ACCADEMIA di FORMAZIONE

SIMTI

Attualità nella gestione delle terapie cellulari avanzate

La selezione del donatore di CSE: aspetti non-immunogenetici

Dr.S.Bregante

UO Ematologia e Terapie Cellulari-SS Programma Trapianti e Terapie Cellulari " Alberto Marmont"
IRCCS Azienda Ospedaliera Metropolitana (IRCCS AOM)

Roma, 25 marzo 2026

La sottoscritta, in qualità di Relatrice
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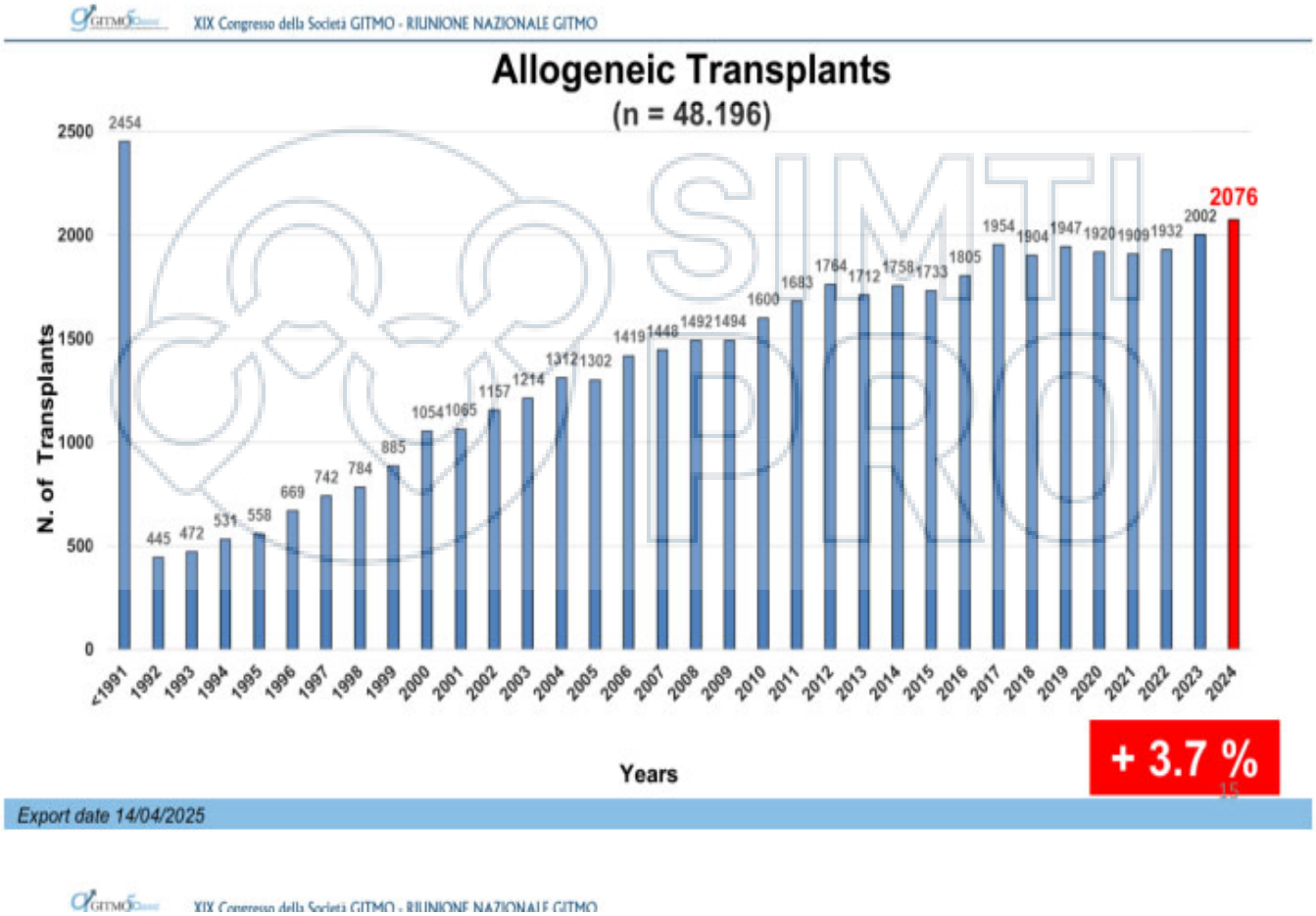
Gruppo Italiano per il Trapianto di Midollo Osseo, cellule staminali emopoietiche e terapia cellulare

Riunione Nazionale GITMO, 05 - 06 maggio 2025

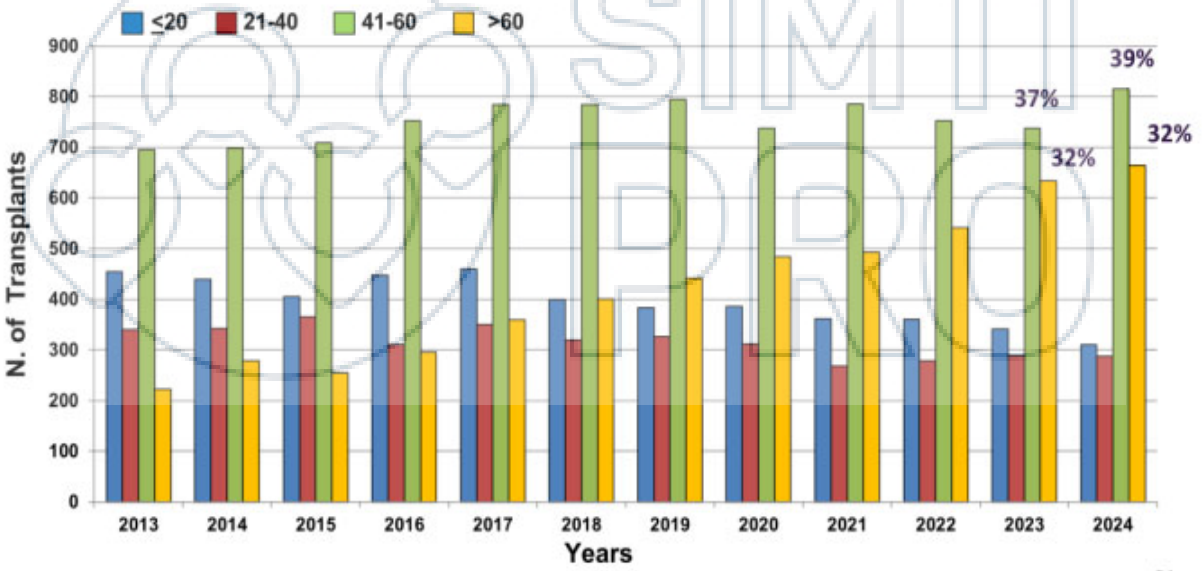


XIX Congresso della Società GITMO - RIUNIONE NAZIONALE GITMO

Gruppo Italiano per il Trapianto di Midollo Osseo, cellule staminali emopoietiche e terapia cellulare

Riunione Nazionale GITMO, 05 - 06 maggio 2025

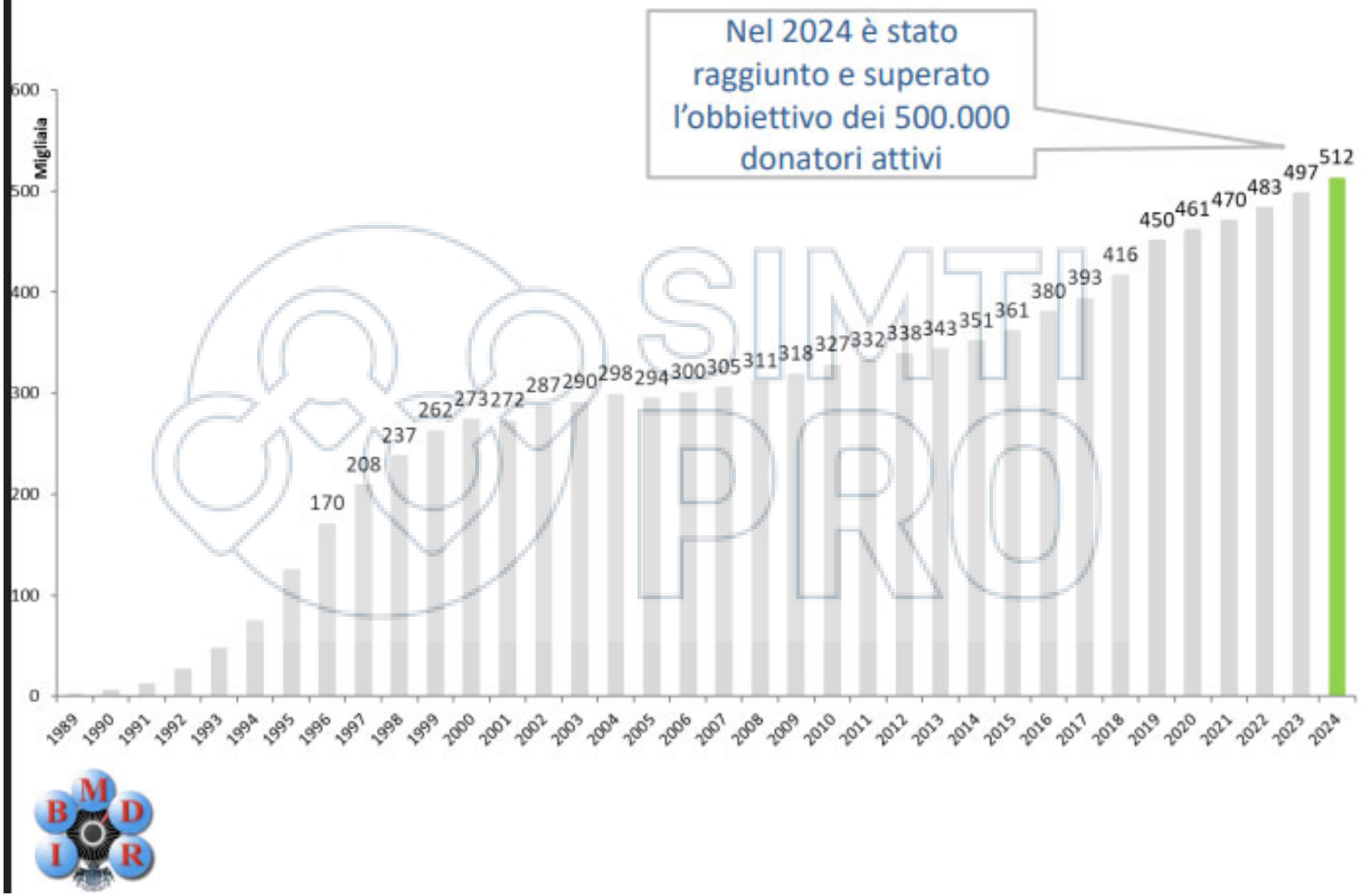
2024 - Allogeneic Transplants: Patient age at transplantation



Export date 14/04/2025

XIX Congresso della Società GITMO - RIUNIONE NAZIONALE GITMO

Il Registro


Nel 2024 è stato raggiunto e superato l'obbiettivo dei 500.000 donatori attivi
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262
273
272
287
290
298
294
300
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327
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351
361
380
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RAZIONALE

- Maggior numero di DR →aumenta probabilità individuare DR HLA identico →Necessaria attenta valutazione criteri non immunologici

- Ottimizzare attecchimento
- Ridurre mortalità non correlata a recidiva (NRM)
- Ridurre rischio GvHD acuta e cronica
- Massimizzare effetto GVL
- Migliorare gestione trasfusionale

EBMT Handbook 2024

-

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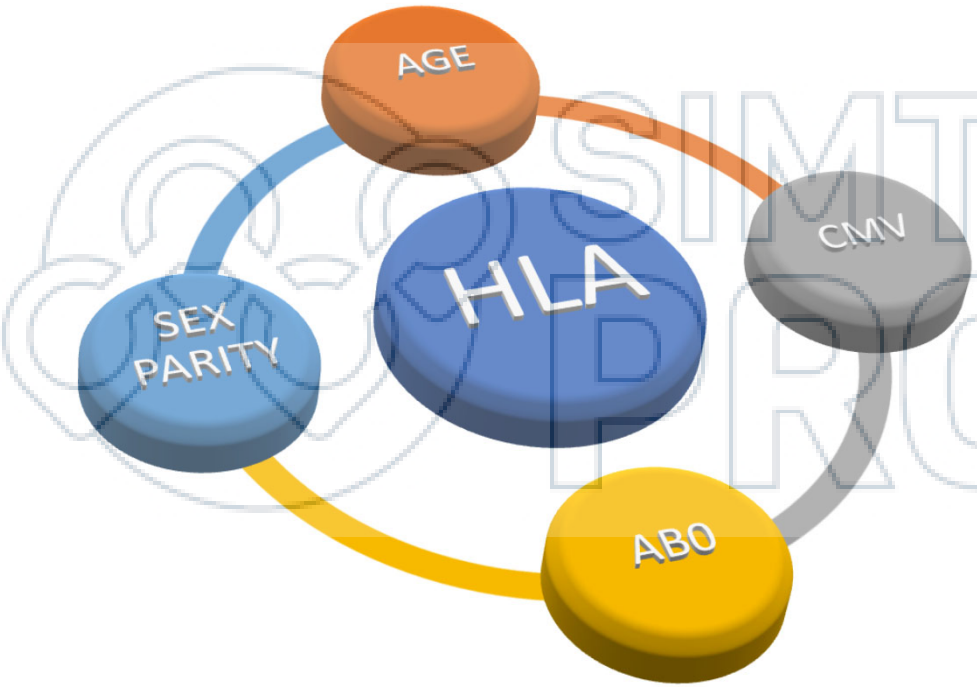
AGE
CMV
HLA
SEX
PARITY
ABO

ETA' DEL DONATORE

A
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E

- Fattore prognostico indipendente
- Donatore < 35 aa associato a :
  - ↓ GVHD cronica
  - ↓ NRM
  - ↑ Overall Survival

A
G
E

TRANSPLANTATION

The effect of donor characteristics on survival after unrelated donor transplantation for hematologic malignancy

Craig Kollman,[1] Stephen R. Spellman,[2] Mei-Jie Zhang,[3,4] Anna Hassebroek,[2] Claudio Anasetti,[5] Joseph H. Antin,[6] Richard E. Champlin,[7] Dennis L. Confer,[2] John F. DiPersio,[8] Marcelo Fernandez-Viña,[9] Robert J. Hartzman,[10] Mary M. Horowitz,[3] Carolyn K. Hurley,[11] Chatchada Karanes,[12] Martin Maiers,[13] Carlheinz R. Mueller,[14] Miguel-Angel Perales,[15] Michelle Setterholm,[13] Ann E. Woolfrey,[16] Neng Yu,[17] and Mary Eapen[3,18]

[1]Jaeb Center for Health Research, Tampa, FL; [2]Center for International Blood and Marrow Transplant Research, National Marrow Donor Program/Be The Match, Minneapolis, MN; [3]Center for International Blood and Marrow Transplant Research and [4]Division of Biostatistics, Institute for Health and Society, Medical College of Wisconsin, Milwaukee, WI; [5]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL; [6]Center for Hematologic Oncology, Dana-Farber Cancer Institute, Boston, MA; [7]Department of Stem Cell Transplantation and Cellular Therapy, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX; [8]Barnes Jewish Hospital, St. Louis, MO; [9]Stanford Hospital & Clinics, Stanford, CA; [10]C.W. Bill Young Marrow Donor Recruitment and Research Program, Department of Defense Marrow Donor Program, Bone Marrow Research Directorate, Naval Medical Research Center, Department of the Navy, Washington, DC; [11]Georgetown University, Washington, DC; [12]City of Hope National Medical Center, Duarte, CA; [13]National Marrow Donor Program/Be The Match, Minneapolis, MN; [14]ZKRD-Zentrales Knochenmarkspender-Register Deutschland, Ulm, Germany; [15]Memorial Sloan-Kettering Cancer Center, New York, NY; [16]Fred Hutchinson Cancer Research Center, Seattle, WA; [17]American Red Cross Blood Services East Division, Dedham, MA; and [18]Department of Medicine, Medical College of Wisconsin, Milwaukee, WI

Key Points

- Donor age and donor-recipient HLA match predict survival after hematopoietic cell transplantation.

There are >24 million registered adult donors, and the numbers of unrelated donor transplantations are increasing. The optimal strategy for prioritizing among comparably HLA-matched potential donors has not been established. Therefore, the objective of the current analyses was to study the association between donor characteristics (age, sex, parity, cytomegalovirus serostatus, HLA match, and blood group ABO match) and survival after transplantation for hematologic malignancy. The association of donor characteristics with transplantation outcomes was examined using either logistic or Cox regression models, adjusting for patient disease and transplantation characteristics associated with outcomes in 2 independent datasets: 1988 to 2006 (N = 6349; training cohort) and 2007 to 2011 (N = 4690; validation cohort). All donor-recipient pairs had allele-level HLA typing at HLA-A, -B, -C, and -DRB1, which is the current standard for selecting donors. Adjusting for patient disease and transplantation characteristics, survival was better after transplantation of grafts from young donors (aged 18-32 years) who were HLA matched to recipients ($P < .001$). These findings were validated for transplantations that occurred between 2007 and 2011. For every 10-year increment in donor age, there is a 5.5% increase in the hazard ratio for overall mortality. Increasing HLA disparity was also associated with worsening survival. Donor age and donor-recipient HLA match are important when selecting adult unrelated donors. Other donor characteristics such as sex, parity, and cytomegalovirus serostatus were not associated with survival. The effect of ABO matching on survival is modest and must be studied further before definitive recommendations can be offered. (*Blood.* 2016;127(2):260-267)

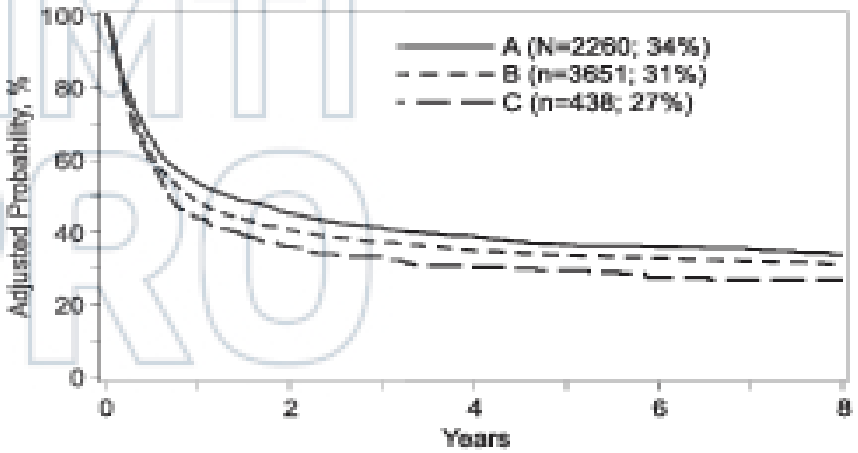


Figure 1. Overall survival. The risk-adjusted 5-year probabilities of overall survival were 36% (95% CI, 34-38), 33% (95% CI, 32-35), and 29% (95% CI, 25-33) for donors aged (A) 18 to 32, (B) 33 to 50, and (C) >50 years, respectively. The corresponding 8-year probabilities of survival were 34% (95% CI, 31-36), 31% (95% CI, 29-32), and 27% (95% CI, 22-31).

A
G
E

REGULAR ARTICLE

blood advances

Relationship of donor age and relationship to outcomes of haploi transplantation with posttransplant cyclophosphamide

Amy E. DeZern,[1,*] Clio Franklin,[1,*] Hua-Ling Tsai,[2] Phil Hollingsworth Imus,[1] Kenneth R. Cooke,[1] Ravi Varadhan,[2] and Rich

[1]Department of Oncology and [2]Department of Oncology Biostatistics, Sidney Kimmel Cancer Center, Baltimore, MD

Leukemia www.nature.com/leu

ARTICLE OPEN

Check for updates

STEM CELL TRANSPLANTATION

Young unrelated donors confer a survival advantage for patients with myeloid malignancies compared to older siblings

Johannes Schetelig[1,2,15✉], Henning Baldauf[2,15], Carina Rave[2], Gesine Bug[3], Lutz P. Müller[4], Eva Maria Wagner-Drouet[5], Francis Ayuketang Ayuk[6], Wolfgang Bethge[7], Matthias Stelljes[8], Thomas Schroeder[9], Friedrich Stölzel[10], Edgar Jost[11], Christoph Schmid[12], Desiree Kunadt[1], Katja Sockel[1], Katharina Egger-Heidrich[1], Jan Moritz Middeke[1], Daniel Fürst[13], Daniel Schefzyk[2], Jürgen Sauter[2], Alexander H. Schmidt[2], Katharina Fleischhauer[14], Martin Bornhäuser[1], on behalf of the German Cooperative Transplant Study Group* and Deutsches Register für hämatopoetische Stammzelltransplantation und Zelltherapie (DRST)*

Transplant Cell Ther. 2023 September ; 29(9): 578.e1–578.e9. doi:10.1016/j.jtct.2023.06.020.

Impact of Donor Age on Allogeneic Hematopoietic Cell Transplantation Outcomes in Older Adults with Acute Myeloid Leukemia

Muhammad Bilal Abid, MD[†,1], Noel Estrada-Merly, MS[2], Mei-Jie Zhang, PhD[3,2], Karen Chen, MS[2], David Allan, MD[4], Christopher Bredeson, MD[4], Mitchell Sabloff, MD[5], Guru Subramanian Guru Murthy, MD[6], Talha Badar, MD[7], Shahrukh Hashmi, MD[8,9,10], Mahmoud Aljurf, MD[11], Mark R. Litzow, MD[12], Partow Kebriaei, MD[13], Christopher S. Hourigan, MD[14], Wael Saber, MD[2]

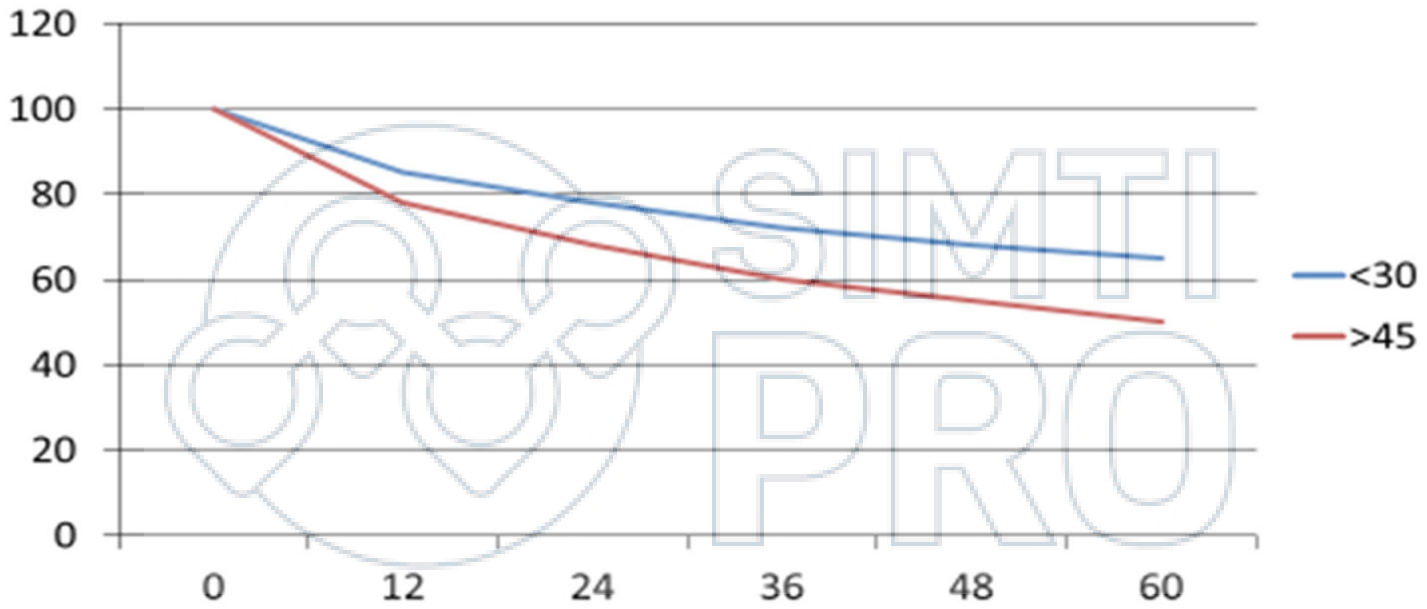
Biol Blood Marrow Transplant. 2018 May ; 24(5): 1049–1056. doi:10.1016/j.bbmt.2018.02.006.

Development of an Unrelated Donor Selection Score Predictive of Survival after HCT: Donor Age Matters Most

Bronwen E. Shaw, MBChB, MRCP, PHD, FRCPath[1], Brent R. Logan, PhD[1], Stephen R. Spellman, MBS[2], Steven GE Marsh, BSc, PhD, ARCS[3], James Robinson, BSc, MSc[3], Joseph Pidala, MD, PhD[4], Carolyn Hurley, PhD[5], Juliet Barker, MBBS[6], Martin Maiers, MS[2], Jason Dehn, MPH[7], Hailin Wang, MPH[1], Mike Haagenson, MS[2], David Porter, MD[8], Effie W. Petersdorf, MD[9], Ann Woolfrey, MD[9], Mary M. Horowitz, MD, MS[1], Michael Verneris, MD[10], Katharine C. Hsu, MD, PhD[6], Katharina Fleischhauer, MD[11], and Stephanie J. Lee, MD, MPH[1,9]

OS IN BASE ETA' DONOR

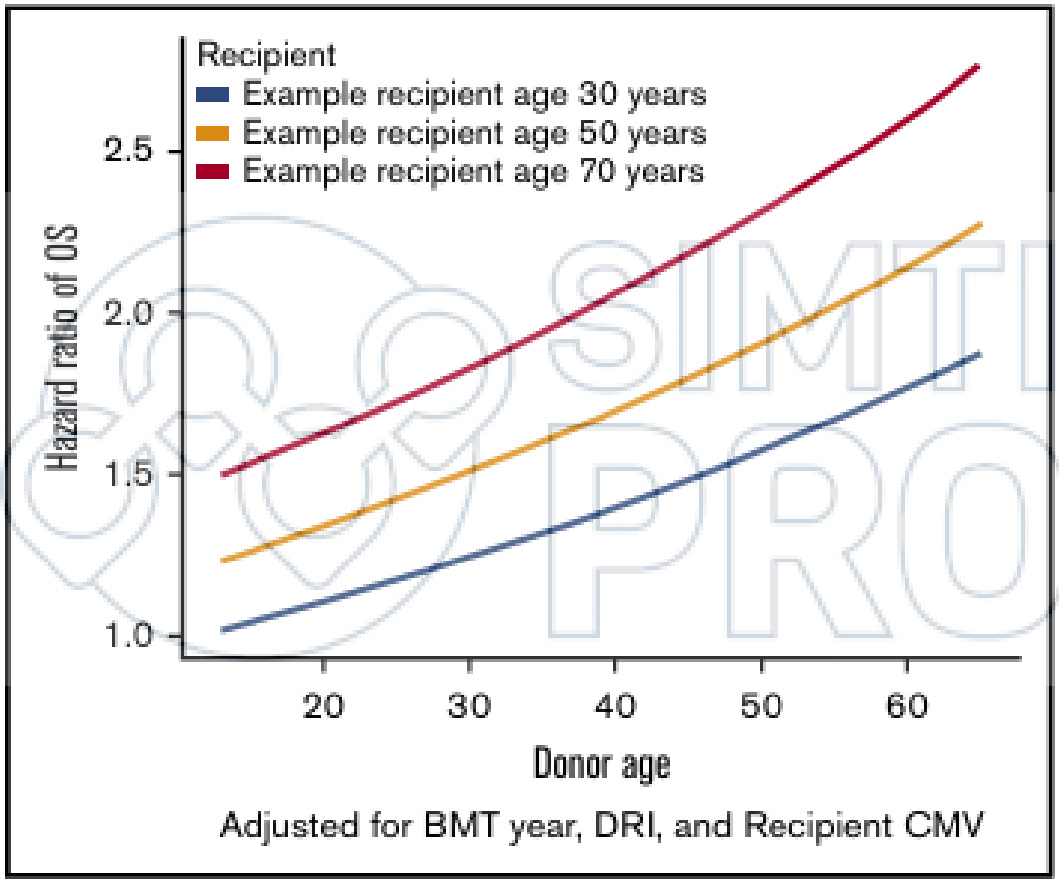
AGE



Schetelig et al., Leukemia 2024

RELATIONSHIP OF DONOR AGE AND RELATIONSHIP TO OUTCOMES OF HAPLOIDENTICAL TRANSPLANTATION WITH PTCY

AGE



DEZERN ET AL 9 MARCH 2021 Xvolume5 , NUMBER5 5 blood Advances

Donor age/outcome aplo HSCT with PTCY

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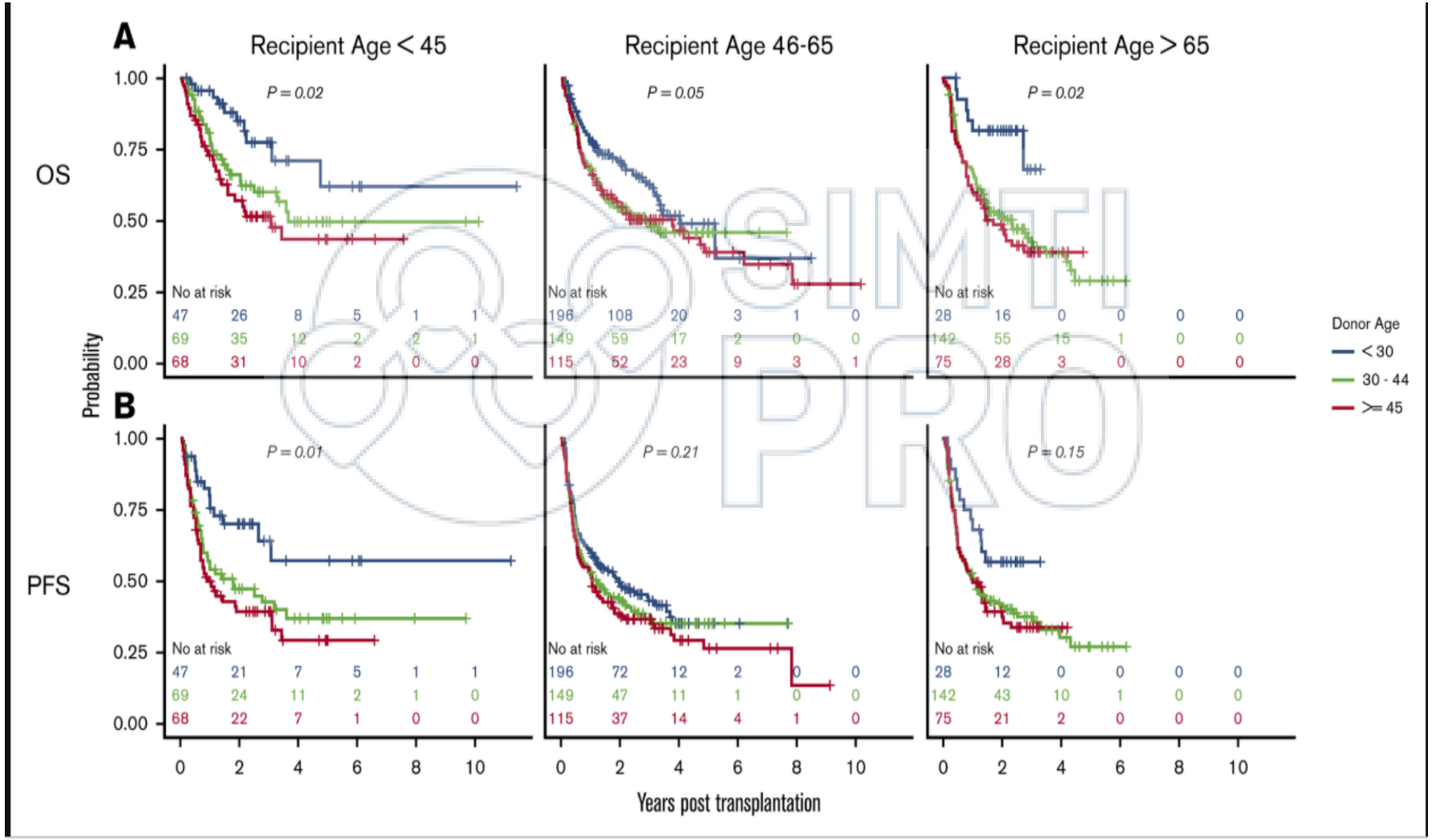


Amy E. DeZern et al,Blood advances Vol5,N.5 March 2021

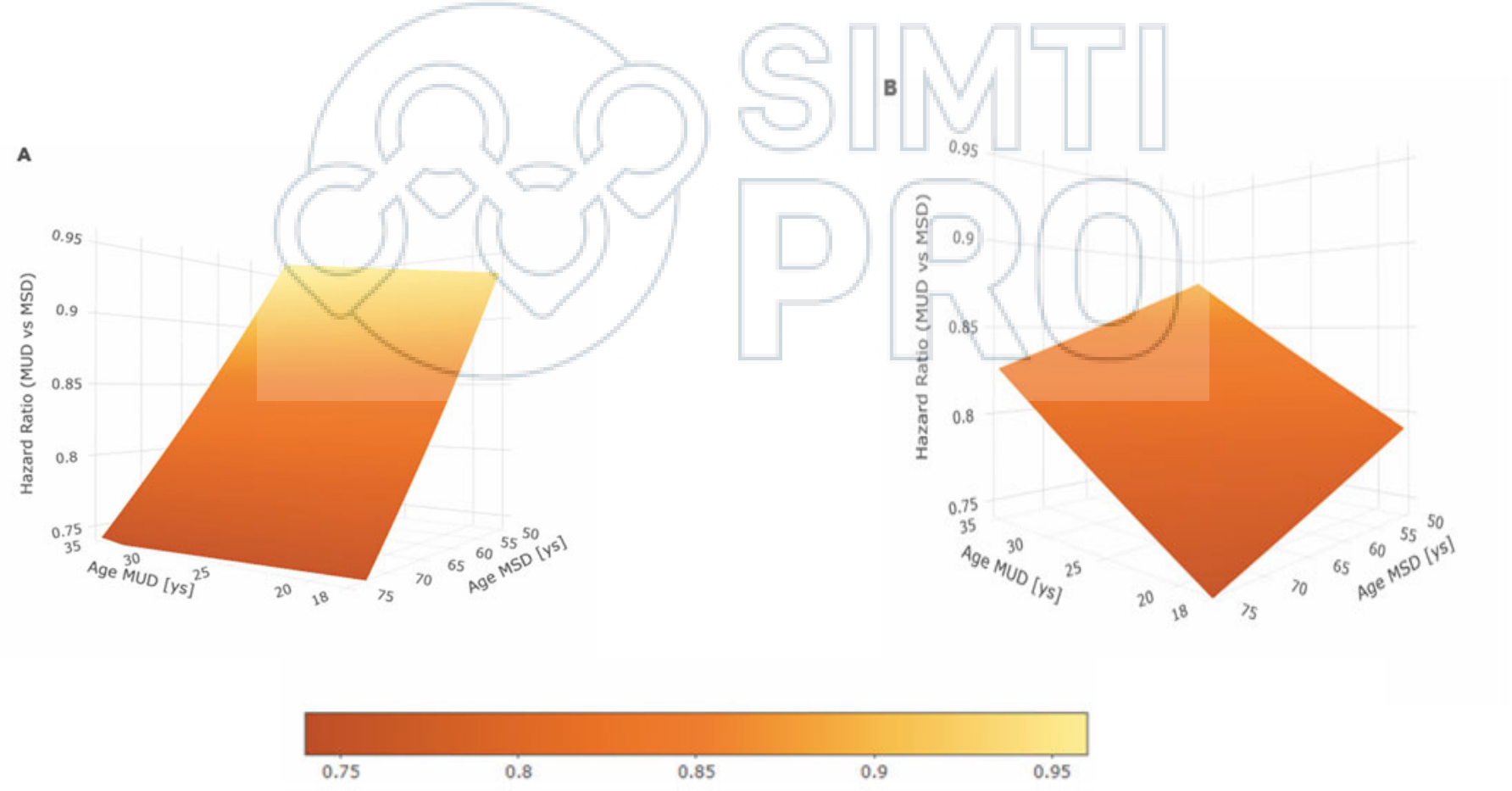
Impact of Donor Age

(Young unrelated donors confer a survival advantage for patients with myeloid malignancies compared to older siblings)

AGE

Event free survival

Overall survival

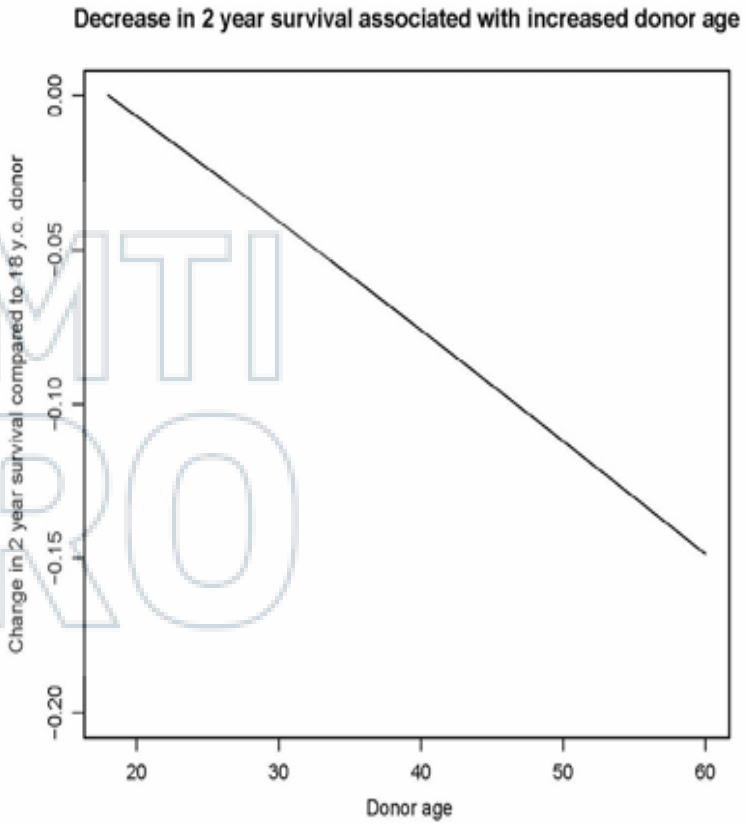


Leukemia (2025) 39:2523–2532

Donor selection score

A
G
E

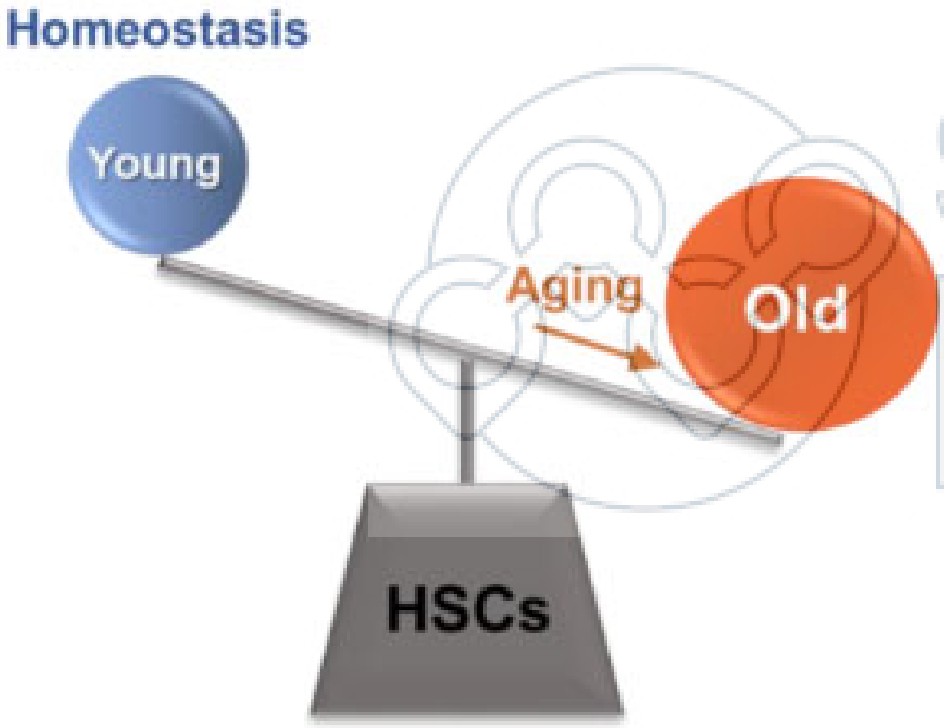
- Results first cohort (1999-2011):
  - 3 donor factors correlate negatively with outcome
    - HLA DBP1 matching
    - Older age
    - CMV mismatching for CMV+ recipients
- Results second cohort (2012-2014):
  - Only age has a negative impact on outcome



B.E. Shaw et al. / Biol Blood Marrow Transplant 24 (2018) 1049–1056

- IL VANTAGGIO DEL DONATORE GIOVANE E' -
BIOLOGICAMENTE DETERMINATO

AGE



↑ DNA demage

↓Self-renewal

Myeloid bias

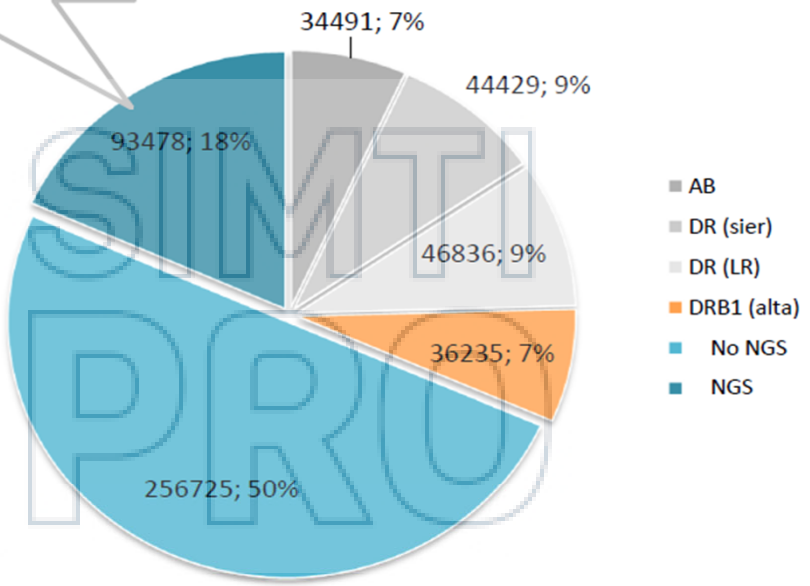
↓ Homing

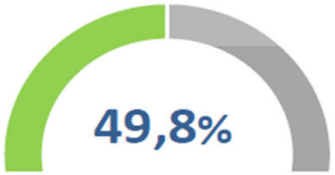
↑GVHD ↑ NRM ↓OS

Il Registro

93.500 NGS (18%)

Fully typed HLA ABC DRB1
350.000 (68,5%)





Dei donatori con età <36 anni

249.114

Dicembre 2024

512.194

A G E

Take home

- Principale fattore non immunologico determinante il buon esito del trapianto
- Impatto su OS, NMR,GVHD
- Tali evidenze hanno comportato un aumento della selezione di donatori con età < 30 anni,

  dal 36 % nel periodo 1988-2006, 51% tra il 1999-2011 ed il 69% tra il 2012 ed il 2014 (Kollmanet al. 2016)

AGE

La DR Femmina

SEX

- Il rischio immunologico legato al sistema **H-Y** è una delle principali cause di complicanze non-HLA nel trapianto di Cellule Staminali Emopoietiche (CSE). Si basa sul riconoscimento di antigeni minori di istocompatibilità codificati dal **cromosoma Y**.

SEX

D/R	Esposizione antigeneH-Y	Rischio GVHD	Impatto Clinico
M/M	**Assente** (Self-Tolerance)	**Basso**	Entrambi hanno il cr Y; il sistema immunitario DR è istruito a non attaccarlo.
M/F	**Assente** (No Target)	**Basso**	DR ha H-Y, ma RIC non lo esprime; manca bersaglio.
F(null)/M	**Potenziale** (Incompatibilità)	**Moderato**	F non conosce H-Y; linfociti T possono riconoscerlo come estraneo nel RIC
F(plurip)/M	**Pre-sensibilizzazione**	**Alto**	F già sensibilizzata l'H-Y in gravidanza . Ha linfociti T memoria.
F/F	**Assente** (No H-Y)	**Minimo**	D/R non hanno cromosoma Y; il conflitto H-Y è biologicamente impossibile.

frontiers | Frontiers in Oncology

TYPE Original Research
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Determining the predictive impact of donor parity on the outcomes of human leukocyte antigen matched hematopoietic stem cell transplants: a retrospective, single-center study

Mojtaba Azari[1,2], Maryam Barkhordar[1,2*], Tanaz Bahri[1,2*], Soroush Rad[2,3], Hosein Kamranzadeh Fumani[2,4], Seied Asadollah Mousavi[1,2], Sahar Tavakoli Shiraji[2,4], Morteza Azari[1,2], Parisa Shafaroudi[1,2] and Mohammad Vaezi[2,3]

S
E
X

Donor parity is often a debated non-human leukocyte antigen (non-HLA) factor that affects the outcome of HSCT. **Various research studies indicate that** individuals receiving grafts from parous female donors exhibit a significantly greater incidence of acute or chronic graft versus host disease (aGVHD or cGVHD) when compared to recipients of male or nulliparous donors

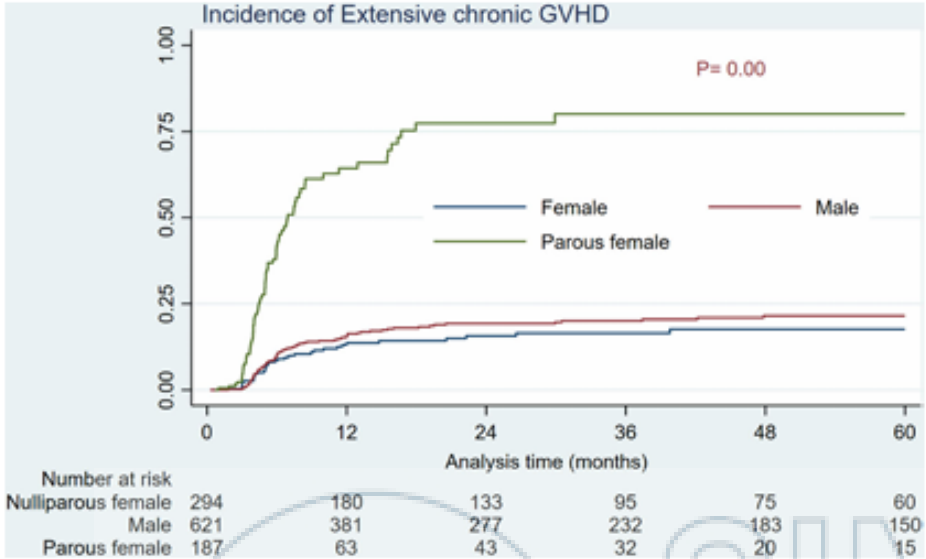


FIGURE 2
Cumulative incidence of extensive chronic GVHD by donor sex/parity.

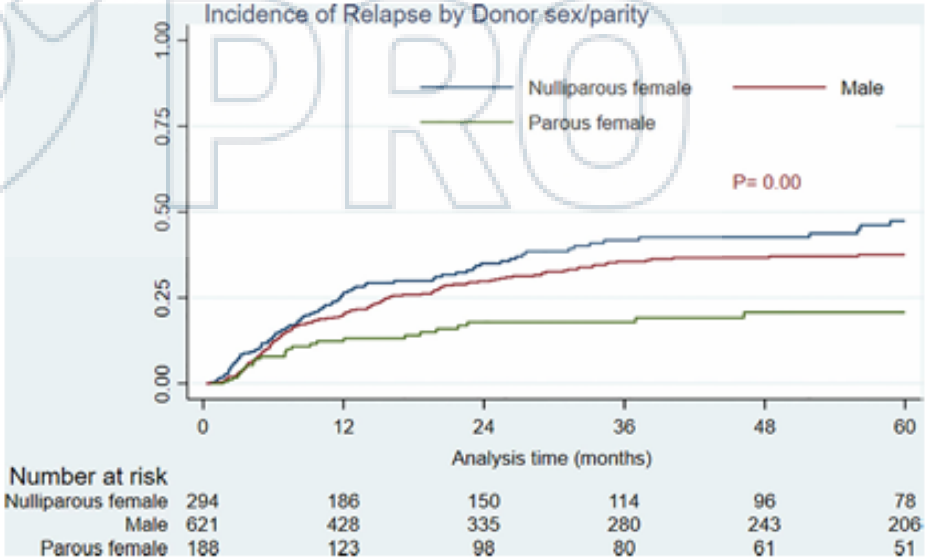


FIGURE 3
Relapse incidence by donor sex/parity.

-

TAKE HOME

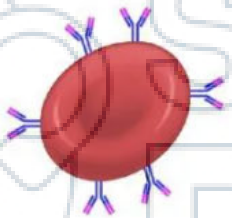
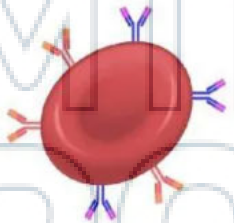
SEX

- Il mismatched sesso è esempio classico di come fattori non HLA possano influenzare significativamente oucome immunologico del trapianto

- Il mismatched sesso, in particolare F/M, è associato ↑ GvHD cronica

A
B
0

-
-

Genotipo	I^AI^A, I^AI^0	I^BI^B, I^BI^0	I^AI^B	I^0I^0
Fenotipo	gruppo A	gruppo B	gruppo AB	gruppo 0
				
Antigeni	A	B	AB	nessuno
				
Anticorpi	anti-B	anti-A	nessuno	anti-A, anti-B

A
B
0

-
-

Genotipo	I^AI^A, I^AI^0	I^BI^B, I^BI^0	I^AI^B	I^0I^0
Fenotipo	g	B	gruppo AB	gruppo 0
Antigeni				ssuno
Anticorpi	anti-B			anti-A, anti-B

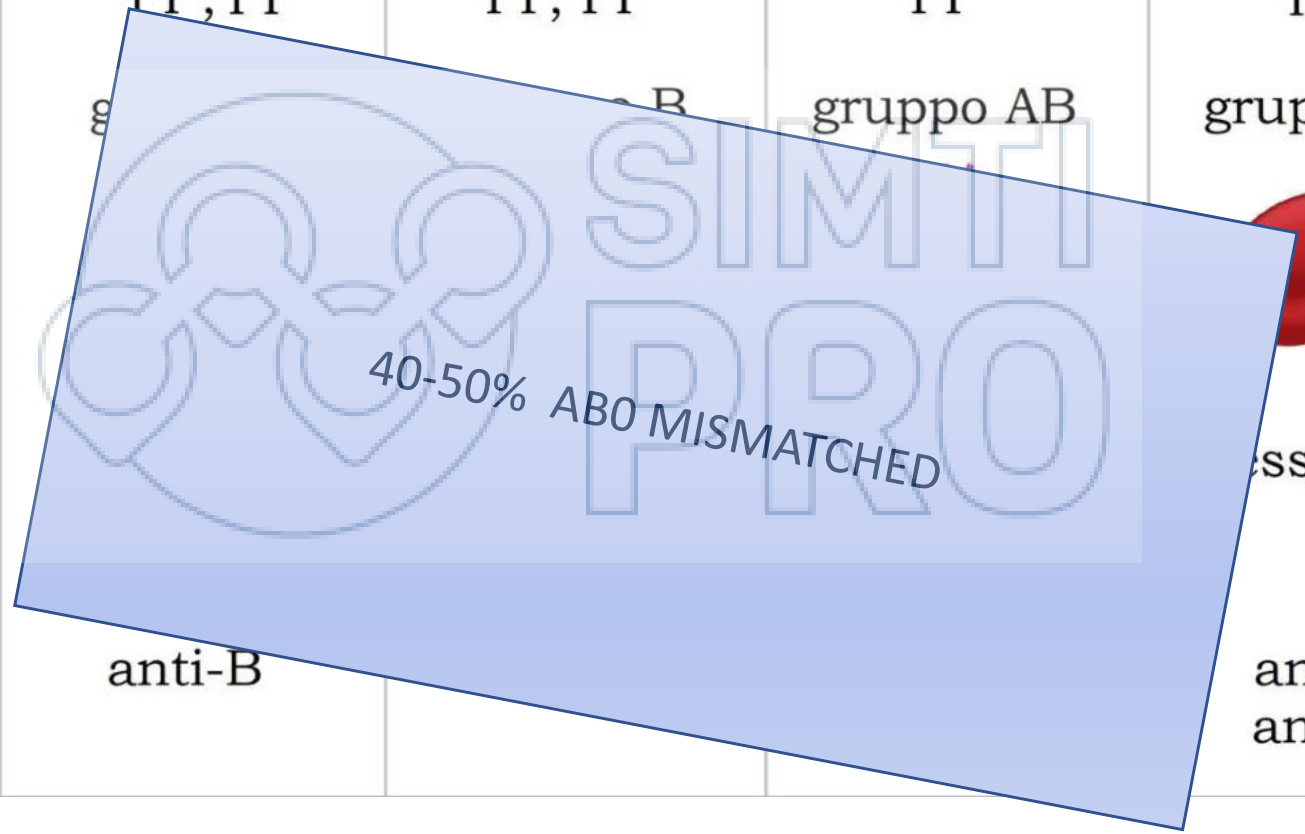


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Table 2. Complications and preventive measures in ABO incompatibility.

Type of Incompatibility	Complications	Causes	Preventive Measures
ABO Major	Immediate hemolysis	Infusion of donor's incompatible RBCs	RBC depletion of BM grafts (>20 mL) No manipulation of red cell contamination in PBSC grafts (<20 mL)
	Delayed hemolysis	Anti-donor IHAs by recipient residual B lymphocytes	Check anti-donor IHA titer Immunoadsorption, plasma exchange (if anti-donor IHA titer is ≥1:32)
	Pure Red Cell Aplasia (PRCA)	Persistence of high titer anti-donor IHAs	
ABO Minor	Immediate hemolysis	High titer IHAs in donor plasma	Check anti-recipient IHA titer Plasma depletion of both PBSC and BM grafts (if anti-recipient IHA titer is ≥1:256)
	Delayed hemolysis	Passenger Lymphocyte Syndrome (PLS) by donor lymphocyte (anti-host IHAs)	
ABO Bidirectional	Immediate hemolysis	Recipient and donor IHAs	Both RBCs and plasma depletion are required
	Delayed hemolysis	IHAs by recipient and donor B lymphocytes	

RBC: red blood cell; BM: bone marrow; PBSC: peripheral blood stem cells; IHAs; isohemagglutinins.

A.Matteocci-L.Pierelli Cells 2024,13,814

A
B
0

Table 4. Delayed immuno-hematologic complications after ABO-incompatible HSCT.

	PRCA	PLS
ABO Incompatibility	Major	Minor
Onset	+30 to +120 days Rule out other causes of anemia: AIHA, TMA, graft failure Bone marrow: absence of erythroid precursors (reticulocytopenia)	+5 to +21 days Rule out other causes of anemia: TMA, bleeding, infection, graft rejection
Risk factors	Pre-HSCT anti-donor IHAs $\geq$ 1:64 Type A anti-donor IHAs Non-myeloablative conditioning HLA-matched related donor and unrelated donor	Unrelated donor Recipient of blood group A Absence of methotrexate in GVHD prophylaxis (cyclosporine only) Reduced intensity
Preventive interventions	Reduction of anti-donor IHAs (residual recipient lymphocytes and plasma cells, abnormal immune tolerance): immunoadsorption, plasma exchange	Plasma reduction in grafts
Immuno-hematologic investigations	Positive DAT: IgG+, C3d+ or both Positive eluate for the presence of anti-A/B IHAs IHA titration	Positive DAT: IgG+, C3d+ or both Positive eluate for the presence of anti-A/B IHAs IHA titration
Treatment	Supportive care: transfusion support Donor lymphocyte infusion (DLI), erythropoietin, IVIG, rituximab Reduction of anti-donor IHAs (plasma exchange) Plasma cell-directed therapy: daratumumab, bortezomib, rituximab	Supportive care: transfuse donor-compatible RBC units Rituximab Plasma exchange

PRCA: pure red cell aplasia; PLS: passenger lymphocyte syndrome; AIHA: autoimmune hemolytic anemia; TMA: thrombotic microangiopathy; GVHD: graft versus host disease; RBC: red blood cells; DAT: direct antiglobulin testing; IHAs: isohemagglutinins.

A.Matteocci-L.Pierelli Cells 2024,13,814

A
B
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Pure red cell aplasia among ABO mismatched hematopoietic stem cell transplant recipier 13-years retrospective study literature review

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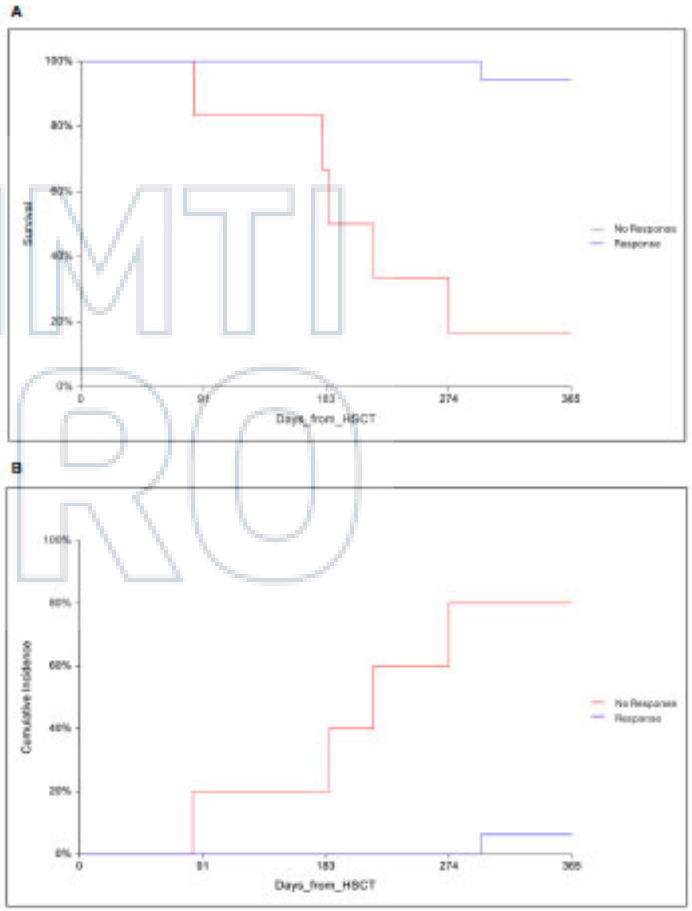

FIGURE 2
(A) One-year overall survival (OS) in responders and non-responders patients with PRCA. (B) One-year cumulative incidence of transplant-related mortality in responders and non-responders patients with PRCA.

A
B
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TABLE 2 PRCA cases: treatment and response.

Patient	Donor	Source	Treatment *(starting day, +d)*	Response Y/N
# 1	MRD	PB	Pre-HSCT PEX (-5, -1 d), rhEPO (+21 d)	N
# 2	MUD	PB	rhEPO (+21 d)	Y
# 3	MUD	PB	rhEPO (+21 d)	Y
# 4	Haplo	BM	Pre-HSCT PEX (-5, -1 d), rhEPO (+20 d)	Y
# 5	MRD	PB	Rh EPO (+20 d), rhEPO + PDN (+30 d)	N
# 6	MUD	PB	rhEPO (+21 d), rhEPO + PEX x 6 + PDN (+110 d)	Y
# 7	Haplo	BM	Pre-HSCT PEX (-5, -1 d), rhEPO (+20 d), rhEPO + PEX x 6 (+90d)	Y
# 8	Haplo	BM	Pre-HSCT PEX (-5, -1 d), rhEPO (+20 d), rhEPO + PEX x 6 + Eltrombopag	Y
# 9	Haplo	BM	rhEPO (+20 d), rh EPO + RTX x 4 (+92 d), rhEPO + PEX x 3 (+150 d)	N
# 10	MRD	PB	rhEPO (+21 d), rhEPO + RTX x 4 + PDN (+110 d), rhEPO + PEX x 12 (+145 d)	N
# 11	MUD	PB	Pre-HSCT PEX (-5, -1 d), rhEPO (+20 d), rhEPO + RTX x 4 (+120 d), rhEPO + PEX x 6 (+150d)	Y
# 12	Haplo	BM	Pre-HSCT PEX (-5, -1 d), rhEPO (+21 d), rhEPO + RTX x 4 (+210 d), rhEPO + PEX x 6 + PDN (+250 d)	Y
# 13	MMUD	PB	Pre-HSCT PEX (-5, -1 d), rhEPO (+20 d), rhEPO + RTX x 4 (+88 d), rh EPO + PEX x 6 (+128 d), rh EPO + Daratumumab x 8 (+180 d)	Y
# 14	Haplo	BM	rhEPO (+20 d), rhEPO + PEX x 6 (+110 d), rhEPO + RTX x 4 (+180 d)	Y
# 15	Haplo	BM	rhEPO (+19 d), rhEPO + RTX x 4 (+94 d)	Y
# 16	MUD	PB	rhEPO (+19 d), rhEPO + RTX x 4 (+120 d)	Y
# 17	Haplo	BM	rhEPO (+20 d), rhEPO + RTX x 4 (+75 d)	Y
# 18	Haplo	BM	Pre-HSCT PEX (-5, -1 d), rhEPO (+21 d), rhEPO + RTX x 4 (+100 d)	Y
# 19	Haplo	BM	rhEPO (+21 d), rhEPO + RTX x 4 + PDN (+120 d)	Y
# 20	MRD	PB	rhEPO (+21 d), rhEPO + RTX x 4 + PDN (+93 d)	N
# 21	MRD	PB	rhEPO (+19 d), rhEPO + RTX x 4 + PDN (+110 d)	Y
# 22	MUD	BM	rhEPO (+21 d), rhEPO + PEX x 6 (+90 d, +165), rhEPO + RTX x 4 + PDN (+300 d)	Y
# 23	MRD	PB	Pre-HSCT PEX (-5, -1 d), rhEPO (+19 d), rhEPO + RTX x 4 (+91 d), rhEPO + Daratumumab x 6 (+130 d)	N
# 24	MMUD	BM	Pre-HSCT PEX (-5, -1 d), rhEPO (+21 d), rhEPO + Daratumumab x 2 (+100 d)	Y

MUD, Matched unrelated donor; MMUD, Mismatched unrelated donor; MRD, Matched related donor; Haplo, haploidentical donor; HSCT, Hematopoietic stem-cell transplantation; BM, bone marrow; PB, peripheral blood stem cell; PDN, prednisone; RTX, Rituximab; DLI, rhEPO, erythropoietin; PEX, plasma exchange; d, the day of first administration; m, month of first administration; n, number of patients.

Metafuni et al.Front. Oncol., 02 July 2024

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B
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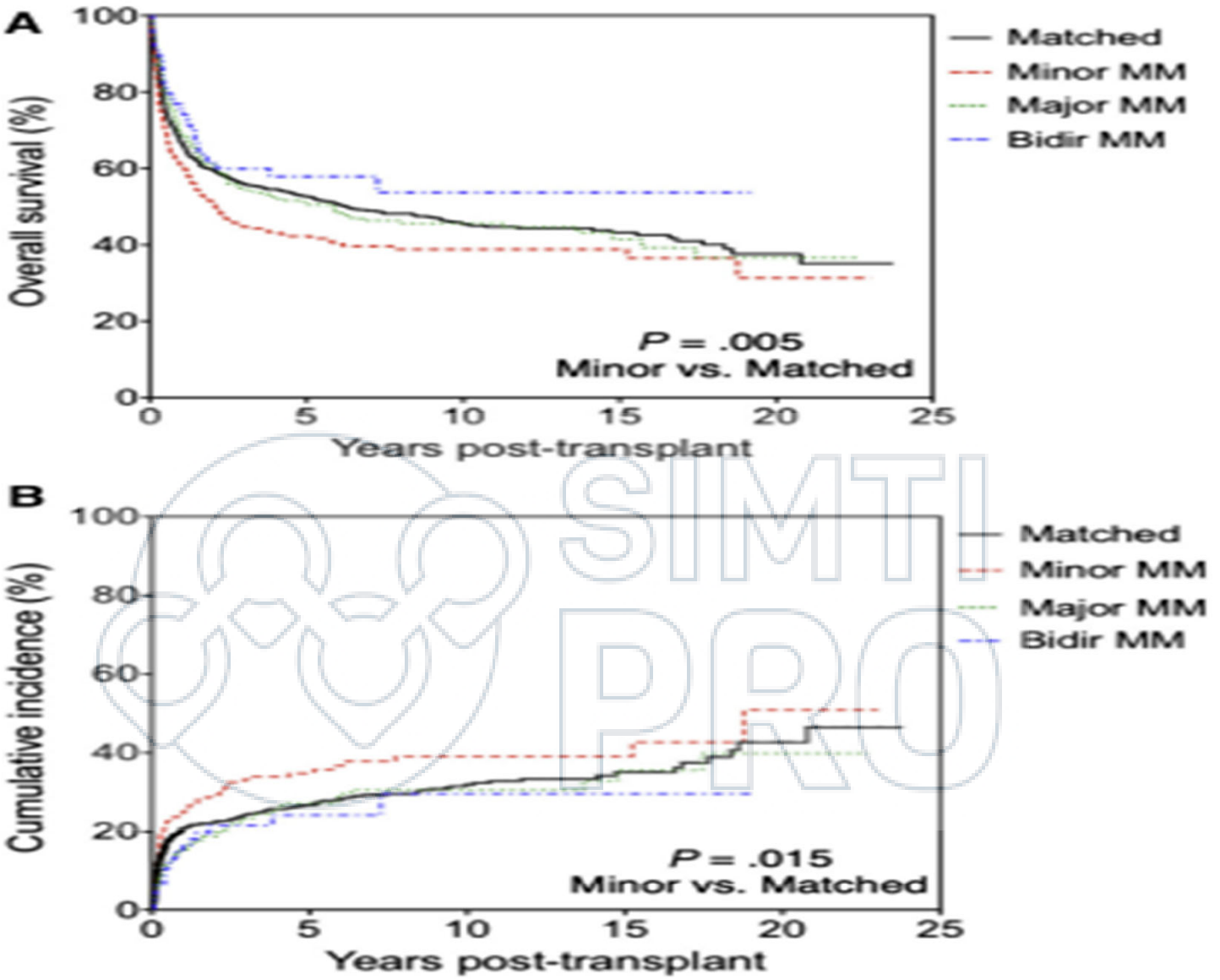

Figure 1. Recipient survival when donor was ABO matched, minor MM, major MM, or bidirectionally MM. Recipients receiving minor-MM grafts experienced a significant overall survival impairment compared with those receiving ABO-matched grafts ($P = .005$) (A). Cumulative incidence of NRM was increased in recipients of ABO minor MM grafts compared with recipients of ABO-matched grafts ($P = .015$) (B).

A.C. Logan et al. / Biol Blood Marrow Transplant 21 (2015) 746e754

A
B
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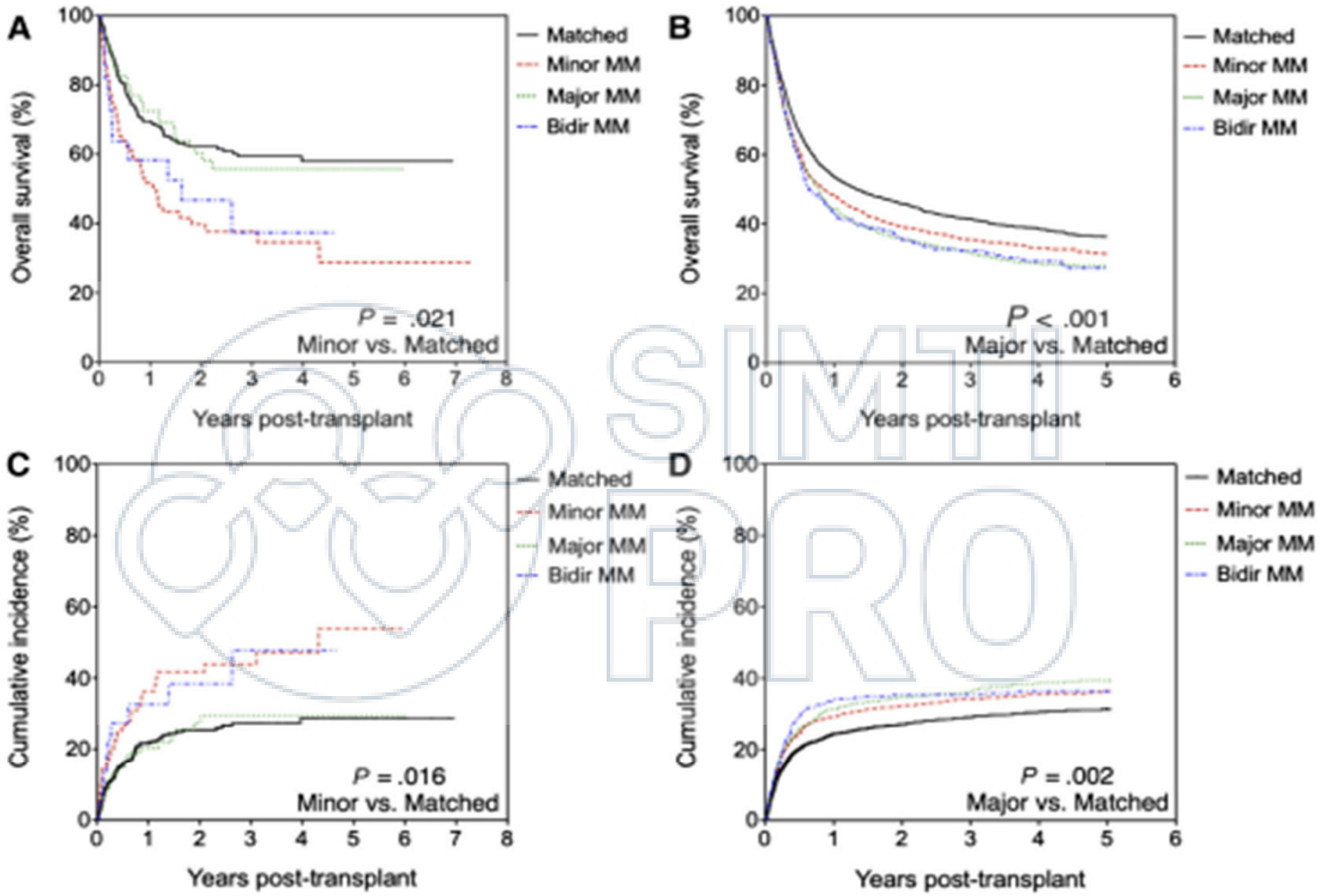

Figure 2. CIBMTR analysis of overall survival and cumulative incidence of NRM in patients receiving ABO-matched, minor MM, major MM, or bidirectionally (Bidir) MM hematopoietic allografts for lymphoma (A and C; data from Ratanatharathorn et al. [18] evaluated for ABO effect) or AML/MDS (B and D; data from Luger et al. [19] evaluated for ABO effect).

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Take home

A
B
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- Mismatched AB0 raramente decide il donatore, ma può avere impatto significativo nella gestione post-trapianto.

MA SONO INDISPENSABILI

- Protocolli condivisi per la gestione dell'incompatibilità AB0
- Protocolli condivisi per il monitoraggio immunoematologico, il supporto trasfusionale e la terapia

Impatto del sierostato CMV su sopravvivenza globale

Sierostato D/R	OS	HR (IC 95%)
D− / R−	riferimento	1.00
D+ / R−	↓ OS	1.15–1.20
D− / R+	↓↓ OS	1.20–1.25
D+ / R+	↓↓ OS	1.20–1.30

Mehta RS et al., Transplant Cell Therapy 2025 | Ljungman P et al., EBMT Handbook 2024

Sierologia CMV e NRM

Sierostato D/R	NRM	HR (IC 95%)
D− / R−	baseline	1.00
D+ / R−	↑ NRM	1.10–1.20
D− / R+	↑↑ NRM	1.20–1.30
D+ / R+	↑↑ NRM	1.25–1.35

Mehta RS et al., Transplant Cell Therapy 2025 | Ljungman P et al., EBMT Handbook 2024

Perché D– / R+ è associato a outcome peggiori?

-
-

Ric CMV + virus latente (CMV già presente- si riattiva dopo trapianto)

Il graft da da DR CMV - non contiene linfociti T CMV –specifici→

Assenza immunità specifica

IS →Ritardo immunoricostituzione CMV-specifica

↑Riattivazione CMV ↑Infezione opportunistiche
↑infiammazione sistemica ↑NRM

-

CMV

Perché è complesso?

⟶ Non rappresenta solo un marker, ma anche un driver biologico:

infiammazione

Immunodepressione

Infezioni

Contribuiscono a NRM

CMV e Letermovir

- ↓ riattivazione precoce
- ***X*** ***non elimina***
- riattivazioni tardive
- Impatto su NRM

- Estesa indicazione a proseguire fino a gg +200

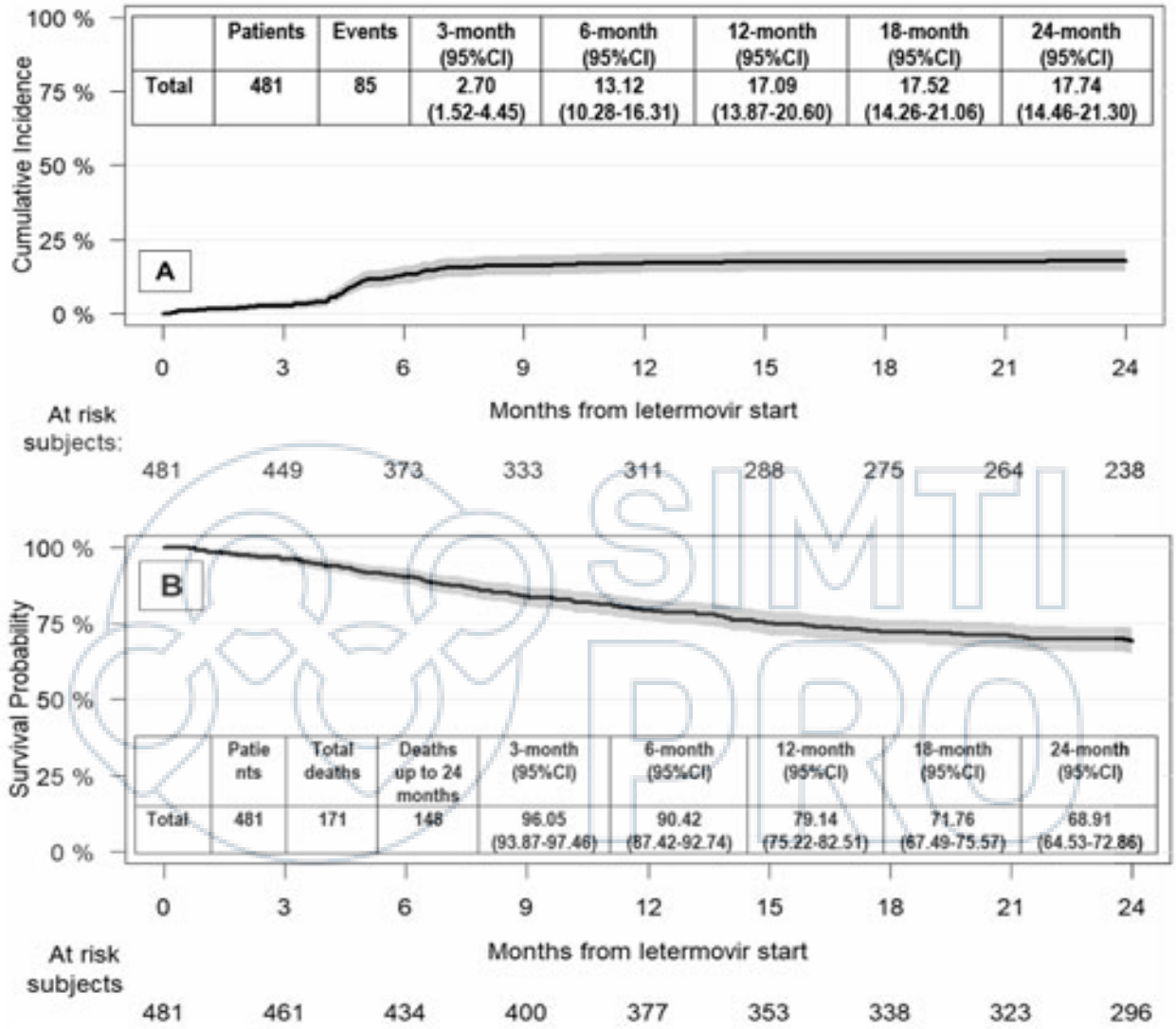

FIGURE 1 | Clinical outcomes: (A) Cumulative incidence of clinically significant CMV infection; (B) probability of overall survival.

J. Styczynski et al Transplant Infectious Disease,2026

Take –home

- Nell’era della profilassi e della terapia pre-emptive , il CMV non è più un criterio dirimente, ma rimane un fattore modulatore nella scelta del donatore capace di influenzare outcome

Gerarchia decisionale

Criterio	Priorità e Raccomandazioni NMDP	Note Cliniche
HLA Match	**8/8 (A, B, C, DRB1)** è lo standard preferito.	In contesti con profilassi PTCy, i match 7/8 mostrano esiti comparabili.
Età del Donatore	**Priorità assoluta ai giovani (< 30-31 anni).**	L'età è considerata più impattante del sesso sulla sopravvivenza globale.
Sesso e Parità	**Preferenza per donatori maschi** o femmine nullipare.	Le donatrici con gravidanze aumentano il rischio di GvHD cronica.
Gruppo ABO	**Donatore ABO-identico** o compatibile.	Considerato se HLA ed età sono equivalenti.
CMV Status	Match CMV (es. donatore negativo per ricevente negativo).	Fattore secondario rispetto a HLA ed età.
Taglia Corporea	Preferenza per donatori di **peso > 80 kg** o con buon rapporto donatore/paziente.	Cruciale per garantire una dose cellulare (CD34+) adeguata.

NMDP GUIDLINES

Secondary characteristic considerations:		
Recommendation	**Evidence Level**	**References**
Donor age: • Donors ≤ 30 years old should be prioritized to maximize OS. 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) Donor weight: • A large patient-donor weight discrepancy should be avoided in the setting of BM HCT.	 +++ ++ ++ + +++	Dehn et al 2024[1] Ciurea et al 2020[39] Kollman et al 2016[61] Spellman et al 2024[68] Mehta et al 2023[69] Anthias et al 2016[88] Sanz et al 2024[94] Murthy et al 2022[98]

CONCLUSIONI

- Quando l'HLA è identico, la scelta del donatore non è più genetica, ma clinica

- Età del donatore e sesso = criterio chiave
- CMV= criterio modulatore
- ABO= criterio gestionale
- DECISIONE FINALE= equilibrio rischio biologico/complessità clinica

CONCLUSIONI

- Quando l'HLA è identico, la scelt re non è più genetica, ma cli
- Età del d
- CMV
- A
- D ischio bi nica

Quando HLA è uguale, il miglior donatore non è più quello compatibile ma quello biologicamente più favorevole

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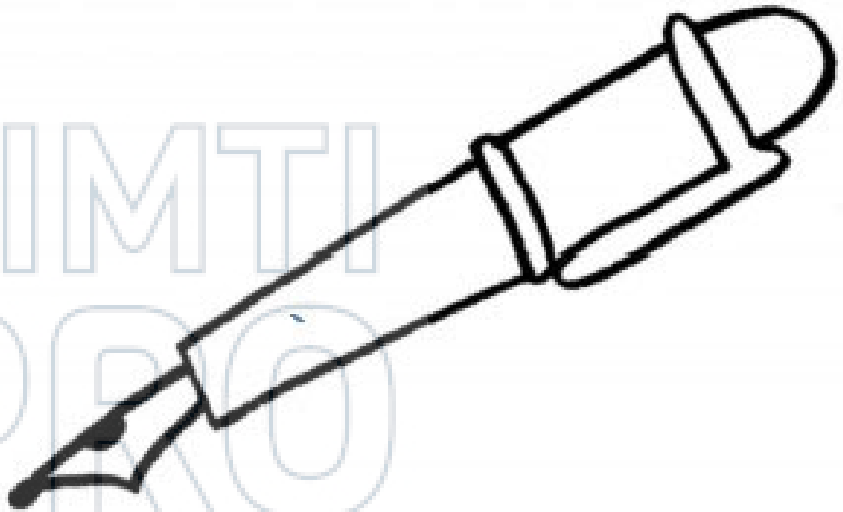

Grazie