Early Mortality After Allogeneic Hematopoietic Cell Transplantation According to Donor Type

A Single-Center Retrospective Cohort Study · early mortality assessed within the first 100 days and at 6 months (180 days) · 183 consecutive adult alloHCT, Buenos Aires, 2017–2024

Eugenia Pérez Lloveras, PhD · Lucrecia Oses, MD · Gonzalo Ferini, MD · Jorge Alberbide, MD
Department of Haematology and Bone Marrow Transplant Unit, Hospital Italiano de Buenos Aires, Argentina

BACKGROUND

The selection of donor type for allogeneic hematopoietic cell transplantation (allo-HCT) remains a critical clinical decision. Post-transplant cyclophosphamide (PTCy) has expanded access to haploidentical donors, yet comparative data on early transplant-related mortality (TRM) across donor types in Latin American centers are limited.

METHODS

- Retrospective single-centre cohort, January 2017 – June 2024; follow-up closed June 2025. Unit of analysis is the transplant.
- **Aalen–Johansen** cumulative incidence with mutually exclusive terminal events; 1−KM was not used, as it overestimates incidence when the competing event is frequent.

OBJECTIVES

Primary To compare **early mortality according to donor type** among HLA-identical sibling (MSD), unrelated (MUD+MMUD) and haploidentical recipients, with emphasis on the cumulative incidence of NRM, RRM and all-cause mortality **at day+100 and at day+180**, and on how much of the NRM falls inside those windows.

Secondary The cumulative incidence of **NRM and RRM according to donor type over full follow-up**, to establish whether the early separation persists.

Secondary Cumulative incidence of mortality due to relapse, GVHD, infection, other and unknown causes; GVHD taken as "any GVHD ever". Also grade III–IV acute GVHD and documented infectious episodes across the same donor groups.

Statistics Donor groups compared by global permutation test (600 permutations), MUD and MMUD pooled; differences without overlapping 95% CIs considered significant.

COHORT

Age at alloHCT, median (IQR)	52 (37–64)
PROCEDURE	
Myeloablative conditioning	74 (40.4%)
Post-transplant cyclophosphamide	89 (48.6%)
Antithymocyte globulin	62 (33.9%)
Graft source: peripheral blood	174 (95.1%)
DONOR	
Donor age, median (IQR)	35 (27–42)
Donor sex, male	111 (60.7%)
Unrelated (MUD 57 + MMUD 18)	75 (41.0%)
Related haploidentical	66 (36.1%)
HLA-identical sibling (MSD)	42 (23.0%)

Table 1. Cohort characteristics (n=183 transplants in 178 patients). Age ≥60 y 34.4%; AML 34.4%; DRI high or very high 33.9%; HCT-CI ≥3 23.0%; RIC 59.6%; grade II–IV acute GVHD 37.7%; chronic GVHD 37.7%; relapse or progression 26.2%.

WHOLE-COHORT BACKDROP

MONTHS	6	12	24	36	60
Non-relapse mortality	14.8	17.0	21.2	**21.2**	22.4
95% CI	10.1–20.3	11.9–22.8	15.6–27.5	15.6–27.5	16.4–28.9
Relapse-related mortality	6.6	12.1	15.7	**17.9**	22.0
95% CI	3.6–10.8	7.9–17.3	10.8–21.4	12.5–24.0	15.7–29.0
Overall survival	—	70.9	63.1	60.9	55.6
Progression-free survival	—	65.0	56.6	54.5	47.7

Table 2. Aalen–Johansen cumulative incidence and Kaplan–Meier survival (%). Relapse or progression, with NRM as competing risk: 18.1% (12.9–24.0) at 12 months, 24.4% (18.3–30.9) at 36. Median follow-up among survivors 42.3 months.

- Of 79 deaths, 41 (51.9%) were NRM and 38 (48.1%) RRM. **21 of the 41 NRM deaths fell within the first 100 days**, which is why the donor comparison is read early. Infection led the causes of NRM (18 deaths, 43.9%), ahead of GVHD (12) and toxicity or other (11).

PRIMARY ENDPOINT — EARLY MORTALITY AT DAY +100 BY DONOR TYPE

A. NON-RELAPSE MORTALITY — global permutation p=0.004

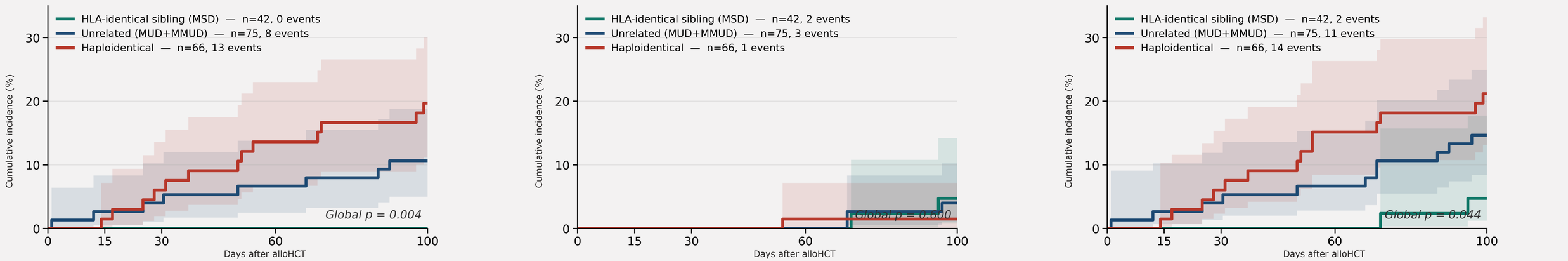
MSD	UNRELATED	HAPLOIDENTICAL
0	**10.7**	**19.7**
0 events; ≤7.1 by rule of three	95% CI 5–19	95% CI 11–30

B. RELAPSE-RELATED MORTALITY — global permutation p=0.800

MSD	UNRELATED	HAPLOIDENTICAL
4.8	**4.0**	**1.5**
95% CI 1–14	95% CI 1–10	95% CI 0–7

C. ALL-CAUSE MORTALITY — global permutation p=0.044

MSD	UNRELATED	HAPLOIDENTICAL
4.8	**14.7**	**21.2**
95% CI 1–18	95% CI 8–25	95% CI 13–33



Early death is almost entirely non-relapse related: 21 of the 27 deaths inside day+100. Whole cohort at day+100 — NRM 11.5%, RRM 3.3%, all-cause 14.8%.

Figure 1. Day+100 window. NRM and RRM by Aalen–Johansen as mutually exclusive competing events; all-cause mortality by 1−Kaplan–Meier. Shaded bands are 95% CIs; global p by permutation test. No NRM event occurred in the MSD group within the first 100 days — its 0% rests on zero events, and its first NRM falls at month 8.1.

SECONDARY — FULL FOLLOW-UP

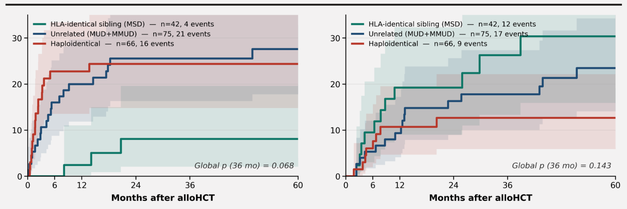


*Figure 2. NRM and RRM by donor type to 60 months, Aalen–Johansen; bands are 95% CIs, global p by permutation test at 36 months. **The early separation attenuates:** NRM is no longer significant, and the burden changes hands — MSD ends with the lowest NRM and the highest RRM, haploidentical the reverse.*

GVHD BY DONOR TYPE

- **Severe acute GVHD does not explain the early haploidentical NRM peak:** at day+180 it is evenly distributed (16.7% / 16.0% / 14.3%; p=0.900). **Chronic GVHD does separate the groups** (p=0.025) — MSD 58.4% at 36 months against 34.2% haploidentical and 32.2% unrelated.

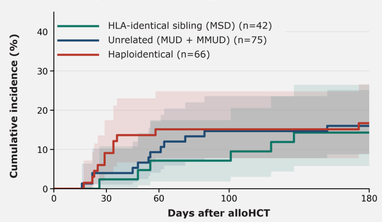


Figure 3. Grade III–IV acute GVHD to day+180; whole cohort 15.9%, 30 events, median onset day+48.

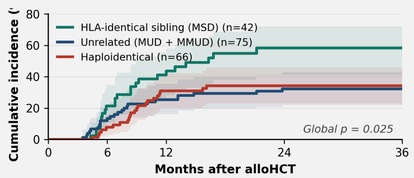


Figure 4. Chronic GVHD to 36 months; whole cohort 40.0%, 69 events. Both panels take death as a competing risk; bands are 95% CIs.

MORTALITY BY CAUSE

CUM. INCIDENCE (%)	6	12	36	60
NRM — infection (18)	6.6	7.7	**8.9**	10.1
NRM — GVHD (12)	3.8	4.4	**6.7**	6.7
NRM — toxicity, other (11)	4.4	4.9	**5.5**	5.5
RRM (38)	6.6	12.1	**17.9**	22.0

Table 3. Four mutually exclusive terminal events summing to total mortality; event counts in brackets. GVHD taken as any GVHD ever.

- **Infection is the leading single cause of NRM** (43.9%), ahead of GVHD (29.3%) and toxicity or other (26.8%). Toxicity has the earliest kinetics, every event inside 18 months; infection is biphasic and still rises after year four.
- All 7 bacterial deaths fell between day0 and month4.5, and **all four speciated isolates were multidrug-resistant**.

INFECTIOUS BURDEN

- 184 episodes in 125 of 183 procedures. **Bacterial episodes were most frequent in haploidentical recipients**; viral and fungal episodes concentrated in the unrelated group. CMV was the commonest organism and reactivated in 45.4% of procedures, yet **no death was attributed to CMV disease.**

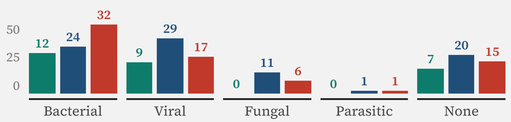


Figure 5. Documented infectious episodes per 100 alloHCT, by category and donor group; figures above each bar are absolute counts. A patient may contribute more than one episode and category. The field carries no event dates, so cumulative incidence cannot be estimated.

CONCLUSIONS

1. Donor type shapes *when* non-relapse death occurs more than how much of it there is: haploidentical NRM is almost entirely peri-transplant, unrelated-donor NRM accrues slowly and ends highest, and MSD recipients had none in the first 6 months.
2. The burden changes hands: MSD carries the lowest NRM with the highest RRM, haploidentical the reverse. Neither difference reached conventional significance here.
3. Acute GVHD does not explain the early haploidentical peak; infection does more of the work, with bacterial episodes concentrated in that group and all speciated bacterial deaths multidrug-resistant.
4. This argues for donor-adapted surveillance: a dense peri-transplant window for haploidentical recipients, vigilance sustained through year four for unrelated donors, and prophylaxis matched to local microbial ecology.

LIMITATIONS & REFERENCES

Retrospective and single-centre; with 41 NRM and 38 RRM events no multivariable analysis was feasible and donor groups are unadjusted. MUD and MMUD were pooled. Causes of death were free text without blinded adjudication; RRM attribution is temporal. The infectious-episode field is missing in 31.7% of procedures and carries no dates.

1. Cibich A, et al. *Transplant Cell Ther.* 2026;32(11):689.e1–13. 2. Penack O, et al. *Blood Adv.* 2020;4(24):6283–90. 3. Shouval R, et al. *Lancet Haematol.* 2019;6(11):e573–84. Approved by the HIBA Ethics Committee (CEPI).

eugenia.perezlloveras@hospitalitaliano.org.ar