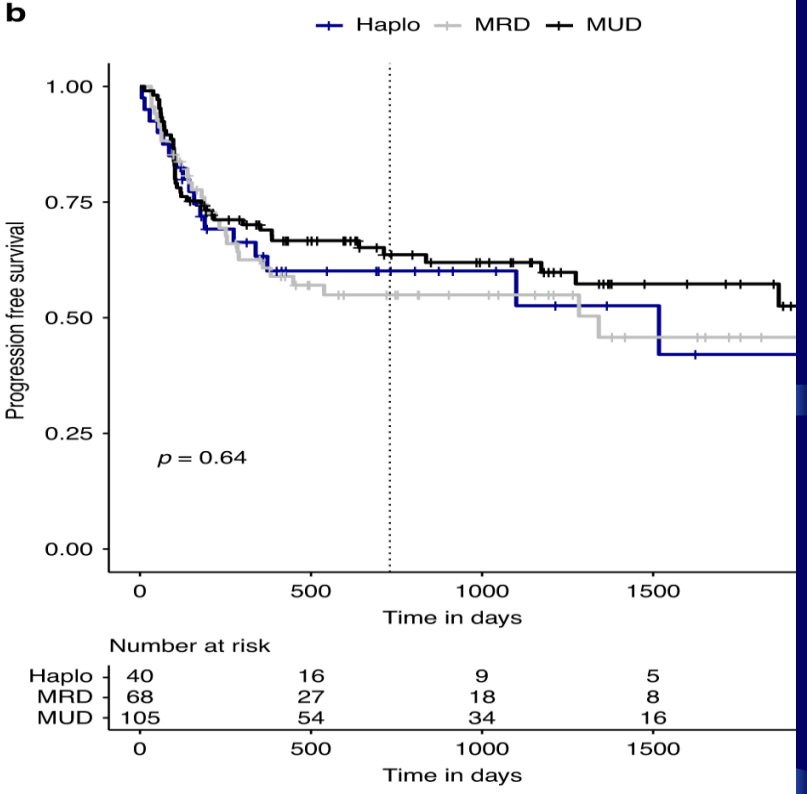
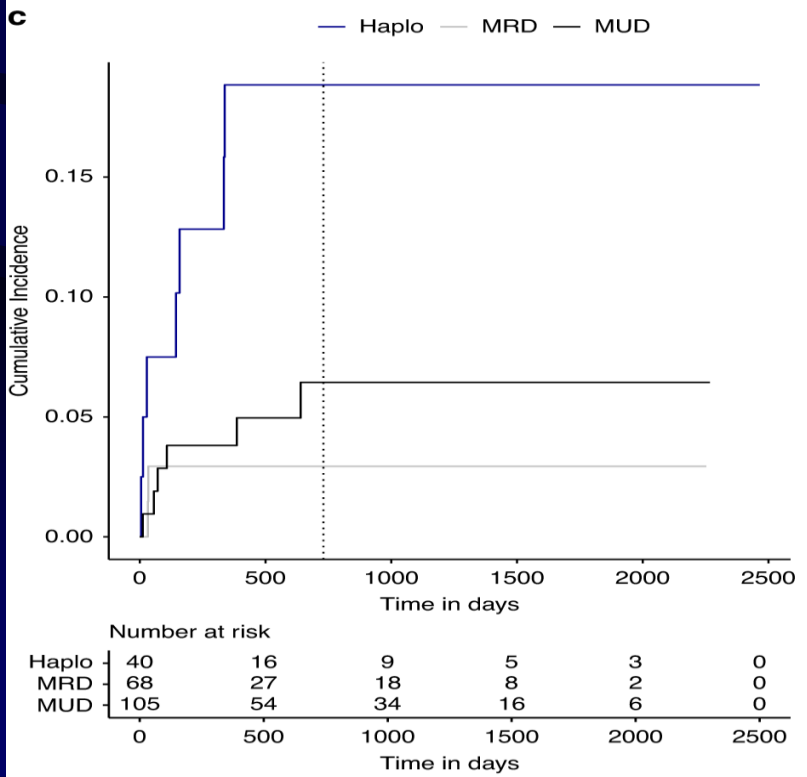


Mehta RS, et al Haploidentical versus Matched Unrelated versus Matched Sibling Donor Hematopoietic Cell Transplantation with Post-Transplantation Cyclophosphamide. Transplant Cell Ther. 2022 Jul

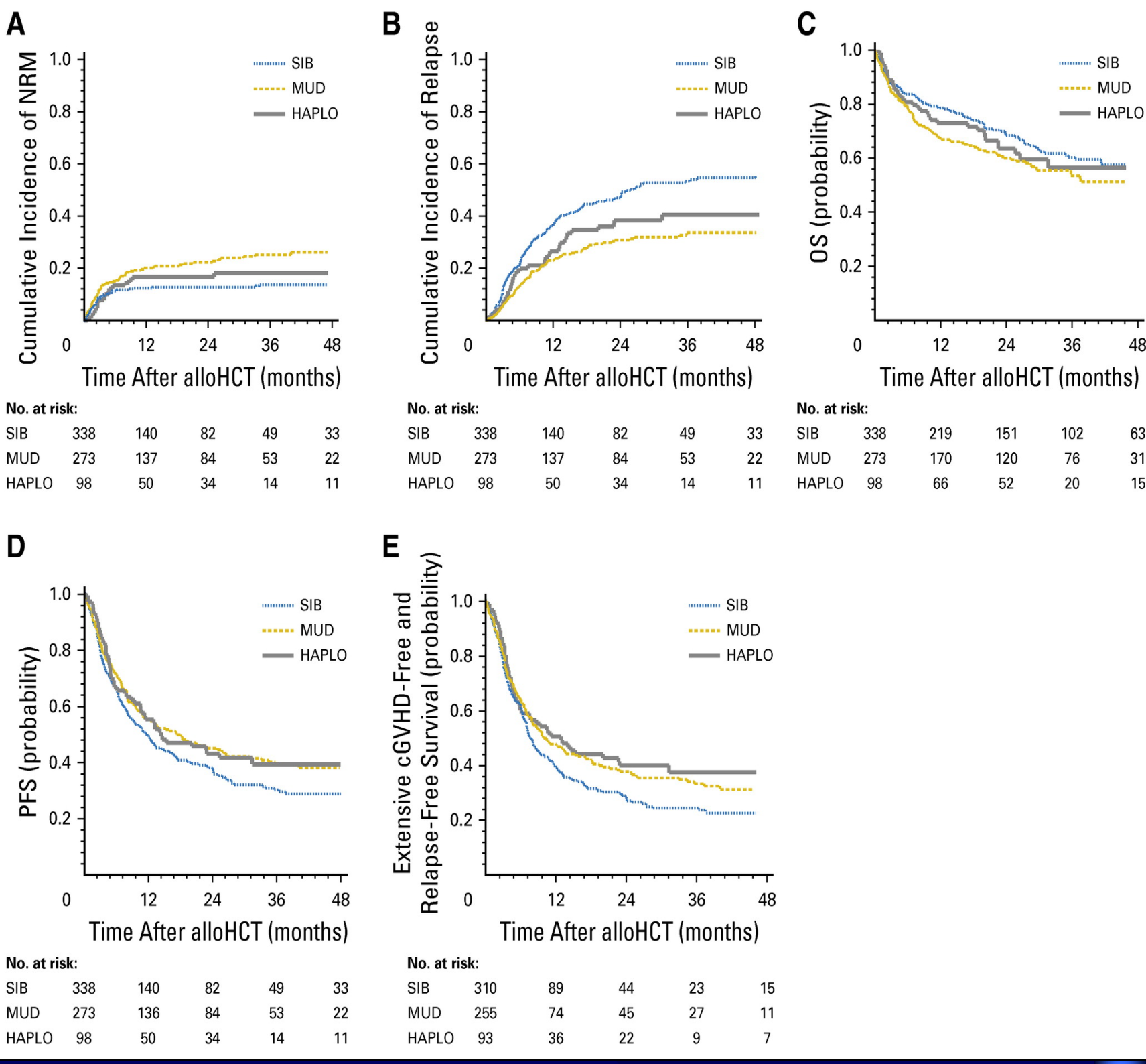






Rieger, M.J., Stolz, S.M., Müller, A.M. *et al.* Haploidentical transplant with posttransplant cyclophosphamide vs matched related and unrelated donor transplant in acute myeloid leukemia and myelodysplastic neoplasm. *Bone Marrow Transplant* **58**, 1121–1129 (2023)

Post-Transplantation Cyclophosphamide-Based Haploidentical Transplantation as Alternative to Matched Sibling or Unrelated Donor Transplantation for Hodgkin Lymphoma: A Registry Study of the Lymphoma Working Party of the European Society for Blood and Marrow Transplantation. *J CO* (2017)



- 25 year old man with MDS
- Related or unrelated donor?

Table 3. Clinical features prompting consideration of clinical testing for a germline predisposition allele(s)

Clinical features
Personal history of ≥2 cancers, one of which is a hematopoietic malignancy (order does not matter)
Personal history of a hematopoietic malignancy plus: • Another relative within two generations with another hematopoietic malignancy, or • Another relative within two generations with a solid tumor diagnosed at age 50 or younger, or • Another relative within two generations with other hematopoietic abnormalities
Presence of a deleterious gene variant in tumor profiling that could be a germline allele, especially if that variant is present during remission[a]
Age of diagnosis of hematopoietic malignancy at an earlier age than average (eg, MDS diagnosed ≤40 years)
Germline status of a variant is confirmed by
Its presence in DNA derived from a tissue source not likely to undergo somatic mutation frequently (eg, cultured skin fibroblasts or hair follicles) AND at a variant allele frequency consistent with the germline (generally considered between 30-60%), or Its presence in at least two relatives at a variant allele frequency consistent with the germline

MDS, myelodysplastic syndrome

[a] Certain gene alleles (eg, *CHEK2* I200T and truncating *DDX41* variants) are overwhelmingly likely to be germline and should prompt consideration of germline testing when identified even once.

Dohner Blood 2022

Alternative donors

- Mismatched unrelated donor
- Haplo-identical
- Umbilical cord blood

Mismatched unrelated donor(MMUD)

9-10% lower overall survival with each additional mismatch

Match	n	Survival (CI)	RR (CI)	P-value
8/8	1840	52 (50-54)	1.00	
7/8	988	43 (40-46)	1.25 (1.13-1.37)	<0.0001
6/8	633	33 (30-37)	1.65 (1.48-1.84)	<0.0001

No difference between alleleic and antigeneic mismatch
B and C mismatches are better tolerated than A/ DR in BM
C mismatches are less well tolerated after PBSC
Difference in survival is dependent on disease status

Haplo donor

- A related donor who shares one haplotype with the patient
- Any 1^0 relative, sibling, parent or offspring

  2^0 or 3^0 relatives
- Almost every patient has a readily avaliabale haplo-identical donor

Early studies

- Early studies in the mid 70th and early 80th explored haplo donors using the same transplant platform as for HLA-matched siblings
- An intense bi-directional allo-responses in both the HVG and GVH direction were seen
- These resulted in high rates of graft failure (~30%) and high rates of severe acute GVHD (>50%) resulting in high rates of NRM (~70%) and low rates of LFS (<20%).
- Haplo BMT was deemed associated with prohibitive toxicity and was largely abandoned.

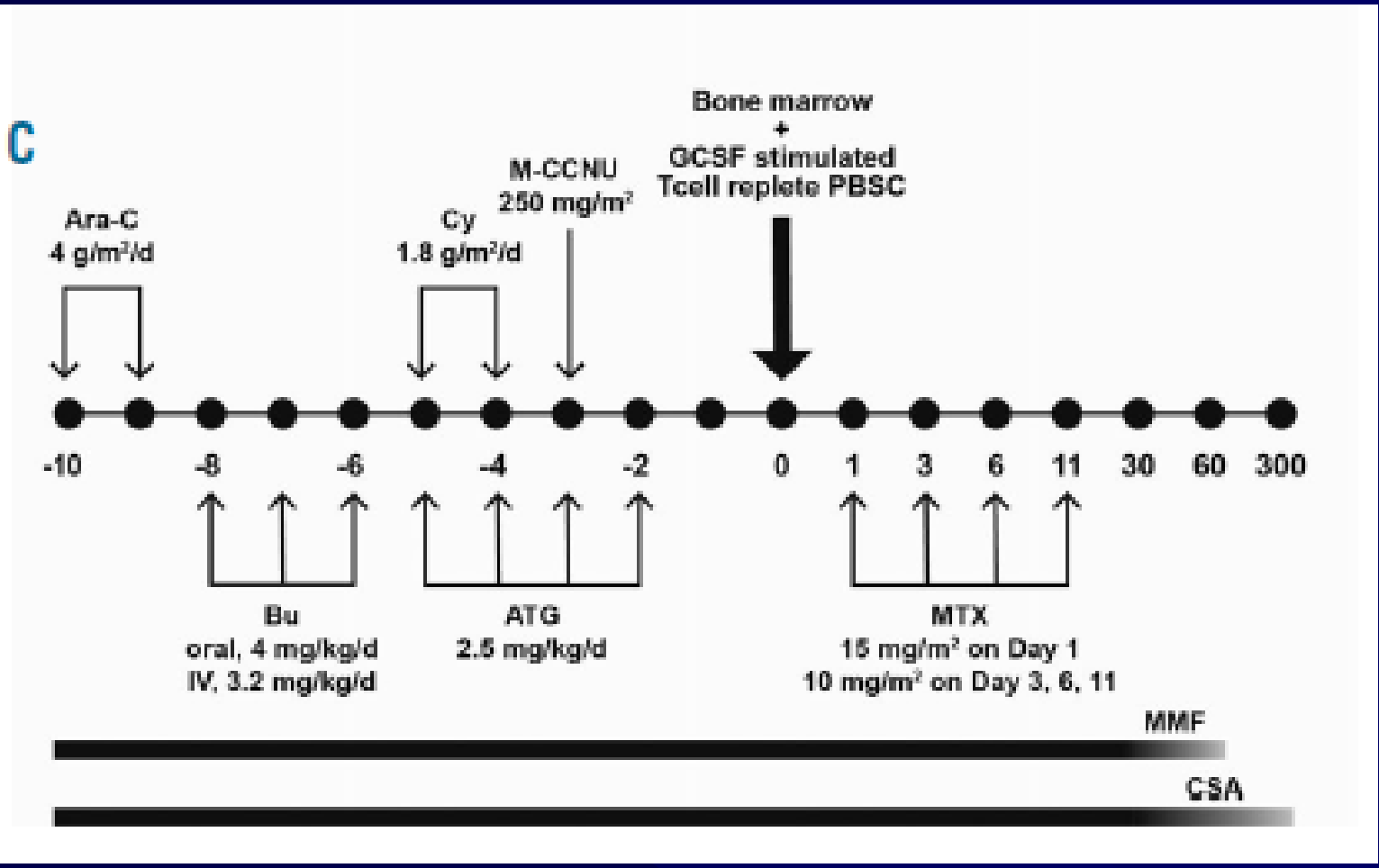
Methods to improve immune reconstitution are highly sophisticated, cumbersome, require very specific expertise and costly. They are therefore limited to very specialized centers.

Non-T depleted Haplo-identical transplant

- Chinese approach: G-CSF primed non-T depleted bone marrow with intensive pre- and post-transplant immune suppression.

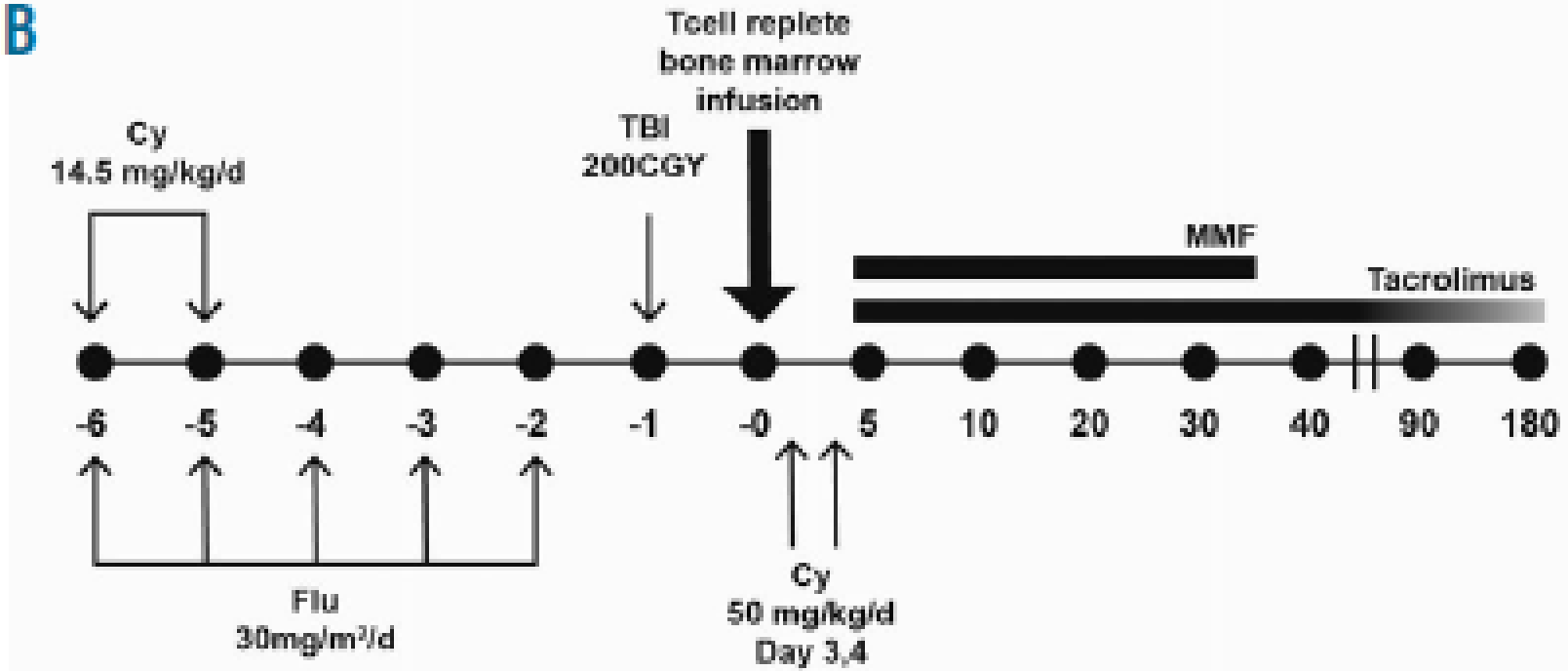
- Baltimore/ Seattle approach: Post-transplant cyclophosphamide

The Beijing regimen

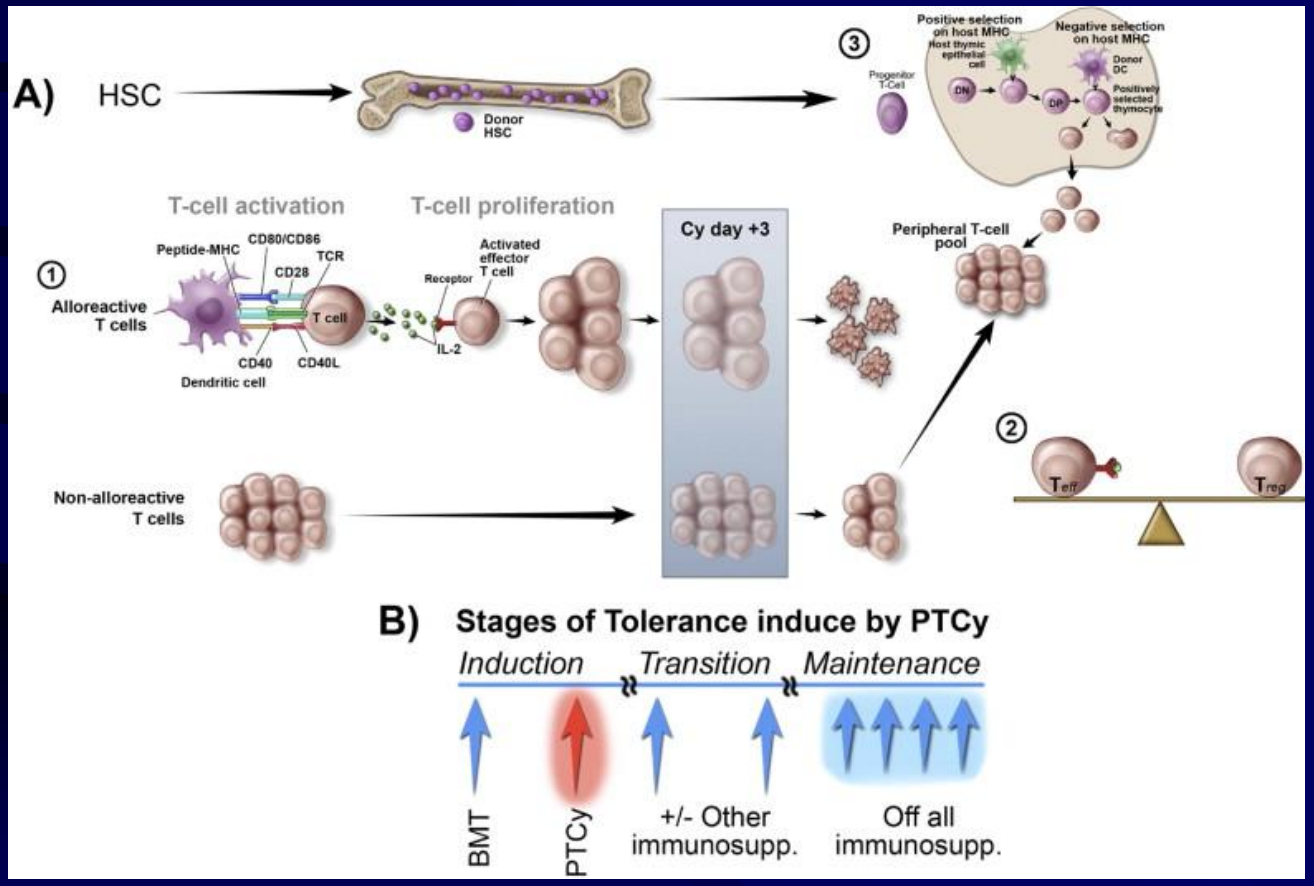


GIAC regimen (G-csf stimulation, Intensified immunosuprresion, Atg, Combined bm and pbsc)

The Baltimore regimen



ההגיון מאחורי PTCy



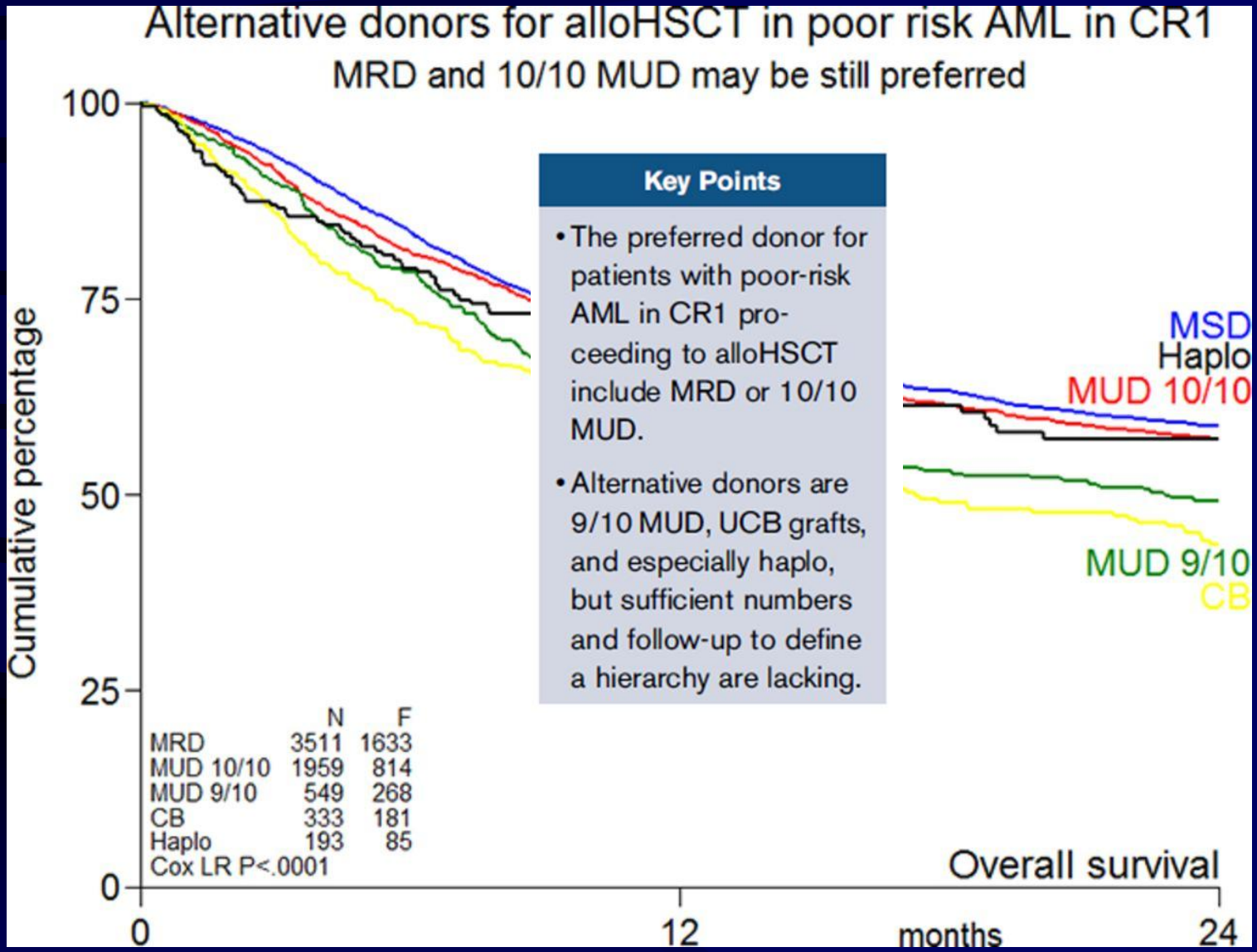
Alternative donors for allogeneic hematopoietic stem cell transplantation in poor-risk AML in CR1

Jurjen Versluis,[1] Myriam Labopin,[2-5] Annalisa Ruggeri,[4,6] Gerard Socie,[7,8] Depei Wu,[9] Liisa Volin,[10] Didier Blaise,[11] Noel Milpied,[12] Charles Craddock,[13] Ibrahim Yakoub-Agha,[14] Johan Maertens,[15] Per Ljungman,[16] Anne Huynh,[17] Mauricette Michallet,[18] Eric Deconinck,[19] Patrice Chevallier,[20] Jakob Passweg,[21] Fabio Ciceri,[22] Mohamad Mohty,[2-4] Jan J. Cornelissen,[1,*] and Arnon Nagler,[5,23,*] on behalf of the Acute Leukemia Working Party of the European Society for Blood and Marrow Transplantation (EBMT)

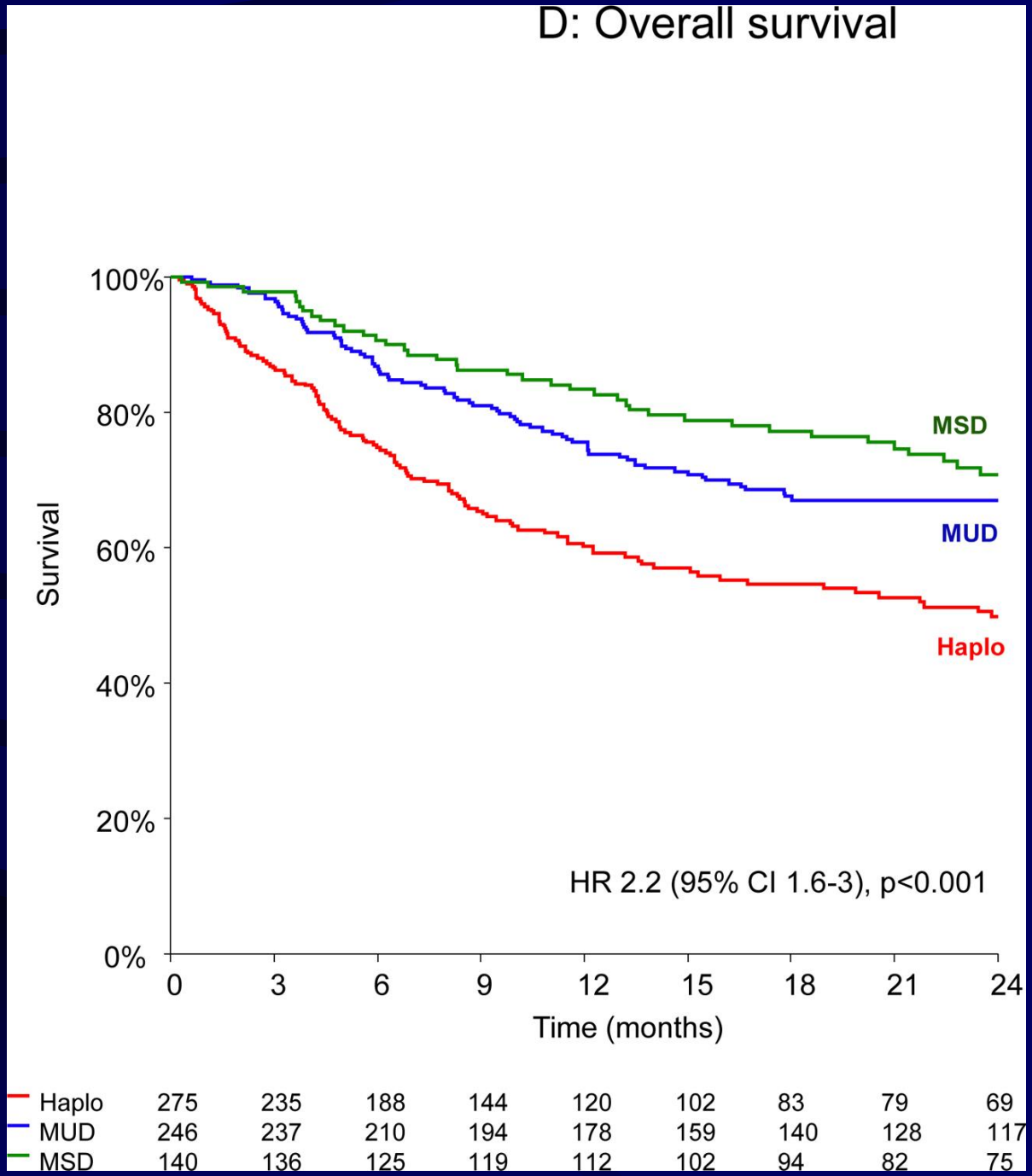
Blood Adv 2017

6545 patients with poor-risk AML in CR1
Transplanted 2000-2014.

MRD	3511 pts
10/10 MUD	1959 pts
9/10 UD	549 pts
Haplo	193 pts
UCB	333 pts

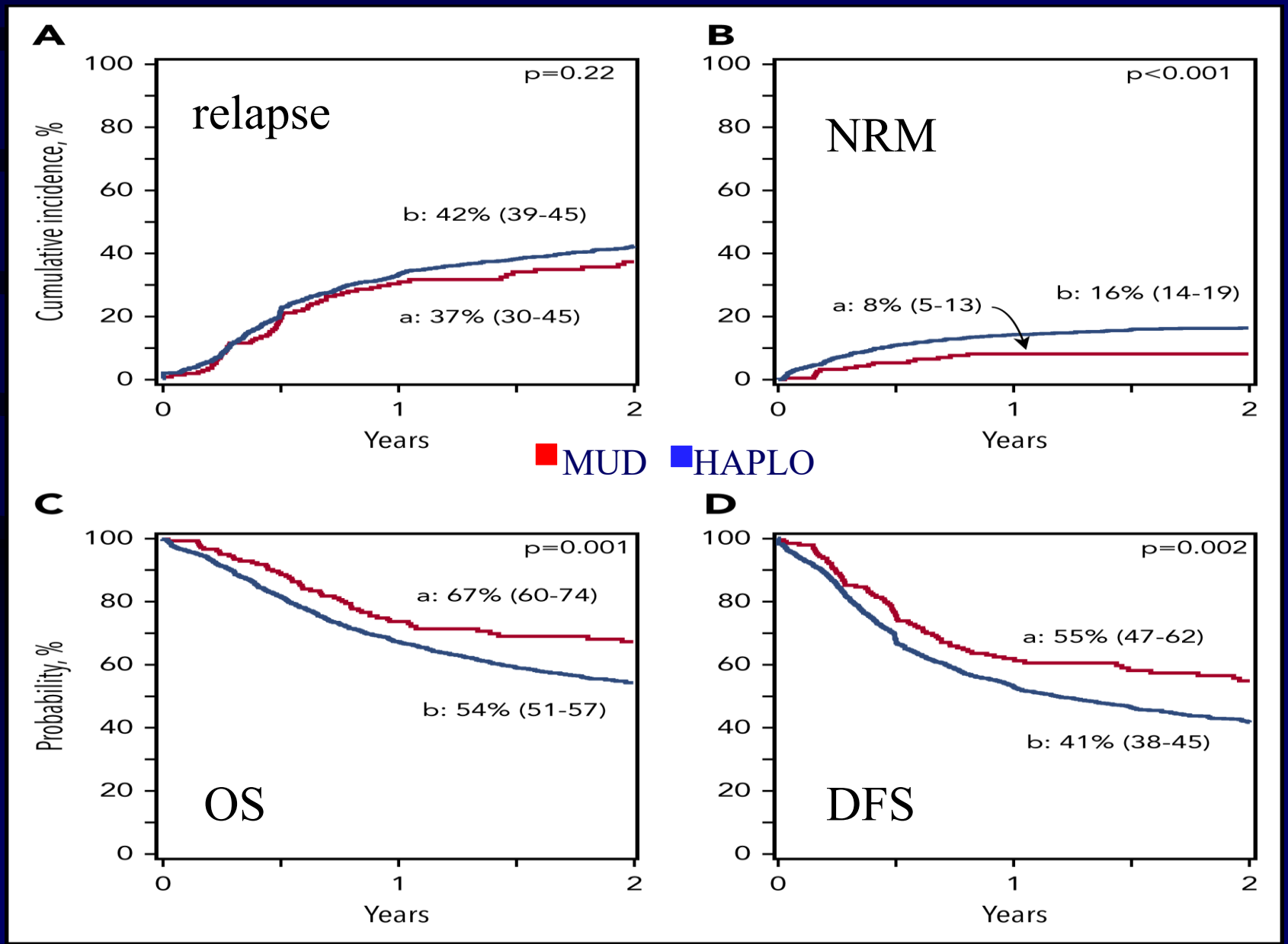


Jurjen Versluis et al. Blood Adv 2017;1:477-485



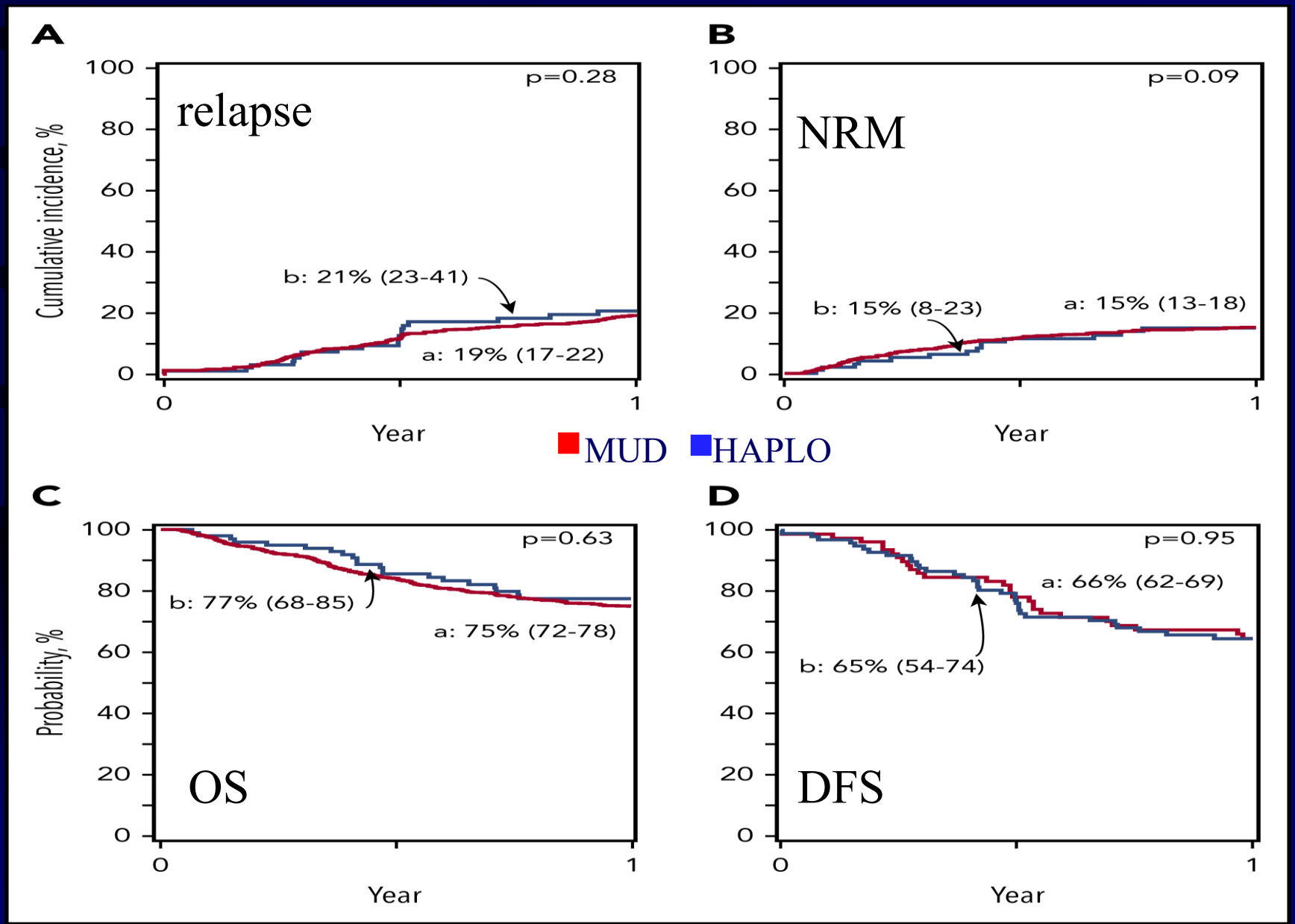
Mehta RS, et al Haploidentical versus Matched Unrelated versus Matched Sibling Donor Hematopoietic Cell Transplantation with Post-Transplantation Cyclophosphamide. Transplant Cell Ther. 2022 Jul

Reduced-intensity regimens



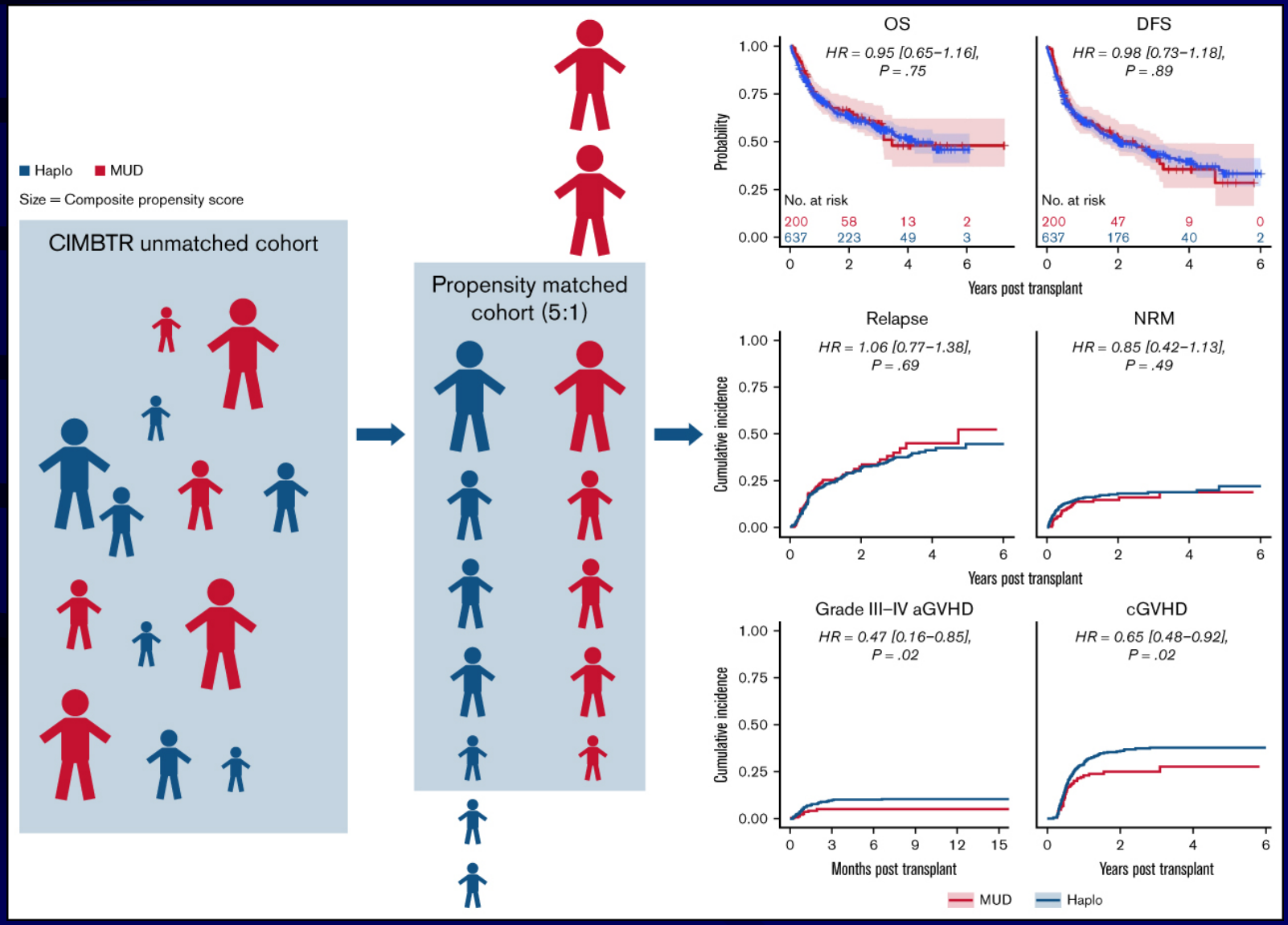
Mahasweta Gooptuet. Al. HLA-haploidentical vs matched unrelated donor transplants with posttransplant cyclophospham ide-based prophylaxis. *Bl ood* 2021; 138 (3): 273–282.

MYELOABLATIVE



Mahasweta Gooptuet. Al. HLA-haploidentical vs matched unrelated donor transplants with posttransplant cyclophospham ide-based prophylaxis. *Bl ood* 2021; 138 (3): 273–282.

HLA-matching with PTCy: a reanalysis of a CIBMTR dataset with propensity score matching and donor age



Alexander Ambinder et. Al. HLA-matching with PTCy: a reanalysis of a CIBMTR dataset with propensity score matching and donor age, Blood Adv, 2022,

COMPLICATIONS

- Cytokine release syndrome
- Cardiotoxicity
- Hemorrhagic cystitis

לסיכום - MUD לעומת HAPLO

	HAPLO	MUD
זמינות	+	-
זמן	+	-
לוגיסטיקה	+	-
אפשרויות בחירה בין תורמים	+	-
Engraftment	-	+
ניסיון	-	+

עדין MUD נחשב לטיפול המועדף בתנאי שלא דוחה את ההשתלה

Donor-specific anti-HLA antibodies (DSA)

- The presence of donor-specific anti-HLA antibodies (DSA) is associated with a 10-fold increased risk of graft failure in haploidentical stem cell transplantation (haplo-SCT). Consensus guidelines from the European Society for Blood and Marrow Transplantation set a mean fluorescence intensity (MFI) >1000 as a cutoff for DSA positivity. In the absence of an alternative donor, it is recommended that patients undergo desensitization therapy, especially with high DSA levels (>5000 MFI)

- The incidence of graft failure in the setting of PT-Cy-based haplo-HSCT, ranges from 0 to 30%.
- Antibody-mediated rejection (DSA) appears to be one of the principal mechanisms of primary graft failure.
- In adult patients with hematologic malignancies, the prevalence of anti-HLA antibodies can be up to 40%; however, not all of these anti-HLA antibodies are directed against donor HLA antigens.
- In haplo-SCT, the prevalence of DSA may range between 10% and 21%. The prevalence of DSA is lower in male recipients (5%) compared with female recipients (86%) , because pregnancy is a cause of these antibodies.

What's New?

- Cyclophosphamide dose
- ATG+PTCy
- Desensitization protocols

Who is the best donor for a related HLA haplotype-mismatched transplant?

Yu Wang,[1] Ying-Jun Chang,[1] Lan-Ping Xu,[1] Kai-Yan Liu,[1] Dai-Hong Liu,[1] Xiao-Hui Zhang,[1] Huan Chen,[1] Wei Han,[1] Yu-Hong Chen,[1] Feng-Rong Wang,[1] Jing-Zhi Wang,[1] Yao Chen,[1] Chen-Hua Yan,[1] Ming-Rui Huo,[1] Dan Li,[1] and Xiao-Jun Huang[1,2]

Blood 2014

Analysis of 1210 transplants in Beijing

Key Points

- There is a need to identify the best HLA haplotype-mismatched related donor.
- Use of young, male, NIMA-mismatched donors results in the best survival after HLA haplotype-mismatched related donor transplants.

Impact of family relationships.

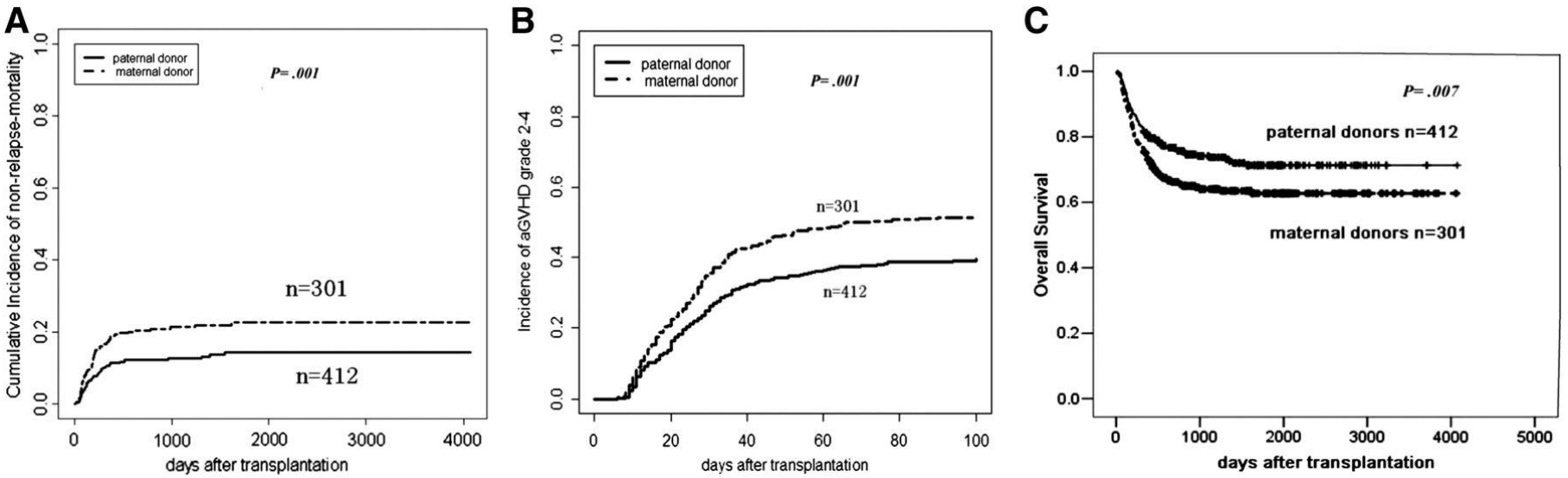
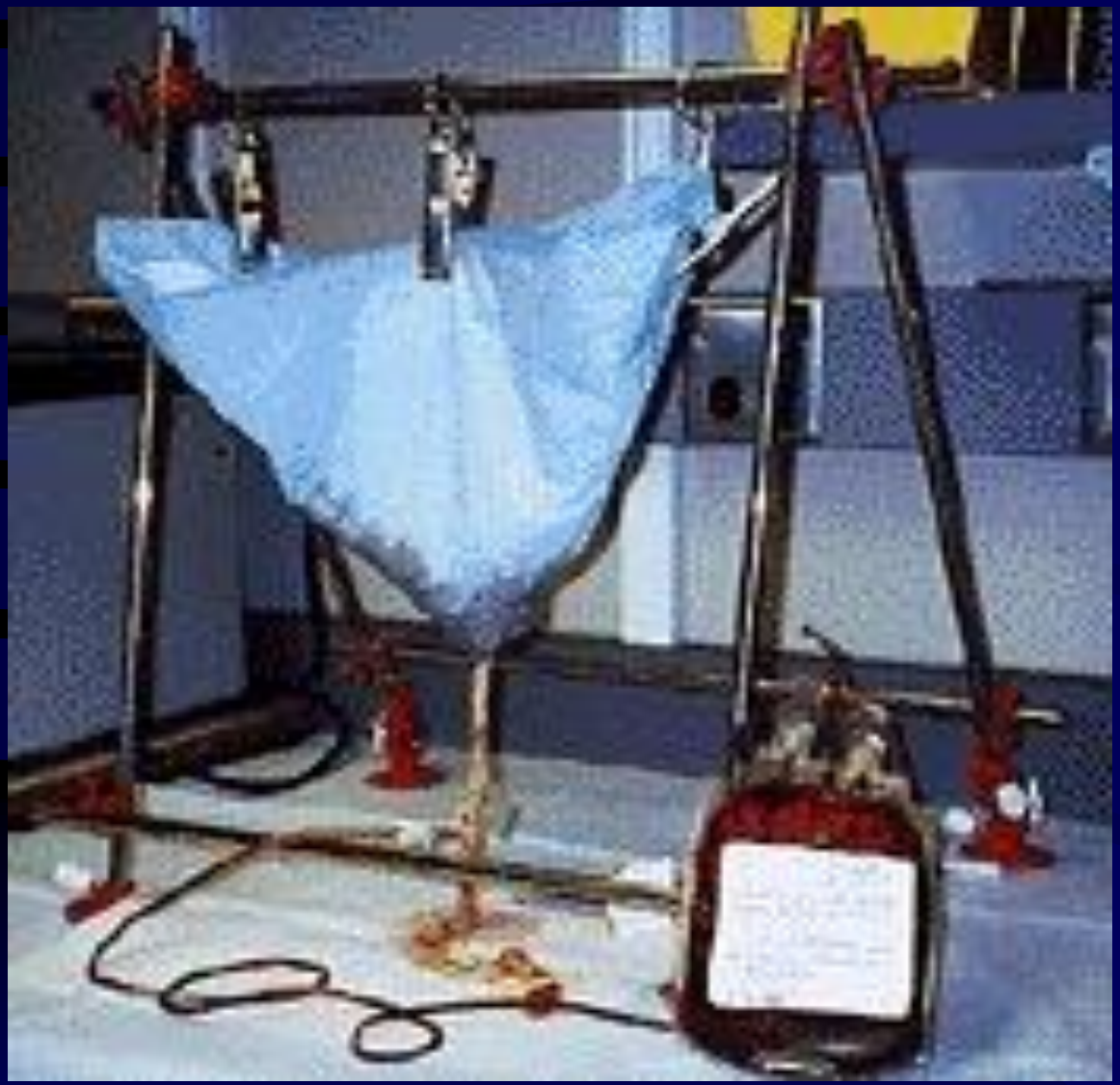


Table 4. Proposed algorithm for donor selection in haploidentical hematopoietic stem cell transplantation (based on GVHD and NRM)

Selection order	Donor source
Most preferred	Child, NIMA-mismatched
2nd choice	Younger brother, NIMA-mismatched
3rd choice	Older sister, NIMA-mismatched or Father
4th choice	Older sibling, NIPA-mismatched
The last choice	Mother

Yu Wang et al. Blood 2014;124:843-850

Umbilical cord blood transplants in adults



Cord blood unit

Healthy newborn

Umbilical cord blood; properties

- Higher proportion of primitive stem cells than bone marrow
- Higher potential for expansion and proliferation
- T-cells have a naïve and immature phenotype and decreased cytokine production.
- Engraftment possible with 10-fold lower number of cells.
  GVHD risk is lower despite wide HLA-mismatching.
  GVL not different.

CBT - advantages

- Rapid availability
- Allows donor-recipient disparity (4/6 vs 10/10)
- Reduced risk for GVHD
- Low risk for transmission of infectious diseases
- No risk to donors

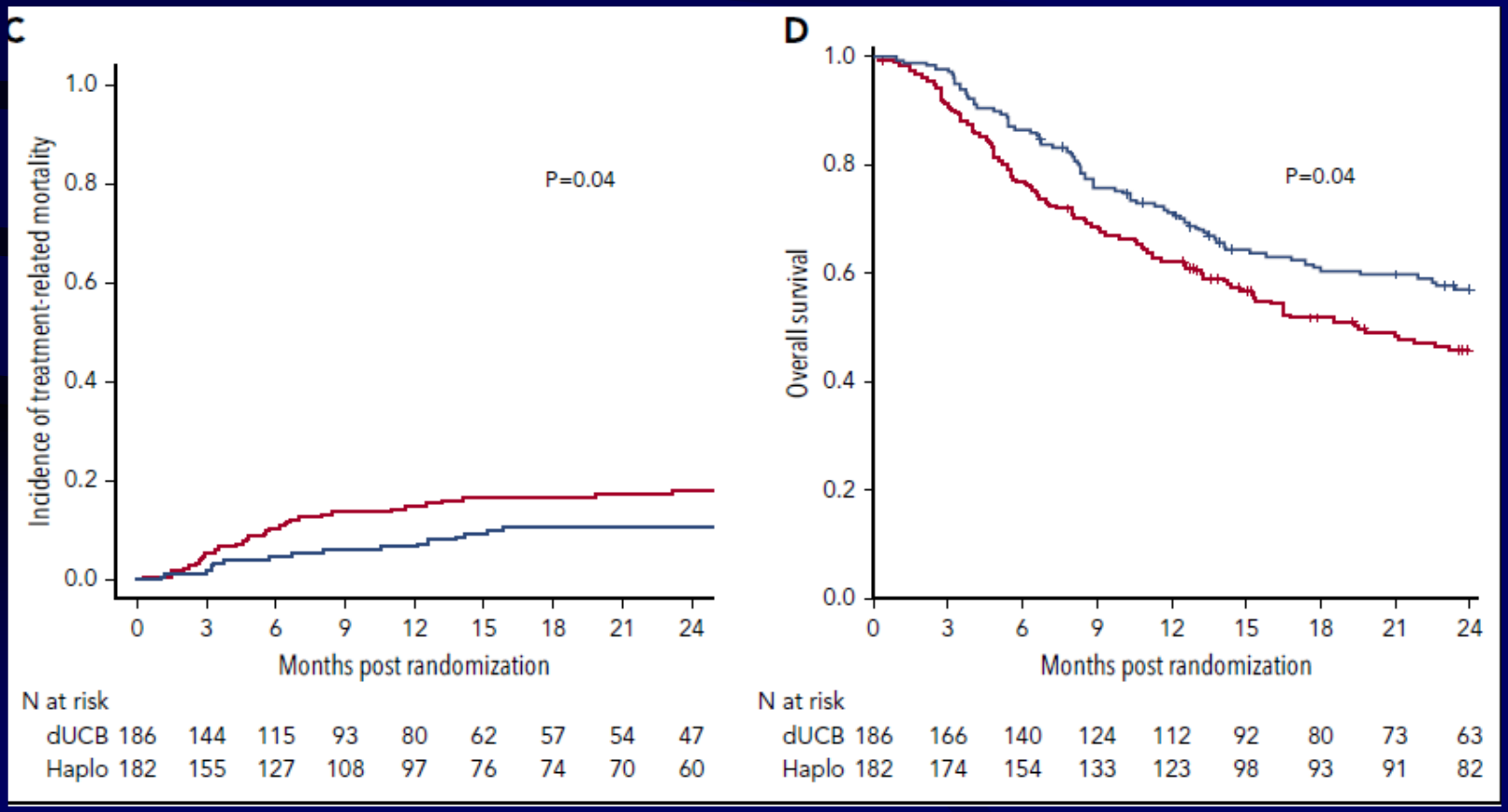
CBT - disadvantages

- Limited cell dose, slow engraftment, higher risk for graft failure.
- Inability to obtain additional collections.
- Less long-term experience

TRANSPLANTATION

Double unrelated umbilical cord blood vs HLA-haploidentical bone marrow transplantation: the BMT CTN 1101 trial

Ephraim J. Fuchs,[1] Paul V. O'Donnell,[2] Mary Eapen,[3] Brent Logan,[4] Joseph H. Antin,[5] Peter Dawson,[6] Steven Devine,[7] Mary M. Horowitz,[3] Mitchell E. Horwitz,[8] Chatchada Karanes,[9] Eric Leifer,[10] John M. Magenau,[11] Joseph P. McGuirk,[12] Lawrence E. Morris,[13] Andrew R. Rezvani,[14] Richard J. Jones,[1] and Claudio G. Brunstein,[15] on behalf of the Blood and Marrow Transplant Clinical Trials Network



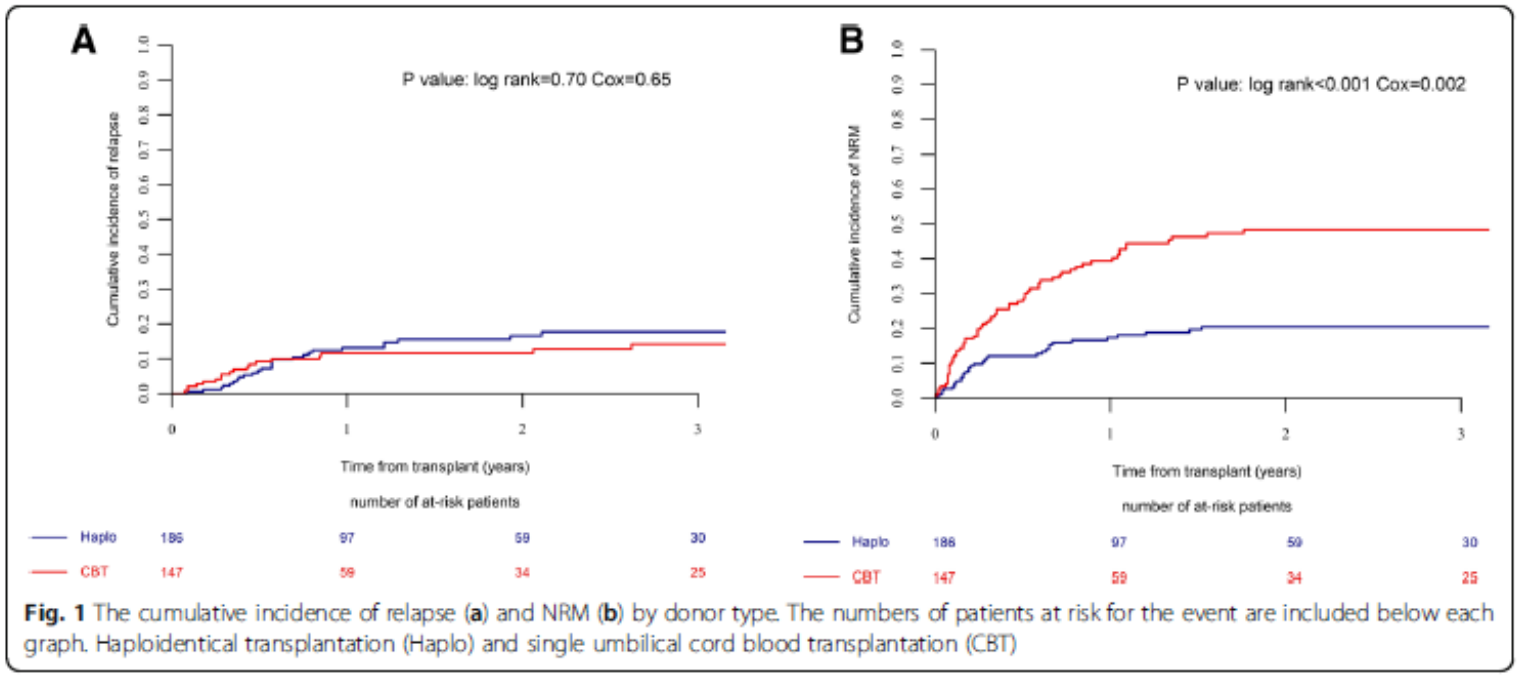


Fig. 1 The cumulative incidence of relapse (**a**) and NRM (**b**) by donor type. The numbers of patients at risk for the event are included below each graph. Haploidentical transplantation (Haplo) and single umbilical cord blood transplantation (CBT)

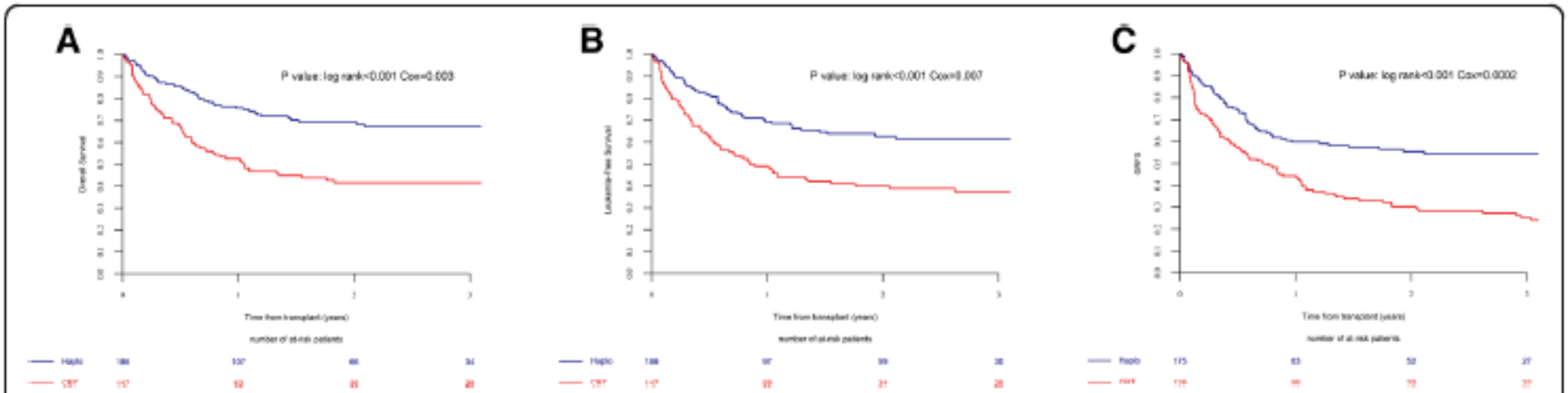


Fig. 2 The estimated probability of overall survival (**a**), leukemia-free survival (**b**), and GRFS (**c**) by donor type. The numbers of patients at risk for the event are included below each graph. Graft-versus-host disease-free relapse-free survival (GRFS), haploidentical transplantation (Haplo), and single umbilical cord blood transplantation (CBT)

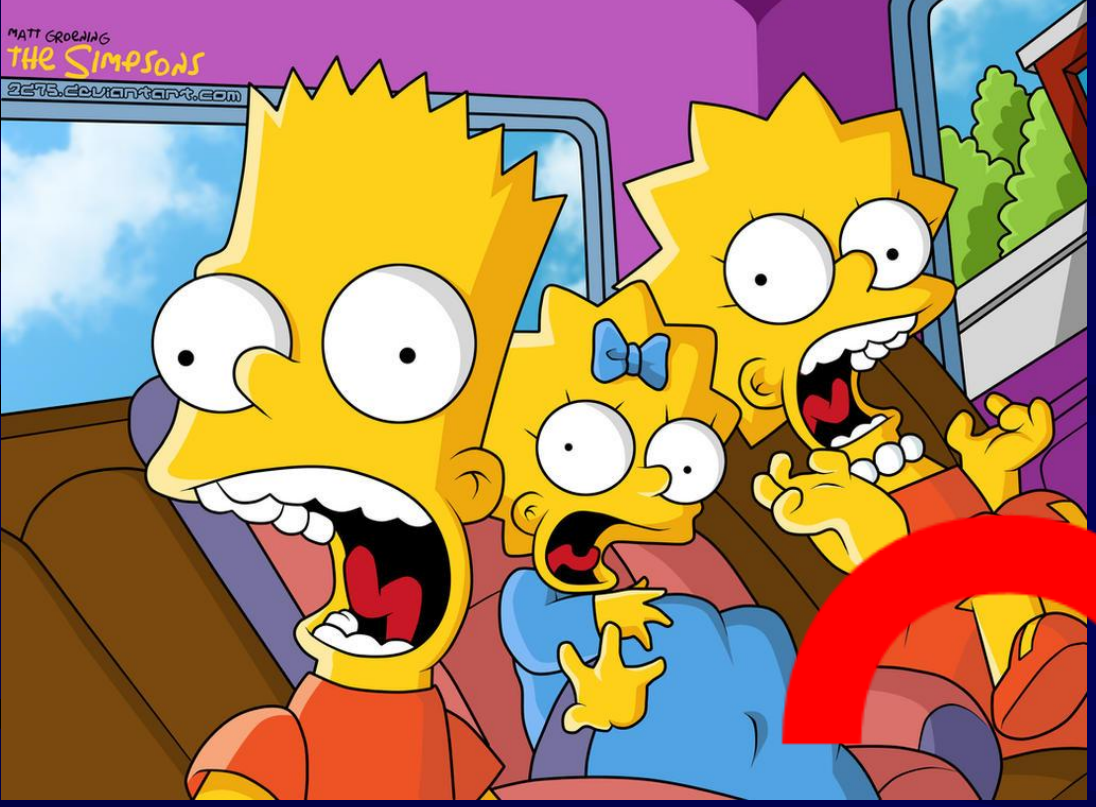
Strategies for Facilitating Engraftment in CBT

- The main obstacle for successful CBT is short term engraftment (long term engraftment is well established)

- Current available approaches:
  - Expansion of CD34+ progenitor cells: HGF
    HGF in conjunction with differentiation blocking agents
  - Simultaneous infusion of CB and highly purified haploidentical CD34+ cells
  - Co-transplantation of CB and mesenchimal cells
  - Intraoseous CBT
  - Co-transplantation of more than one CB unit

	MUD	CB	Haplo
Donor availability	Limited Mismatches tolerated poorly	frequent Mismatches tolerated well	Unlimited
Time availability	slow	Relatively rapid	rapid
engraftment	good	Major obstacle	Good (regimen dep.)
GVHD	frequent	Less frequent	~MUD
Immune reconstitution	Relatively rapid	slow	Major obstacle
OS	Similar?		

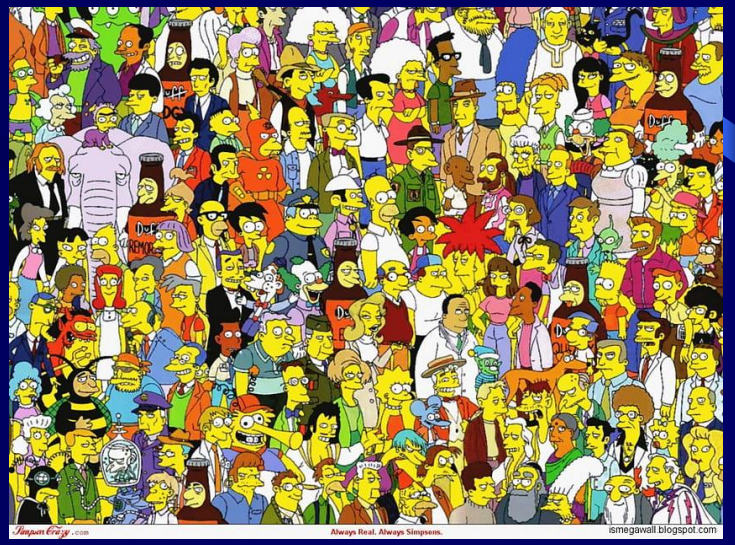
אז במי בוחרים?



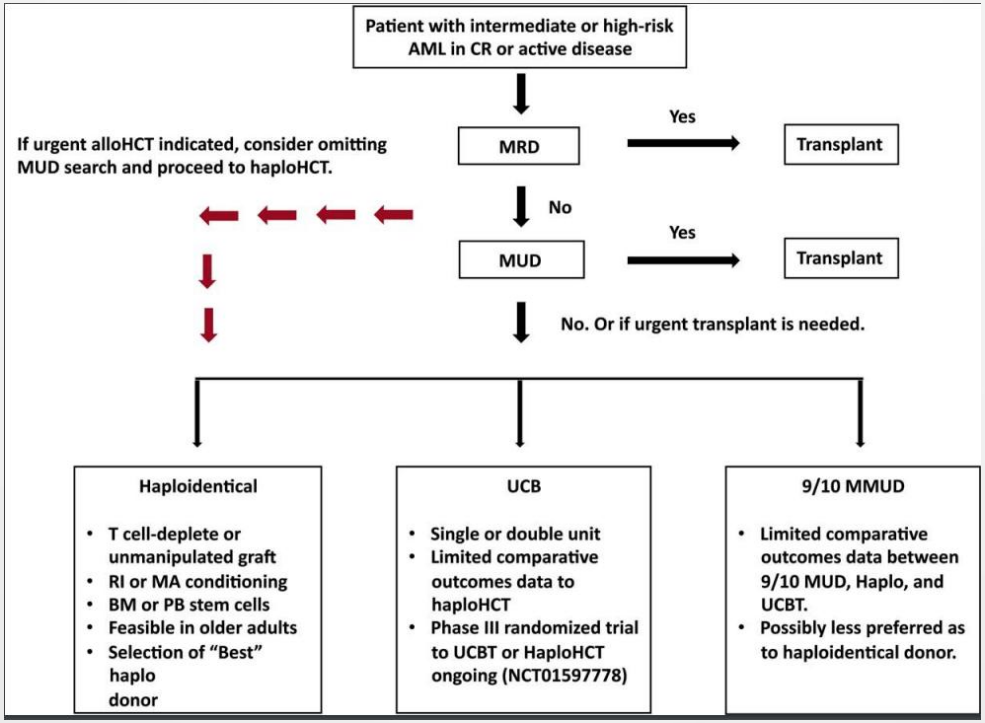
Matched sibling donor is generally the 1st choice

Haploidentical is the 3rd

Unrelated matched donor the 2nd



Recommended donor choice algorithm for adults with intermediate or high-risk AML with an indication for allogeneic HCT



Lee CJ. Haematologica 2017 Sep 7. pii: haematol.2017.176107. doi: 10.3324/haematol.2017.176107. [Epub ahead of print]

Additional considerations in donor selection

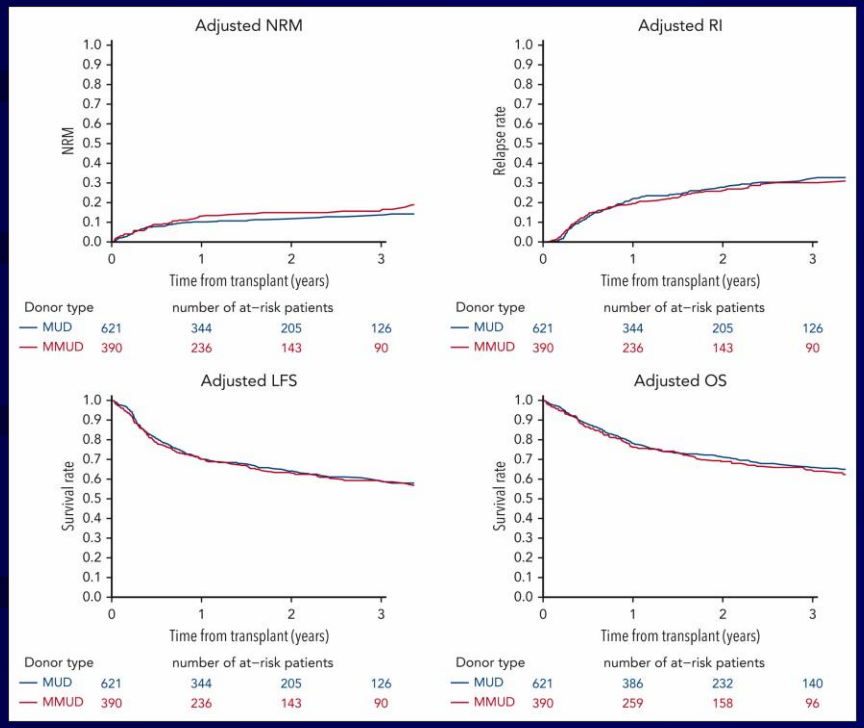
- Donor age
- Gender and parity
- CMV status
- Blood type
- Extended typing: HLA DP, DRB 3/4/5
- Donor specific HLA antibodies (for mismatched donors)

- A 65 year old man with AML needs allogeneic SCT
- He has a 70 year old health HLA-matched sister
- A 22 year old 10/10 matched unrelated male donor is also identified.
- Who is the best donor?

- CHIP 16% of donors> 55 years, similar survival

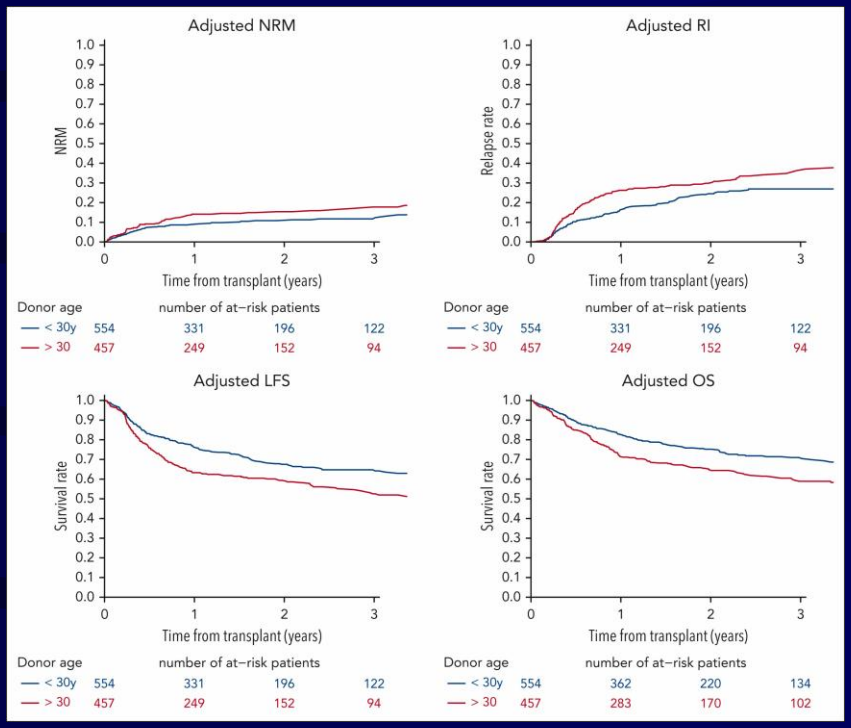
Young (<35 years) haploidentical versus old (≥35 years) mismatched unrelated donors and vice versa for allogeneic stem cell transplantation with post-transplant cyclophosphamide in patients with acute myeloid leukemia in first remission: a study on behalf of the Acute Leukemia Working Party of the European Society for Blood and Marrow Transplantation BMT AUG 2024

Younger unrelated donors may be preferable over HLA match in the PTCy era: a study from the ALWP of the EBMT



Jaime Sanz,Myriam Labopin,Goda Choi,Alexander Kulagin,Jacopo Peccatori,Jan Vydra,Péter Reményi,Jurjen Versluis,Montserrat Rovira,Didier Blaise,Hélène Labussière-Wallet,Juan Montoro,Simona Sica,Ellen Meijer,Maija Itälä-Remes,Nicolaas Schaap,Claude Eric Bulabois,Simona Piemontese,Mohamad Mohty,Fabio Ciceri, Younger unrelated donors may be preferable over HLA match in the PTCy era: a study from the ALWP of the EBMT, Blood, 2024, Figure 1.

Younger unrelated donors may be preferable over HLA match in the PTCy era: a study from the ALWP of the EBMT



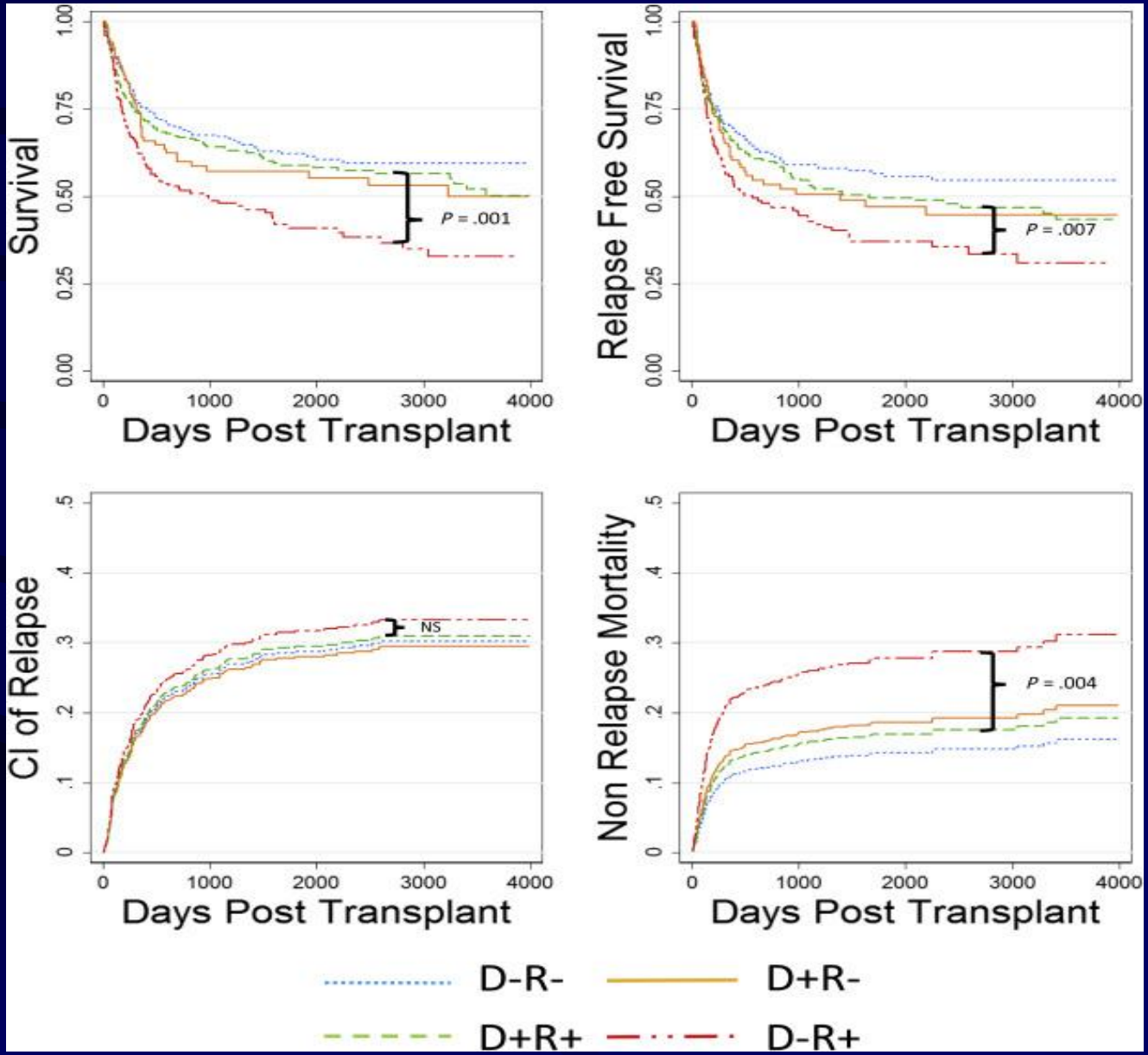
Jaime Sanz,Myriam Labopin,Goda Choi,Alexander Kulagin,Jacopo Peccatori,Jan Vydra,Péter Reményi,Jurjen Versluis,Montserrat Rovira,Didier Blaise,Hélène Labussière-Wallet,Juan Montoro,Simona Sica,Ellen Meijer,Maija Itälä-Remes,Nicolaas Schaap,Claude Eric Bulabois,Simona Piemontese,Mohamad Mohty,Fabio Ciceri, Younger unrelated donors may be preferable over HLA match in the PTCy era: a study from the ALWP of the EBMT, Blood, 2024, Figure 2.

Better to be young, at least as a donor

GENDER

- Allo-HCT from female donors to male recipients (female-to-male allo-HCT) is a well-established risk factor for inferior survival outcomes in allo-HCT using bone marrow or peripheral blood.
- The inferior survival in female-to-male allo-HCT is probably due to greater incidence of chronic GVHD and non-relapse mortality
- The biological explanation is that naïve female-donor lymphocytes recognize several proteins encoded by the Y chromosome of a male recipient, which are called H-Y minor histocompatibility antigens.

CMV STATUS



Amit Kalra et. Al Impact of Donor and Recipient Cytomegalovirus Serostatus on Outcomes of Antithymocyte Globulin–Conditioned Hematopoietic Cell Transplantation, Biology of Blood and Marrow Transplantation, Volume 22, Issue 9, 2016,Pages 1654-1663

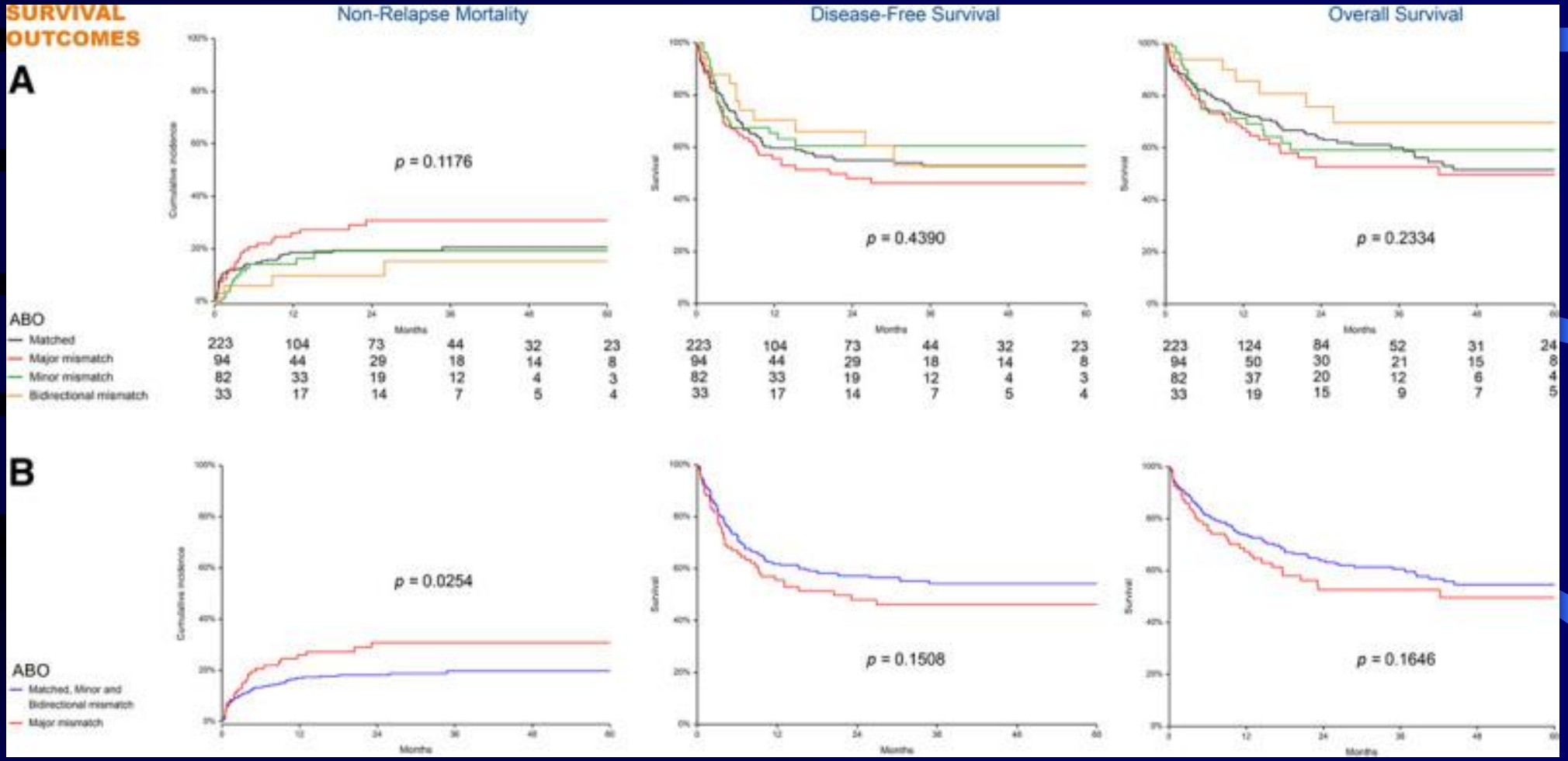
ABO MISMATCH

Mismatch Type	Blood Type	
	Recipient	**Donor**
Major	O	A, B, AB
	A	AB
	B	AB
Minor	A	O
	B	O
	AB	O, A, B
Bidirectional	A	B
	B	A

Mismatch Type	ABO Blood Type		Potential Clinical Consequence	Etiology	Potential Interventions
	Recipient	Donor			
Major	O	A, B, AB	• Acute hemolytic episode • Delayed RBC engraftment	• Transfusion of incompatible red blood cells • Recipient anti-donor isohemagglutinins	• Red blood cell reduction of stem cell product
Major	A	AB	• Pure red blood cell aplasia	• Loss of immature stem cells from processing with ABO antigens expressed on granulocytes and platelets	• Therapeutic plasma exchange in recipient to reduce isohemagglutinins before transplantation (uncommon in United States) • Promote donor erythropoiesis via erythropoietin administration
Major	B	AB	• Delayed granulocyte and platelet engraftment		
Minor	A	O	• Acute hemolytic episode	• Donor plasma with elevated isohemagglutinin titers/small blood volume recipient • Passenger lymphocytes producing isohemagglutinins	• Plasma reduction • Continual clinical monitoring between days +5 and 15 for signs/symptoms of hemolysis (including laboratory monitoring with LDH, bilirubin, CBC, DAT)
Minor	B	O	• Delayed hemolysis secondary to passenger lymphocyte syndrome		
Minor	AB	O, A, B			
Bidirectional	A	B	• Combination of major and minor consequences	• Combination of major and minor etiologies	• Combination of major and minor interventions
Bidirectional	B	A			

LDH indicates lactate dehydrogenase; DAT, direct antiglobulin test.

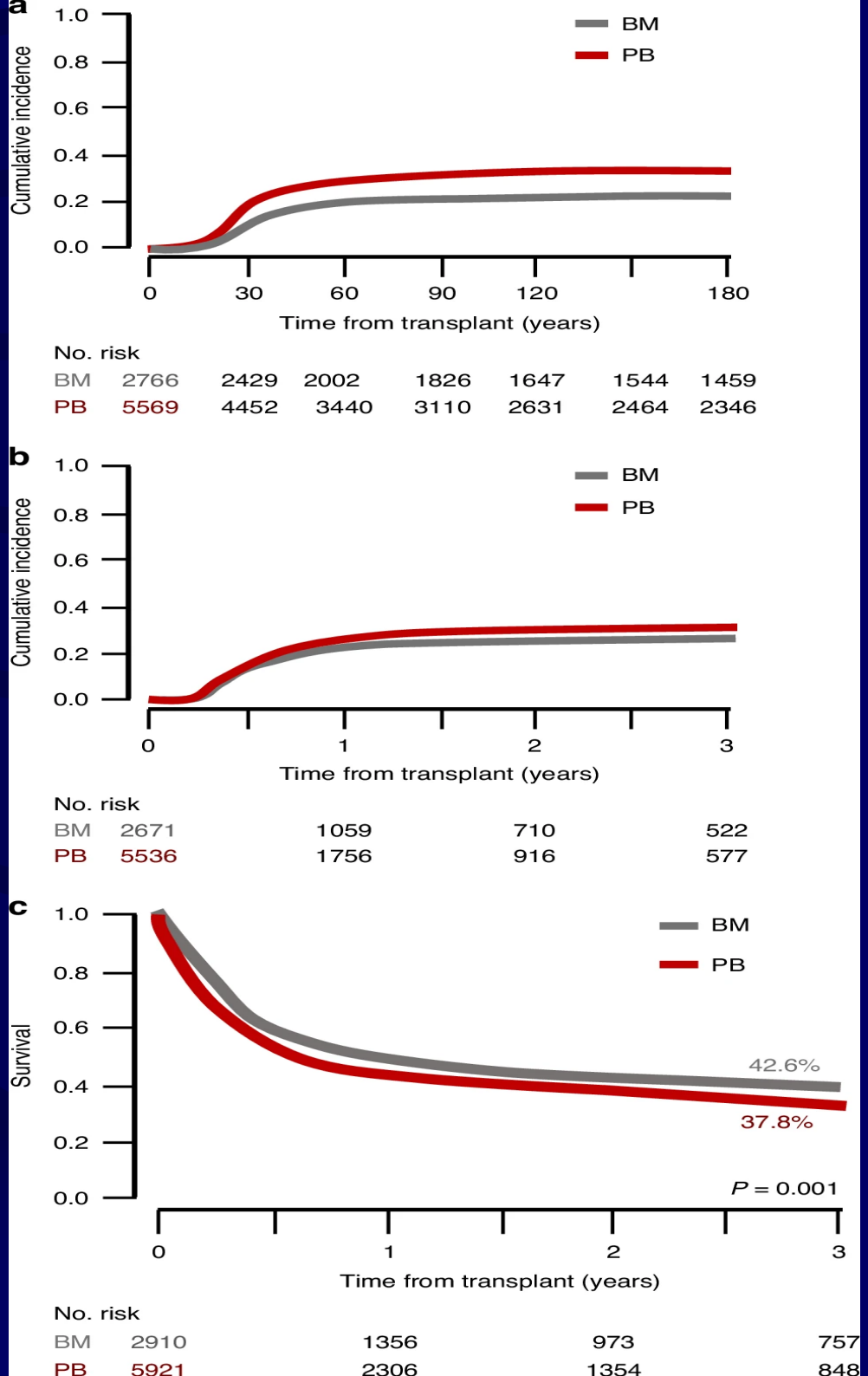
ABO


SURVIVAL OUTCOMES
A
Non-Relapse Mortality
Disease-Free Survival
Overall Survival
p = 0.1176
p = 0.4390
p = 0.2334
ABO
Matched
Major mismatch
Minor mismatch
Bidirectional mismatch
223 104 73 44 32 23
94 44 29 18 14 8
82 33 19 12 4 3
33 17 14 7 5 4
223 104 73 44 32 23
94 44 29 18 14 8
82 33 19 12 4 3
33 17 14 7 5 4
223 124 84 52 31 24
94 50 30 21 15 8
82 37 20 12 6 4
33 19 15 9 7 5
B
p = 0.0254
p = 0.1508
p = 0.1646
ABO
Matched, Minor and Bidirectional mismatch
Major mismatch

Bone marrow vs. peripheral blood

- Bone marrow as a stem cell source is associated with a significantly lower risk of cGVHD and extensive cGVHD compared to peripheral blood stem cells, with similar overall and disease-free survival rates.
- Peripheral blood stem cells (PBSCs) offer the advantage of faster neutrophil and platelet engraftment and lower risk of graft failure.
- AGVHD rates may also be modestly increased with PBSCs, though the difference is less pronounced

Rocha, V., Labopin, M., Raiola, A.M. *et al.* Use of bone marrow cells is associated with improved outcomes when compared to peripheral blood stem cell after haplo-identical transplants with post transplant cyclophosphamide, a study from of the CTIWP-EBMT. *Bone Marrow Transplant* (2025



a cumulative incidence (CI) of grade II-IV acute GVHD, **b**. CI of cGVHD, **c**. probability of GRFS by BM versus PBSC graft.

Conclusions

- The last decade has seen significant advances in alternative donor transplant such that almost every patient can find a donor.
- A haploidentical donor is easily and rapidly available.
- Non T- depleted haploidentical transplant, in particular with PTCy emerged as a widely feasible strategy.
- Will haplo-transplant ultimately replace MUD?
- Relapse remains a major problem after transplant.
- Randomized studies are required to determine the best alternative donor and the transplant platform.

Thank you for your attention

Vered.stavi@gmail.com

תודה לפרופ' אביחי שמעוני על שיתוף השקופיות