

Quali rimangono a tutt'oggi le indicazioni per la reinfusione di cellule staminali midollari?

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Corso di Formazione GITMO

Trapianto e terapie cellulari: cellule, donatori e condizionamenti

Udine, 8-9 Ottobre 2026

Aula Polifunzionale Ospedale di Udine

Disclosures of Name Surname

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

“Is there still a clear standardized recommendation to use bone marrow as first choice in adult allo-HSCT?”

“Or are there situations in which the preference for bone marrow is a choice?”

“Is there still a clear standardized recommendation to use bone marrow as first choice in adult allo-HSCT?”

Probably not.

“Or are there situations in which the preference for bone marrow is a choice?”

Yes, there are.

BM vs PB: differences in graft composition

PB → ↑ CD34⁺ cell dose → more hematopoietic progenitors

PB → markedly ↑ CD3⁺, CD4⁺ and CD8⁺ T-cell dose → greater effector-cell burden

PB → ↑ mature immune-cell content (T, NK and B cells)

BM → ↓ T-cell burden + relatively more regulatory/tolerogenic immune profile

Collins NH et al. Biol Blood Marrow Transplant 2010, Mehta et al. Transplantation and Cellular Therapy 2021, Chang YJ et al. Journal of Translational Medicine. 2015, Lundqvist A et al Frontiers in Immunology. 2021..

BM vs PB: from graft composition to clinical outcomes

PB → ↑ CD34⁺ cell dose → more hematopoietic progenitors

→ faster engraftment / ↓ graft failure

PB → markedly ↑ CD3⁺, CD4⁺ and CD8⁺ T-cell dose → greater effector-cell burden

→ ↑ alloreactivity / ↑ inflammatory drive → ↑ CRS / ↑ GVHD, but potentially ↑ GVL

PB → ↑ mature immune-cell content (T, NK and B cells)

→ faster immune reconstitution / earlier immune competence

BM → ↓ T-cell burden + relatively more regulatory/tolerogenic immune profile

→ ↓ alloreactivity / ↓ inflammatory drive → ↓ CRS / ↓ GVHD, potentially at the cost of less GVL

Practical considerations

BM

- **More complex collection:** OR + anesthesia + longer donor recovery
- **Higher donor burden:** approx. 4-fold higher serious adverse events than PBSC
- **Graft adequacy:** TNC target may be difficult to achieve, especially with **donor–recipient weight mismatch**
- **Product constraints:** limited cryopreservation; ABO-related manipulation may reduce cell dose

PB

- **Simpler collection:** G-CSF mobilization + outpatient leukapheresis
- **Lower resource utilization:** no OR/anesthesia, shorter hospitalization and fewer transfusions
- **Lower transplant-related costs**
- **Donor safety:** long-term follow-up shows **no increased risk of malignancy, autoimmune disease or serious late adverse events** after G-CSF

Seftel M et al Transplant Cell Ther 2021, Prokopishyn N. Biol Blood Marrow Transplant 2019, Shaw B. Biol Blood Marrow Transplant 2015

Choosing BM is not enough

BM harvest is a complex, team-dependent procedure

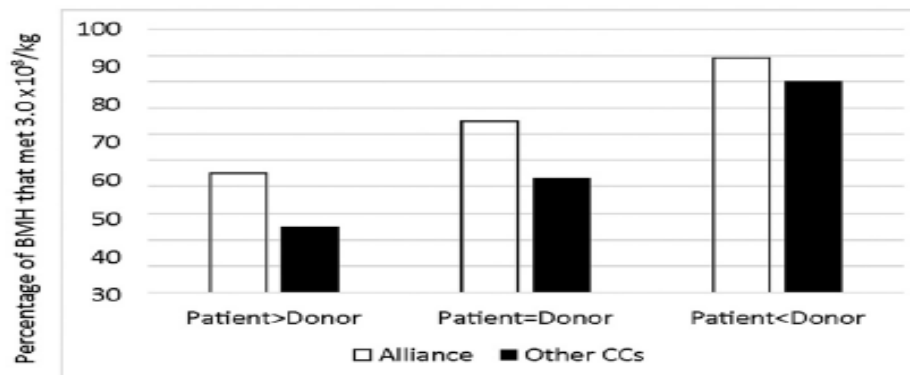
Requires a **trained multidisciplinary team**: collectors, anesthesiologist, scrub/circulating nurses and product-handling staff

Declining use of BM may lead to **loss of expertise and inadequate staff training**

Center experience matters: higher-volume centers produce grafts with **higher TNC concentration**

Low-volume centers are also associated with **greater donor toxicity**

NMDP Marrow Alliance 2022:
Target: TNC $\geq 3.0 \times 10^8/\text{kg}$ recipient weight

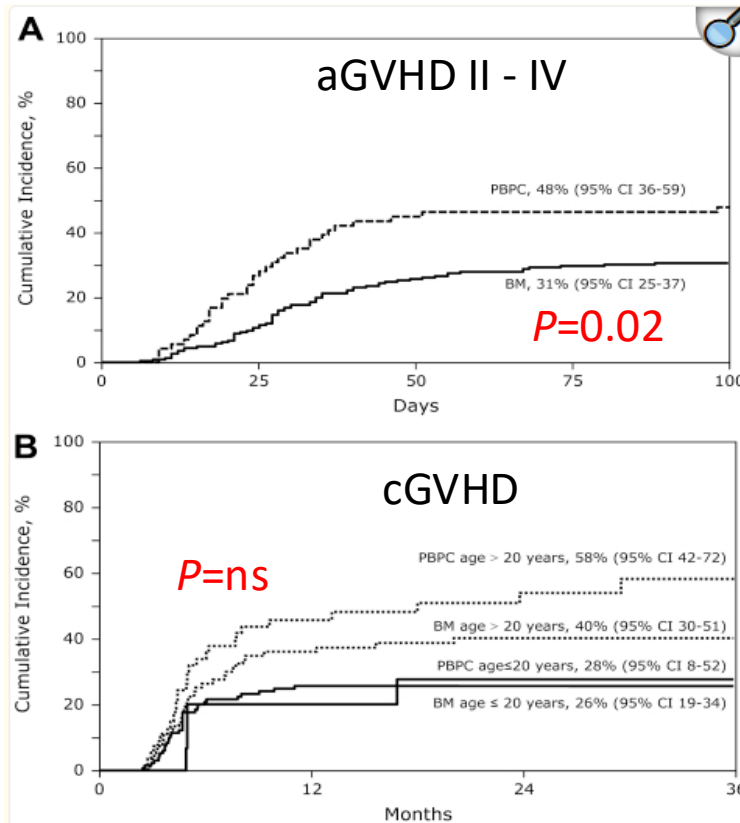


Murakami et al. Transplantation and Cellular Therapy 2024

SAA: BM > PB

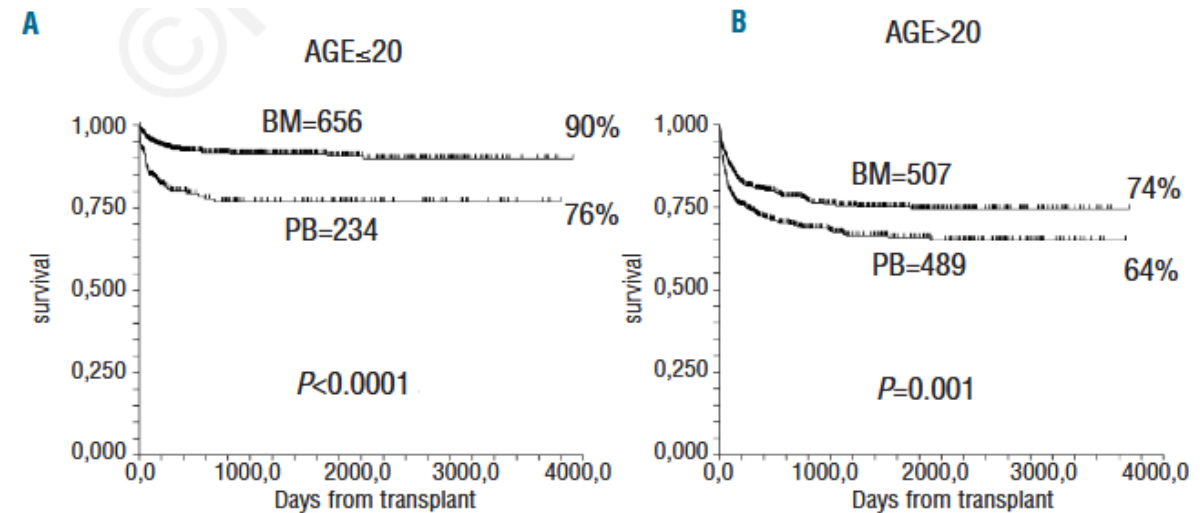
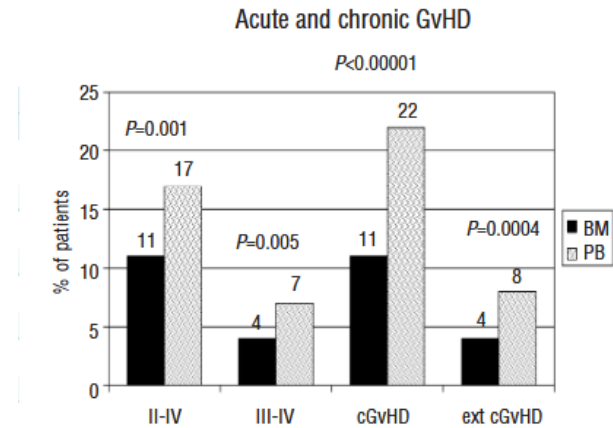
CIBMTR centers that contribute data prospectively on consecutive transplantations.

SAA BM = 225 PB = 71 from MUD // 2000 - 2008



The 3-y OS adjusted for poor performance and no TBI were 61% after PB 76% after BM ($P=0.02$);

EBMT SAA BM = 1163 PB = 723 from MSD // 1999 - 2009



Eapen M Blood 2011

Bacigalupo et al. Haematologica 2012

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BM associated with less GVHD and better survival in both MSD and MUD SAA

ASTCT 2024 → BM preferred graft source Strong recommendation – moderate certainty of evidence.

“For selected patients with:

- serious ongoing infections before HSCT,*
- those where the donor only gives consent for PB collection,*
- or when there are clinical concerns about large donor-recipient weight disparity*
- the ability to harvest adequate TNC / kg, clinicians*

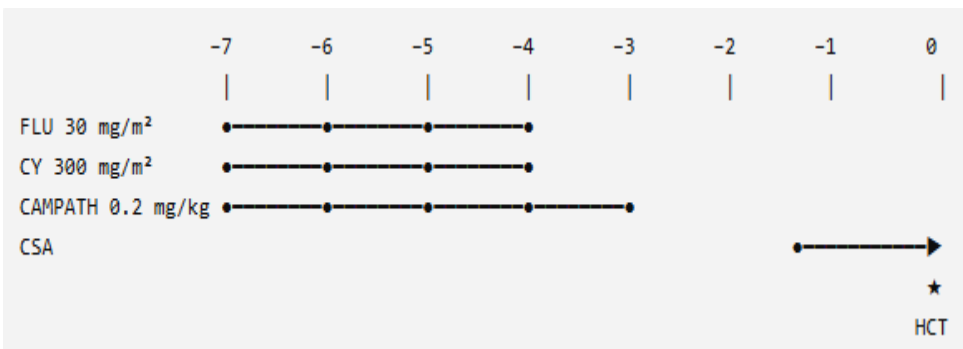
may use PB as graft source while accepting a higher risk of GVHD”.

ASH 2026 → no specific recommendation on BM vs PB graft source

Iftikhar et al Transplantation and Cellular Therapy 2024, Scheinberg et al. Blood 2026

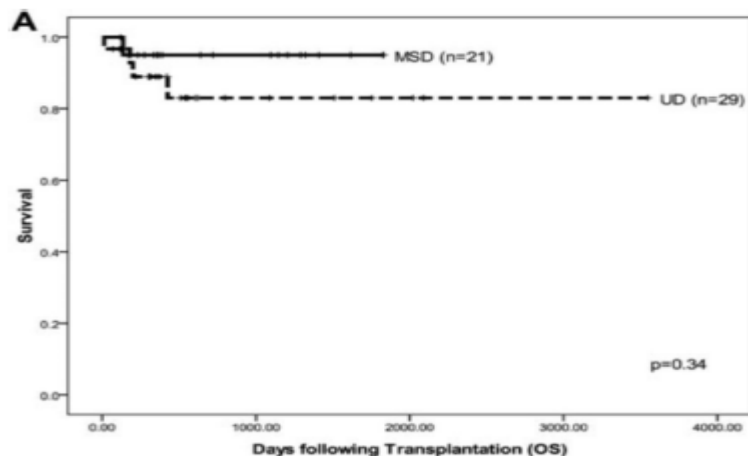
SAA: can modern GVHD prophylaxis mitigate the impact of graft source?

ALEMTUZUMAB // UK experience



Alemtuzumab-based conditioning: PBSC or BM

aGVHD 13.5%, (I-II) ; cGVHD 4%

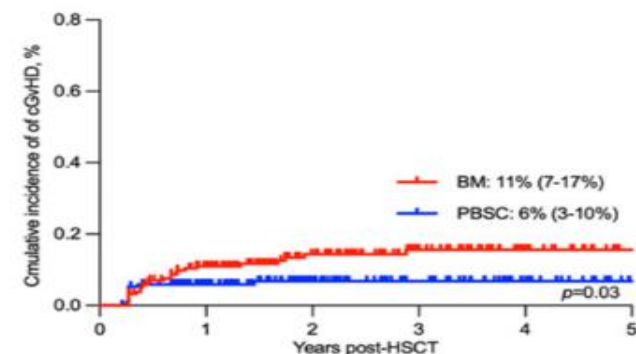
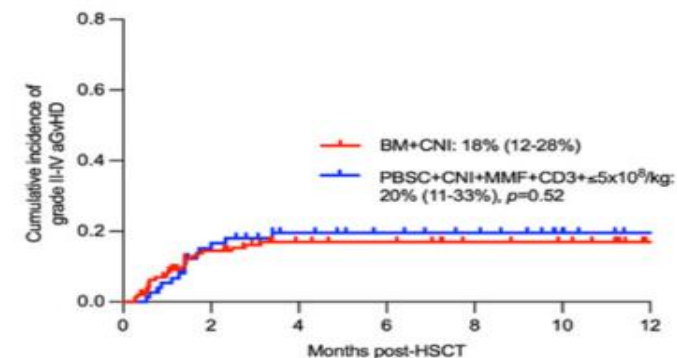


Shaw et al., *Br J Haematol.* 2011 Marsh et al., *Blood* 2011 *Transplant Cell Ther.* 2024.

Dual GVHD prophylaxis:

- 1) Alemtuzumab,
- 2) 2) CD3⁺ T cell dose $\leq 5 \times 10^8/\text{kg}$ reduces GVHD after PBSC transplantation.

Retrospective multicenter study 397 children: BM = 202, PBSC = 195)



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Role of age and donor type in 3,646 severe aplastic anemia patients undergoing hematopoietic stem cell transplantation in 2011-2020: a retrospective EBMT-SAAWP study

A retrospective study of the EBMT Severe Aplastic Anemia Working Party to investigate:

- The impact of (older) age on overall survival of HSCT for AA
- The possible improvement over time
- The possible impact of age on other clinically meaningful transplant outcomes
- The impact of age split by donor type
- **The possible impact of other factors**

In all first allogeneic HSCT performed at EBMT centers in the decade 2011-2020 (minimum follow up 3 years)

Data collected from the EBMT PROMISE database



On behalf of the Severe Aplastic Anemia Working Party
of the European Society for Blood and Marrow Transplantation

Courtesy of Antonio M Risitano

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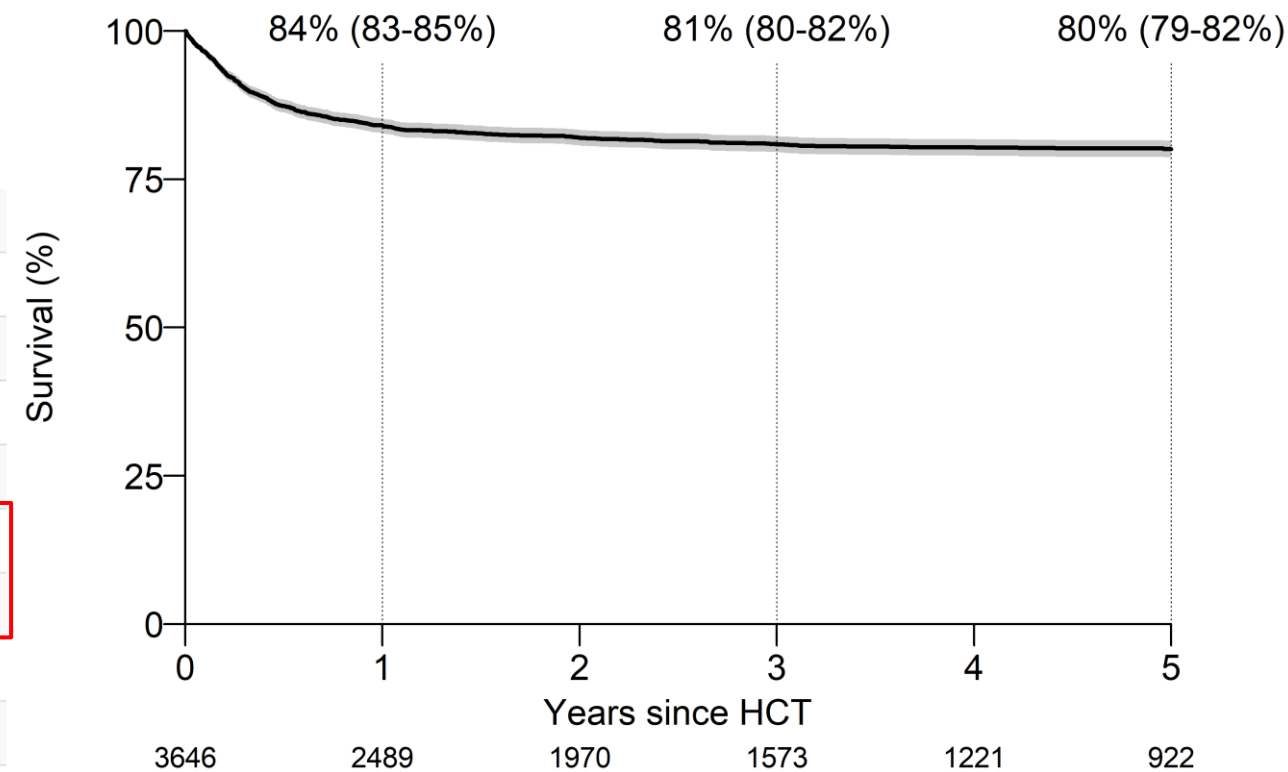
Results

Overall survival - global

- Total number of included patients: 3646
- Patients received a first HCT between 2011 and 2020.
- Transplants were performed in 365 centers.

Cause of death

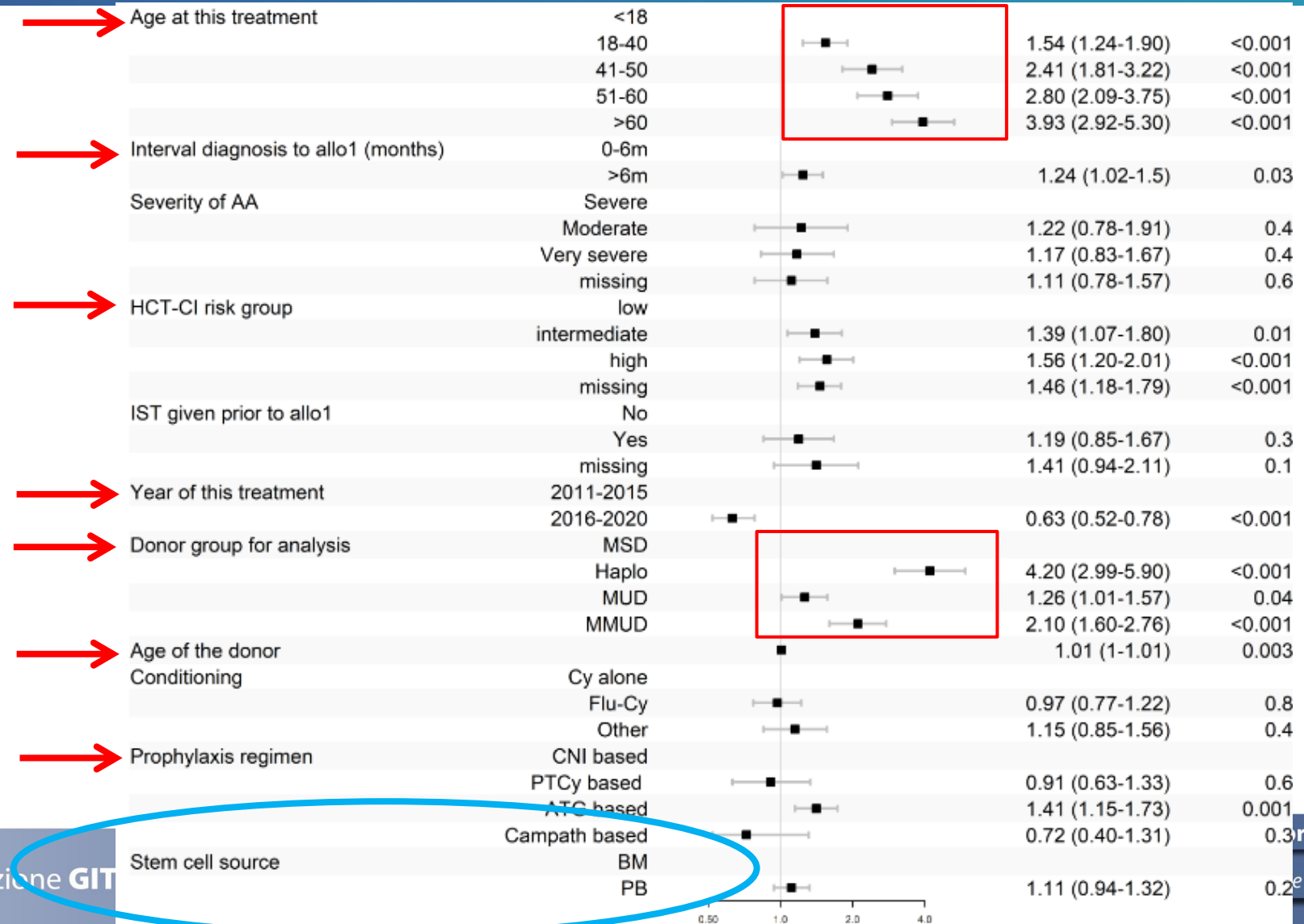
Group	Total		≤3yrs FU		>3yrs FU	
	Missing	N (%)	Missing	N (%)	Missing	N (%)
Total		602 (100%)		573 (95.2%)		29 (4.8%)
death relapse/progression	25 (4.2%)	22 (3.8%)	22 (3.8%)	22 (4.0%)	3 (10.3%)	0 (0.0%)
secondary malignancy/PTLD		34 (5.9%)		25 (4.5%)		9 (34.6%)
gvhd		86 (14.9%)		82 (14.9%)		4 (15.4%)
infection		289 (50.1%)		285 (51.7%)		4 (15.4%)
organ damage/failure		54 (9.4%)		51 (9.3%)		3 (11.5%)
toxicity		12 (2.1%)		11 (2.0%)		1 (3.8%)
HSCT-related death		29 (5.0%)		28 (5.1%)		1 (3.8%)
other		51 (8.8%)		47 (8.5%)		4 (15.4%)



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Age and overall survival - multivariable

Multivariable analysis for overall survival



β -Thalassemia: is bone marrow still the preferred graft?

Adult TDT: contemporary real-world EBMT /Hemoglobinopathy Working Party — 2010–2021

- 206 adults, median age 22.1 years (range 18–44.8)
- PBSC was the predominant graft source: 59.3%
- 2-year OS: 84.4% (95% CI 78.1–89.0)
- 2-year EFS: 80.8% (95% CI 73.9–86.1)
- Severe GVHD remained relatively limited: grade III–IV aGVHD 9.5% and extensive cGVHD 7.2%

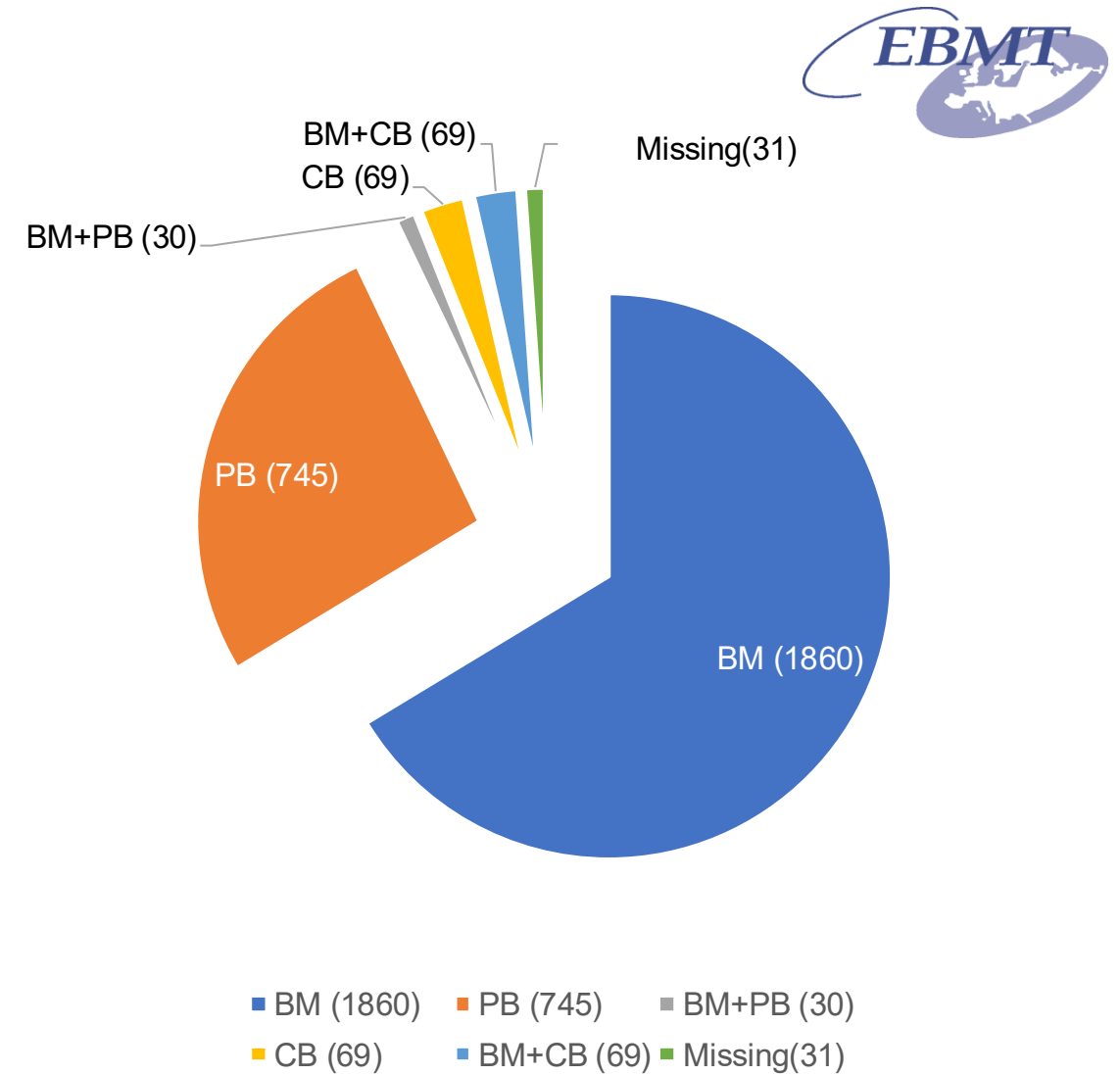
Current recommendations for stem-cell source in TDT

Guideline / Consensus	Recommendation
International Expert Panel / EBMT, 2014	Avoid PBSC because of increased chronic GVHD
TIF Guidelines, 2025	BM is usually preferred; no anti-malignancy effect is required
EBMT Guidelines, 2026	No specific BM vs PBSC recommendation

Baronciani D, et al. Blood. 2024;144(Suppl 1) Angelucci E, et al. Haematologica. 2014; Pinto VM, et al. TIF Guidelines for the Management of TDT, 5th ed. 2025. Essa M, et al. BMT. 2026.

Stem cell source

- children: 69.2 % received bone marrow
- adults: 59.3 % adults received PBSC

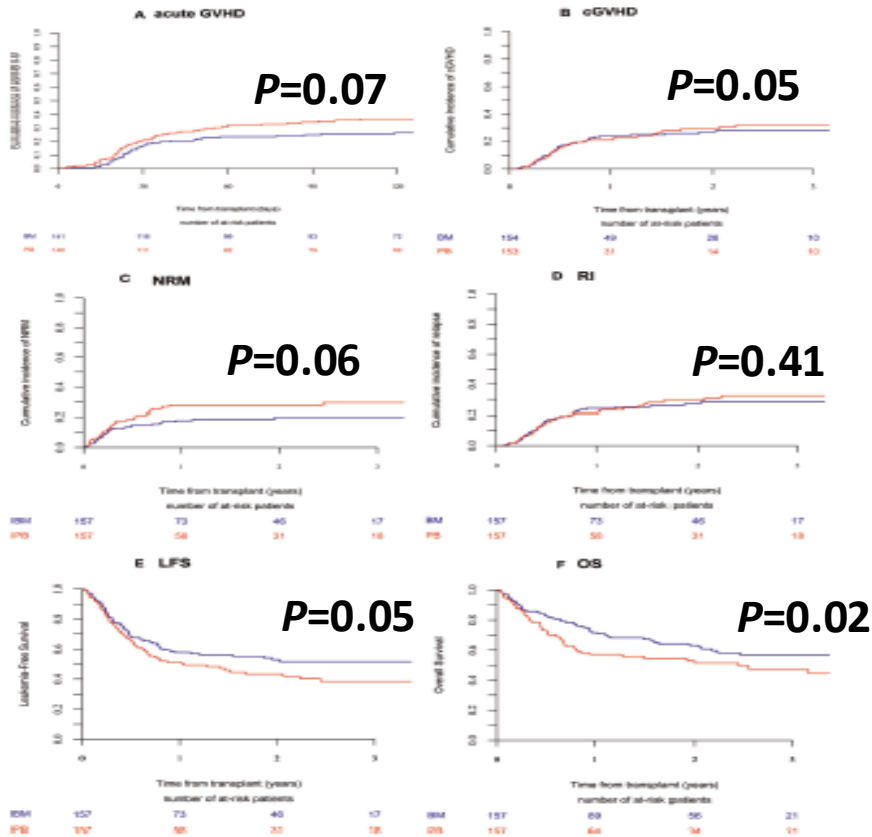


Haplo-PTCy: is BM associated with better outcomes?

	aGVHD II–IV	aGVHD III–IV	cGVHD	Relapse	NRM	OS	GRFS / LFS
Ruggeri 2018 <i>Cancer</i> (n = 451)	21% vs 38% (<i>P</i> <0.001)	4% vs 14% (<i>P</i> <0.001)	22% vs 18% (<i>P</i> =0.39)	22% vs 21% (<i>P</i> =0.73)	23% vs 19% (<i>P</i> =0.46)	55% vs 56% (<i>P</i> =0.88)	44% vs 43% (<i>P</i> =0.90)
Nagler 2020 <i>Leukemia</i> (n = 314, ALL)	HR 1.54 (<i>P</i> =0.01)	HR 1.76 (<i>P</i> =0.01)	HR 1.47 (<i>P</i> =0.04)	HR 1.23 (<i>P</i> =0.41)	HR 1.23 (<i>P</i> =0.37)	HR 1.59 (<i>P</i> =0.02)	HR 1.42 (<i>P</i> =0.03)
Mehta 2021 <i>Transplant Cell Ther</i> (n = 264)	32% vs 23% (<i>P</i> =0.07)	SR-aGVHD 9% vs 32% (<i>P</i> <0.001)	8% vs 22% (<i>P</i> <0.001)	= (<i>P</i> =n.s.)	= (<i>P</i> =n.s.)	= (<i>P</i> =n.s.)	<i>P</i><0.05
Rocha 2026 <i>BMT</i> (n = 8,854)	HR 1.53 (<i>P</i> <0.0001)	HR 1.42 (<i>P</i> <0.0001)	HR 1.34 (<i>P</i> <0.001)	HR 1.02 (<i>P</i> =0.79)	HR 1.22 (<i>P</i> =0.002)	HR 1.13 (<i>P</i> =0.008)	HR 1.20 (<i>P</i> <0.001)

Haplo-PTCy: who may benefit most from BM? The case of ALL

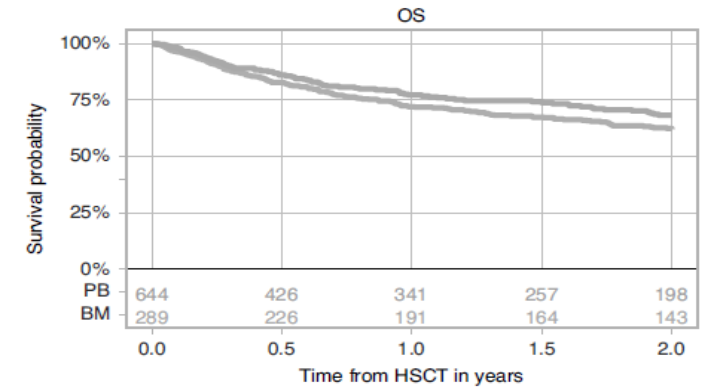
EBMT: ALL patients undergoing haplo HSCT
2010 – 2018 BM= 157 PB= 157



CI of GF:
BM = 10, 6%
PB = 3, 2%
($P = 0.04$).

Nagler et. al Leukemia 2020

EBMT: ALL patients undergoing haplo HSCT
2010-2022 BM= 289 PB= 644



Outcome	Stem cell source ⁴	
	HR (95% CI)	p-value
aGVHD grades II–IV	1.14 (0.83–1.57)	0.42
aGVHD grades III–IV	1.2 (0.71–2.01)	0.5
cGVHD any grade	1.38 (0.98–1.95)	0.07
cGVHD extensive	1.09 (0.67–1.78)	0.74
NRM	1.26 (0.84–1.89)	0.25
Relapse	1.38 (0.97–1.95)	0.07
OS	1.48 (1.09–2.02)	0.01
LFS	1.31 (0.99–1.73)	0.06
GRFS	1.28 (1.01–1.62)	0.04

BM used as reference

Sanz et al. BMT 2026

Take home messages

- *Differences in graft source remain biologically and clinically relevant.*
- *BM should be considered when GVL is not required (non-malignant diseases).*
- *In haploidentical HSCT, BM may be preferred in selected patients in whom limiting inflammatory toxicity (CRS and GVHD) is particularly relevant (ALL).*
- *High-quality prospective randomized trials comparing BM and PBSC are still lacking.*
- *The benefit of choosing BM depends on the ability of an experienced multidisciplinary team to deliver a high-quality BM graft.*

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Grazie.



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