Società Italiana di Ematologia

QUINTO EVENTO NAZIONALE

SIE incontra i pazienti

13 maggio 2026

Bologna, Royal Hotel Carlton

Disclosures of Emanuele Angelucci

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Vertex							DMC
MBS							DMC
Menarini			X				
Pharmacosmos			X				
Johnson & Johnsonx			X				

IRCCS AOM
AZIENDA OSPEDALIERA METROPOLITANA

IRCCS Ospedale Policlinico San Martino

PROGRAMMA TRAPIANTI E TERAPIE CELLULARI ALBERTO MARMONT

Il ruolo attuale del trapianto allogenico

Emanuele Angelucci

UO Ematologia e Terapie Cellulari

Agenda

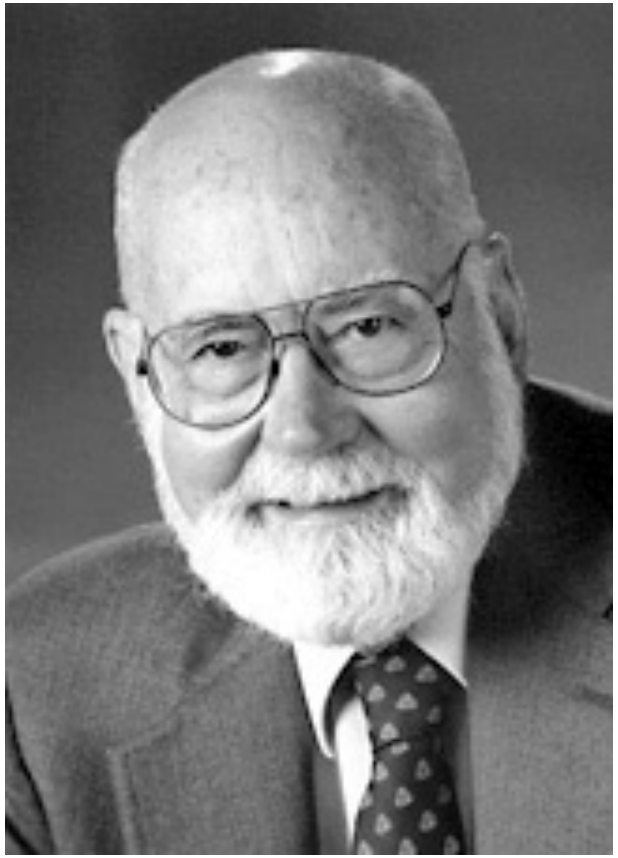
- Il trapianto allogenico
- Ruolo attuale
- Recenti avanzamenti

Prime esperienze

- Il **15 Ottobre 1958**, in un incidente nucleare in Yugoslavia (a Vinca) sei Fisici rimasero irradiati (400 rads) e svilupparono rapidamente aplasia midollare.
- A Parigi, Georges Mathe, offrì a questi fisici la possibilità di una terapia di salvataggio. Trasferiti nella sua unità sterile a Villejuif, ricevettero infusioni multiple di midollo osseo da parenti. Il sistema HLA non era noto e la funzione del sistema linfocitario non era ben conosciuta.
- Cinque individui sopravvissero. Essi mostrarono veloce recupero della emopoiesi (provata allogenica almeno in un caso per genotipo eritrocitario) seguita da ricostituzione autologa senza GvHD.
- Questo evento rimane la prima volta che il trapianto di midollo osseo allogenico è stato usato con intento terapeutico e con successo e rimane una pietra angolare nella storia del trapianto nell'uomo.

Nel 1957 E.D. Thomas iniziò a descrivere i primi trapianti di cellule staminali emopoietiche midollari nell’uomo

(Thomas ED, Lochte HL, Jr., Lu WC, Ferrebee JW. Intravenous infusion of bone marrow in patients receiving radiation and chemotherapy. N Engl J Med 1957;257:491-6.)



Of one thing I am sure, the last word has not been written on the subject

Robert Good. *Lancet 1968;2:1366-9*.

Nel 1968 due bambini furono sottoposti con successo a trapianto di cellule staminali emopoietiche da donatore familiare identico:

Il primo affetto da una immunodeficienza legata al cromosoma X

Gatti RA, Meuwissen HJ, Allen HD, Hong R, Good RA. Immunological reconstitution of sex-linked lymphopenic immunological deficiency. Lancet 1968;2:1366-9.)

Il secondo affetto dalla sindrome di Wiskott-Aldrich *(Bach FH, Albertini RJ, Joo P, Anderson JL, Bortin MM. Bone-marrow transplantation in a patient with the Wiskott-Aldrich syndrome. Lancet 1968;2:1364-6 17).*

Haematopoietic Stem cells Transplantation (HSCT)

ORIGINAL ARTICLE FREE PREVIEW ARCHIVE

Intravenous Infusion of Bone Marrow in Patients Receiving Radiation and Chemotherapy

1957

E. Donnall Thomas, M.D.†, Harry L. Lochte, Jr., M.D.‡, Wan Ching Lu, Ph.D.§,

E. Donnall Thomas, Nobel Prize in Physiology or Medicine, 1990.

"***For their discoveries concerning organ and cell transplantation for the treatment of human diseases***"

American Journal of Pathology • Volume 108, Issue 2, Pages 196 - 205 • 1982

Acute and chronic graft-versus-host disease in dogs given hemopoietic grafts from DLA-nonidentical littermates. Two distinct syndromes

Atkinson K.; Shulman H.M.; Deeg H.J.; Weiden P.L.; Graham T.C.; Thomas E.D.; Storb R.

Graft-versus-host disease: a review

A J Barrett MD MRCPath *Department of Haematology, Charing Cross and Westminster Medical School, Westminster Hospital, London SW1*

Keywords: graft-versus-host disease, T cells, marrow transplant, immune recovery

Presidential Address to Section of Pathology, 10 January 1986

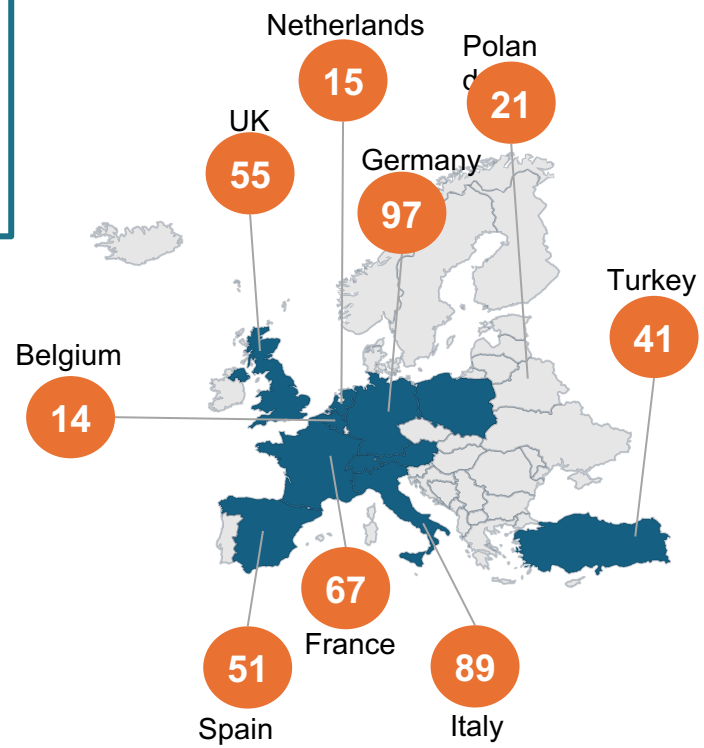
Historical background

Graft-versus-host reactions (GVHR) after bone marrow transplantation were first observed in mouse recipients of bone marrow and spleen from donor mice of different strains. The condition was described by Barnes and Loutit in 1954[1]: affected mice would survive the initial period of myelosuppression following irradiation (primary disease) and later, between three to six weeks after transplantation, develop a debilitating, wasting condition initially called secondary disease. For some years there was a debate about the nature of the GVHR because it was not clear whether the disease was a host-versus-graft or graft-versus-host effect. After a series of conflicting experiments, the demonstration by van Bekkum[2] that GVHR severity was directly related to the num-

Figure 1. Rash of acute GVHD

The EBMT is a not-for-profit, international collaboration of healthcare professionals

Top 10 countries in terms of number of centres



- Established in 1974
- 7209 members and 681 centres located in 78 different countries
- Centres contribute data voluntarily
- Currently in the database
  - >740,000 HSCT total (2020)[1]
  - >40,000 new HSCT per year
  - >3,000 CAR T-cell therapies (Feb 22)[2]

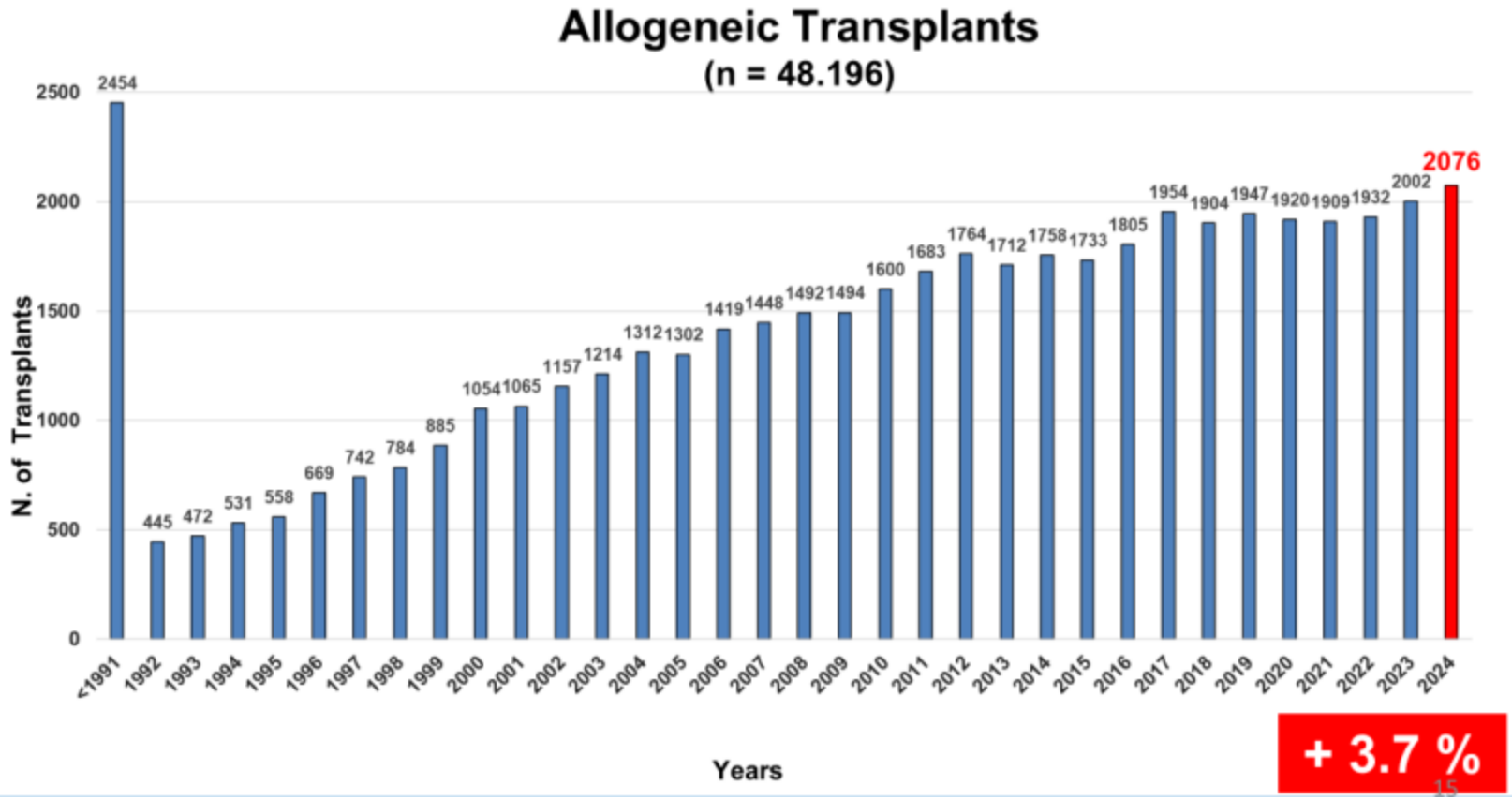
** Not shown on the map: 30 centres from China*

[1] *EBMT annual report 2023*

[2] *EBMT Registry February 2022*

Programmi Trapianto 88
(Allo 61)

Allogeneic Transplants (n. 45.111)


Allogeneic Transplants
(n = 48.196)
N. of Transplants
Years
2500
2000
1500
1000
500
0
2454
445
472
531
558
669
742
784
885
1054
1065
1157
1214
1312
1302
1419
1448
1492
1494
1600
1683
1764
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1954
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2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
2021
2022
2023
2024
+ 3.7 %

Diseases requiring allogeneic hematopoietic stem cell transplantation with curative intent.

Hematologic Malignancies (~75–80%)

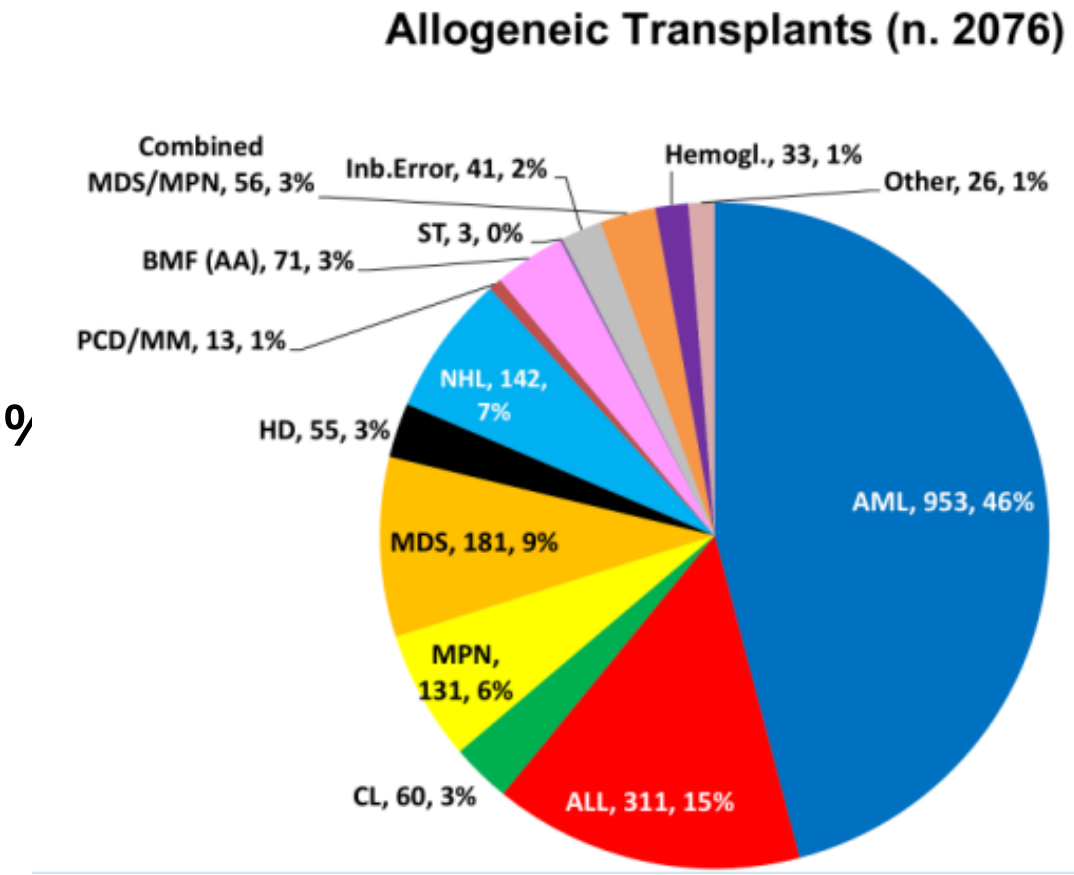
- Acute Myeloid Leukemia (AML) — ~35–40%
- Acute Lymphoblastic Leukemia (ALL) — ~15–20%
- Myelodysplastic Syndromes (MDS) — ~10–12%

Non-malignant Hematologic Diseases (~15–20%

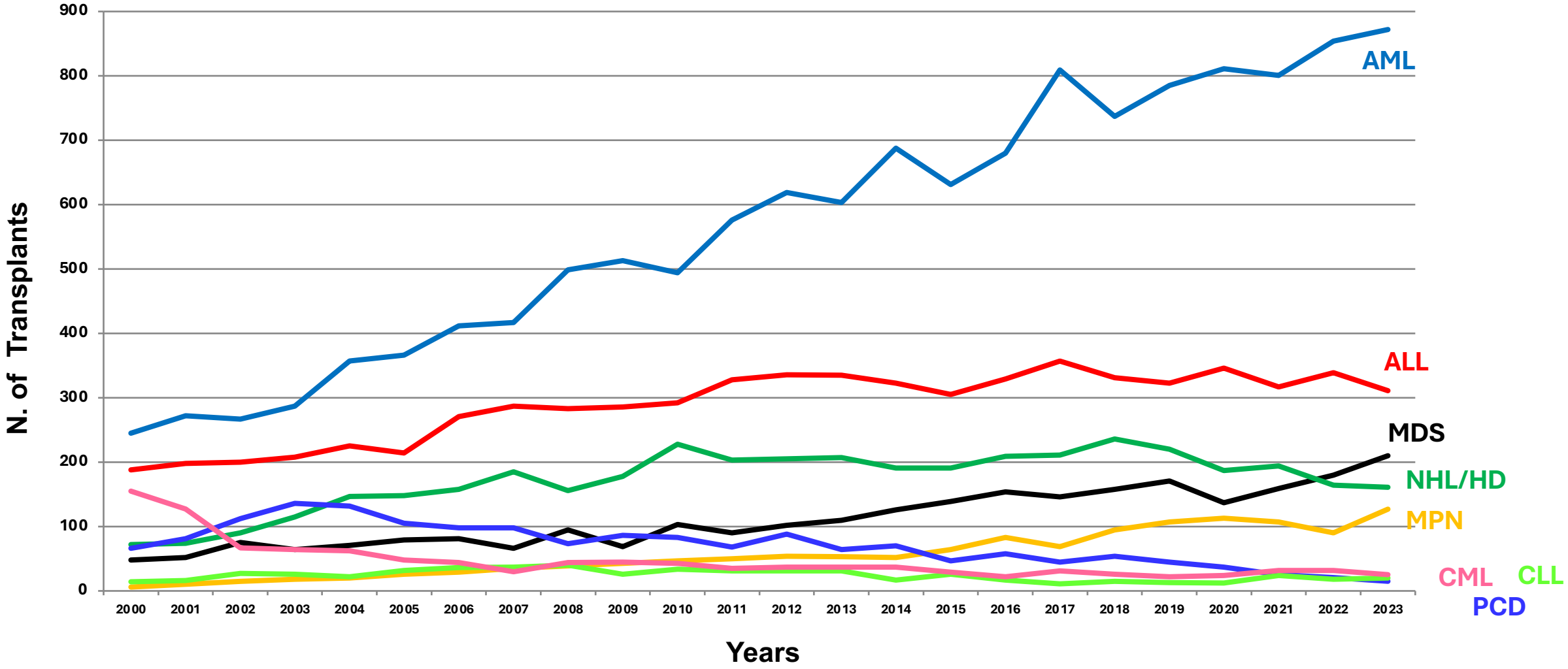
- Aplastic anemia — ~6–8%
- β-thalassemia — ~3–5%
- Sickle cell disease — ~2–4%

Inherited Metabolic Disorders (~3–5%)

- Hurler syndrome (MPS I)
- Adrenoleukodystrophy



GITMO data: Number of Allogeneic HCTs in Italy by Selected Disease



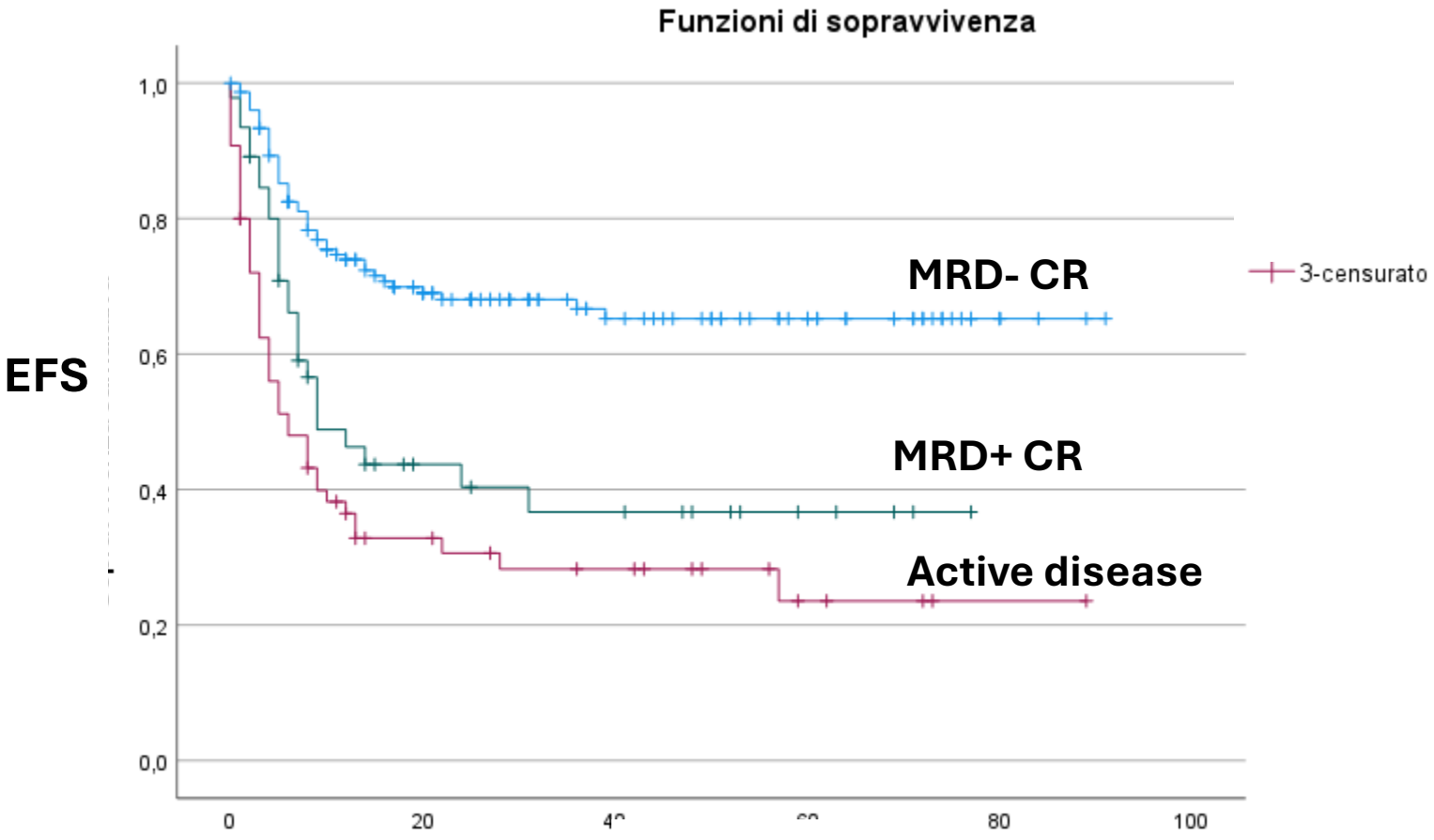
Export date 01/03/2024

Posizione nel 2026

- Terapia curative (Chemio-immunoterapia)
  - Terapia di consolidamento
  - Ruolo in malattia attiva

- Terapia curative / sostitutiva

Terapia di consolidamento / ruolo in malattia attiva



Months from allo HSCT

Confronti pairwise

		1		2		3	
	RCDEEP	Chi-quadrato	Sign.	Chi-quadrato	Sign.	Chi-quadrato	Sign.
Log Rank (Mantel-Cox)	1			12,971	<,001	39,979	<,001
	2	12,971	<,001			2,785	,095
	3	39,979	<,001	2,785	,095		

Recent and ongoing progreses

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DONOR

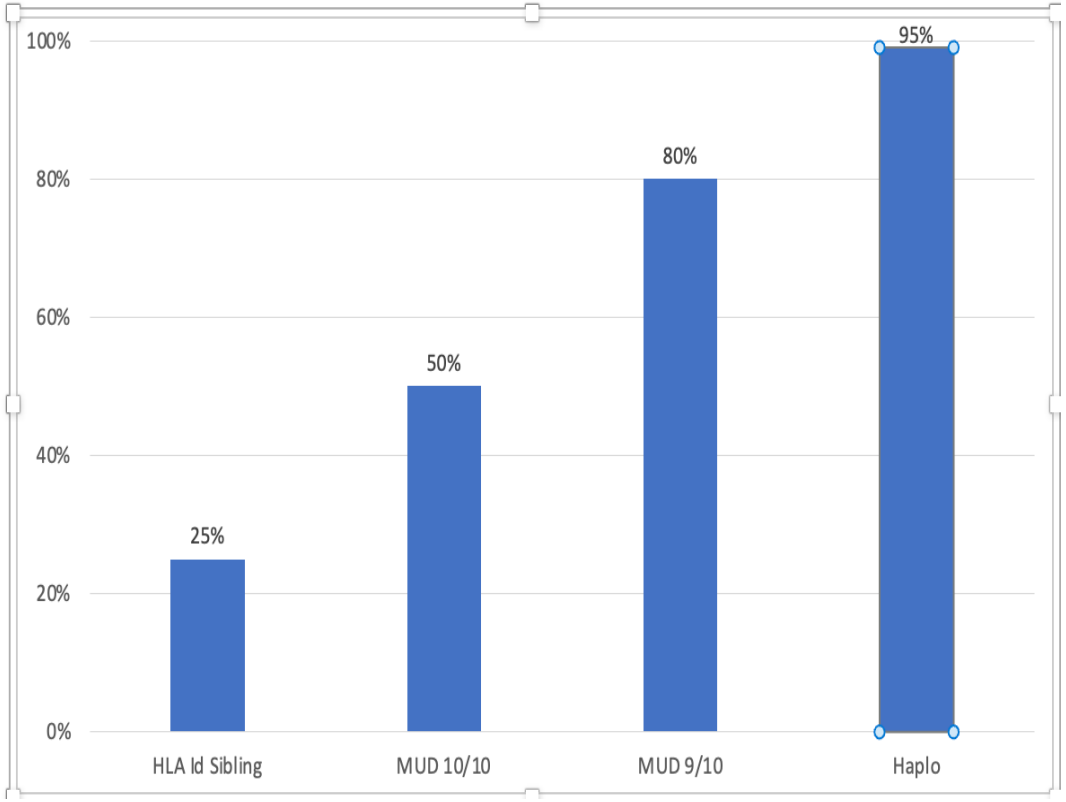
Algorithm for donor selection for adult patients with hematological malignancies

HLA-identical sibling donor

HLA-10/10 matched unrelated donor
Beyond HLA: donor age> CMV-matching, sex-matching, ABO-matching

HLA-9/10 matched unrelated donor;
HLA-mismatched related donor; cord blood Beyond HLA: donor specific antibodies, specific center experience

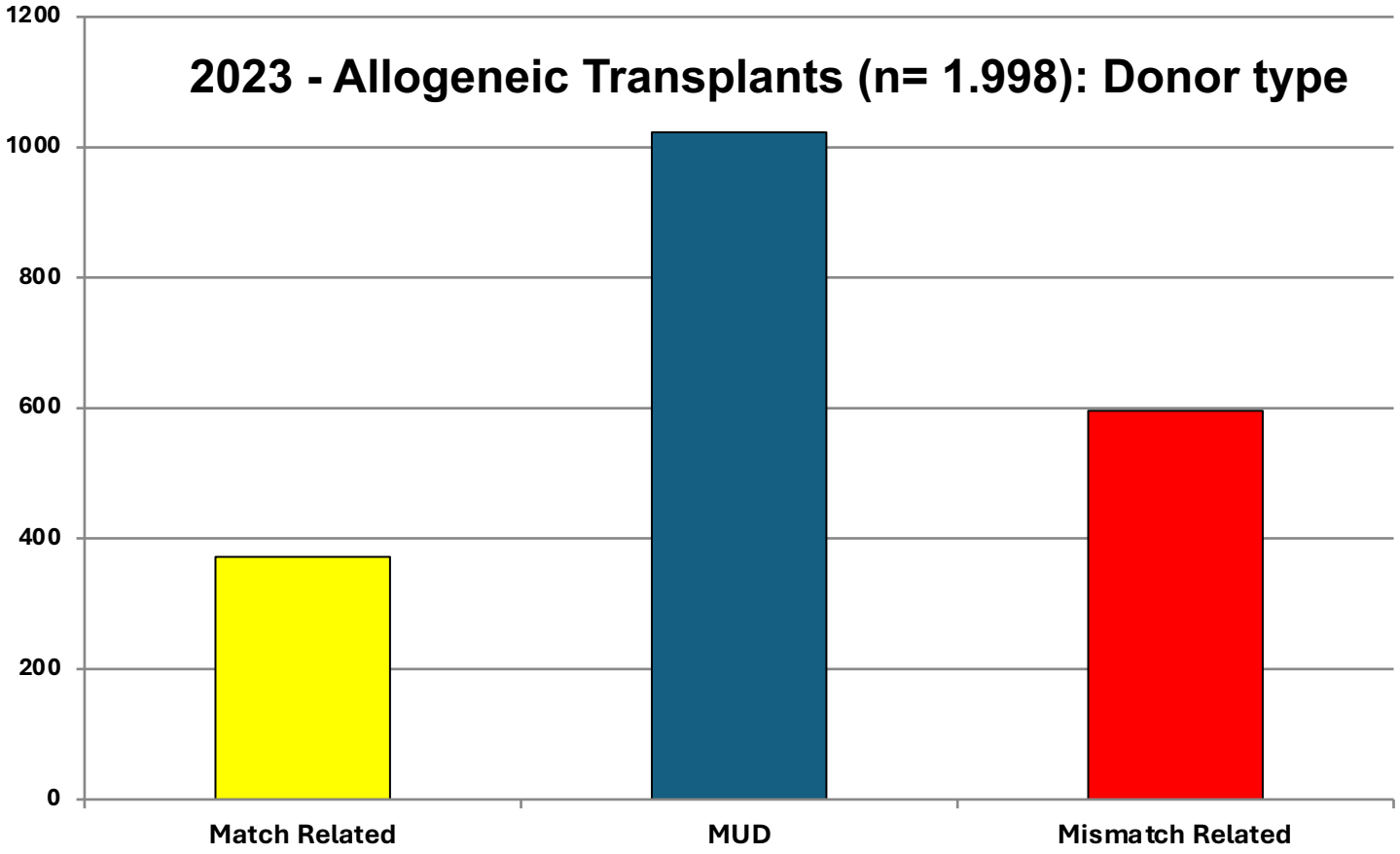
Probability to Find a Donor

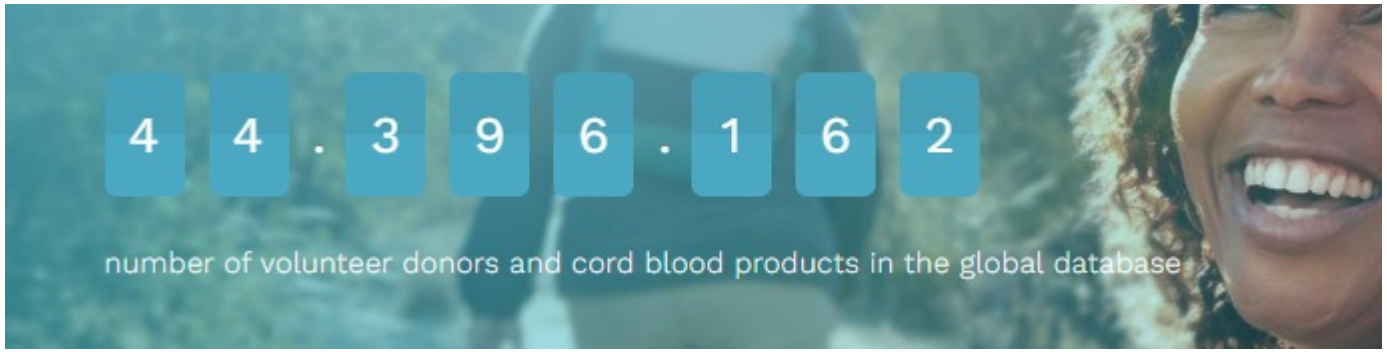


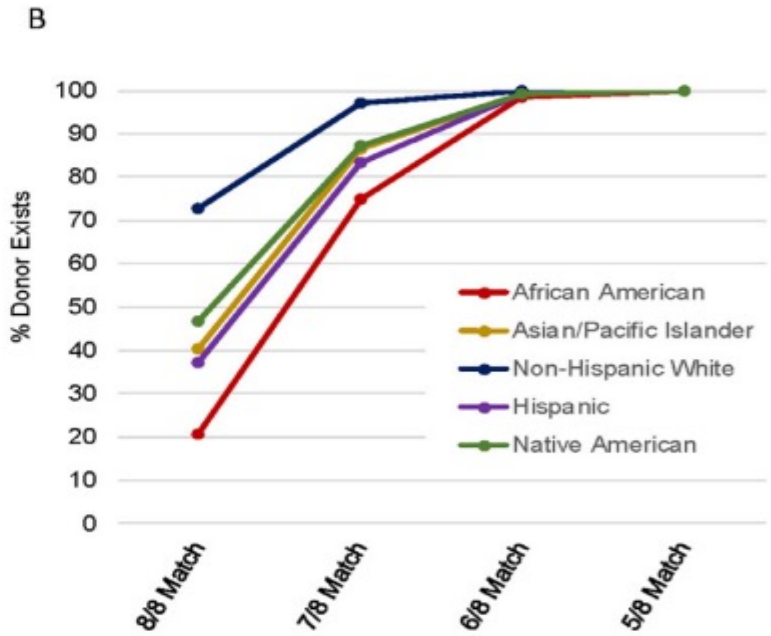
Role of anti HLA ab

F. Ayuk and A. Balduzzi, EBMT Handbook 2019

Donors







Global stem cell donor registries

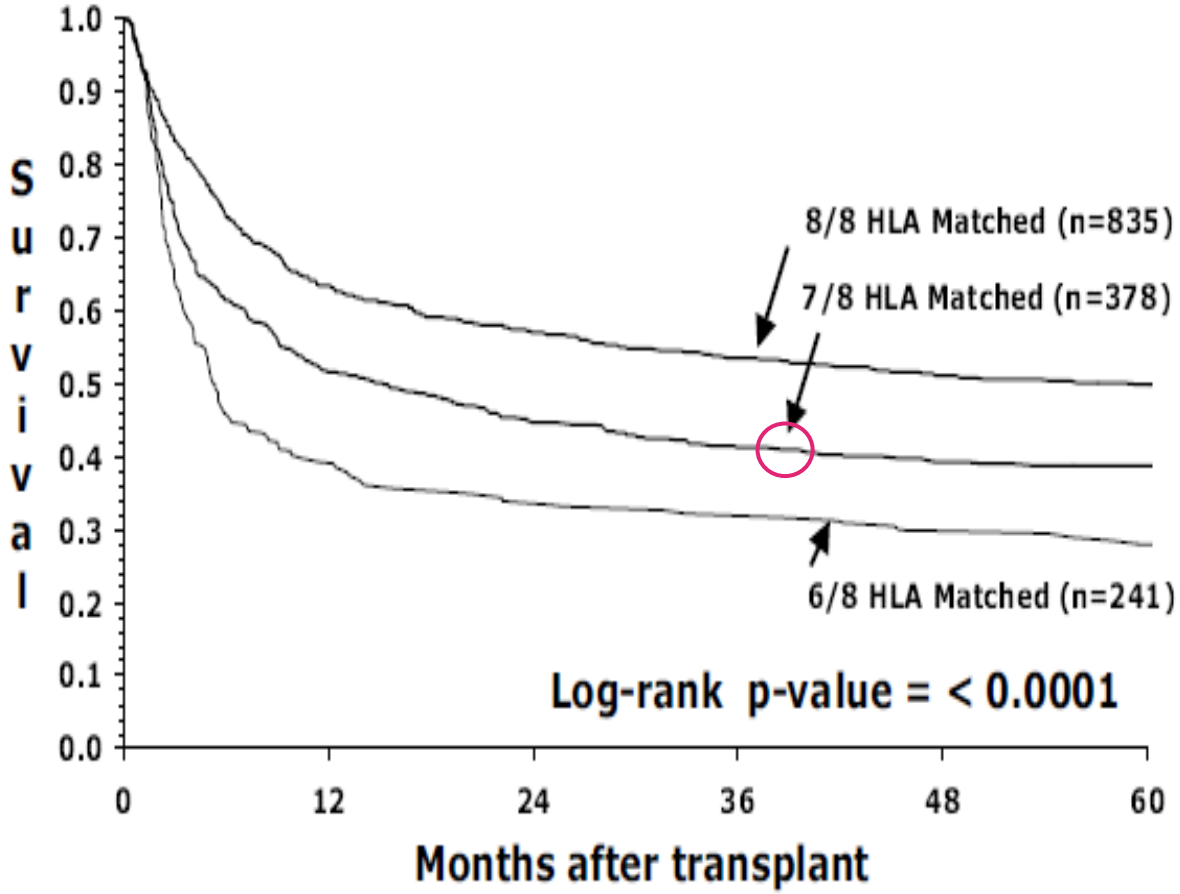
- **~ 43–44 million registered volunteer donors worldwide**
- **~ 750,000 cord blood units**
- registries in **>55 countries**

Global database coordinated by the World Marrow Donor Association (WMDA)

Jimenez et al, Transplantation and cellular therapy 2025

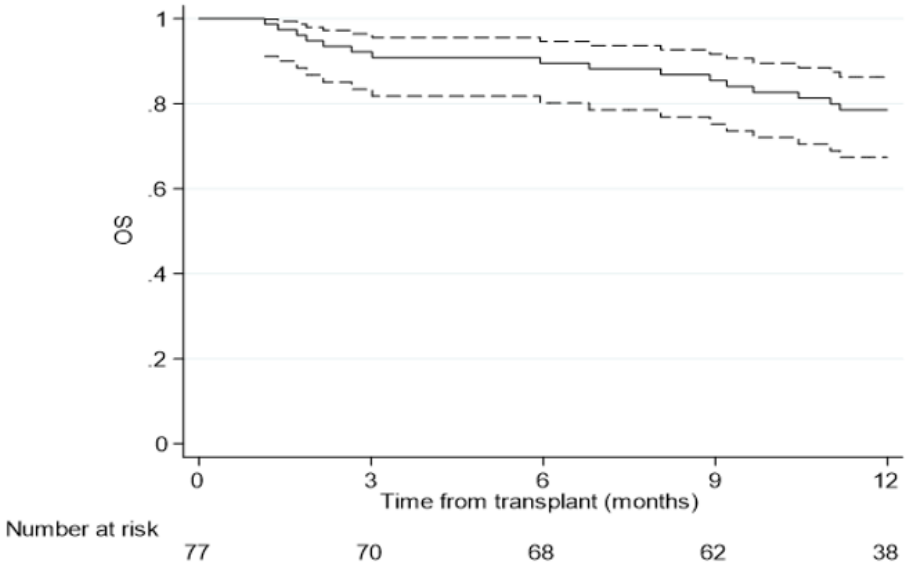
OVERALL SURVIVAL 1 LOCUS MISMATCHED

2007 .....



2025

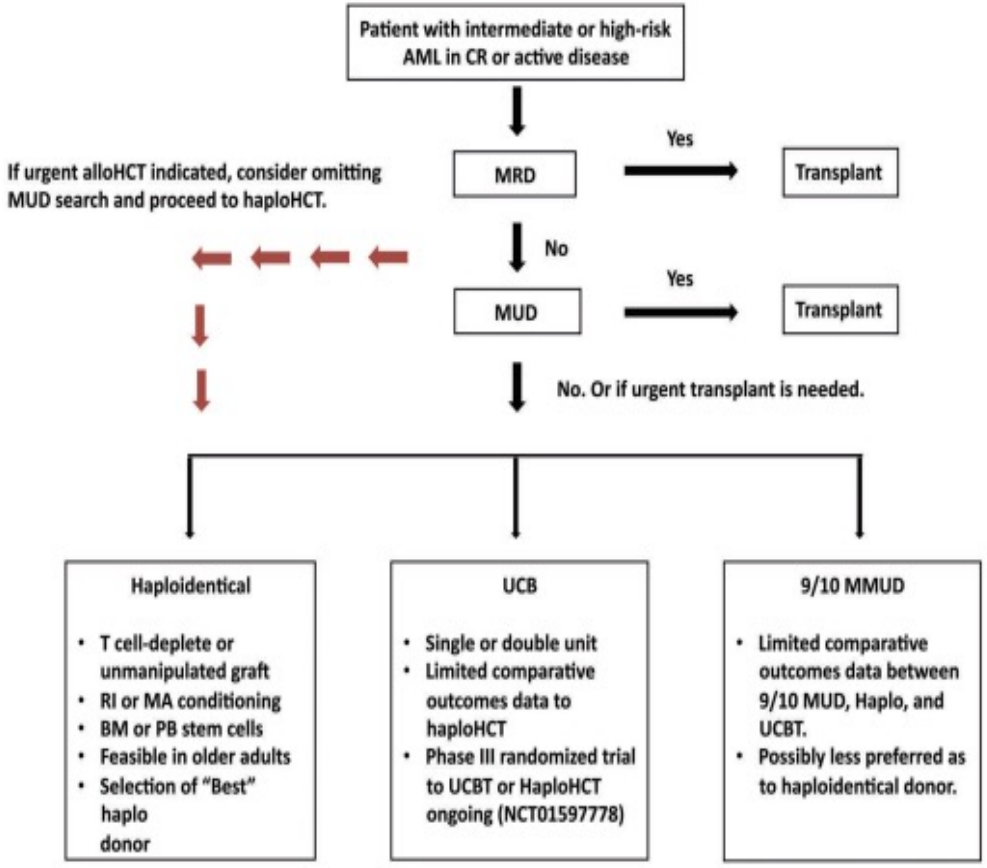
HLA matched 7/8

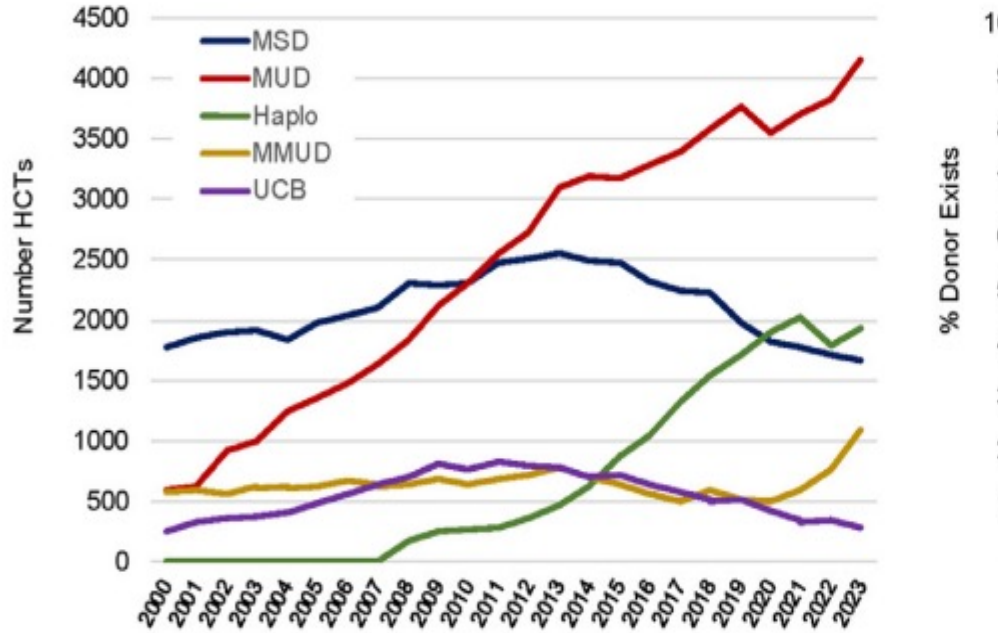


The 1-year overall survival was 78.5%
(95%CI: 67.4-86)

Lee et al Blood 2007,Raiola et al, Blood Advanced 2025

Donor: Selection





Ciceri et al Haematologica 2017,Jimenez et al, Transplantation and cellular therapy 2025

Si sta accumulando evidenza che l'età del donatore possa essere importante come (forse di più) del grado di compatibilità

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COMORBIDITIES

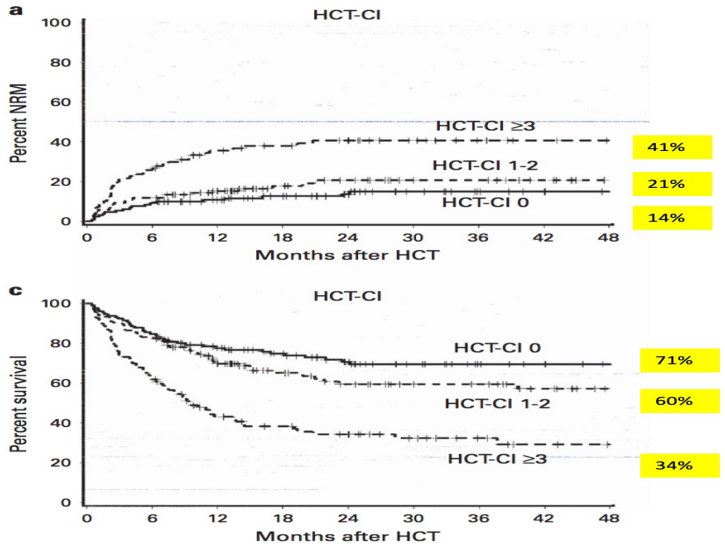
Hematopoietic cell transplantation (HCT)-specific comorbidity index

Blood 2005;106:2912-9

Comorbidity	Definitions of comorbidities included in the new HCT-CI	HCT-CI weighted scores
Arrhythmia	Atrial fibrillation or flutter, sick sinus syndrome, or ventricular arrhythmias	1
Cardiac‡	Coronary artery disease,§ congestive heart failure, myocardial infarction, or EF ≤ 50%	1
Inflammatory bowel disease	Crohn disease or ulcerative colitis	1
Diabetes	Requiring treatment with insulin or oral hypoglycemics but not diet alone	1
Cerebrovascular disease	Transient ischemic attack or cerebrovascular accident	1
Psychiatric disturbance†	Depression or anxiety requiring psychiatric consult or treatment	1
Hepatic, mild‡	Chronic hepatitis, bilirubin > ULN to 1.5 × ULN, or AST/ALT > ULN to 2.5 × ULN	1
Obesity†	Patients with a body mass index > 35 kg/m^2	1
Infection†	Requiring continuation of antimicrobial treatment after day 0	1
Rheumatologic	SLE, RA, polymyositis, mixed CTD, or polymyalgia rheumatica	2
Peptic ulcer	Requiring treatment	2
Moderate/severe renal‡	Serum creatinine > 2 mg/dL, on dialysis, or prior renal transplantation	2
Moderate pulmonary‡	DLco and/or FEV_1 66%-80% or dyspnea on slight activity	2
Prior solid tumor‡	Treated at any time point in the patient's past history, excluding nonmelanoma skin cancer	3
Heart valve disease	Except mitral valve prolapse	3
Severe pulmonary‡	DLco and/or FEV_1 ≤ 65% or dyspnea at rest or requiring oxygen	3
Moderate/severe hepatic‡	Liver cirrhosis, bilirubin > 1.5 × ULN, or AST/ALT > 2.5 × ULN	3

http://www.hctci.org/Home/Calculator

Sorror, Blood 2013



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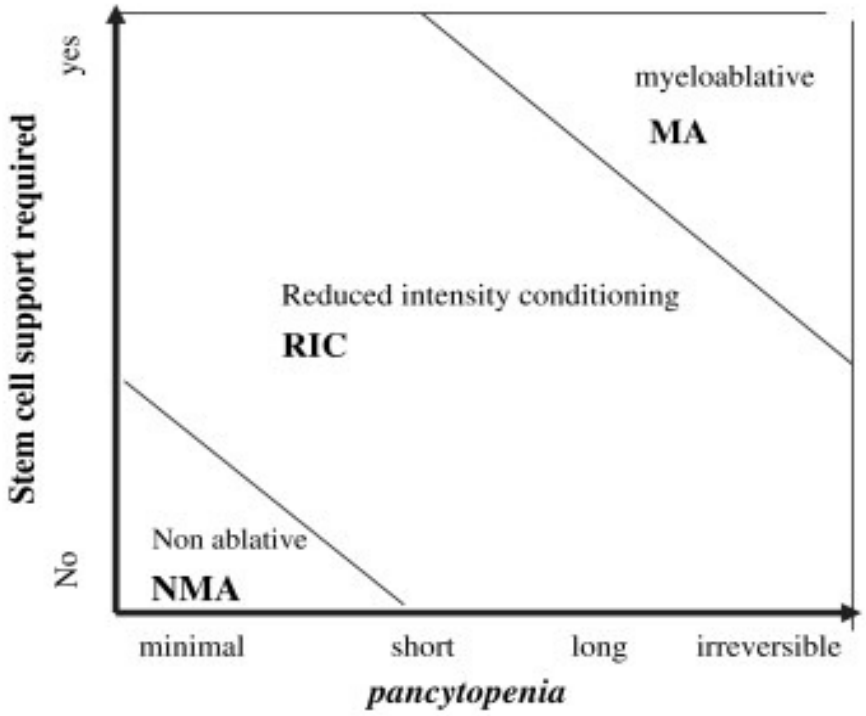
3) Reduced intensity (RIC) and reduced toxicity regimen (RTC) have been utilized in patients ineligible for standard myeloablative HSCT

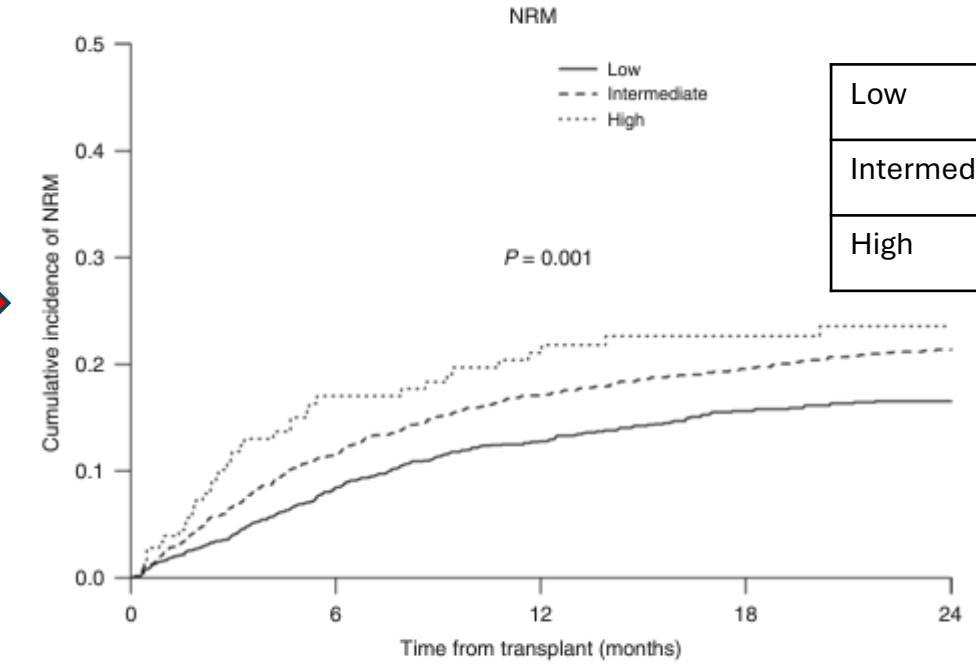
Defining the Intensity of Conditioning Regimens: a predictive numeric score

MAC **RIC** **NMA**



Bacigalupo et al. BMT 2009

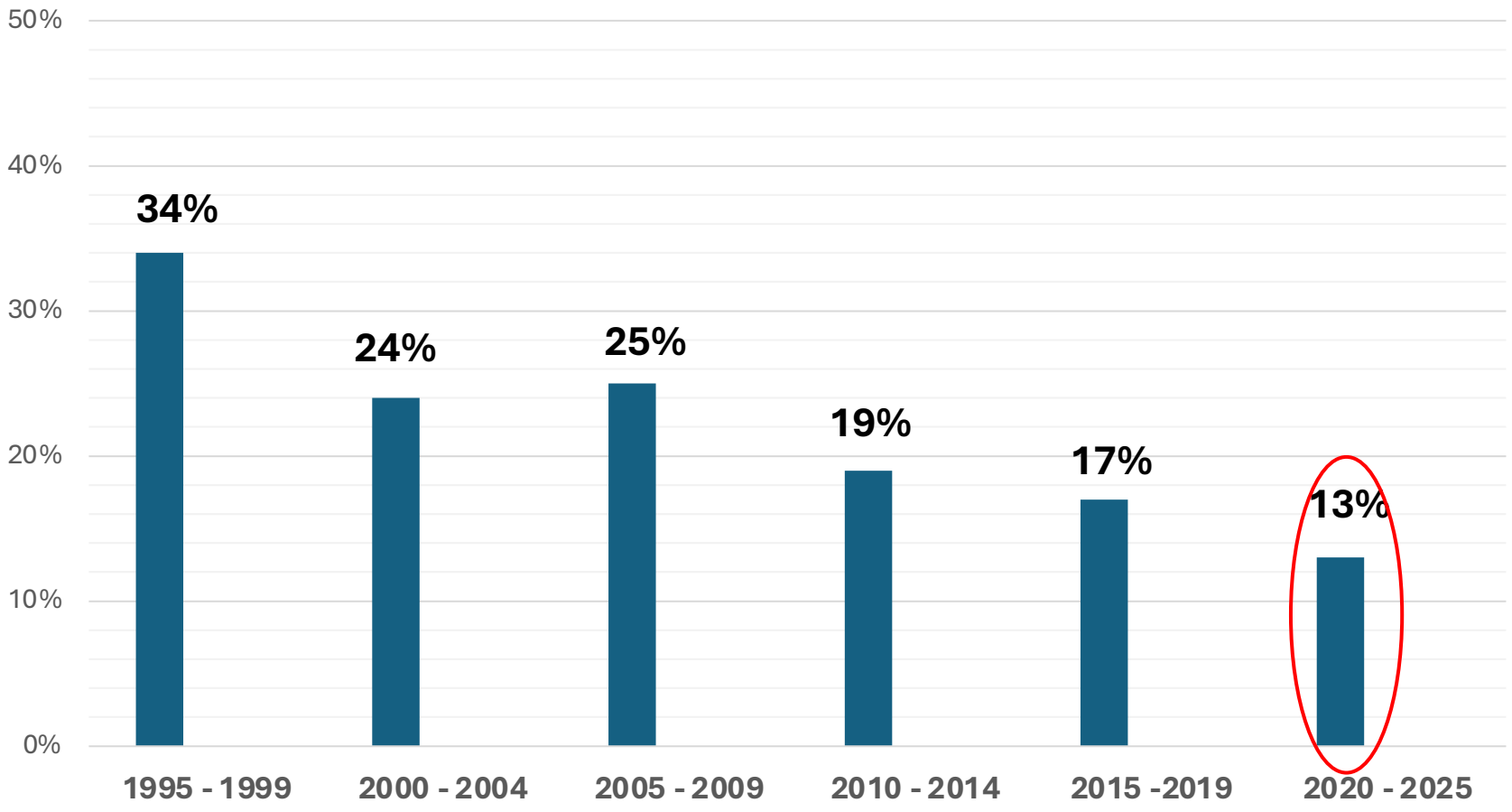
Transplant Condidioning Intensity: low, intermediate, high



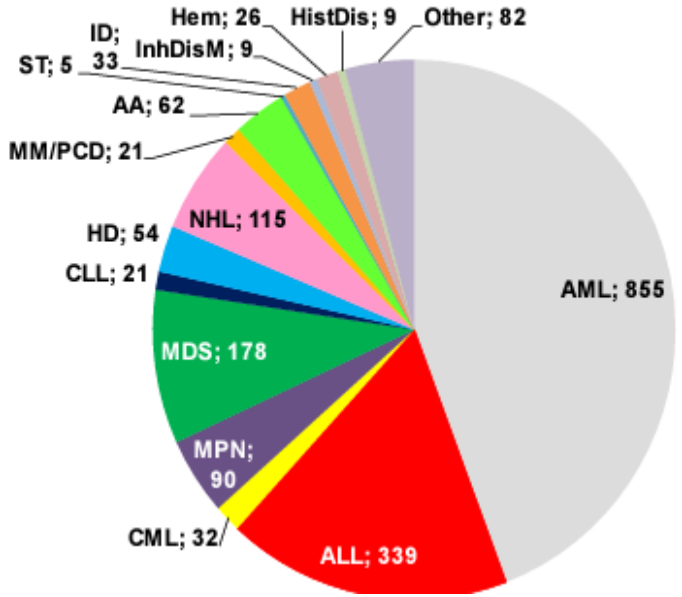
Low	≤2.5
Intermediate	2.6-3.5
High	≥3.6

Spyridonitis et al. BMT 2020; 55: 1114-1125

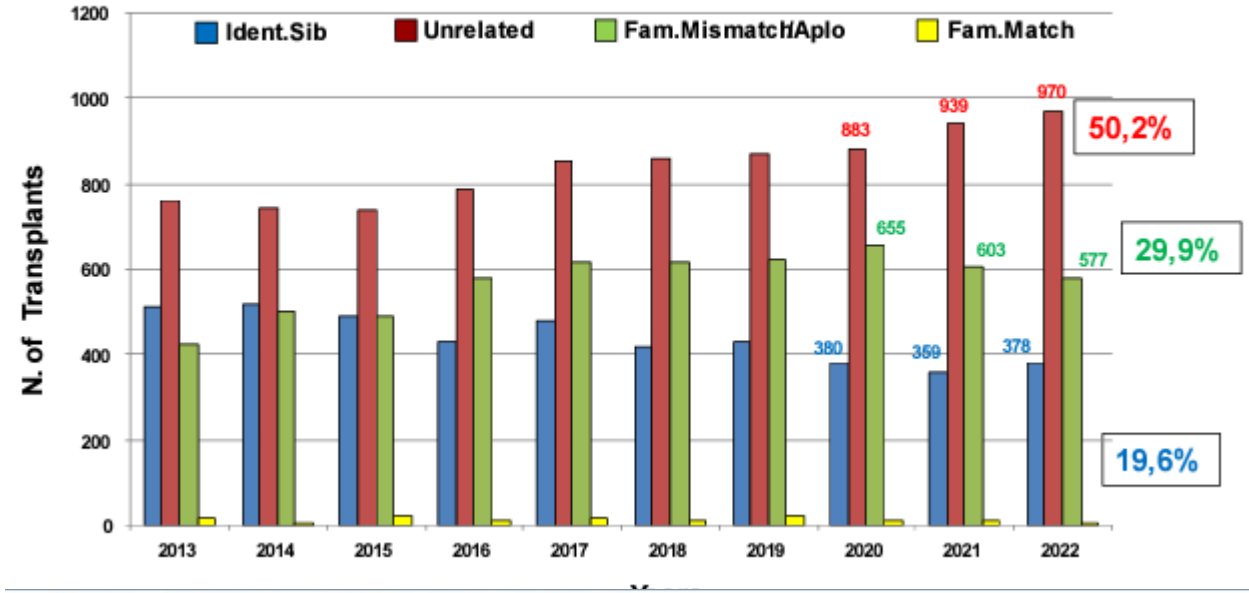
Non relapse mortality



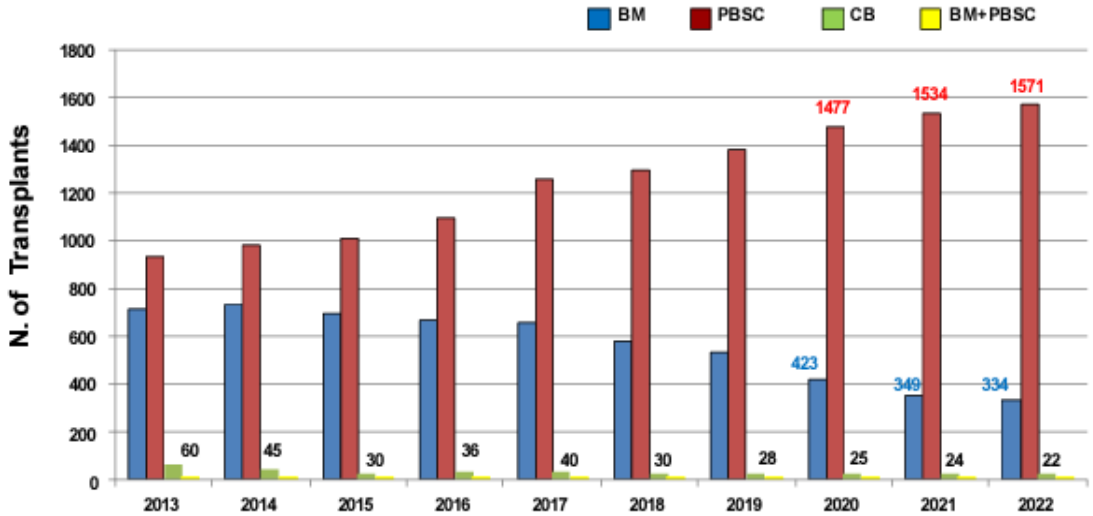
Allogeneic Transplants - Indications 2023



Allogeneic Transplants – Donor type

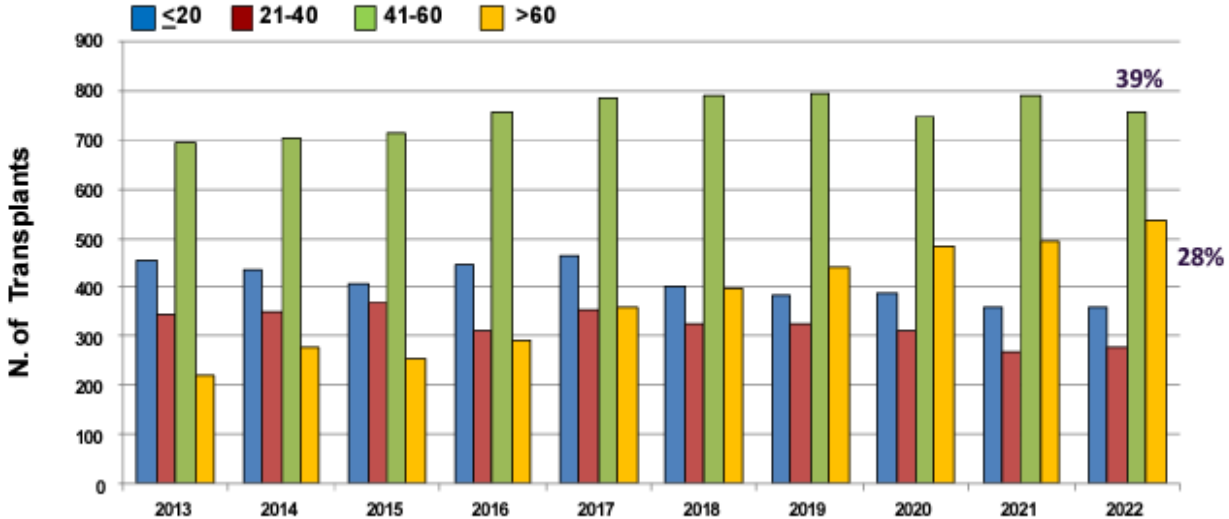


Allogeneic Transplants – Source of HSC



Export date 09/03/2023

Allogeneic Transplants – Patient age at transplantation



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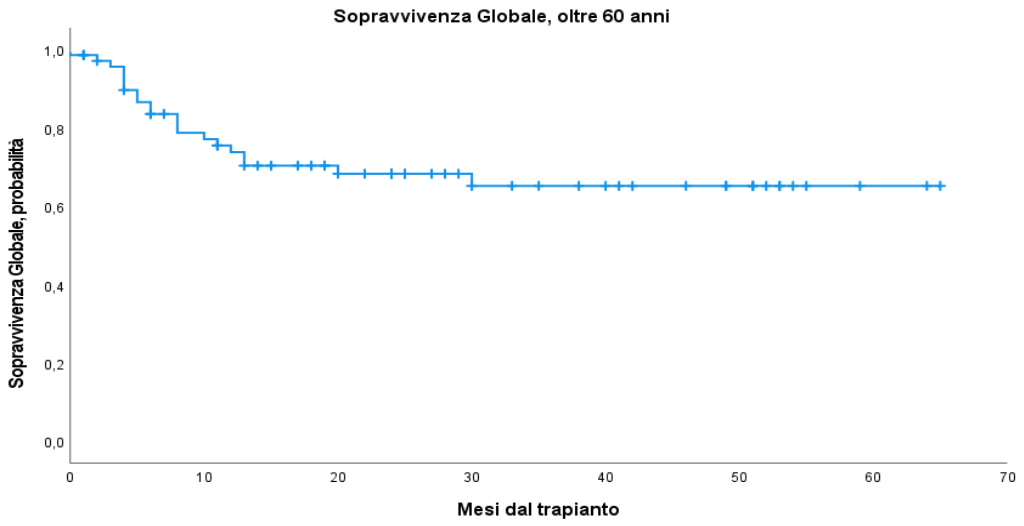
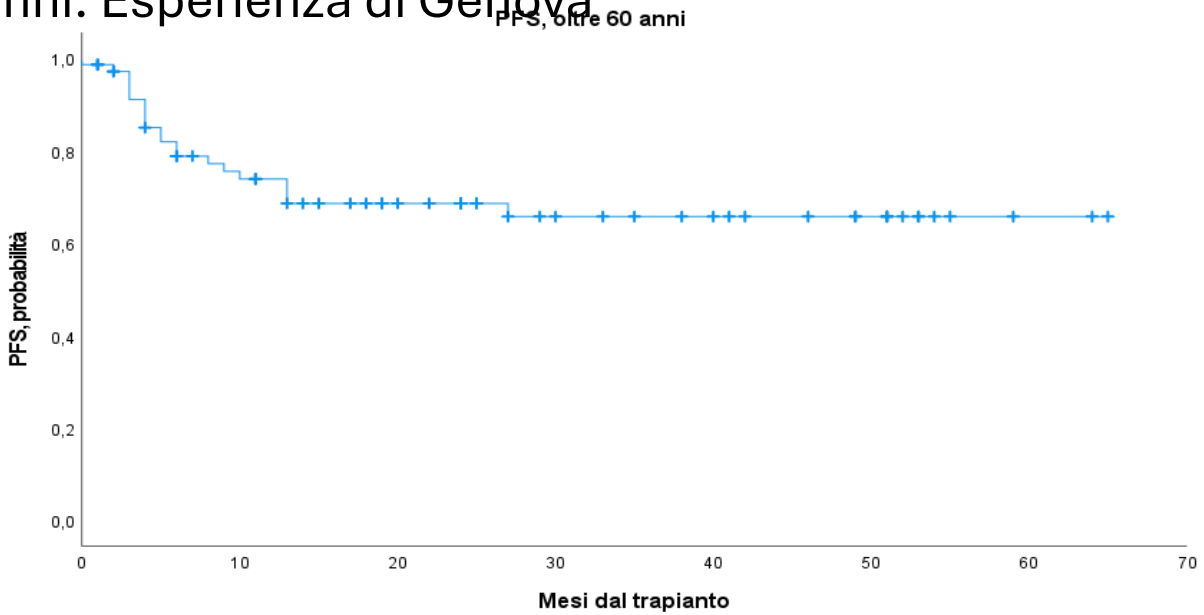
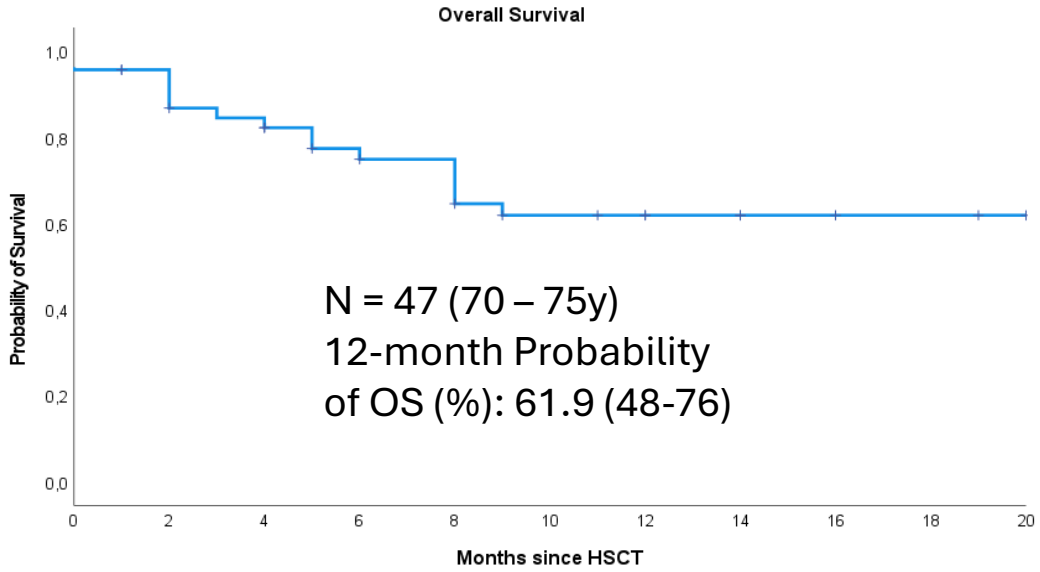
Trapianto in Leucemia Mieloide acuta > 60 e > 70 anni. Esperienza di Genova

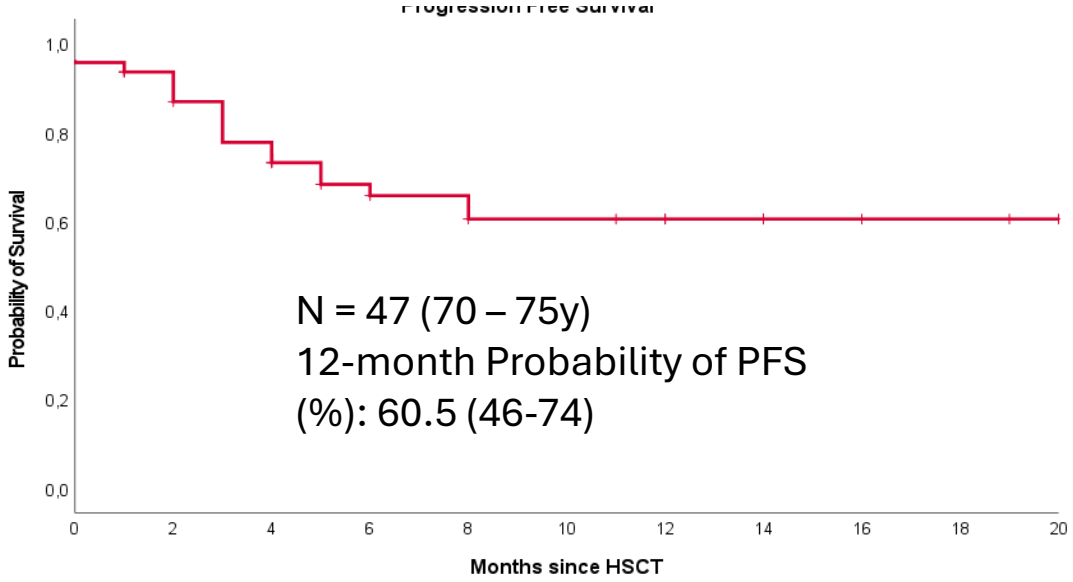






N = 47 (70 – 75y)
12-month Probability of OS (%): 61.9 (48-76)

FU, median duration: 12 months (95% CI: 6-33)



N = 47 (70 – 75y)
12-month Probability of PFS (%): 60.5 (46-74)

FU, median duration: 12 months (95% CI: 6-33)

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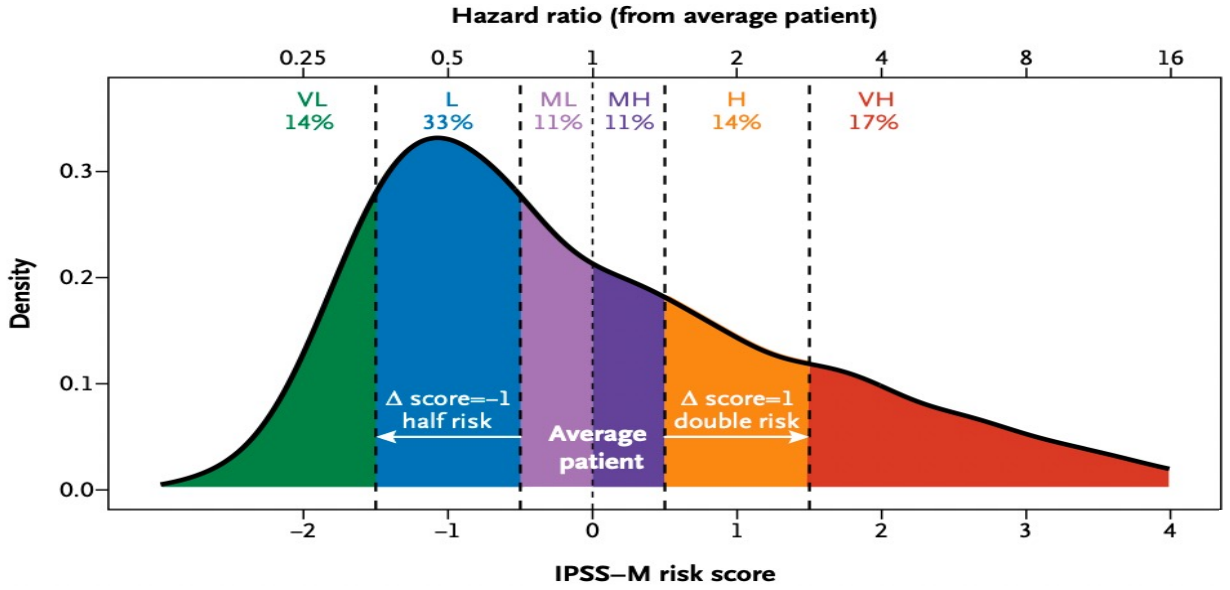
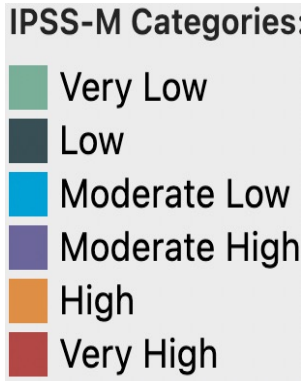
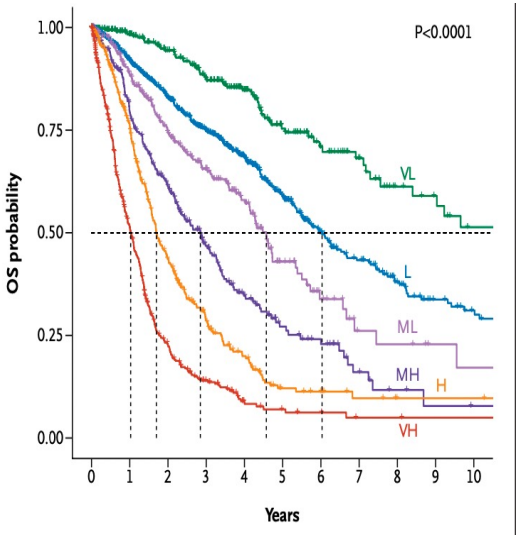
PROGNOSTIC SCORES

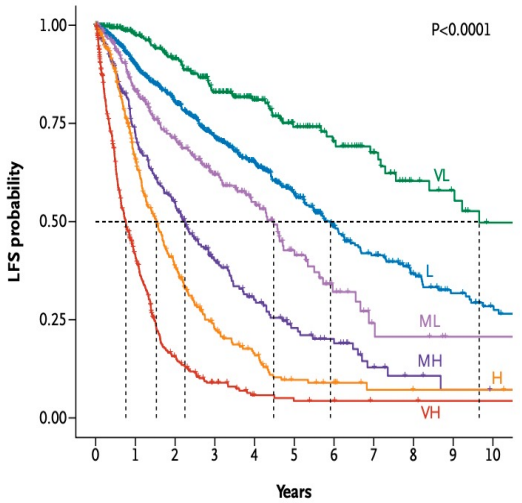
IPSS-Molecular





- Restratification of pts from IPSS-R to IPSS-M: 46% of pts change risk group
- 50% of int-risk shift to high risk





Bernard et al NEJM Evidence 2022

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- New conditioning /reduced intensity /standardization conditioning
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- Better knowledge of transplant and diseases pathophysiology mechanism
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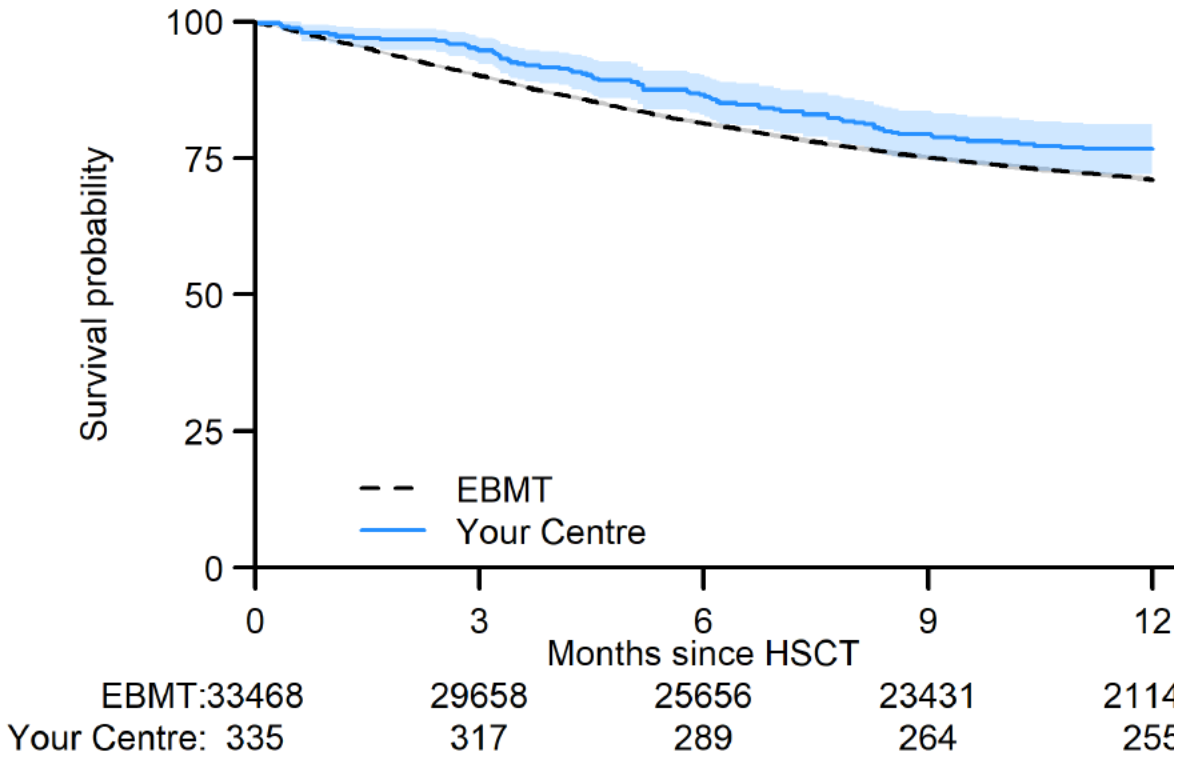
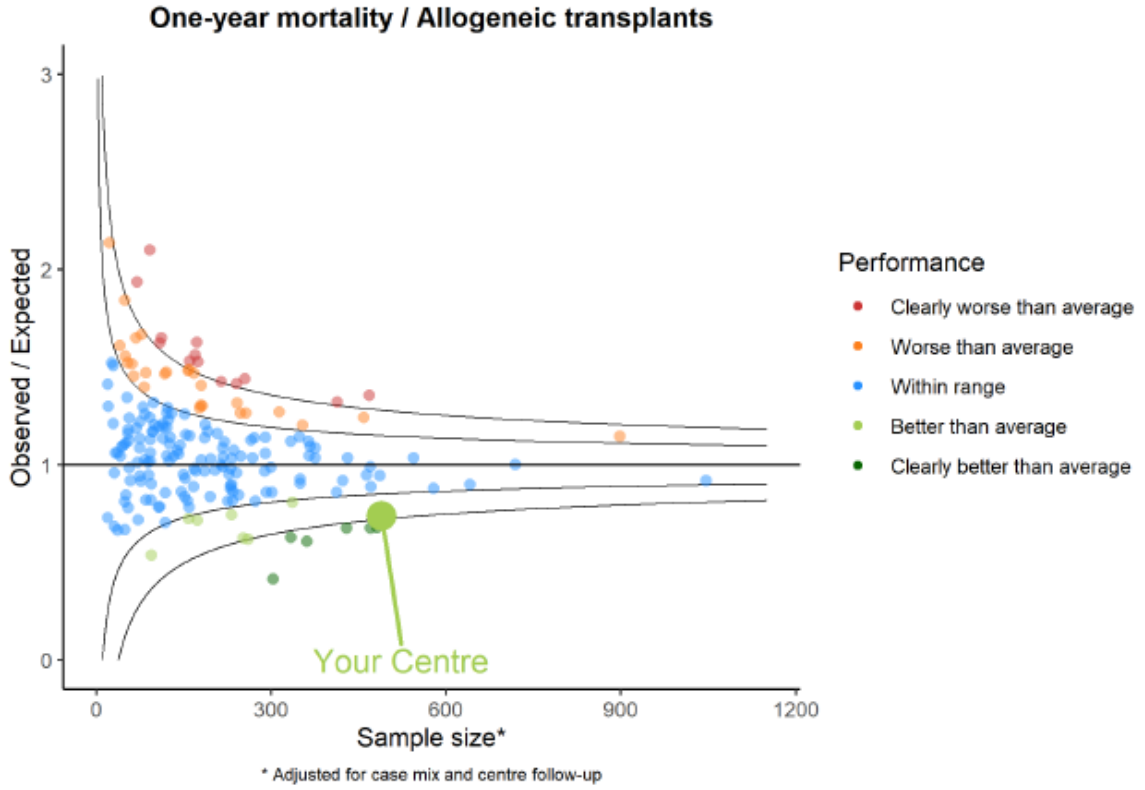
- Comorbidity index
- GITMO / EBMT / JACIE / Benchmarking project
- Cost saving

EBMT-JACIE Benchmarking project.

Allogeneic transplantation (288 centers, 49612 patients)



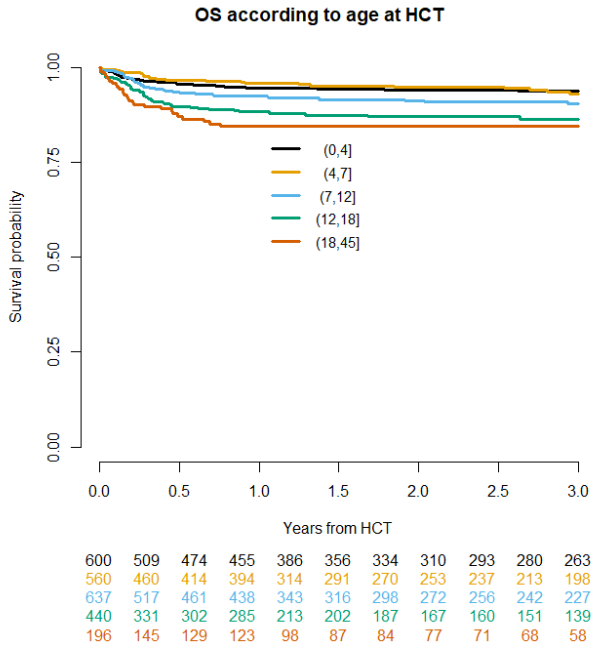


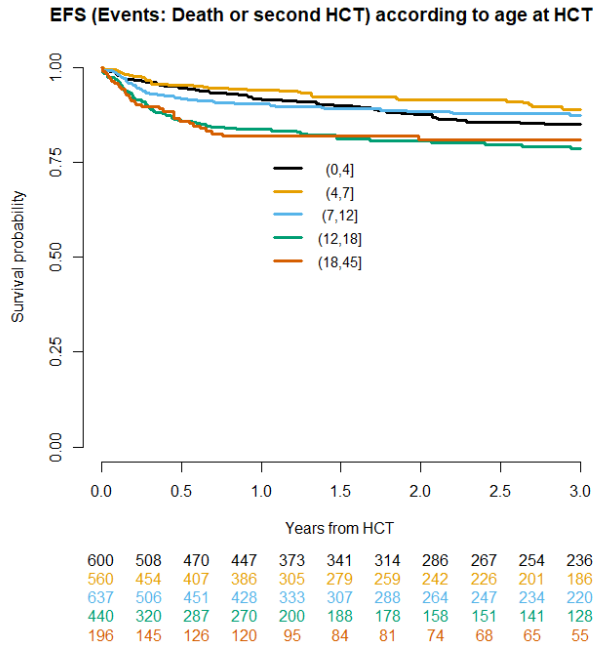
Posizione nel 2026

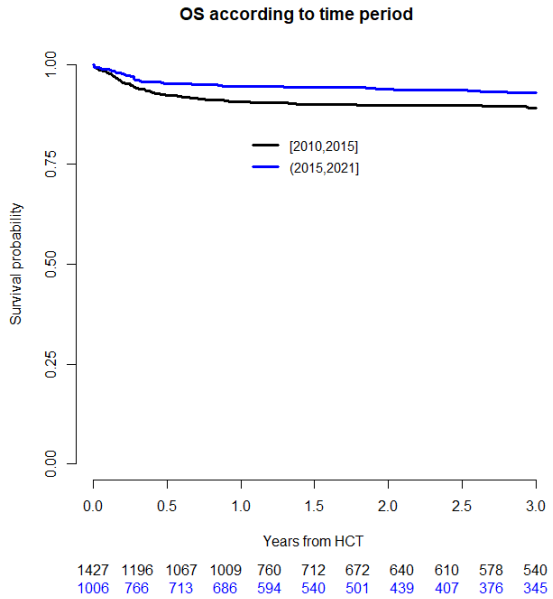
- Terapia curative (Chemio-immunoterapia)
  - Terapia di consolidamento
  - Ruolo in malattia attiva

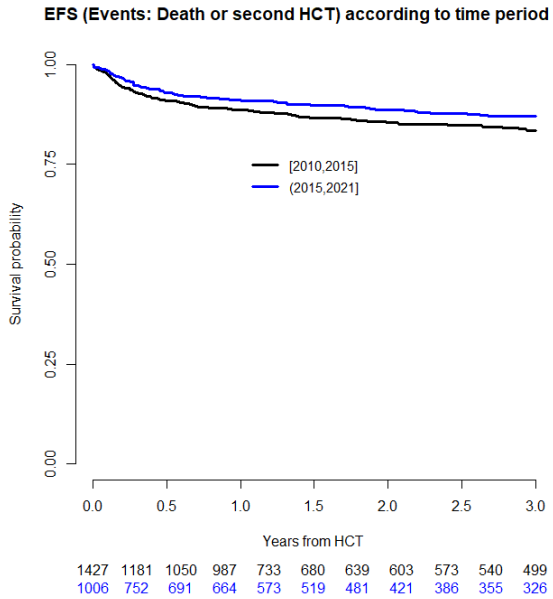
- Terapia curative / sostitutiva

EBMT Hemoglobinopathies WP
TDT: age as a factor in OS & GFRS

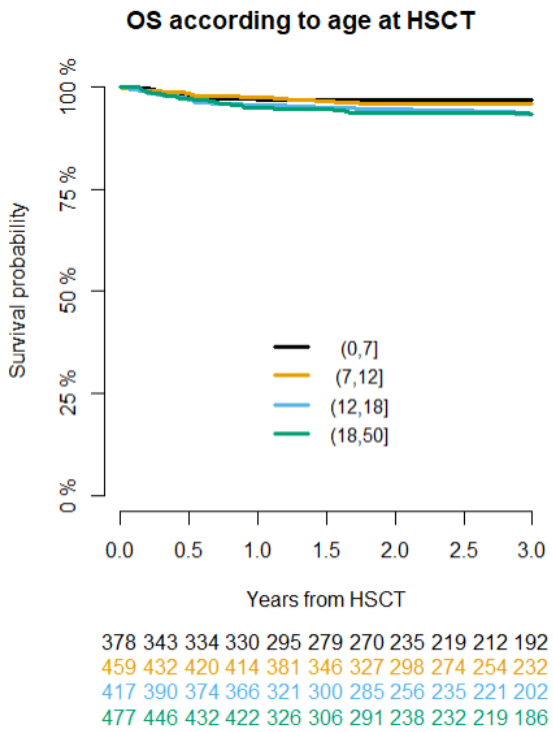


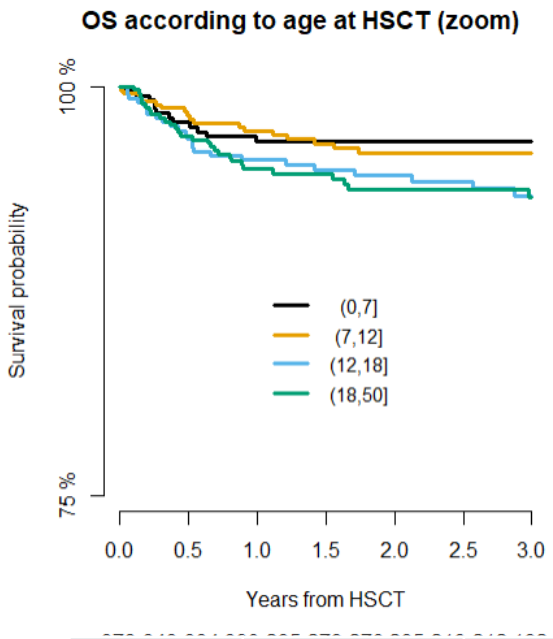




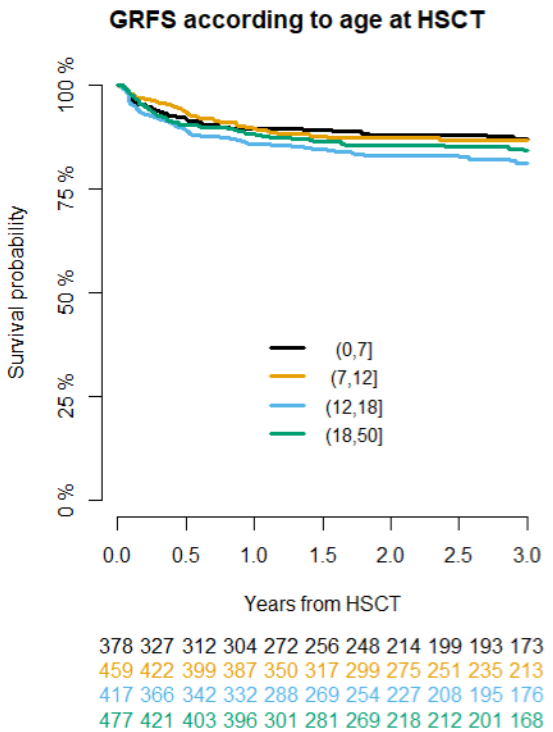


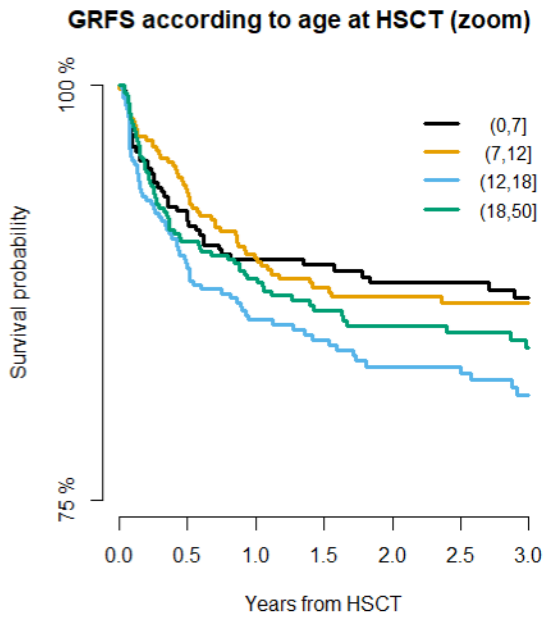
EBMT Hemoglobinopathies WP SCD: age as a factor in OS & GFRS





age	OS	
	HR (95% CI)	p value
(0,4]	1	
(7,12]	1.27 (0.61-2.67)	0.52
(12,18]	2.01 (1.01-3.99)	0.047
(18,45]	2.47 (1.23-4.94)	0.01





age	GRFS	
	HR (95% CI)	p value
(0,4]	1	
(7,12]	0.6 (0.29-1.23)	0.16
(12,18]	0.72 (0.36-1.44)	0.35
(18,45]	1.17 (0.62-2.2)	0.63

Recent and ongoing progreses

- 40.000.000 volunteers donors worldwide
- Haplo transplant
- Increased infectious diseases treatment and prophylaxis
- New conditioning /reduced intensity /standardization conditioning
- Decreased Transplant Related Mortality (TRM)
- Increased medical care bridging to transplant
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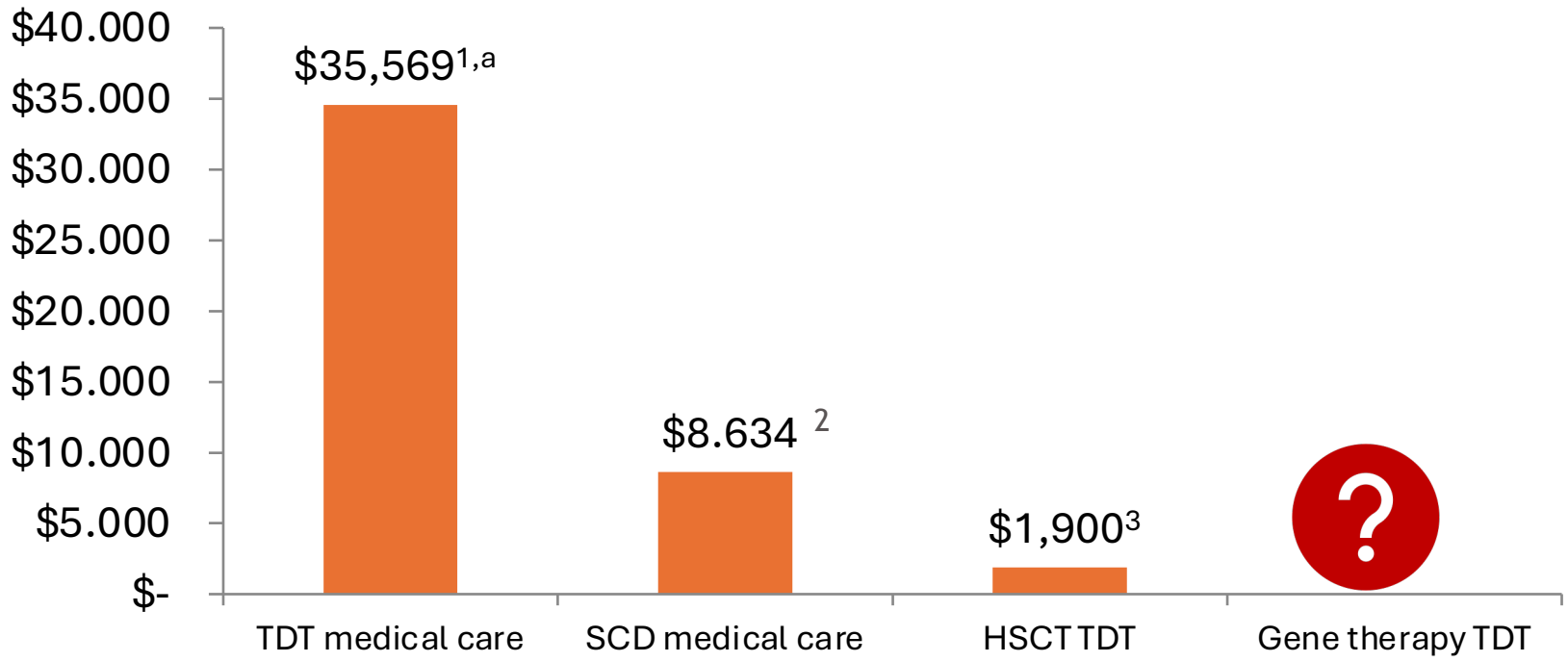
Cost-effectiveness of HSCT vs. medical care in thalassemia and SCD USD per expected life year

USD per expected life year



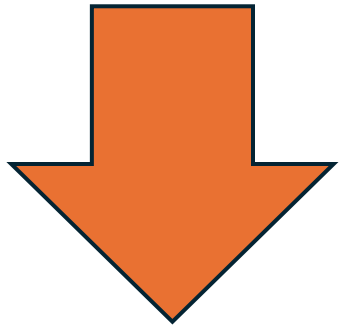
The wholesale acquisition cost of a single dose of gene therapy ranges from **$2.2 million to $2.8 million**[4]

[a] USD calculated based on EUR values provided in source and may very slightly. HSCT, hematopoietic stem cell transplantation; SCD, sickle cell disease; TDT, transfusion-dependent thalassemia. 1. Angelucci E, et al. Blood. 2017;130(Suppl.1):3368; 2. Kauf TL, et al. Am J Hematol. 2009;84:323–327; 3. Speaker's own expert opinion.

4. The Medical Letter on Drugs and Therapeutics. Casgevy for Beta Thalassemia. 2024. Available from: https://secure.medicalletter.org/system/files/private/TML-article-1702d.pdf. Accessed Sep 2024.

Recent and ongoing progreses

Close connection between the hematology and transplant centers



Planned and common patients’ journey

MEDICINES CAN CURE DISEASES BUT ONLY DOCTORS CAN CURE PATIENTS.

C. G. Jung

Società Italiana di Ematologia

QUINTO EVENTO NAZIONALE

SIE incontra i pazienti

Grazie per la vostra gentile attenzione

13 maggio 2026

Bologna, Royal Hotel Carlton

IRCCS AOM
AZIENDA OSPEDALIERA METROPOLITANA

IRCCS Ospedale Policlinico San Martino

PROGRAMMA TRAPIANTI E TERAPIE CELLULARI ALBERTO MARMONT