Carbapenem-resistant gram-negative rod colonization does not compromise outcomes after allogeneic hematopoietic cell transplantation

A single-center study of 658 consecutive patients (2012–2022)

N. Stocker, F. Malard, A. Banet, Z. Van de Wyngaert, S. Sestili, S. Jolivet, M.J. Bastos, J.-L. Meynard, F. Barbut, A. Bonnin, L. Ricard, R.M. Martin Rojas, A. Couprie, F. Kaoui, Z. Marjanovic, O. Legrand, S. Leclercq, M. Mohty, E. Brissot

· Sorbonne Université, Hôpital Saint-Antoine, AP-HP, Service d'Hématologie Clinique et Thérapie Cellulaire, Paris, France
· Sorbonne Université, INSERM, Centre de Recherche Saint-Antoine (CRSA), Paris, France
· FHU S2C-HOPE, Sorbonne Université, AP-HP, INSERM et Institut Universitaire de Cancérologie (IUC), Paris, France

KEY MESSAGE

When systematic screening and strict infection-control measures are applied, CR-GNR carriage by itself should not preclude or delay allo-HCT in patients with an otherwise valid transplant indication.

INTRODUCTION

- Carbapenem-resistant gram-negative rods (CR-GNR) are an increasing threat in allogeneic hematopoietic cell transplantation (allo-HCT).
- CR-GNR carriage is still used to defer or contraindicate transplantation, yet evidence of its actual impact on transplant outcomes remains limited.
- We assessed the outcomes of CR-GNR carriers in a large, unselected single-center cohort spanning a decade of allo-HCT practice.

METHODS

- **Patients.** 658 consecutive patients receiving a first allo-HCT at Saint-Antoine Hospital, January 2012 to December 2022.
- **Screening.** Rectal swab, stool and urine cultures before allo-HCT and weekly thereafter. Carriers were strictly isolated in single rooms; no decolonization strategy was used.
- **Statistics.** Cumulative incidence by the Aalen-Johansen estimator in a competing-risk framework, compared by Gray's test; survival by Kaplan-Meier and log-rank; cause-specific Cox models adjusted for age, DRI, HCT-CI, lineage, donor type and transplant period.

658
allo-HCT recipients
consecutive first transplants, 2012–2022

→ **Systematic screening**
Rectal swab, stool and urine before allo-HCT, then weekly

→ **59 vs 599**
carriers vs non-carriers
carriage in 9.0% of patients

86 mo
median follow-up
in survivors

RESULTS

- **No outcome differed between carriers and non-carriers at 5 years.**
- **Balanced groups.** Carriers and non-carriers did not differ for age (median 56 vs 56 y), sex, myeloid lineage (81 vs 74%), disease risk index, HCT-CI ≥3, donor type (haploidentical 47 vs 39%), stem cell source or transplant period (all P>0.10). Thiotepa-based conditioning was more frequent in carriers (78 vs 63%, P=0.03).
- **Isolates.** Citrobacter freundii 37%, Enterobacter cloacae 24%, Escherichia coli 22%, Klebsiella pneumoniae 12%.
- **Engraftment and GvHD.** Neutrophil (15 vs 16 d) and platelet recovery (21 vs 17 d) were similar. Grade II-IV acute GvHD at day 180 (19 vs 20%, P=0.79) and chronic GvHD at 24 months (21 vs 27%, P=0.57) did not differ.

Table 1. Outcomes at 5 years

Outcome at 5 years, % (95% CI)	Carriers (n=59)	Non-carriers (n=599)	P
Relapse	37% (25–49)	32% (28–35)	0.29
Non-relapse mortality	27% (17–39)	23% (20–26)	0.67
Progression-free survival	35% (23–47)	45% (41–49)	0.15
Overall survival	42% (29–55)	53% (49–57)	0.17

Figure 1. Adjusted hazard ratios for CR-GNR colonization

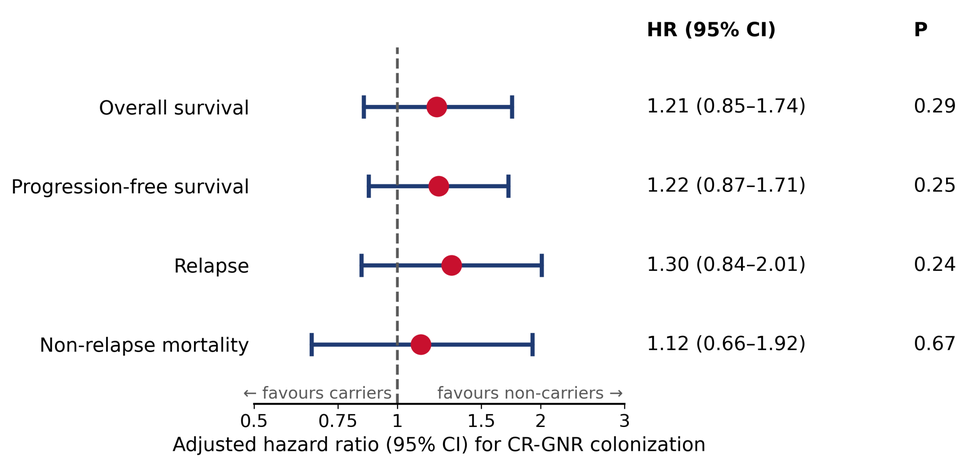


Figure 2. Cumulative incidence of relapse and non-relapse mortality

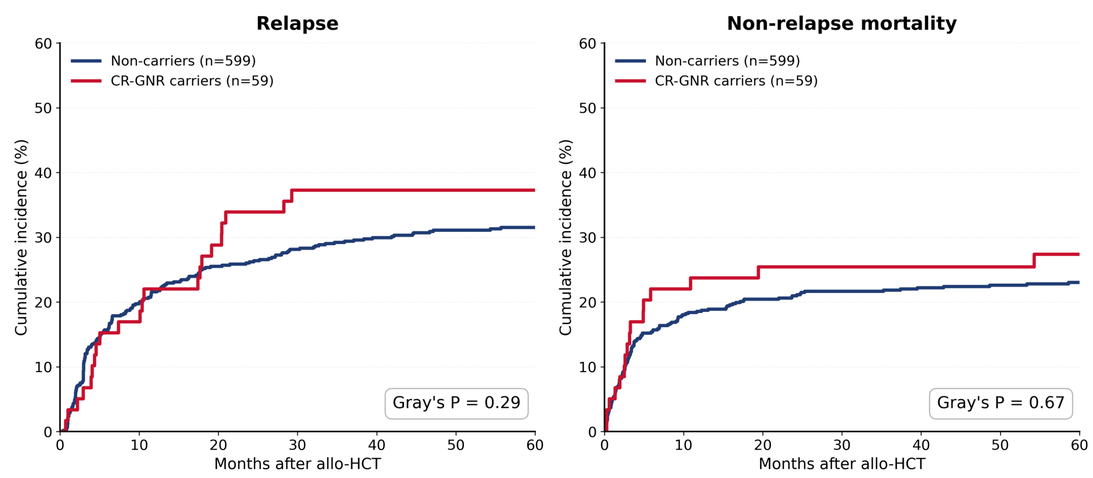
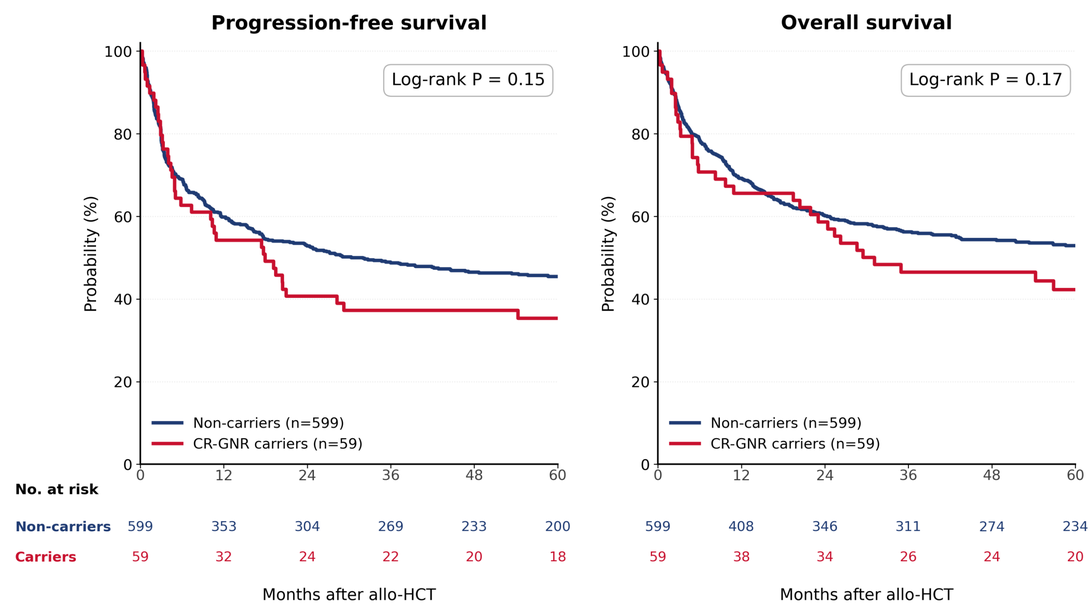


Figure 3. Progression-free and overall survival



MULTIVARIABLE ANALYSIS

- **Colonization was not an independent prognostic factor.**
- After adjustment for age, disease risk index, HCT-CI, lineage, donor type and transplant period, CR-GNR colonization was not independently associated with any outcome (Figure 1).
- Overall survival was driven by high or very-high disease risk index (HR 1.85, 1.47-2.33), age (HR 1.22 per 10 years, 1.12-1.33) and myeloid lineage (HR 0.65, 0.50-0.85).
- Death was attributed to infection in 31% of carriers and 28% of non-carriers (P=0.39).

CONCLUSION

- CR-GNR colonization was not associated with impaired engraftment, GvHD, relapse, non-relapse mortality or survival, and was not an independent prognostic factor.
- With 59 carriers, the study excludes a large detrimental effect (HR ≥1.7 for overall survival) but not a moderate one. Findings are limited by the retrospective, unmatched design and the absence of time-dependent modelling of colonization (possible immortal-time bias).

REFERENCES

1. Averbuch D, et al. Bone Marrow Transplant. 2017;52:1030-1037.
2. Girmenia C, et al. Biol Blood Marrow Transplant. 2015;21:1226-1233.
3. Satlin MJ, et al. Clin Infect Dis. 2017;64:1583-1591.
4. Tacconelli E, et al. Clin Microbiol Infect. 2014;20(Suppl 1):1-55.

ACKNOWLEDGEMENTS & CONTACT

The authors thank the nursing and infection-control teams of the Department of Clinical Hematology and Cellular Therapy, and the Microbiology laboratory, Saint-Antoine Hospital.

Contact: nicolas.stocker@aphp.fr