XIX Congresso della Società GITMO

RIUNIONE NAZIONALE GITMO

TORINO, CENTRO CONGRESSI LINGOTTO, 5 - 6 MAGGIO 2025

Selezione del donatore – Non solo HLA

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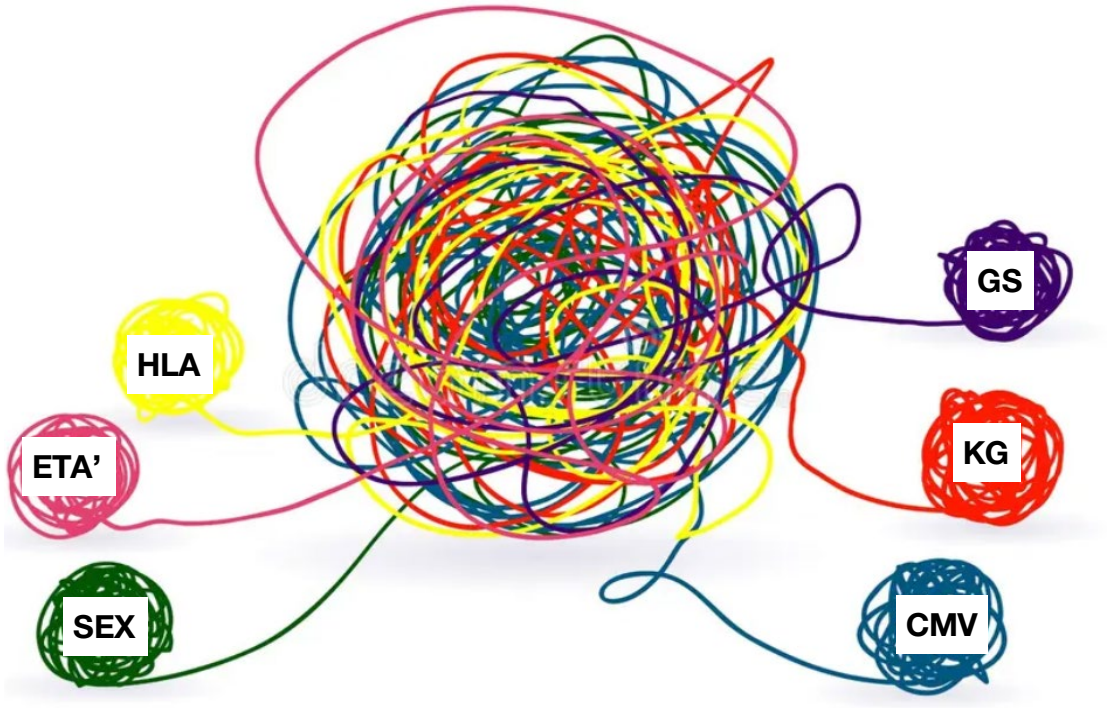
Ematologia e UTMO,

IRCCS Ospedale San Raffaele, Milano

Disclosures

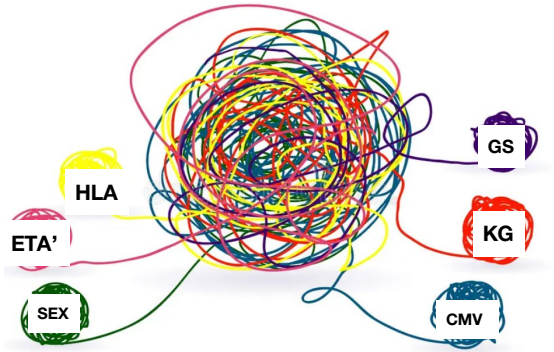
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
MEDAC							x

CRITERI DI SELEZIONE DEL DONATORE DI CSE



CRITERI DI SELEZIONE DEL DONATORE DI CSE

Tempistica del trapianto



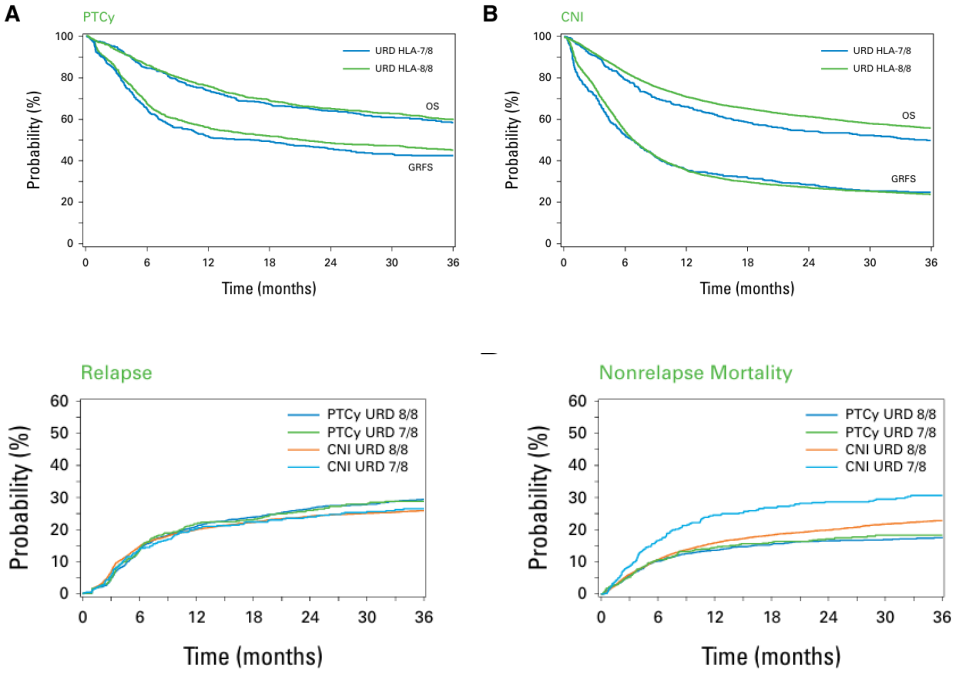
Stato di malattia

Tipologia di malattia

HLA

CRITERI DI SELEZIONE DEL DONATORE DI CSE - HLA

AL or MDS, MUD 8/8 or MMUD 7/8 – PTCy or CNI – CIBMTR



Shaffer BC et al. Blood. 2024, J Clin Oncol 42:3277-3286

CRITERI DI SELEZIONE DEL DONATORE DI CSE - HLA

ALL, CR1 – PTCy (EBMT)

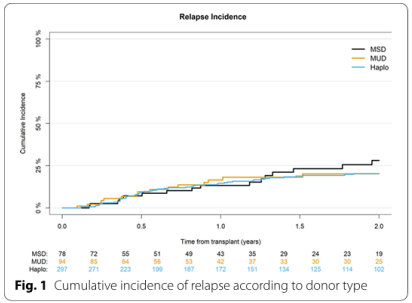


Fig. 1 Cumulative incidence of relapse according to donor type

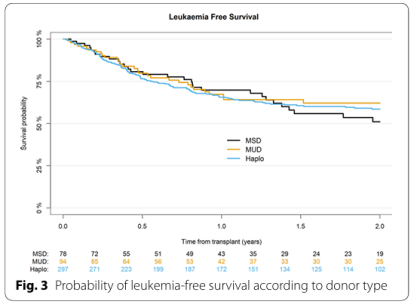


Fig. 3 Probability of leukemia-free survival according to donor type

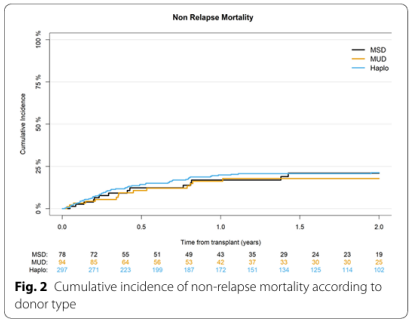


Fig. 2 Cumulative incidence of non-relapse mortality according to donor type

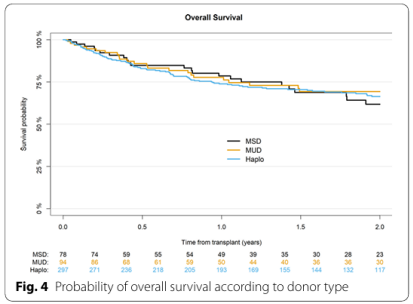


Fig. 4 Probability of overall survival according to donor type

Sanz et al. J Hematol Oncol. 2021

AML, CR1 – PTCy (EBMT)

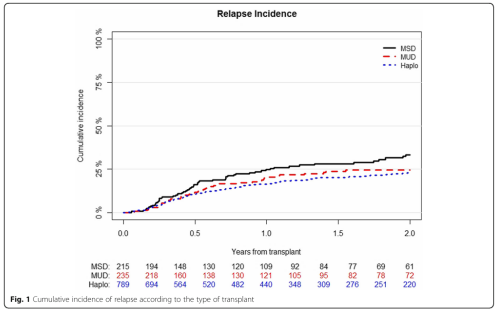


Fig. 1 Cumulative incidence of relapse according to the type of transplant

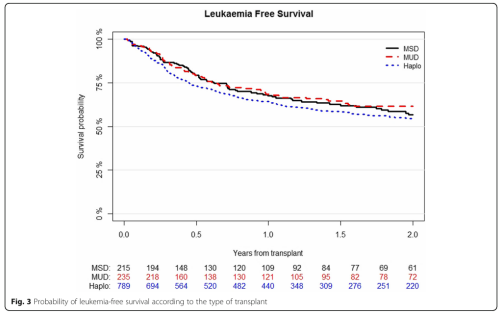


Fig. 3 Probability of leukemia-free survival according to the type of transplant

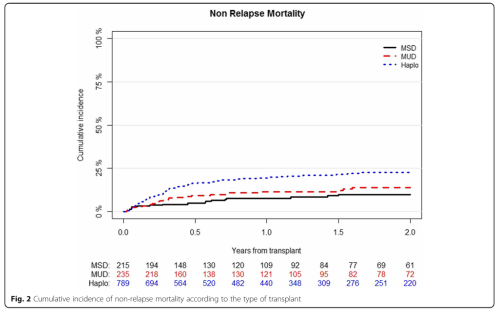


Fig. 2 Cumulative incidence of non-relapse mortality according to the type of transplant

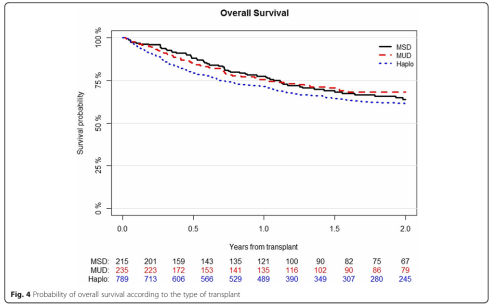
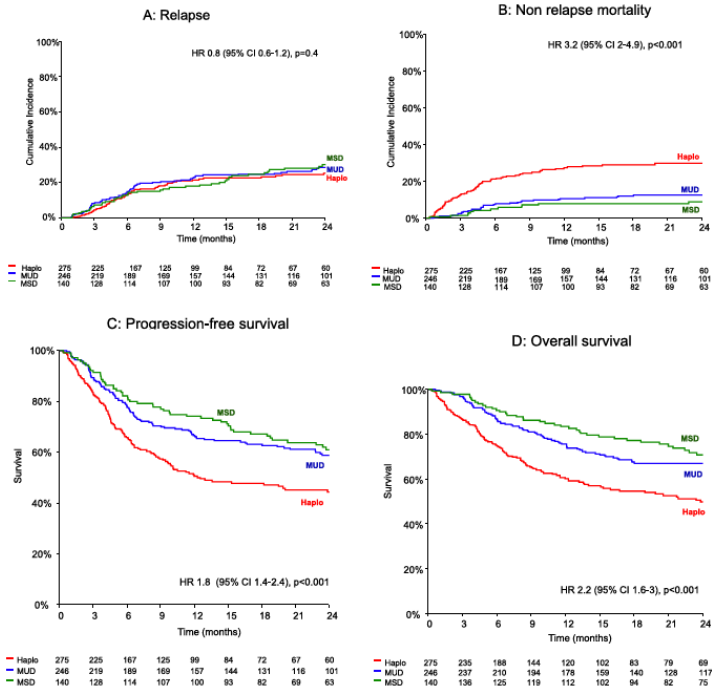


Fig. 4 Probability of overall survival according to the type of transplant

Sanz et al. J Hematol Oncol. 2020

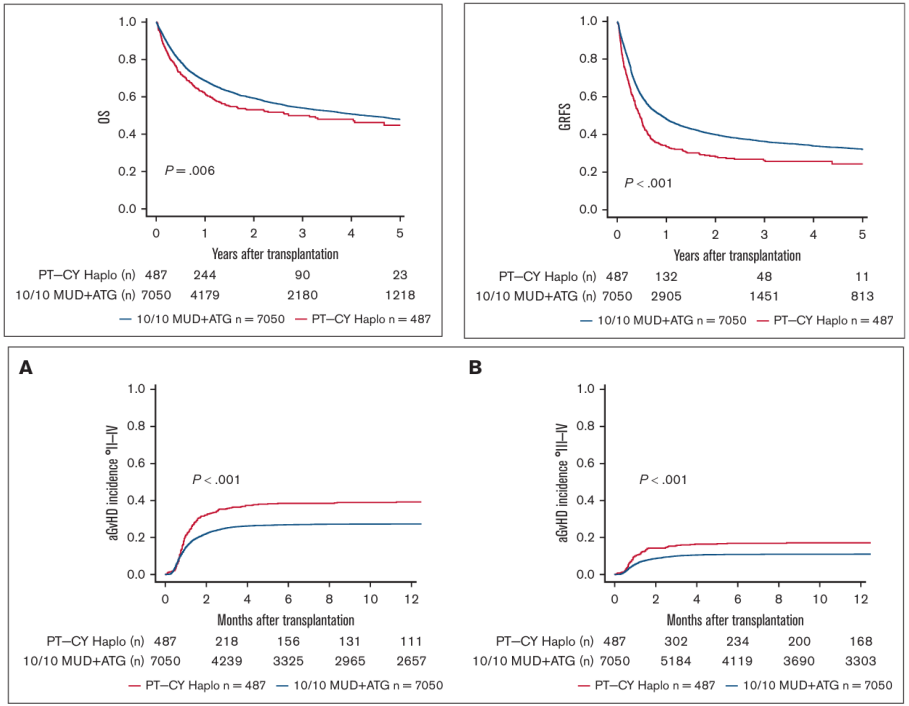
CRITERI DI SELEZIONE DEL DONATORE DI CSE - HLA

All disease – PTCy (single center - USA)



R.S. Mehta et al. Transplantation and Cellular Therapy (2022)

All disease – Haplo PTCy/ MUD ATG (Germany)



A Arslan et al. Blood Advances (2024)

CRITERI DI SELEZIONE DEL DONATORE DI CSE – HLA

IMMUNOPEPTIDOMA

HLA – IMMUNOPEPETIDOMA – DPB1

A

DPB1* alleles	TCE-3 group	TCE core group	Immunogenicity
09:01 10:01 17:01*	1	1	
03:01 14:01 45:01*	2	2	
Other	3	Non-Core	
02:01 04:01 04:02 23:01		Core	

* TCE group assignment includes other less common alleles detemined based on their FD_{allele} scores, using the algorithm described by Crivello et al. (reference #14).

B

Recipient DPB1 Group on Unshared Haplotype

Donor DPB1 Group on Unshared Haplotype	TCE-3 →	1	2	3	
↓	TCE-core	1	2	NC	C
1	1	PMM	NPMM	NPMM	NPMM
2	2	NPMM	PMM	NPMM	NPMM
3	NC	NPMM	NPMM	C-NPMM-Bidirectional	C-NPMM-HVG
	C	NPMM	NPMM	C-NPMM-GVH	C-PMM

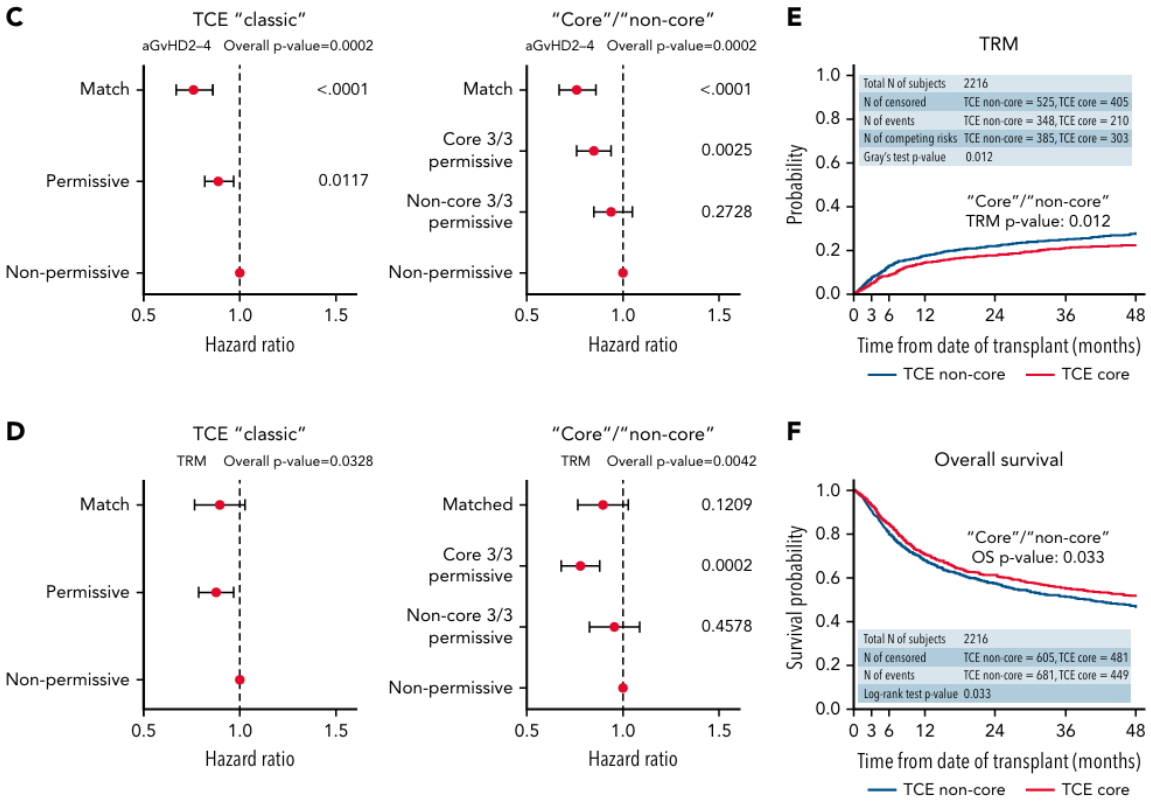
= indicates a NPMM by conventional TCE-3 model = indicates a PMM by conventional TCE-3 but NPMM by TCE-Core

C, core; NC, non-core; HVG, host-versus-graft direction only; GVH, graft-versus-host direction only; PMM, permissive mismatch; NPMM, non-permissive mismatch.

Figure 1. TCE-Core model. (A) TCE-3 versus TCE-Core immunogenicity groups. (B) TCE-3 versus TCE-Core permissiveness categories.

Fuchs EJ, et al. Blood. 2022 Mar. 139(10):1452-1468

HLA – IMMUNOPEPETIDOMA – DPB1



E. Arrieta-Bolanos et al. Blood (2022)

HLA – IMMUNOPEPETIDOMA – DPB1

S.R. Solomon et al. / Transplantation and Cellular Therapy 30 (2024) 608.e1–608.e10

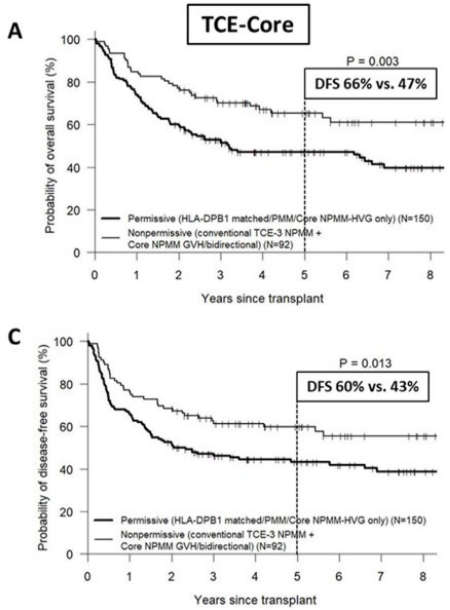


Figure 4. Survival outcomes based on HLA-DPB1 NPMM by TCE-Core versus TCE-3 algorithms. (A) TCE-Core OS; (B) TCE-3 OS; (C) TCE-Core DFS; (D) TCE-3 DFS.

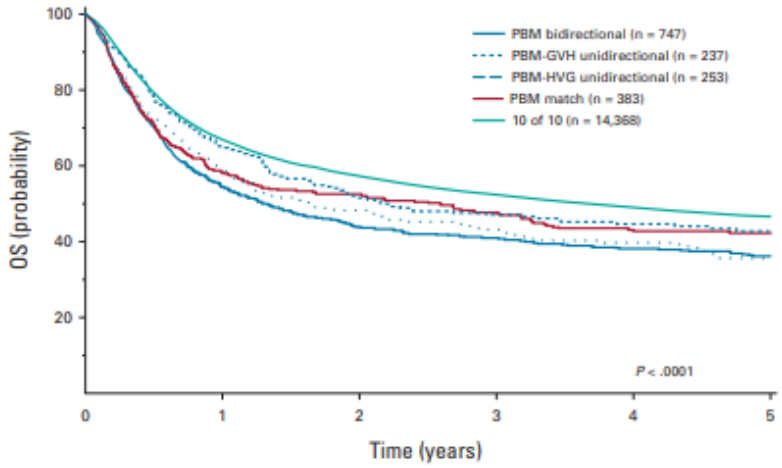
HLA – IMMUNOPEPETIDOMA – Peptide Binding Motif (mm classe I)

Example, No.	PBM Group			Immunopeptidome	PBM Status	Direction
	Shared	Donor	Recipient			
1	PBM-x	PBM-x	PBM-x	Low divergence	Match	None
2	PBM-x	PBM-y	PBM-y			
3	PBM-x	PBM-z	PBM-z			
4	PBM-x	PBM-y	PBM-z	High divergence	Mismatch	Bidirectional
5	PBM-x	PBM-x	PBM-y			Unidirectional GVH
6	PBM-x	PBM-y	PBM-x			Unidirectional HVG

Crivello P et al. J Clin Oncol. 2023 May 1;41(13):2416-2427

HLA – IMMUNOPEPETIDOMA - Peptide Binding Motif

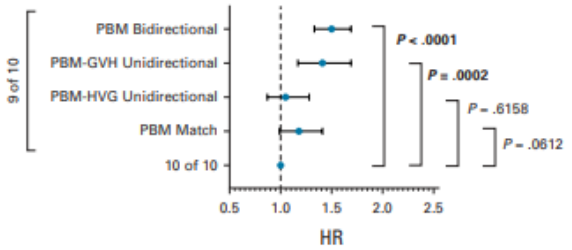
A



No. at risk:

PBM bidirectional	747	386	273	224	165	126
PBM-GVH unidirectional	237	134	96	72	57	42
PBM-HVG unidirectional	253	158	118	95	80	60
PBM match	383	211	171	135	98	82
10 of 10	14,368	9,419	6,949	5,299	4,013	2,919

B



Crivello P et al. J Clin Oncol. 2023 May 1;41(13):2416-2427

CRITERI DI SELEZIONE DEL DONATORE DI CSE – combining HLA

All disease

		PTCy No			PTCy Yes			
End Point	Subgroups	No. (events)	HR (99% CI)	*P*	No. (events)	HR (99% CI)	*P*	Interaction *P*[a]
OS	10 of 10	11,943 (4,867)	1		898 (276)	1		.43
	9 of 10	2,924 (1,393)	1.22 (1.13 to 1.33)	<.001	511 (210)	1.32 (1.04 to 1.68)	.003	
	10 of 10	11,943 (4,867)	1		898 (276)	1		.42
	Class I mM	2,117 (1,050)	1.29 (1.18 to 1.41)	<.001	408 (168)	1.32 (1.02 to 1.71)	.006	
	Class II mM	807 (343)	1.05 (0.91 to 1.21)	.39	103 (42)	1.32 (0.86 to 2.04)	.09	
	10 of 10	11,943 (4,867)	1		898 (276)	1		.69
	Low-res[b] match	515 (230)	1.1 (0.92 to 1.32)	.15	64 (27)	1.31 (0.77 to 2.2)	.19	
	Low-res[b] mM	1,602 (820)	1.36 (1.23 to 1.51)	<.001	344 (141)	1.33 (1.01 to 1.75)	.007	
	10 of 10	11,943 (4,867)	1		898 (276)	1		.75
	PBM-GVH[c] match	648 (310)	1.14 (0.98 to 1.33)	.03	128 (52)	1.28 (0.86 to 1.9)	.11	
	PBM-GVH[c] mM	1,153 (586)	1.42 (1.26 to 1.59)	<.001	214 (93)	1.5 (1.09 to 2.06)	<.001	
GRFS	10 of 10	11,147 (6,472)	1		845 (407)	1		.72
	9 of 10	2,645 (1,662)	1.16 (1.08 to 1.25)	<.001	486 (280)	1.2 (0.97 to 1.47)	.02	
	10 of 10	11,147 (6,472)	1		845 (407)	1		.74
	Class I mM	1,912 (1,240)	1.24 (1.14 to 1.34)	<.001	389 (226)	1.22 (0.98 to 1.52)	.02	
	Class II mM	733 (422)	0.99 (0.87 to 1.13)	.79	97 (54)	1.1 (0.76 to 1.61)	.50	
	10 of 10	11,147 (6,472)	1		845 (407)	1		.36
	Low-res[b] match	469 (287)	1.09 (0.93 to 1.28)	.14	59 (28)	0.82 (0.5 to 1.36)	.32	
	Low-res[b] mM	1,443 (953)	1.29 (1.18 to 1.42)	<.001	330 (198)	1.31 (1.04 to 1.65)	.002	
	10 of 10	11,147 (6,472)	1		845 (407)	1		.90
	PBM-GVH[c] match	589 (381)	1.15 (1 to 1.32)	.008	122 (69)	1.16 (0.83 to 1.63)	.26	
	PBM-GVH[c] mM	1,032 (676)	1.32 (1.18 to 1.47)	<.001	202 (123)	1.39 (1.06 to 1.82)	.002	

E Arrieta-Bolanos et al. J Clin Oncol. 2024 Aug 42:3287-3299

ETA’

CRITERI DI SELEZIONE DEL DONATORE DI CSE – ETA'

AML CR1/2, MUD 10/10 or MMUD 9/10 – Donor age cut-off 30y PTCy – EBMT

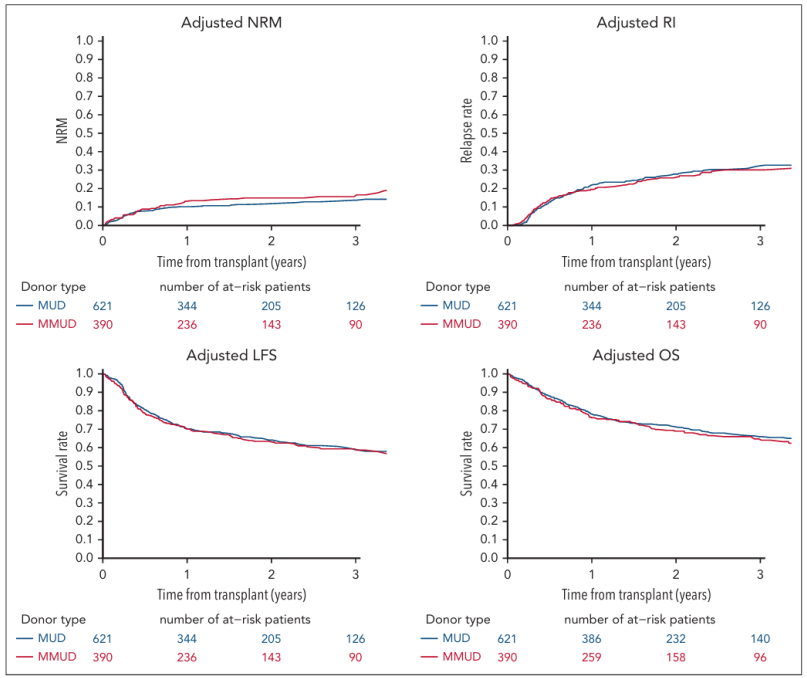


Figure 1. Adjusted cumulative incidence of NRM and relapse, and probability of LFS and OS for MUDs or MMUDs. RI, relapse.

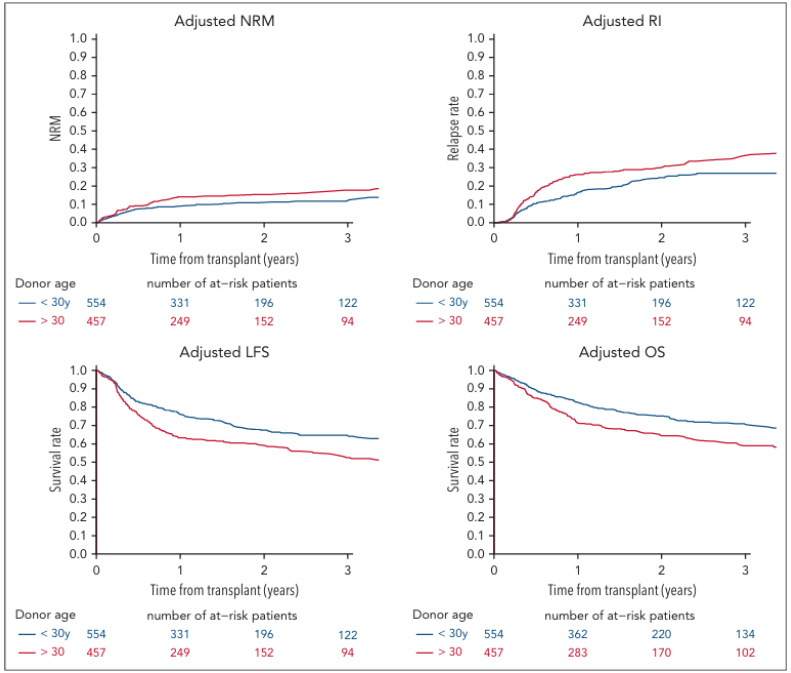
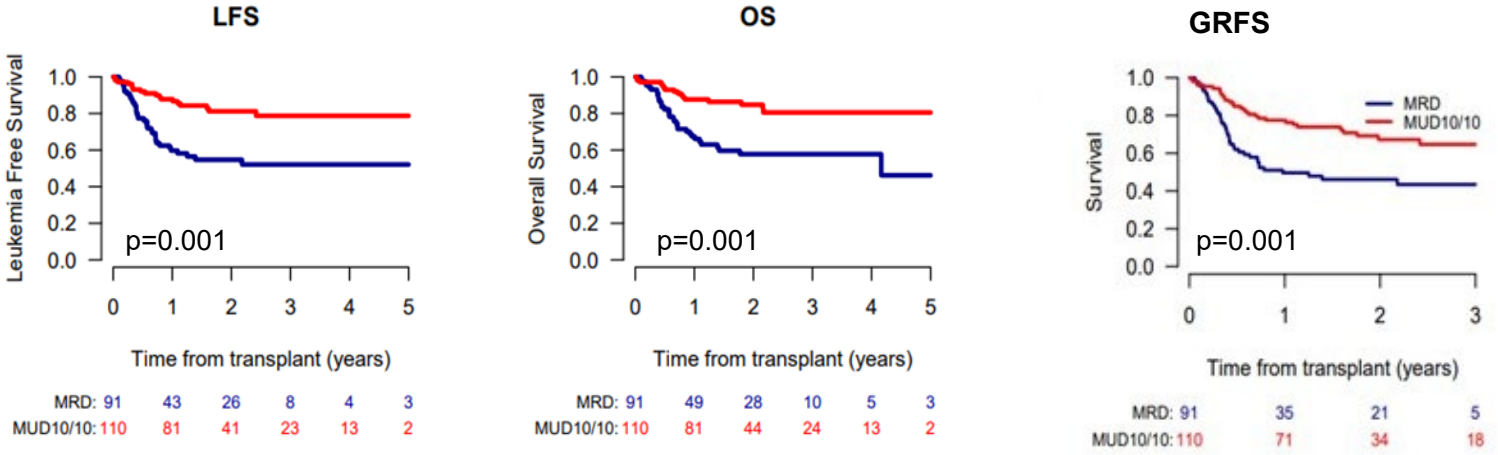


Figure 2. Adjusted cumulative incidence of NRM and relapse, and probability of LFS and OS according to donor age. RI, relapse.

Sanz J, et al. Blood. 2024, Vol 143

CRITERI DI SELEZIONE DEL DONATORE DI CSE – ETA'

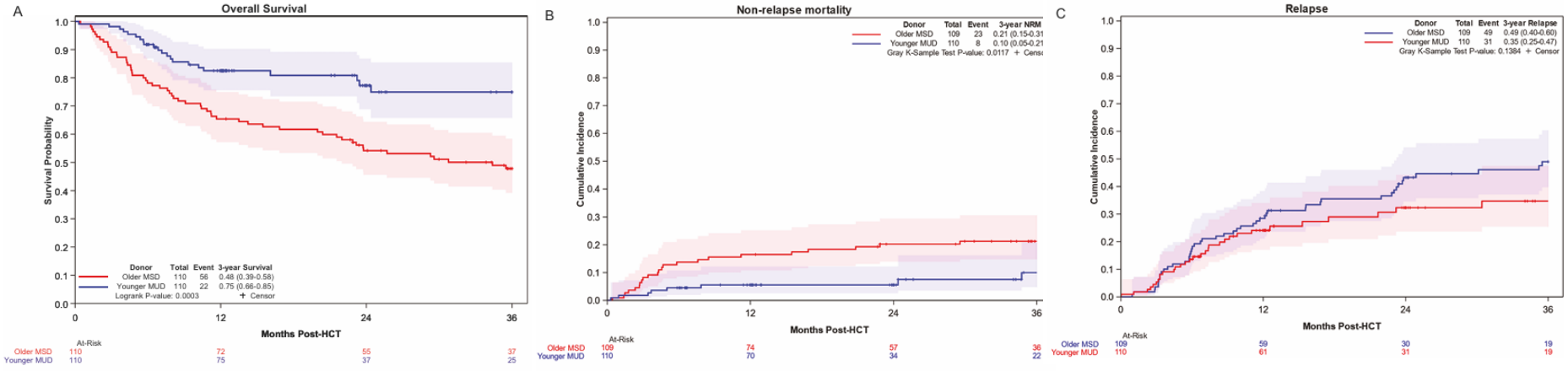
AML CR1, age 50, MUD <40y or MSD > 50y, **TCI Int-High**, PTCy – EBMT



Piemontese S, et al. Leukemia. 2024, 38: 2016-2022

CRITERI DI SELEZIONE DEL DONATORE DI CSE – ETA'

AML or ALL, MUD ≤ 35y or MSD ≥ 45Y, PTCy – CIBMTR

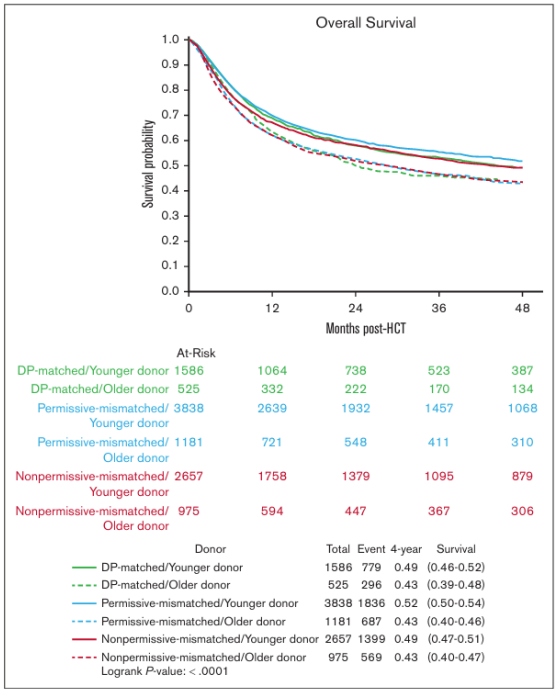


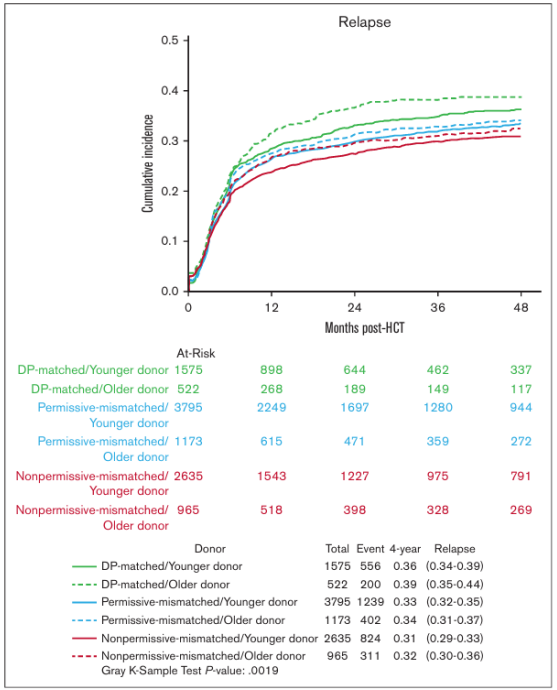
Ramdial J, et al. Leukemia. 2024, 38: 1432-1434

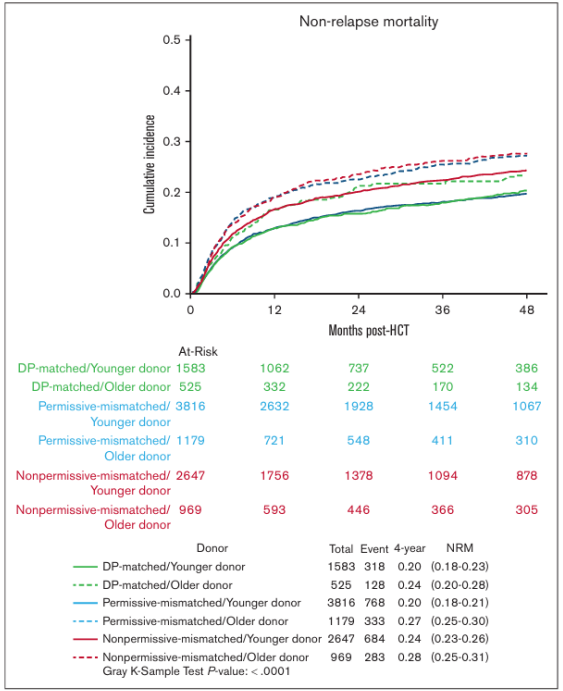
HLA-ETA’

CRITERI DI SELEZIONE DEL DONATORE DI CSE – ETA'/DPB1

AML or ALL, MUD ≤ 35y, DP TCE 3, **PTCy unknown** – CIBMTR



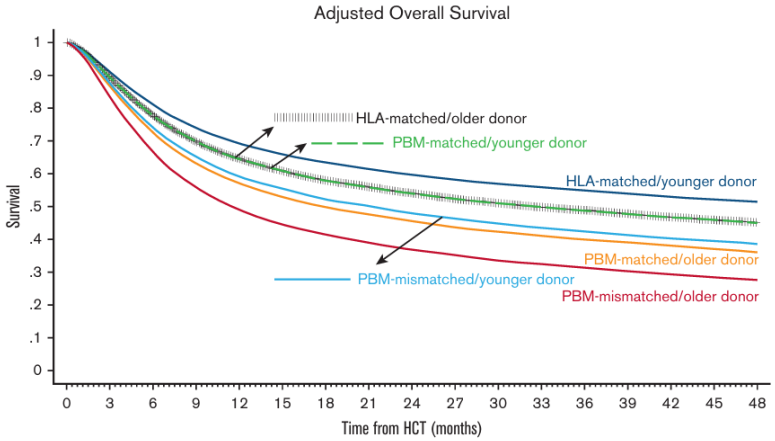




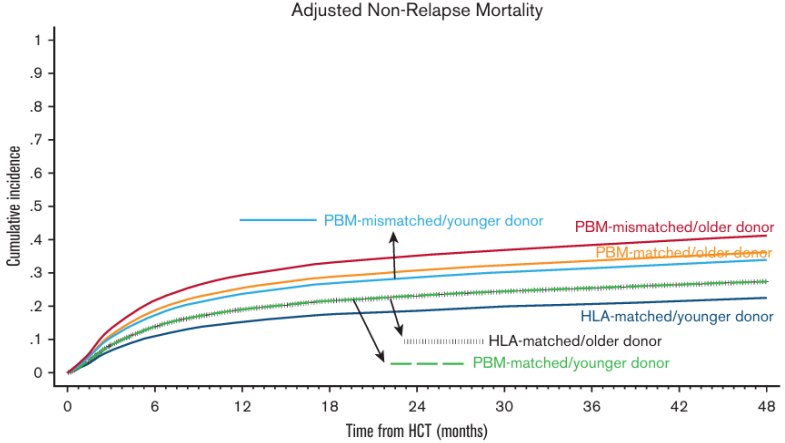
Mehta RS, et al. Blood Adv. Oct 2024, Vol 8

CRITERI DI SELEZIONE DEL DONATORE DI CSE – ETA'/PBM

AML or ALL, MUD ≤ 35y, PBM m/mm, **PTCy excluded** – CIBMTR

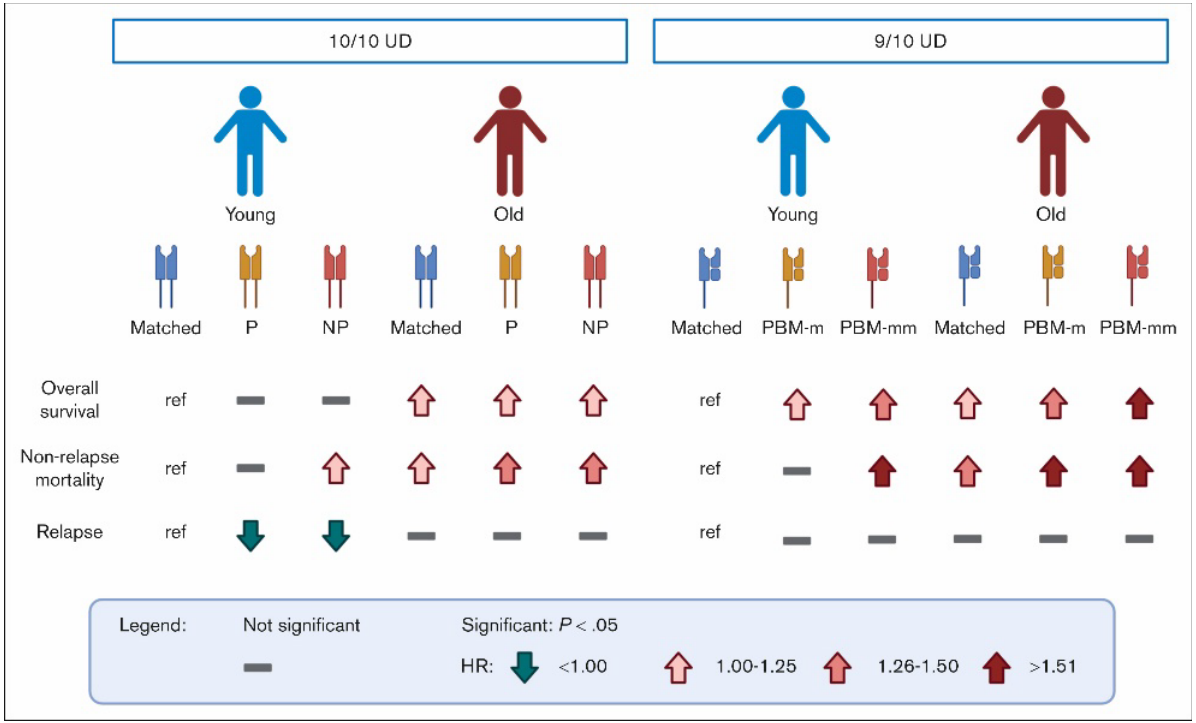


Number at risk



Mehta RS, et al. Blood Adv. May 2024, Vol 8

"What makes a good Samaritan: age, HLA matching, or both?"



Crivello P, Blood Adv, 2024

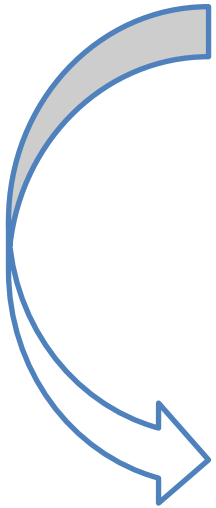
CRITERI DI SELEZIONE DEL DONATORE DI CSE - Conclusioni

- **HLA** ed **ETA'** sono le caratteristiche principali da prendere in considerazione
- Il **donatore full matched giovane** rappresenta il riferimento (a prescindere dalla parentela)
- La **giovane età del donatore** (30? 35? 40?) può mitigare l'effetto negativo del mismatch
- La **compatibilità/permissività a livello del DPB1** e **PBM** possono ulteriormente migliorare la selezione dei donatore matched e mismatched **ma tali algoritmi devono essere validati nel contesto della PTCy**

RINGRAZIAMENTI

MEMBRI DELLA COMMISSIONE GITMO-ALOGENICO RISTRETTA

- Adulto aplo:	Genova (GE01, CIC 274)	Dott.ssa A.M. Raiola
	Milano (MI06, CIC 354)	Dott.ssa S. Bramanti
	Perugia (PG01, CIC 794)	Dott.ssa A. Carotti
- Pediatrico aplo:	Roma (CV01, CIC 796)	Dott.ssa D. Pagliara
- Adulto MUD:	Bergamo (BG01, CIC 658)	Dott.ssa A. Grassi
	Milano (MI07, CIC 813)	Dott.ssa S. Piemontese
	Roma (RM03, CIC 307)	Dott.ssa P. Chiusolo
- Pediatrico MUD:	Torino (TO02, CIC 305)	Dott. F. Saglio
Rappresentante GITMO TMO allogenico:		Dott. M. Algeri
Rappresentante IBMDR:		Dott.ssa S. Pollichieni



Dott.ssa Ilaria Capolsini

RINGRAZIAMENTI

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- Pediatrico MUD:	Torino (TO02, CIC 305)	Dott. F. Saglio
Rappresentante GITMO TMO allogenico:		Dott. M. Algeri
Rappresentante IBMDR:		Dott.ssa S. Pollichieni

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Presidente GITMO – **Massimo Martino**