XIX Congresso della Società GITMO

RIUNIONE NAZIONALE GITMO

TORINO, CENTRO CONGRESSI LINGOTTO, 5 - 6 MAGGIO 2025

Profilassi della GVHD nel trapianto da mismatched unrelated donor (MMUD)

Anna Maria Raiola

IRCCS Ospedale Policlinico San Martino

Genova

OSPEDALE POLICLINICO SAN MARTINO
Sistema Sanitario Regione Liguria
Istituto di Ricovero e Cura a Carattere Scientifico

Disclosures of Name Surname

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
No disclosure							

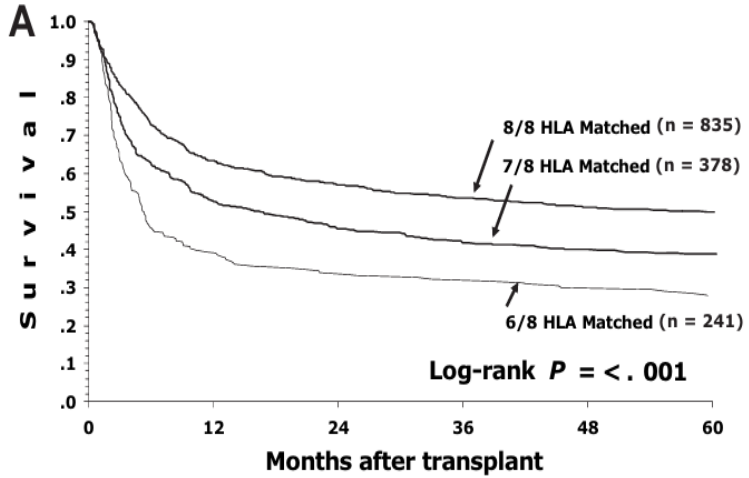
Mismatched Unrelated Donor

7/8: single antigen or allele mismatch at HLA-A, -B, -C, or -DRB1

Lee et al. Blood 2007

Mismatched Unrelated Donor

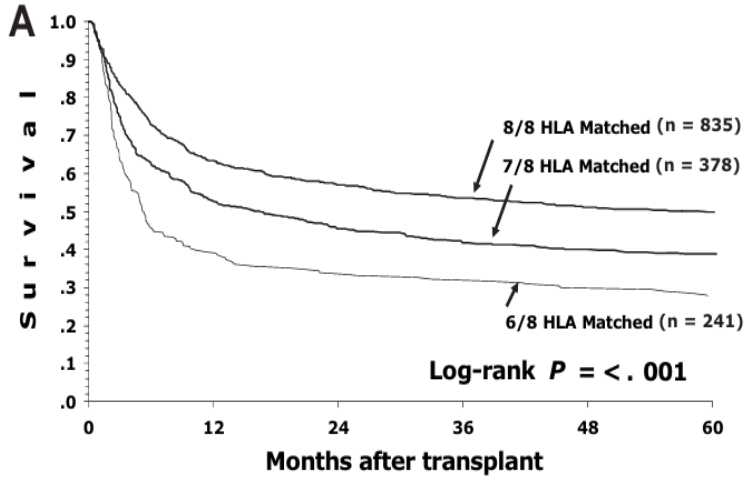
7/8: single antigen or allele mismatch at HLA-A, -B, -C, or -DRB1



Lee et al. Blood 2007

Mismatched Unrelated Donor

7/8: single antigen or allele mismatch at HLA-A, -B, -C, or -DRB1



Lee et al. Blood 2007

-Multiple mismatches at the low expression HLA loci DP, DQ, and DRB3/4/5 are associated with adverse outcomes in HSCT.

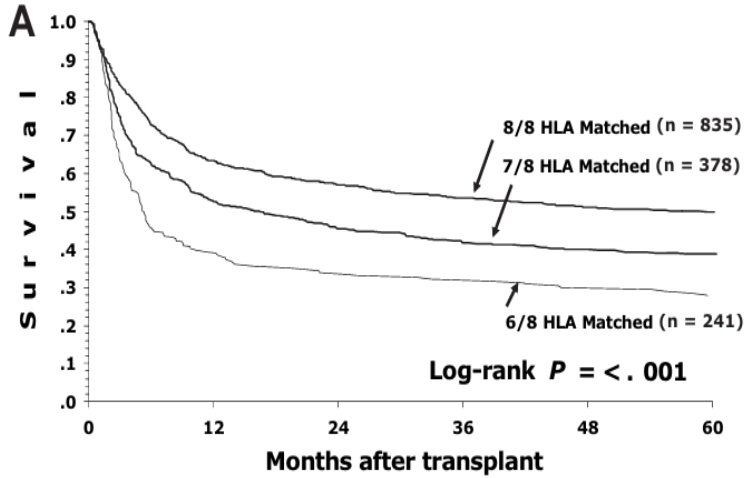
- Mismatches in HLA-DQ were more common in the transplants presenting a single mismatch at DRB1 than in those with a single mismatch at the class I loci or matched in 8/8 alleles (10%).

-HLA DP: permissive and non permissive mismatched.

Fernandez-Vina et al. Blood 2013
Fleischhauer K. et al. Blood 2017
Dehne et. al Blood 2019

Mismatched Unrelated Donor

7/8: single antigen or allele mismatch at HLA-A, -B, -C, or -DRB1



Lee et al. Blood 2007

-Multiple mismatches at the low expression HLA loci DP, DQ, and DRB3/4/5 are associated [illegible] adverse outcomes in HSCT.

- Mismatches in HLA-DQ were [illegible]ore common in the transplants presenting a singl[illegible]ismatch at DRB1 than in those with a single mismatch at the class I loci or matched in 8/8 alleles (10%).

-HLA DP: permissive and non permissive mismatched.

Fernandez-Vina et al. Blood 2013
Fleischhauer K. et al. Blood 2017
Dehne et. al Blood 2019

Prophylaxis and management of graft-versus-host disease after stem-cell transplantation for haematological malignancies: updated consensus recommendations of the European Society for Blood and Marrow Transplantation

Olaf Penack, Monia Marchetti*, Mahmoud Aljurf, Mutlu Arat, Francesca Bonifazi, Rafael F Duarte, Sebastian Giebel, Hildegard Greinix, Mette D Hazenberg, Nicolaus Kröger, Stephan Mielke, Mohamad Mohty, Arnon Nagler, Jakob Passweg, Francesca Patriarca, Tapani Ruutu, Hélène Schoemans, Carlos Solano, Radovan Vrhovac, Daniel Wolff, Robert Zeiser, Anna Sureda, Zinaida Peric*

Lancet Haematology 2024

Recommendations on prophylaxis of GvHD: HSCT from a MMUD

"For recipients of allogenic HSCT from MMUD,
GVHD prophylaxis including **rATG or PTCy should be preferred to prophylaxis with neither rATG nor PTCy**

Moderate quality comparative evidence of ATG versus PTCy, suggests a possible amelioration of non-relapse mortality with PTCy, but the residual uncertainty does not allow to favour one strategy over another"

Prospective trials: ATG in MMUD

	HLA match level Source/Disease/Cond	ATG	aGVHD/cGVHD	NRM/relapse/OS
Kroger 2009	*9/10 (n: 91)* *BM or PB* *All* *MAC RIC*	*ATG F60 mg/kg*	*aGVHD II – IV : 40%* *cGVHD: 46%*	*NRM (3y.) 31%* *Relapse (5y.) 27%* *OS (5y.) 55%*
Kroger 2009	*6-8/10(n.67)* *BM or PB* *All* *MAC RIC*	*ATG F90 mg/kg*	*aGVHD II – IV : 40%* *cGVHD: 36%*	*NRM (3y.) 33%* *Relapse (5y.) 26%* *OS (5y.) 41%*
Spinner 2017	*9/10 (n.72)* *NMA (TLI)* *PB* *All*	*ATG T 7,5 mg/kg*	*aGVHD II – IV : 21%* *cGVHD: 31%*	*NRM (2y.) 17%* *Relapse (2y.) 40%* *OS (2y.) 58%*

Prospective trials: ATG in MMUD

	HLA match level Source/Disease/Cond	ATG	aGVHD/cGVHD	NRM/relapse/OS
Kroger 2009	*9/10 (n: 91)* *BM or PB* *All* *MAC RIC*	*ATG F60 mg/kg*	*aGVHD II – IV : 40%* *cGVHD: 46%*	*NRM (3y.) 31%* *Relapse (5y.) 27%* *OS (5y.) 55%*
Kroger 2009	*6-8/10(n.67)* *BM or PB* *All* *MAC RIC*	*ATG F90 mg/kg*	*aGVHD II – IV : 40%* *cGVHD: 36%*	*NRM (3y.) 33%* *Relapse (5y.) 26%* *OS (5y.) 41%*
Spinner 2017	*9/10 (n.72)* *NMA (TLI)* *PB* *All*	*ATG T 7,5 mg/kg*	*aGVHD II – IV : 21%* *cGVHD: 31%*	*NRM (2y.) 17%* *Relapse (2y.) 40%* *OS (2y.) 58%*
Robin EBMT 2019	*9/10 (n.443)* *RIC (70) MAC (30)* *BM or PB* *MDS*	In vivo T cell depletion	*aGVHD II – IV : 35%* *cGVHD: 39%*	*NRM (3y.) 40%* *Relapse (3y.) 27%* *OS (2y.) 38%*

Prospective trials: PTCy in MMUD

1) *Baltimore*

NCT01203722 *NCT01203722*

2) *NMDP*

NCT02793544 *ACCESS Trial* *NCT04904588*

3) *GITMO*

NCT03270748 *EURODRACT 2017-003530-85*

Prospective trials: PTCy in MMUD

1) *Baltimore*

Prospective study of nonmyeloablative, HLA-mismatched unrelated BMT with high-dose posttransplantation cyclophosphamide

Kasamon Y. et al Blood Advanced 2016

NCT01203722

Nonmyeloablative, HLA-Mismatched Unrelated Peripheral Blood Transplantation with High-Dose Post-Transplantation Cyclophosphamide

Rappazzo C. et al Transplantation and Cellular Therapy 2021

NCT01203722

Prospective trials: PTCy in MMUD

2) NMDP

Three-Year Outcomes in Recipients of Mismatched Unrelated Bone Marrow Donor Transplants Using Post-Transplantation Cyclophosphamide: Follow-Up from a National Marrow Donor Program-Sponsored Prospective Clinical Trial

NCT02793544

Shaw. et al JCO 2021
Shaw. et al Transplantation and Cellular Therapy 2023

Posttransplant cyclophosphamide as GVHD prophylaxis for peripheral blood stem cell HLA-mismatched unrelated donor transplant

Al Malki et al. Blood Advanced 2021
Al Malki et al. Tandem Meetings 2025

ACCESS Trial NCT04904588

1)Baltimore

29 patients, median age: 54 years (range22-74)
Diagnoses: AML(38%)
HLA match level: 7/8: 82%, 6/8: 18%.
Conditioning regimens: NMA
OS at one year post HCT was 93% (95% CI:85 -100%).

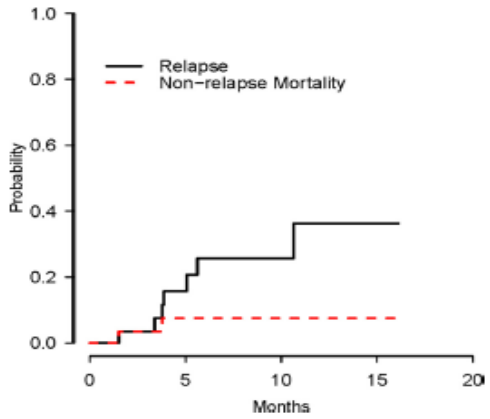


Figure 2. Probabilities of NRM and relapse. The CuI of NRM at 12 months was 7% (90% CI, NA to 16%), and the CuI of relapse at 12 months was 29% (90% CI, 8% to 50%).

CI of aGVHD II-IV was **15%** (90% CI, 3% to 26%).
CI of cGVHD at 12 months was **23%** (90% CI, 1% to 46%).
GRFS at 1 year was **41%** (90% CI, 23% to 73%).

Rappazzo et al. Transplantation and Cellular Therapy. 2021

2)NMDP

75 patients, median age: 46 years (range20-65)
Diagnoses: AML(44%), ALL(39%).
HLA match level: 7/8: 69%, 6/8: 25%, 5/8: 4%, 4/8 :1%.
Conditioning regimens: MAC
OS at one year post HCT was 84% (95% CI:73-90%).

Table 1

Clinical Endpoint	One year estimate (%) (95% CI)#
GVHD-free, relapse free survival (GRFS)	48% (36-59%)
Primary graft failure by Day 28	1% (0-7%)
Non-relapse mortality (NRM)	11% (5-19%)
Relapse	23% (14-34%)
Acute GVHD grade III-IV	8% (3-16%)*
NIH moderate/severe chronic GVHD	10% (4-19%)

* 6-month estimate
# OS and GRFS using Kaplan-Meier method; Primary graft failure using proportion and exact binomial CI; NRM, relapse, and GVHD using cumulative incidence method.

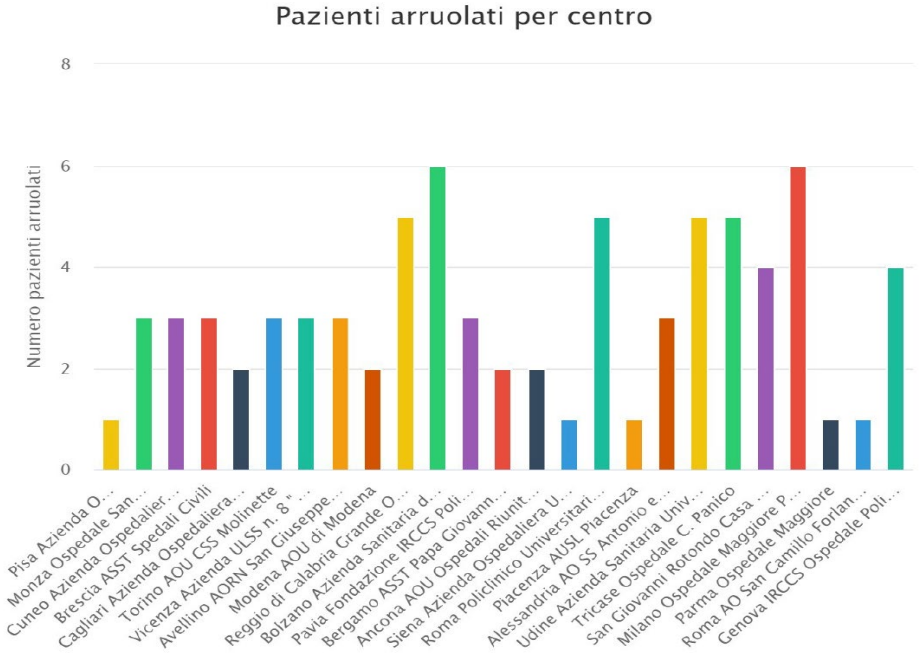
Al Malki et al. Blood Advanced 2021
Al Malki et al. Tandem Meetings 2025

Prospective trials: PTCy in MMUD

3) **Posttransplant cyclophosphamide as GVHD prophylaxis in patients receiving mismatched unrelated HCT: the PHYLOS trial**

GITMO

- Prospective, single-arm trial
- Primary end point: CI aGVHD
- 77 patients (AML/MDS in CR) (Jan. 2020–Nov. 2022).
- 7/8 HLA-matched unrelated donors
- Conditioning: Busulfan + Fludarabine
- GvHD prophylaxis: PTCy + CNI + MMF
- 93.5% PBSC grafts



NCT03270748 EURODRACT 2017-003530-85

Raiola et al. Blood Advances 2025

Posttransplant cyclophosphamide as GVHD prophylaxis in patients receiving mismatched unrelated HCT: the PHYLOS trial

PATIENTS	**77**
Age (years), median (min-max)	53(range 19–65)
HCT-CI 0-2 ≥ 3	 64 (83,1%) 13 (16,9%)
DISEASE **AML** 64 (83,1%)	
Cytogenetic risk (ELN 2022) Favorable Intermediate Adverse	 14 (21,9%) 37 (57,8%) 13 (20,3%)
No CR post induction therapy ≥ II ° CR	15 (23,4%) 11 (17%)
MRD positive at transplant Molecular markers NPM AML1/ETO bcr/abl IF	 14/64 (21%) 11 (17%) 2 (3%) 1. (1%) 14/64 (21%)
MDS 13 (16,9%)	
HSCT up front	5

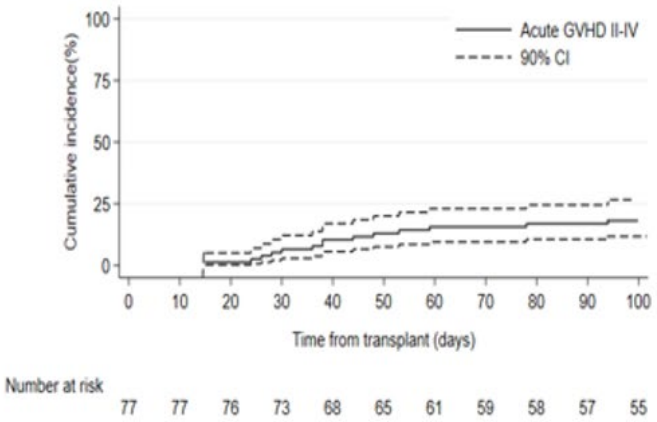
8.5 Flow chart of treatment

TREATMENT											
Days	**-6**	**-5**	**-4**	**-3**	**-2**	**-1**	**0**	**1**	**3**	**4**	**5**
Conditioning regimen											
Busulfan 0·8 mg/kg four times per day during 2 h infusions for four consecutive days (16 doses from day −6 through day −3; total dose of 12·8 mg/kg)	X	X	X	X							
Fludarabine 40 mg/m^2 per day for four consecutive days (from day −6 through day −3) for a total dose of 160 mg/m^2	X	X	X	X							
Transplant							X				
Prophylaxis of GVHD											
Cyclophosphamide 50 mg/kg intravenously day + 3and +4 after transplant (total dose:100 mg/kg).									X	X	
Cyclosporine (CsA) or **Tacrolimus** (IV and then po) beginning day 5 with dose adjusted to maintain a therapeutic level - to be continued for at least 100 days.											X→ 100
Micofenolate 15mg/kg twice from day +5 to +35.											X→ 35
G-CSF 5 ug/kg from day +5 until engraftment.											X

NCT03270748 EURODRACT 2017-003530-85

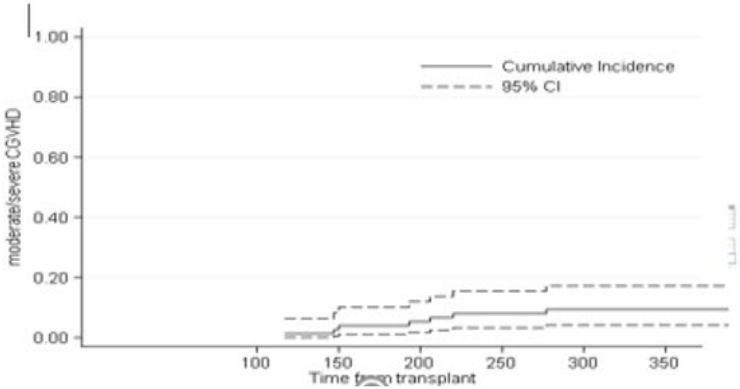
Raiola et al. Blood Advances 2025

aGVHD II - IV



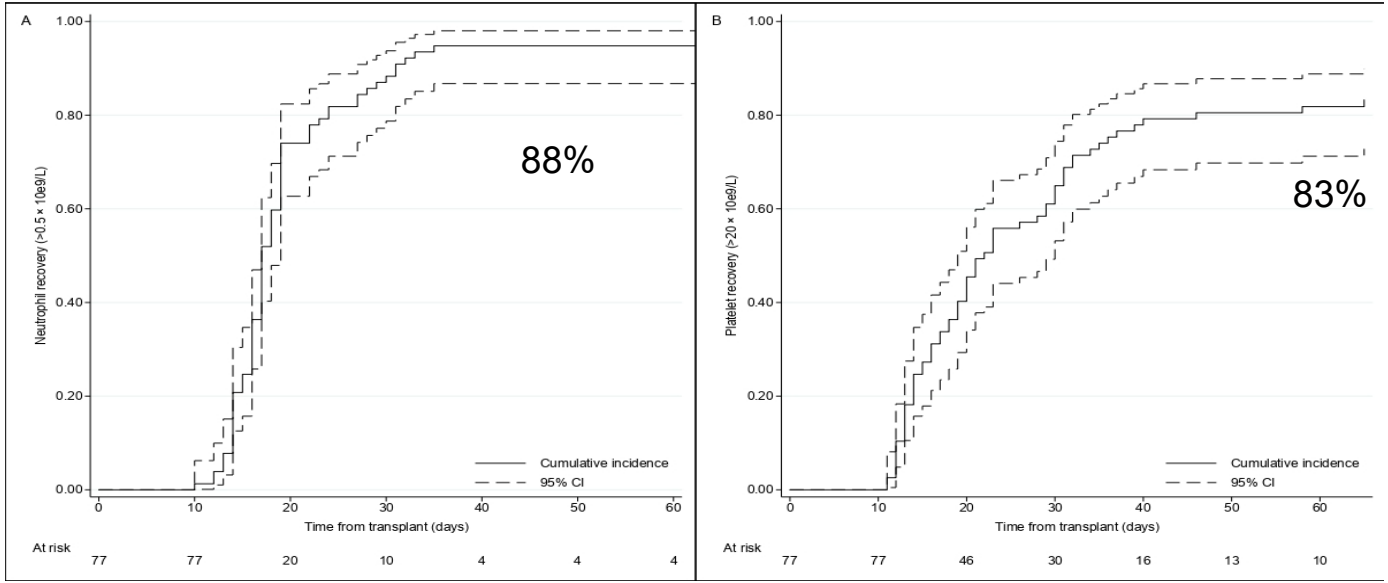
The 100-day cumulative incidence (CI) of grade II-IV aGVHD was 18.2% (90%CI: 11.6 – 25.9) (14 patients) and **6.5%** (95%CI: 2.9-12.1) **for grade III-IV** (5 patients)

cGVHD moderate - severe



The 1-year CI of **moderate/severe cGVHD 9.2%** (95% CI: 4.1 - 17.2) (7 patients).

Raiola et al. Blood Advances 2025



Engraftment

GF: 5 patients

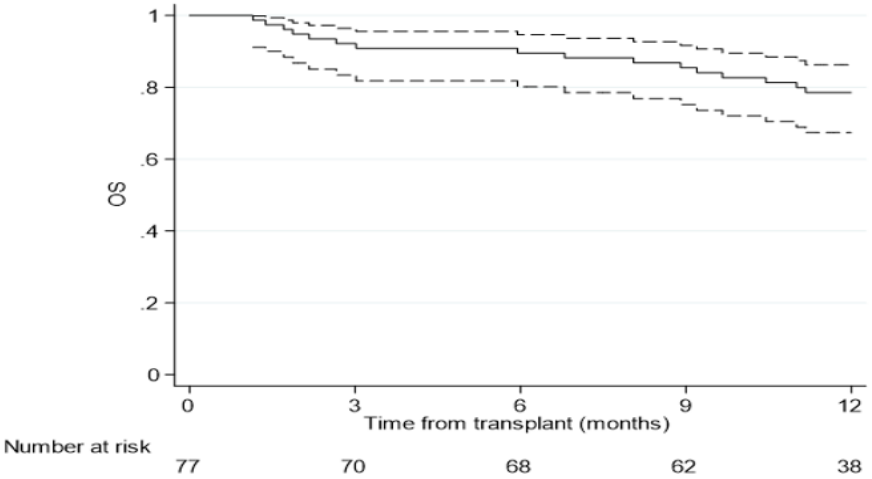
71 patients (92%) had full-donor chimerism by day +30 (BM and PB CD3+ cells) .

Median time (days) to neutrophil recovery was + 17 (range 10 – 35)

Median time to platelet recovery was +22 (range 11 – 137).

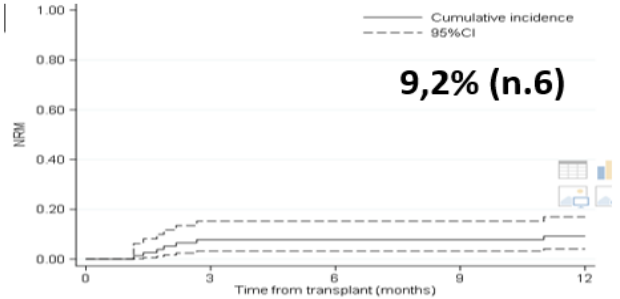
Raiola et al. Blood Advances 2025

OS

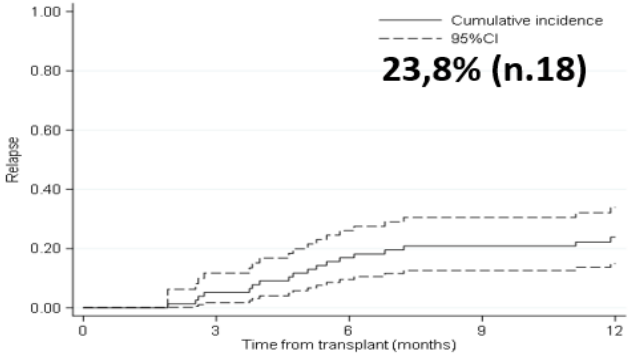


The 1-year overall survival was 78.5%
(95%CI: 67.4-86)

NRM



Relapse



Raiola et al. Blood Advances 2025

Posttransplant cyclophosphamide as GVHD prophylaxis in patients receiving mismatched unrelated HCT: the PHYLOS trial

RESULTS

	Number of events	Estimate	95% CI	
CI of aGVHD at 100 days				
Any grade	28	**39.0%**	28.1%	49.6%
Grade II-IV	14	**18,2%**	10,6%	27, 6%
Grade III-IV	5	**6,5**	3,1%	15,1%
CI of cGVHD at 12 months				
Any grade	10	**13,4%**	6,9%	22,1%
Moderate/severe	7	**9,2%**	4,1%	17,2%
CI of Relapse at 12 months	18	**23,8%**	14,9%	33,9%
CI of NRM at 12 months	7	**9,1%**	4,0%	16,9%
GRFS at 12 months	33	**55,3%**	43,4%	65,7%
OS at 12 months	16	**78,6%**	67,4%	86,3%

Raiola et al. Blood Advances 2025

Phylos vs Baltimora vs NMDP

RESULTS

Phylos GITMO	Number of events	Estimate	Baltimora	NMDP
CI of aGVHD at 100 days				
Grade II-IV	14	18,2%	15%	-
Grade III-IV	5	6,5%	6%	8%
CI of cGVHD at 12 months				
Any grade	10	13,4%	23%	-
Moderate/severe	7	9,2%	0	10%
CI of Relapse at 12 months	18	23,8%	29%	23%
CI of NRM at 12 months	7	9,1%	7%	11%
GRFS at 12 months	33	55,3%	41%	48%
OS at 12 months	16	78,6%	93%	84%

PTCy vs ATG: retrospective studies

Posttransplant cyclophosphamide vs antithymocyte globulin in HLA-mismatched unrelated donor transplantation

Age ≥ 18 years
Diagnosis of AML (all phases)
Transplant from 9/10 MUD HR **EBMT registry**
ATG vs PTCy
Transplant performed between 2011-2017

	ATG n.179	PTCy n.93	
Class I mm	**75%**	**73%**	
MAC	**50%**	**50%**	
PB	**92%**	**91%**	
Active disease	**28%**	**29%**	
Median fu	**27m**	**14m**	**p <.01**

Battipaglia et al. Blood 2019

PTCy versus ATG as graft-versus-host disease prophylaxis in mismatched unrelated stem cell transplantation

Age ≥ 18 years
All diagnosis (AL 58%)
Transplant from 9/10 MUD HR **EBMT registry**
ATG vs PTCy
Transplant performed between 2018-2021

	ATG n.1140	PTCy n.583
Class I mm	**ND**	**ND**
MAC	**55%**	**54%**
PB	**100%**	**100%**
Active disease	**38%**	**34%**
Median fu	**2.4 y**	**2.2y**

Penack et al. Blood Cancer Journal 2024

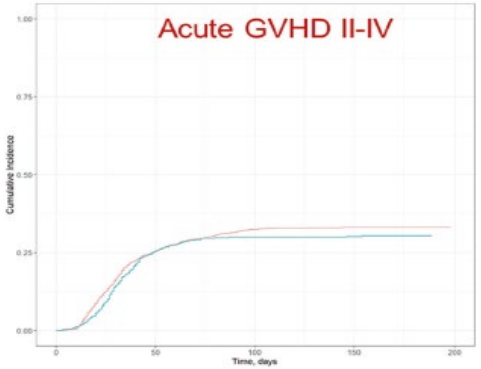
Posttransplant cyclophosphamide vs antithymocyte globulin in HLA-mismatched unrelated donor transplantation

	aGVHD II–IV (95% CI)	aGVHD III–IV (95% CI)	cGVHD (2y) (95% CI)	cGVHD, extensive (2y) (95% CI)
PTCy	30 (21-40)	9 (4 -16)	39 (26-51)	17 (9-28)
ATG	32 (26-40)	19 (13-25)	36 (28-44)	20 (14-28)
p	0.39	**<.04**	0.35	0.31

Propensity score matching // 1identified patient who received PTCY was matched with 2 patients who received ATG.

Battipaglia et al. Blood 2019

PTCy versus ATG as graft-versus-host disease prophylaxis in mismatched unrelated stem cell transplantation



ATG: 32%
PTCy: 29%

PTCy vs ATG

Outcome	HR(95%CI)	p-value
aGVHD II-IV	***0.83*** ***(0.66 - 1.04)***	*0.11*
aGVHD III-IV	***0.78*** ***(0.59 - 1.05)***	*0.10*
cGVHD	***0.95*** ***(0.74 – 1.22)***	*0.67*
Extensive cGVHD	***0.83*** ***(0.63 – 1.10)***	*0.2*

Penack et al. Blood Cancer Journal 2024

Posttransplant cyclophosphamide vs antithymocyte globulin in HLA-mismatched unrelated donor transplantation

Outcome	PTCy	ATG	p-value
NRM (95%CI)	***16** (9-25)*	***29** (22-36)*	*.06*
Relapse (95%CI)	***29** (20-40)*	***37** (29-44)*	*.31*
OS (95%CI)	***56** (43-68)*	***38** (30-46)*	*.07*
PFS (95%CI)	***55** (43-66)*	***34** (27-42)*	***<.05***
GRFS (95%CI)	***37** (25-49)*	***21** (14-28)*	***<.03***

Propensity score matching // 1identified patient who received PTCY was matched with 2 patients who received ATG.

Battipaglia et al. Blood 2019

PTCy versus ATG as graft-versus-host disease prophylaxis in mismatched unrelated stem cell transplantation

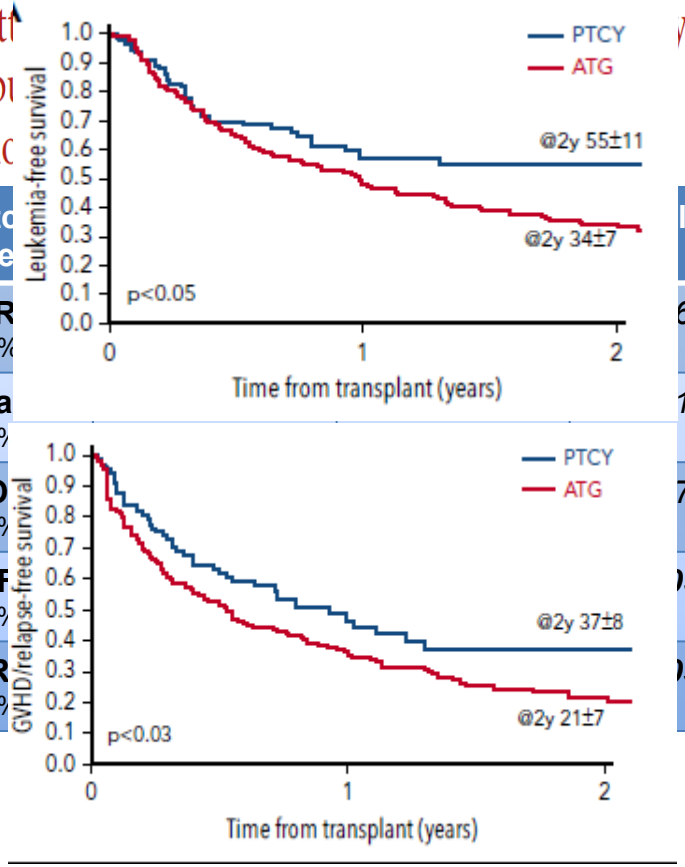
PTCy vs ATG

Outcome	HR(95%CI)	p-value
NRM	***0.74** (0.56 - 0.97)*	***0.028***
Relapse	***0.82** (0.67 - 1.01)*	*0.068*
OS	***0.77** (0.65 - 0.90)*	***<0.001***
PFS	***0.78** (0.67 - 0.91)*	***0.001***
GRFS	***0.80** (0.68 - 0.94)*	***0.006***

Multivariate Cox analysis: HR for PTCy vs. rATG, adjusted for potential risk factors and variables with significant difference across the groups.

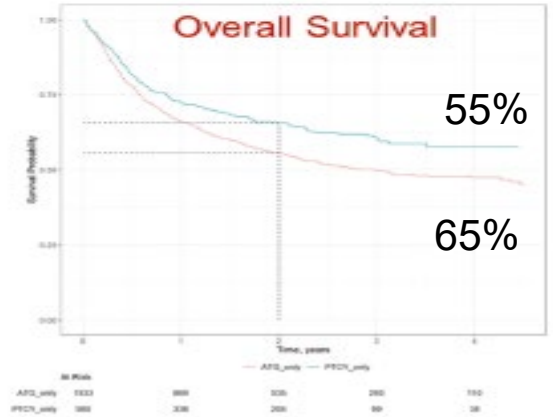
Penack et al. Blood Cancer Journal 2024

Post
globu
donc
yte



Outc e	lue
NR (95%	6
Rela (95%	1
O (95%	7
PF (95%	05
GR (95%	03

Battipaglia et al. Blood 2019



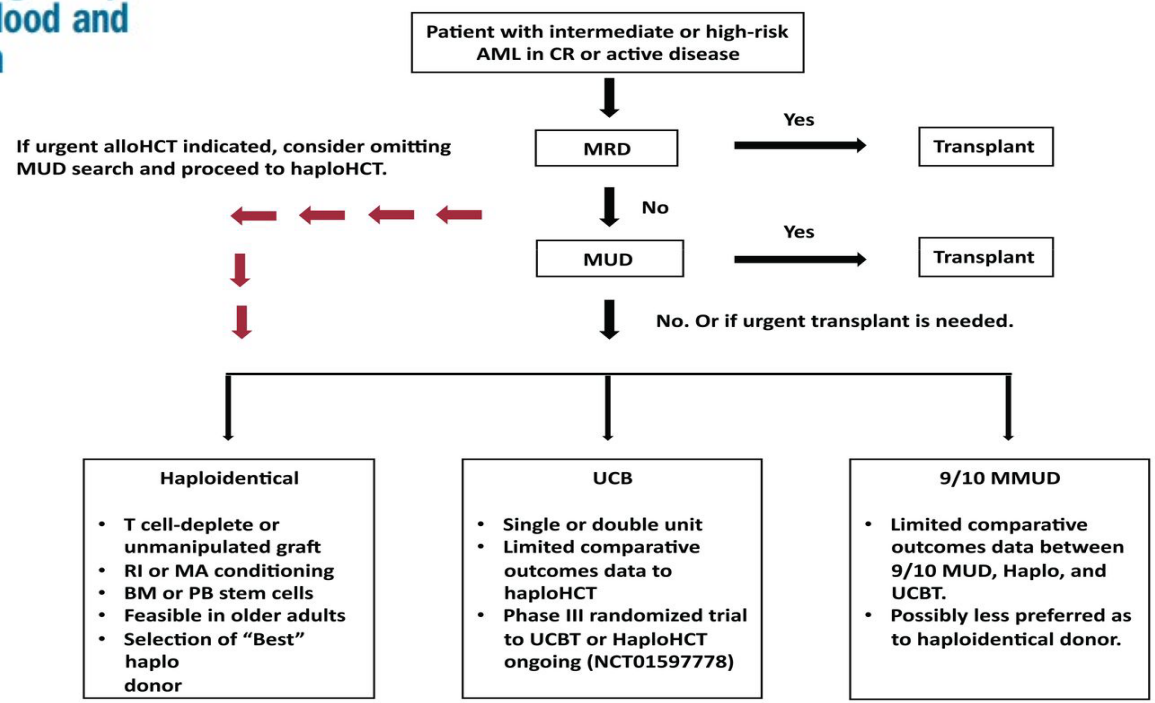
value
.028
.068
.001
.001
.006

. rATG,
ables with

Penack et al. Blood Cancer Journal 2024

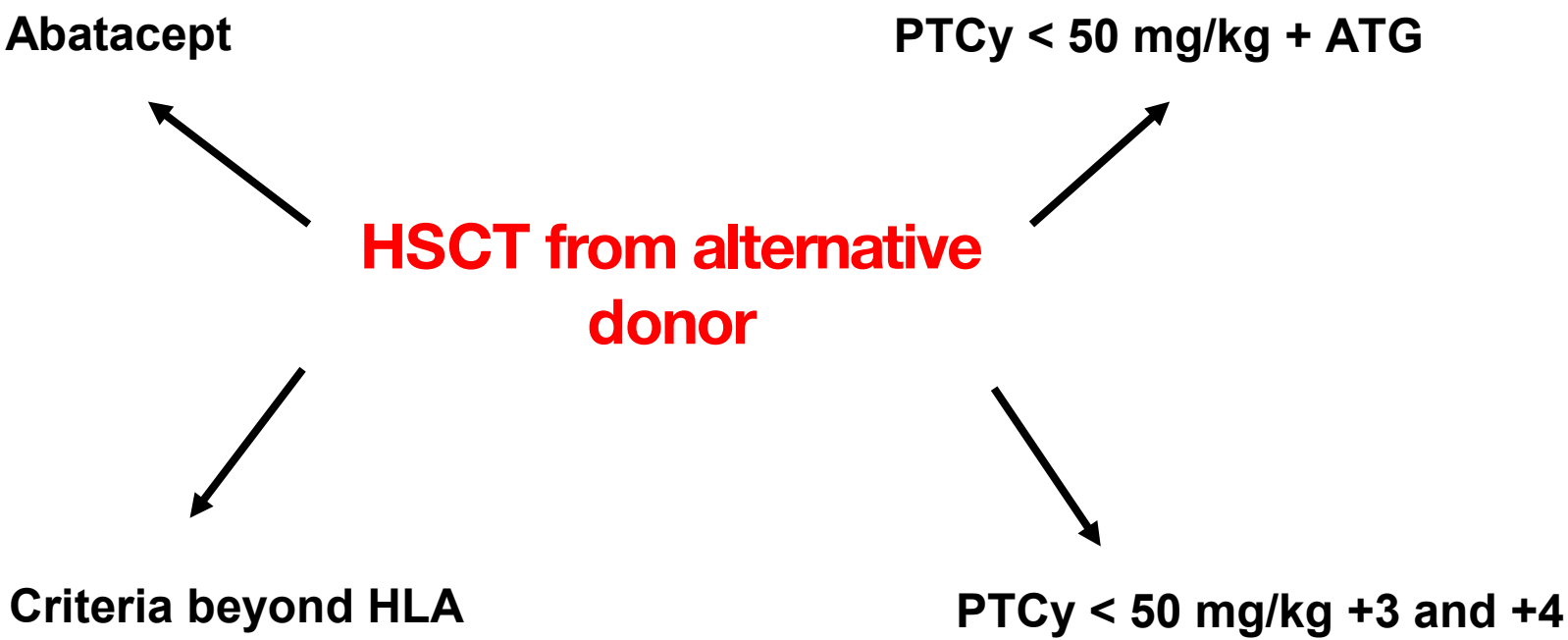
Haploidentical hematopoietic cell transplantation for adult acute myeloid leukemia: a position statement from the Acute Leukemia Working Party of the European Society for Blood and Marrow Transplantation

Lee et al Haematologica 2018



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

HSCT from alternative donor


Abatacept
PTCy < 50 mg/kg + ATG
HSCT from alternative donor
Criteria beyond HLA
PTCy < 50 mg/kg +3 and +4

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

Blood 2024

Jaime Sanz,[1] Myriam Labopin,[2] Goda Choi,[3] Alexander Kulagin,[4] Jacopo Peccatori,[5] Jan Vydra,[6] Péter Reményi,[7] Jurjen Versluis,[8] Montserrat Rovira,[9] Didier Blaise,[10] Hélène Labussière-Wallet,[11] Juan Montoro,[1] Simona Sica,[12] Ellen Meijer,[13] Maija Itälä-Remes,[14] Nicolaas Schaap,[15] Claude Eric Bulabois,[16] Simona Piemontese,[5] Mohamad Mohty,[17] and Fabio Ciceri[5,18]

	UD-HSCT
No. of patients	1011
Follow-up in months, median (IQR)	26 (24-29)
Year of HSCT, n (%)	
2011-2013	10 (1)
2014-2015	63 (6)
2016-2017	187 (18)
2018-2019	330 (33)
2020-2021	421 (42)
Age, median (range), y	54 (18-77)
Disease status at transplant, n (%)	
CR1	837 (83)
CR2	174 (17)
Conditioning intensity, n (%)	
Myeloablative	548 (54)
Reduced intensity	463 (46)

Retrospective analysis EBMT
AML in 1° or 2°CR
Primary end point was LFS.

Donor/recipient HLA match, n (%)	
Considering HLA-A, -B, -C, DR, and DQ	
10/10 MUD	621 (61)
9/10 MMUD	390 (39)
Considering HLA-A, -B, -C, and DR	
8/8 MUD	670 (66)
7/8 MMUD	341 (34)
Locus mismatch	
HLA-A	155 (15)
HLA-B	80 (8)
HLA-C	67 (7)
HLA-DR	39 (4)
HLA-DQ	49 (5)

	Overall
Outcome*	% (95% CI)
aGVHD	
Grade 2-4	24 (22-27)
Grade 3-4	7 (6-9)
cGVHD	
Overall	31 (28-35)
Extensive	12 (10-15)
NRM	12 (10-14)
Relapse incidence	25 (22-27)
LFS	64 (60-67)
OS	70 (67-73)
GRFS	52 (49-56)

From January
2010 to December 2021

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

Retrospective analysis EBMT
AML in 1° or 2°CR
Primary end point was LFS.

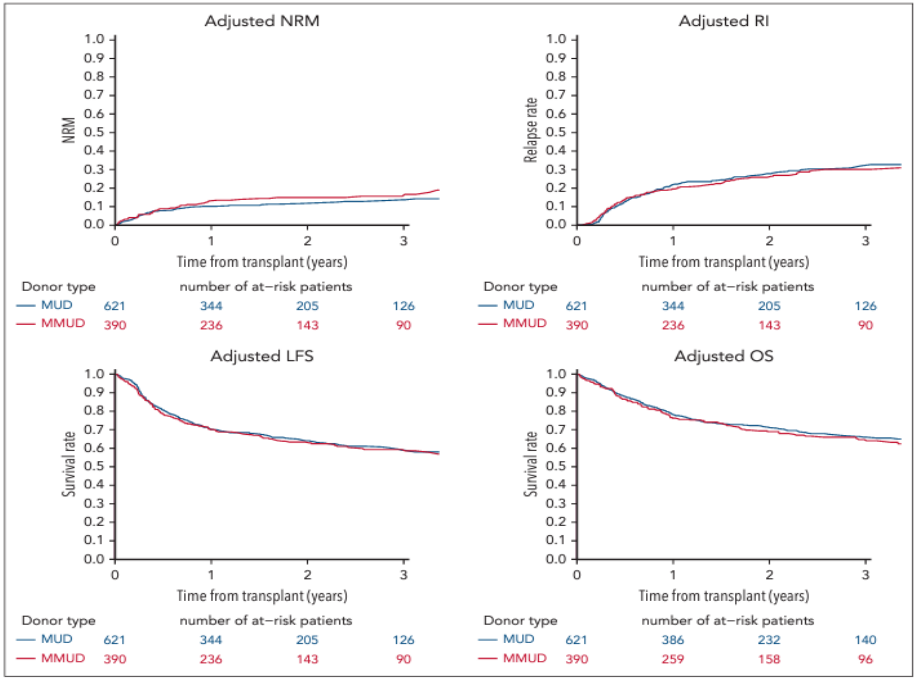


Figure 1. Adjusted cumulative incidence of NRM and relapse, and probability of LFS and OS for MUDs or MMUDs. RI, relapse.

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

Retrospective analysis EBMT
AML in 1° or 2°CR
Primary end point was LFS.

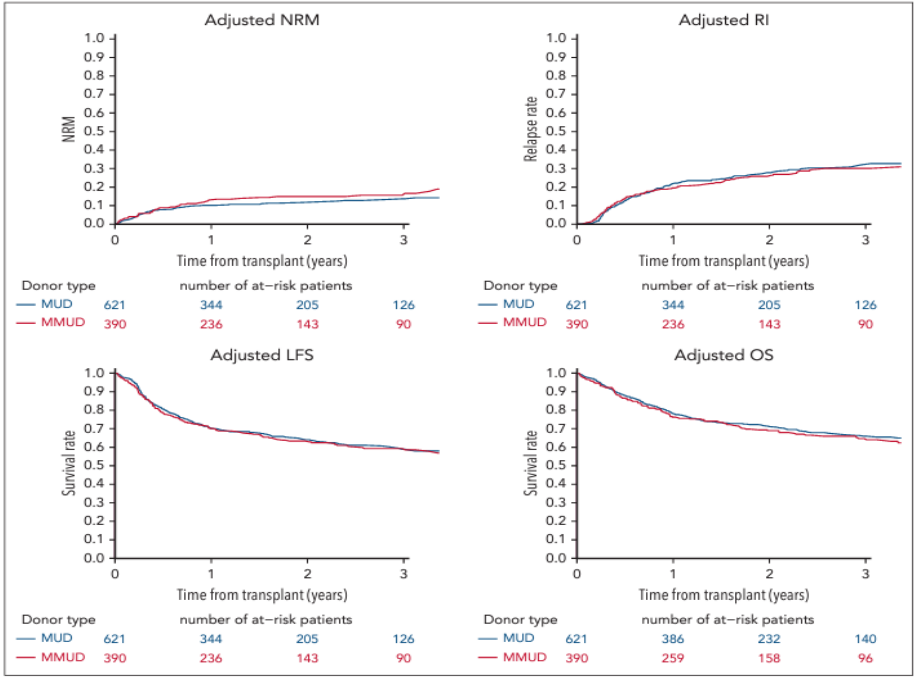


Figure 1. Adjusted cumulative incidence of NRM and relapse, and probability of LFS and OS for MUDs or MMUDs. RI, relapse.

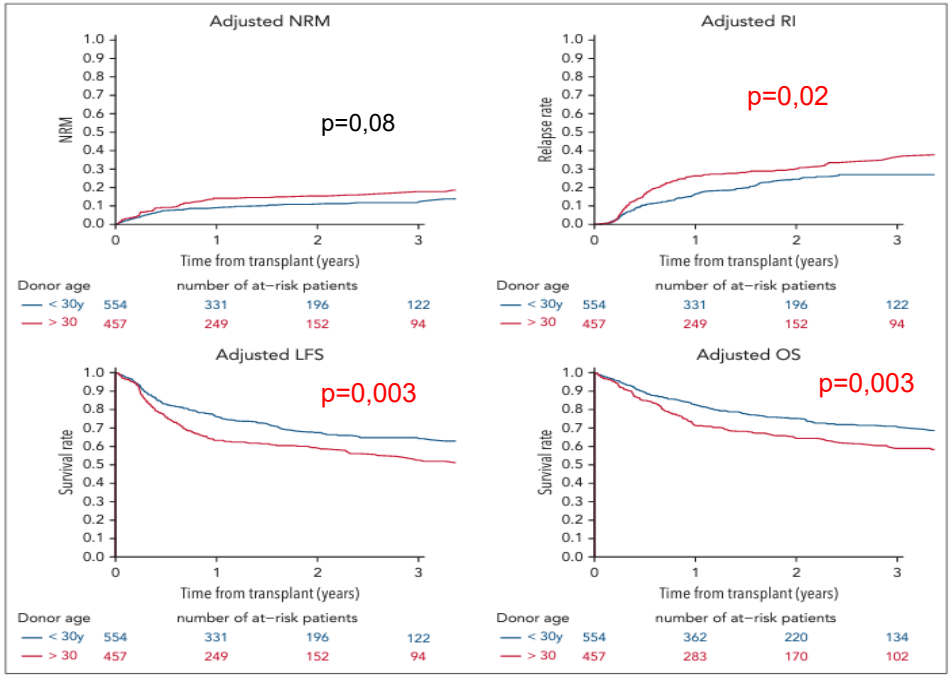


Figure 2. Adjusted cumulative incidence of NRM and relapse, and probability of LFS and OS according to donor age. RI, relapse.

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

Retrospective analysis EBMT
AML in 1° or 2°CR
Primary end point was LFS.

Donor-related variables	Primary end point		Secondary end points											
	LFS		aGVHD 3-4		cextGVHD		NRM		RI		OS		GRFS	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Donor/recipient HLA mismatch														
10/10 MUD	1		1		1		1		1		1		1	
9/10 MMUD	1.04 (0.83-1.31)	.72	1.33 (0.8-2.19)	.27	1.26 (0.84-1.91)	.27	1.39 (0.93-2.08)	.11	0.91 (0.69-1.2)	.52	1.09 (0.85-1.41)	.5	1.14 (0.94-1.37)	.19

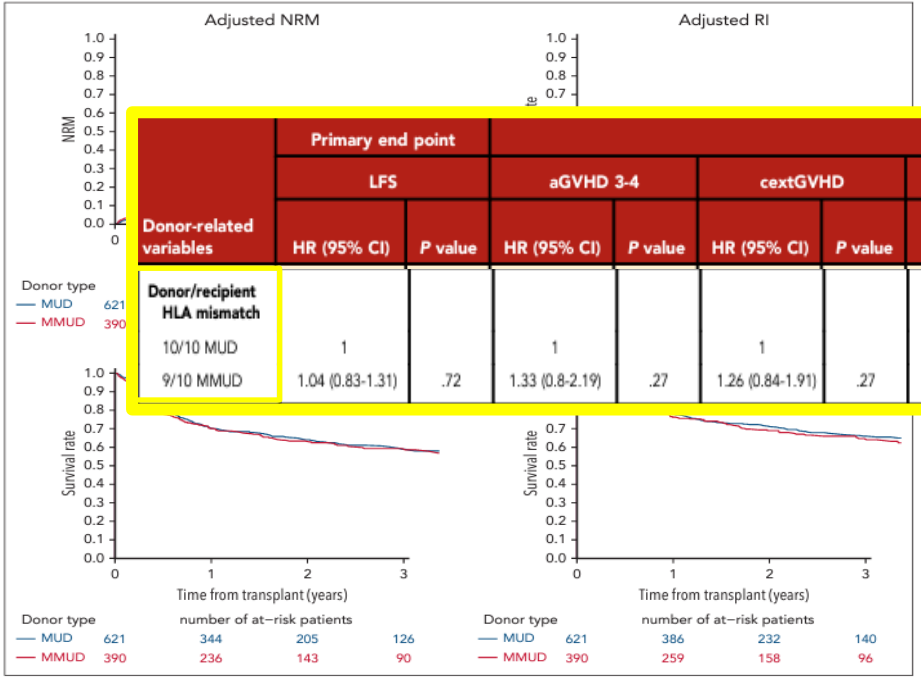


Figure 1. Adjusted cumulative incidence of NRM and relapse, and probability of LFS and OS for MUDs or MMUDs. RI, relapse.

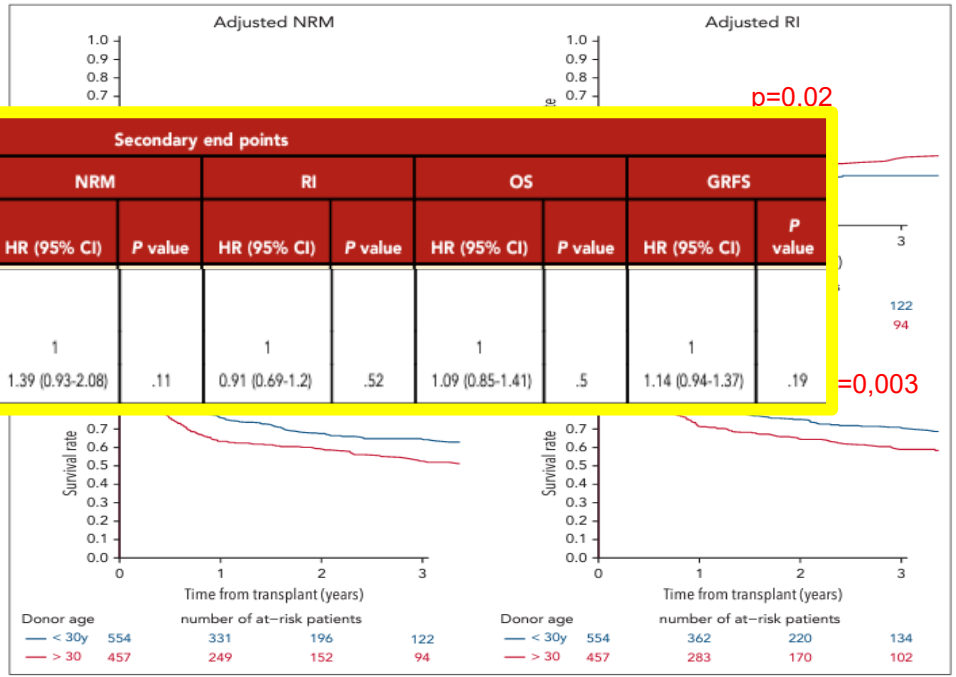


Figure 2. Adjusted cumulative incidence of NRM and relapse, and probability of LFS and OS according to donor age. RI, relapse.

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

Retrospective analysis EBMT
AML in 1° or 2°CR
Primary end point was LFS.

	Primary end point		Secondary end points											
	LFS		aGVHD 3-4		cextGVHD		NRM		RI		OS		GRFS	
Donor-related variables	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Donor age↑														
<30 y	1		1		1		1		1		1		1	
≥30 y	**1.4 (1.12-1.74)**	**.003**	1.37 (0.84-2.23)	.2	1.1 (0.74-1.64)	.6	1.42 (0.97-2.09)	.08	**1.38 (1.06-1.8)**	**.02**	**1.45 (1.14-1.85)**	**.003**	**1.29 (1.07-1.56)**	**.007**

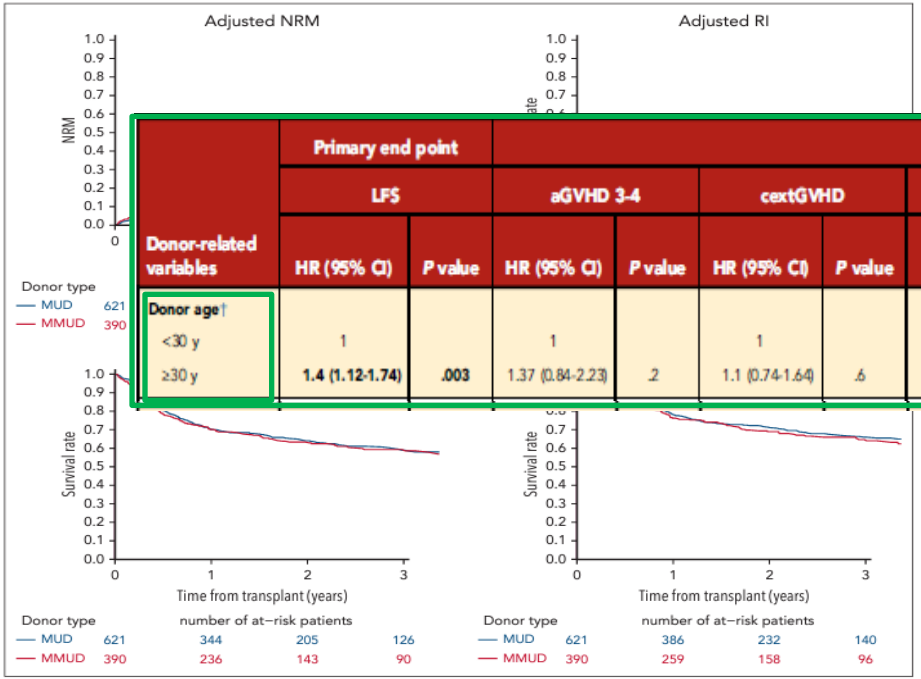


Figure 1. Adjusted cumulative incidence of NRM and relapse, and probability of LFS and OS for MUDs or MMUDs. RI, relapse.

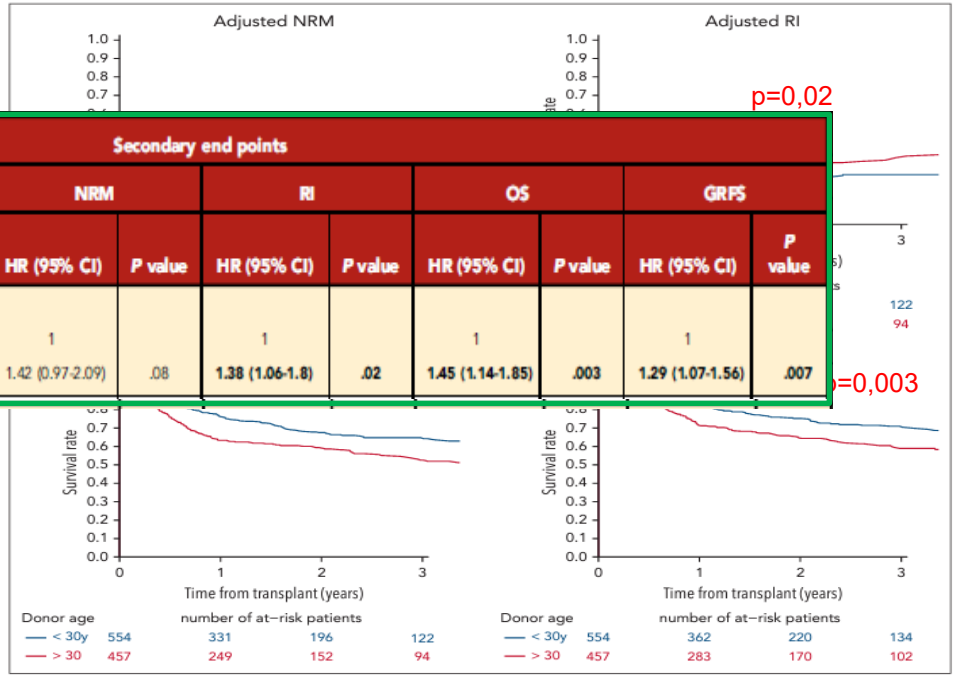
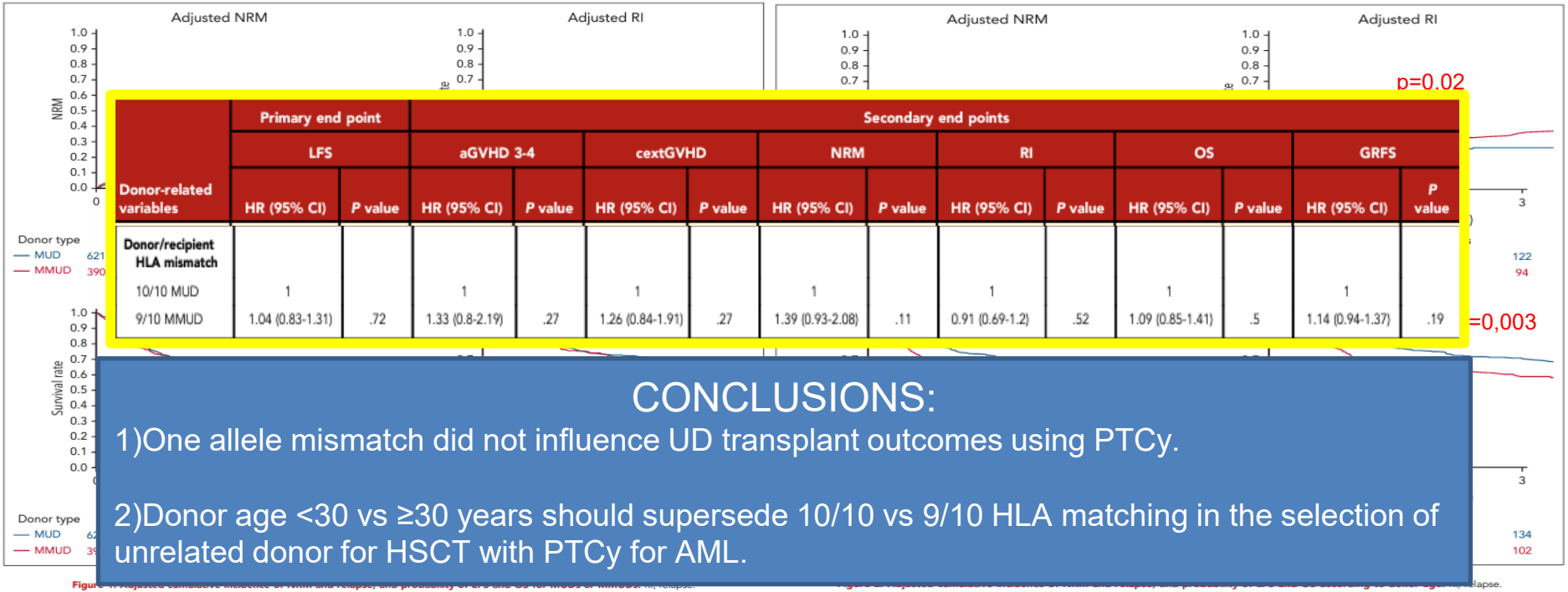


Figure 2. Adjusted cumulative incidence of NRM and relapse, and probability of LFS and OS according to donor age. RI, relapse.

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

Retrospective analysis EBMT
AML in 1° or 2°CR
Primary end point was LFS.



Donor-related variables	Primary end point: LFS HR (95% CI)	LFS P value	Secondary end points: aGVHD 3-4 HR (95% CI)	aGVHD 3-4 P value	cextGVHD HR (95% CI)	cextGVHD P value	NRM HR (95% CI)	NRM P value	RI HR (95% CI)	RI P value	OS HR (95% CI)	OS P value	GRFS HR (95% CI)	GRFS P value
Donor/recipient HLA mismatch														
10/10 MUD	1		1		1		1		1		1		1	
9/10 MMUD	1.04 (0.83-1.31)	.72	1.33 (0.8-2.19)	.27	1.26 (0.84-1.91)	.27	1.39 (0.93-2.08)	.11	0.91 (0.69-1.2)	.52	1.09 (0.85-1.41)	.5	1.14 (0.94-1.37)	.19

CONCLUSIONS:

1)One allele mismatch did not influence UD transplant outcomes using PTCy.

2)Donor age <30 vs ≥30 years should supersede 10/10 vs 9/10 HLA matching in the selection of unrelated donor for HSCT with PTCy for AML.

Phase II Trial of Costimulation Blockade With Abatacept for Prevention of Acute GVHD

Watkins et al. JCO 2021

Abatacept in combination with CNI/MTX was approved by the US Food and Drug Administration (FDA) for aGVHD prophylaxis in recipients of HLA-MUD or 1-allele HLAMMUD HCT, aged ≥2 years (Dec 2021)

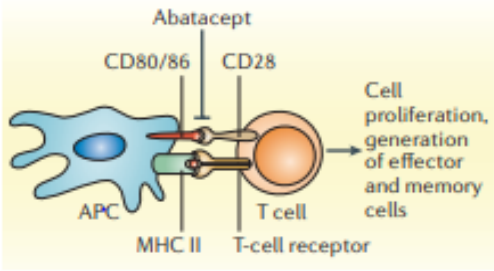
ABA2; ClinicalTrials.gov identifier: NCT01743131

Adults and children with hematologic malignancies under two strata:

1) A randomized, double-blind, placebo-controlled stratum (8/8-HLA-matched URD), comparing CNI/MTX plus abatacept with CNI/MTX plus placebo.

2)A single-arm stratum (7/8-HLA-mismatched URD) comparing CNI/MTX plus abatacept versus CNI/MTX CIBMTR controls.

The primary end point was day +100 grade 3-4 AGVHD, with day +180 severe-AGVHD-free-survival (SGFS) a key secondary end point.

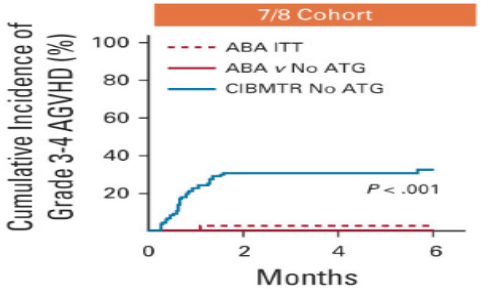


Moreland et al. NATURE REVIEWS | DRUG DISCOVERY 2007

Phase II Trial of Costimulatio[n] Blockade With Abatacept for Prevention of A[GVHD]

kins et al. JCO 2021

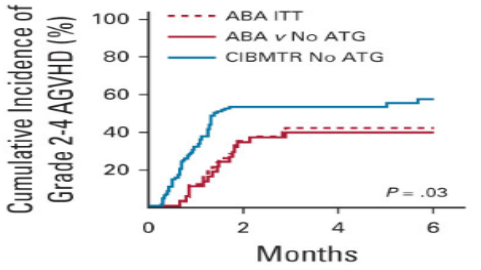
Abatacept in combination with CNI/MTX w[as] [ad]opted by the Food and Drug Administration (FDA) for aGVHD pro[phylaxis] [after] MUD or 1-allele HLAMMUD HCT, aged ≥2 years (

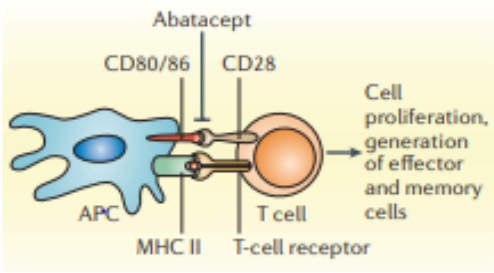


Trials.gov identifier: NCT01743131

Adults and children with hematologic malignanc
1) A randomized, double-blind, placebo-controlled [trial] comparing CNI/MTX plus abatacept with CNI/M[TX]

2)A single-arm stratum (7/8-HLA-mismatched URD [transplants] versus CNI/MTX CIBMTR controls.





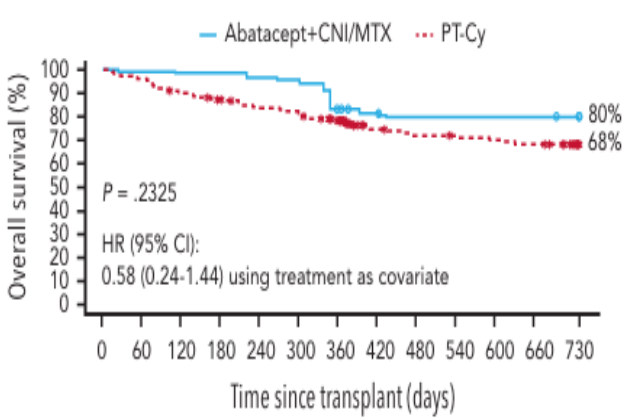
The primary end point was day +100 grade 3-4 A[GVHD]-free-survival (SGFS) a key secondary end point.

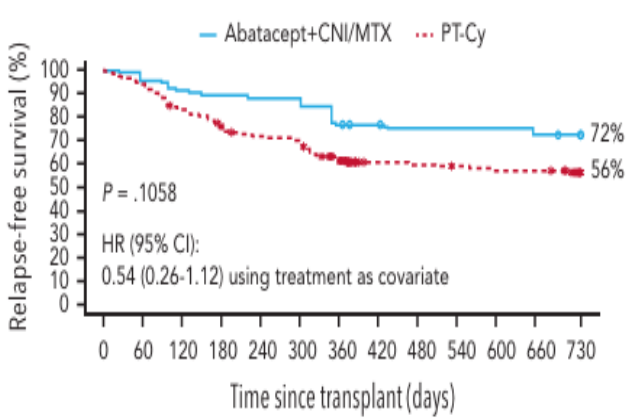
Moreland et al. NATURE REVIEWS | DRUG DISCOVERY 2007

TRANSPLANTATION

Abatacept for acute graft-versus-host disease prophylaxis after unrelated donor hematopoietic cell transplantation

Leslie S. Kean,[1-3,*] Linda J. Burns,[4,*] Tzuyung D. Kou,[5] Roxanne Kapikian,[5,6] Karissa Lozenski,[5] Amelia Langston,[7] John T. Horan,[8] Benjamin Watkins,[9] Muna Qayed,[10] Brandi Bratrude,[1] Kayla Betz,[1] Xiao-Ying Tang,[4] Mei-Jie Zhang,[4] Sean E. Connolly,[5] Martin Polinsky,[5] Brian Gavin,[5] Andres Gomez-Caminero,[5] and Marcelo C. Pasquini[4]





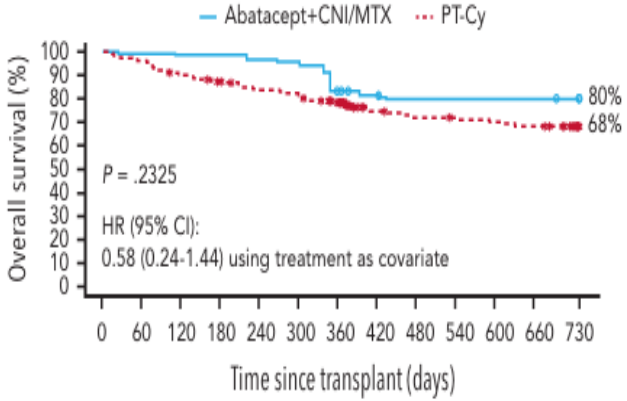
- **Retrospective cohort study - CIBMTR registry database.**
- **1° HCT between 2011 and 2018 from an 7/8 HLA-MMUD or 8/8 HLAMUD.**
- **GVHD prophylaxis with CNI/MTX (with or without ATG, and with or without abatacept) or PT-Cy.**
- **The primary end points were day-180, 1year, and 2-year OS and RFS.**

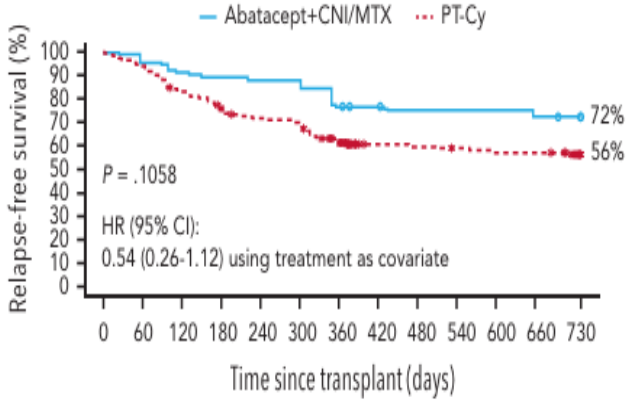
Blood 2024

TRANSPLANTATION

Abatacept for acute graft-versus-host disease prophylaxis after unrelated donor hematopoietic cell transplantation

Leslie S. Kean,[1-3,*] Linda J. Burns,[4,*] Tzuyung D. Kou,[5] Roxanne Kapikian,[5,6] Karissa Lozenski,[5] Amelia Langston,[7] John T. Horan,[8] Benjamin Watkins,[9] Muna Qayed,[10] Brandi Bratrude,[1] Kayla Betz,[1] Xiao-Ying Tang,[4] Mei-Jie Zhang,[4] Sean E. Connolly,[5] Martin Polinsky,[5] Brian Gavin,[5] Andres Gomez-Caminero,[5] and Marcelo C. Pasquini[4]





- **Retrospective cohort study - CIBMTR registry database.**
- **1° HCT between 2011 and 2018 from an 7/8 HLA-MMUD or 8/8 HLAMUD.**
- **GVHD prophylaxis with CNI/MTX (with or without ATG, and with or without abatacept) or PT-Cy.**
- **The primary end points were day-180, 1year, and 2-year OS and RFS.**

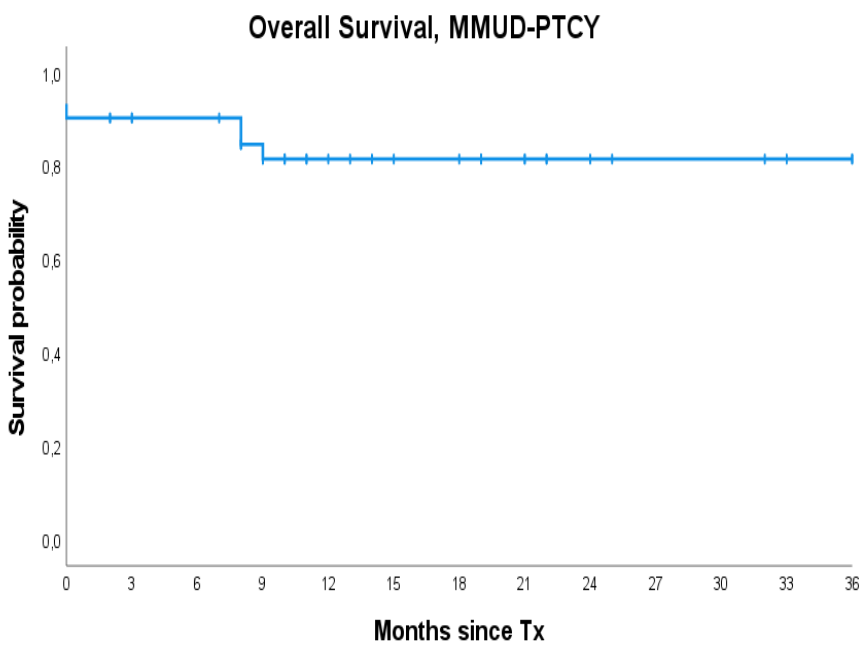
*For 7/8 MMUD and 8/8 MUD recipients, abatacept + CNI/MTX prophylaxis **improved** survival outcomes vs CNI/MTX and CNI/MTX + ATG; **outcomes were similar to PT-Cy–based regimens.***

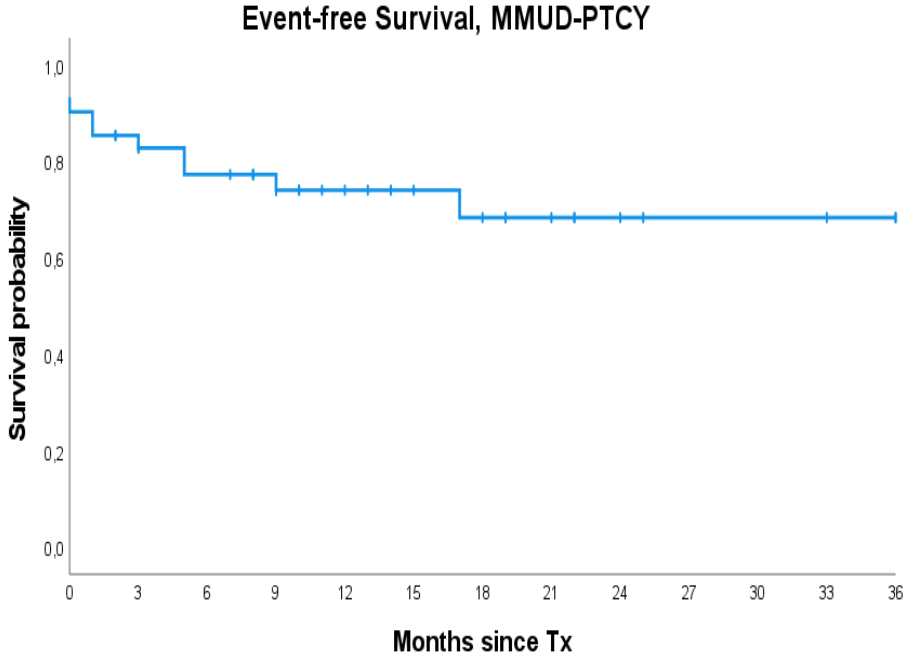
Blood 2024

MMUD PTCy
Genova IRCCS San Martino

N.Pts 41
Median age: 59 (range 19 -75)
Sorror>3: 38% (n. 16)
AML 23 (62%), ALL 5, IM 6, Lymphoma 4, MDS 3
II° allogeneic HSCT: 3
Active disease at transplant: 14 (34%)
PB 100%
Years of transplants: June 2020–December 2024

Median FU: 13 m. (5 – 59)

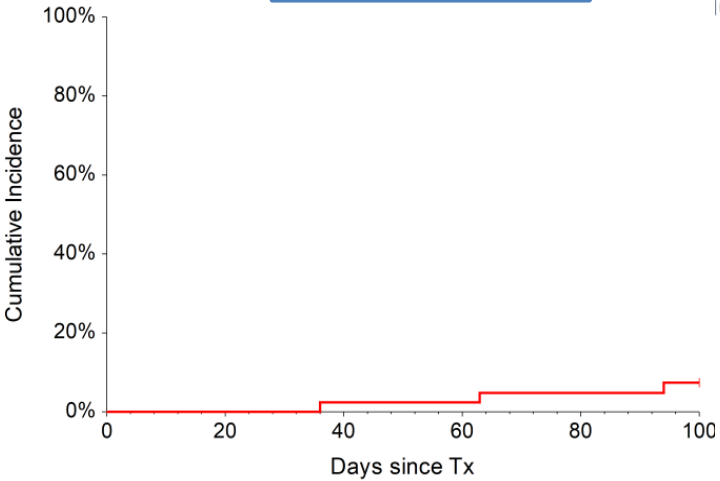




36 month OS (95%CI): 81% (69-93)

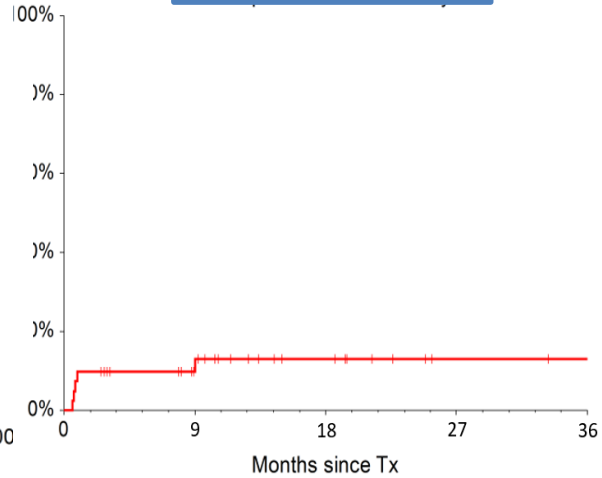
36month EFS (95%CI): 68% (52-84)

aGVHD



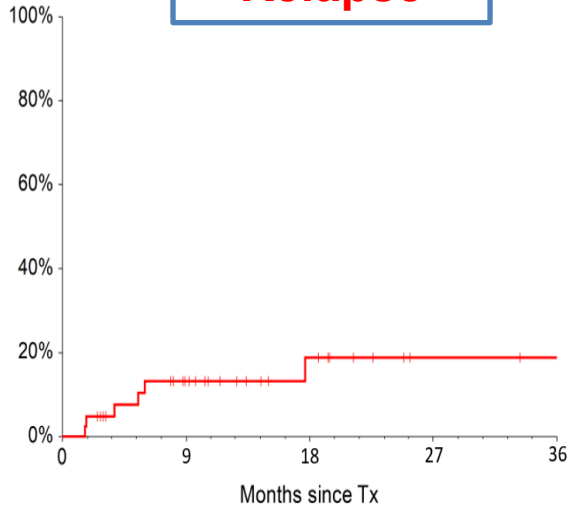
100day aGVHD II - IV (95%CI):
7.3% (2.4-21.7)

NRM

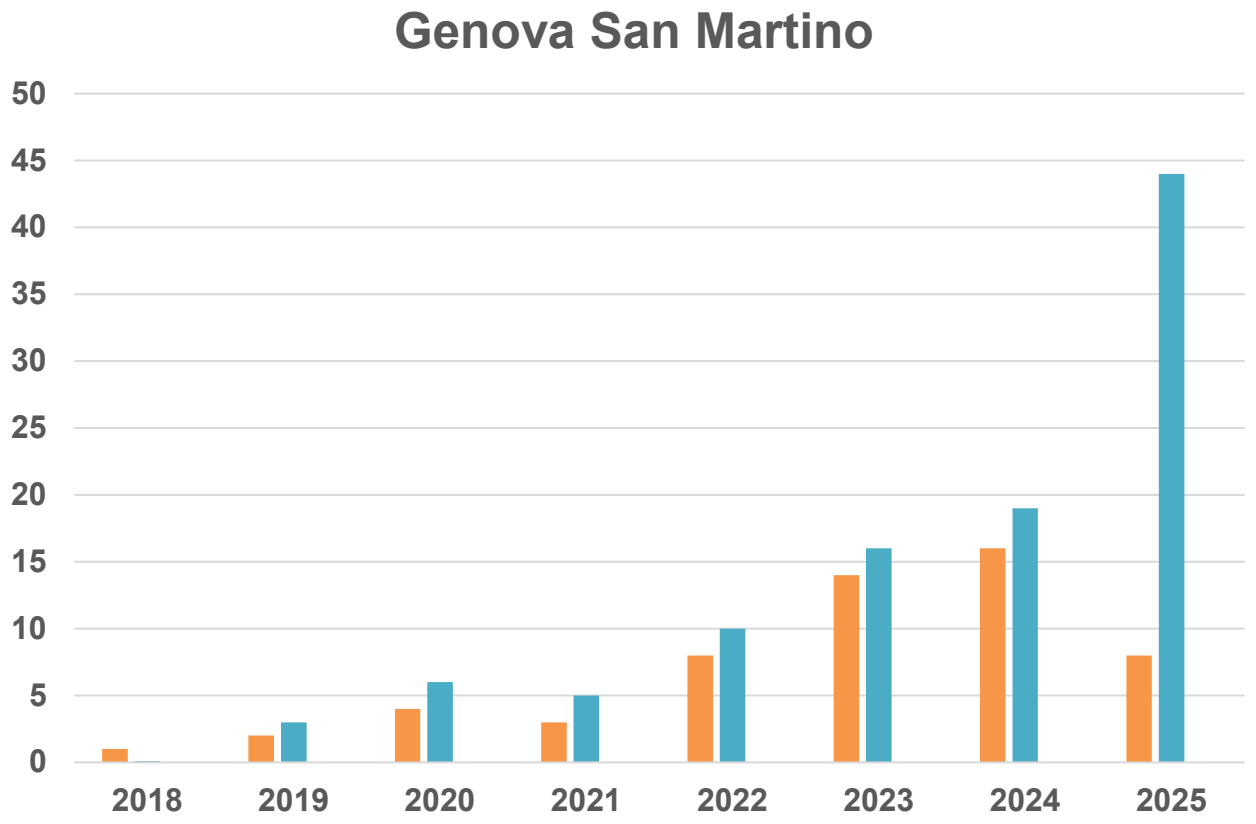


36 m. NRM (95%CI):
12.9% (5.6-29.6)

Relapse



36 m. Relapse (95%CI):
18.8% (8.6-41.1)


Genova San Martino
50
45
40
35
30
25
20
15
10
5
0
2018
2019
2020
2021
2022
2023
2024
2025
MMUD n./y
MMUD %/y

Grazie per l'attenzione!

Programma Trapianti e Terapie Cellulari *"Alberto Marmont"*
IRCCS Ospedale Policlinico San Martino, Genova.

Emanuele Angelucci

Alessandra Bo
Stefania Bregante
Alida Dominietto
Massimiliano Gambella
Anna Ghiso
Carmen di Grazia
Antonella Laudisi
Riccardo Varaldo
I colleghi dell'Ematologia Generale, del CCS e del CTO
Infermieri OSS
Pazienti e familiari