COMPARATIVE SAFETY AND EFFICACY OF CALCINEURIN INHIBITOR (CNI)-FREE VS CNI-BASED GVHD PROPHYLAXIS FOLLOWING ALLOGENEIC HCT: A REAL-WORLD TRINETX-BASED PROPENSITY-MATCHED ANALYSIS

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Introduction

- Graft-versus-host disease (GVHD) remains a major complication following allogeneic hematopoietic stem cell transplantation (allo-HCT).
- Calcineurin inhibitor (CNI)-based prophylaxis with tacrolimus or cyclosporine has been the conventional standard; however, these agents carry risks of nephrotoxicity and immune suppression.
- Emerging strategies, including CNI-free regimens with sirolimus and post-transplant cyclophosphamide, may improve outcomes, but comparative real-world data on safety and efficacy remain limited

Aim

To determine whether CNI-free prophylaxis reduces GVHD incidence and toxicity without compromising survival outcomes.

Objectives

To evaluate the comparative safety and efficacy of CNI-free versus CNI-based GVHD prophylaxis in adult allo-HCT recipients using real-world, multicenter data.

Methods

- Retrospective cohort analysis (TriNetX US Collaborative Network, 69 healthcare organizations).
- Population consisting of Adults (≥18 years) with hematologic malignancies undergoing allo-HCT (2017–2025).
- CNI-based: Tacrolimus/cyclosporine ±methotrexate/mycophenolate mofetil (MMF).
- CNI-free: Sirolimus + MMF + post-transplant cyclophosphamide.
- Propensity score matching (1:1) – 199 patients per arm.
- Outcomes including incidence of GVHD, neutropenia, mortality, renal toxicity, infections, and healthcare utilization (730-day follow-up).

Table 1. Baseline demographics of CNI-free and CNI-based cohorts after propensity score matching (n=199 per group).

			Demographics			
Cohort			Mean ± SD	Patients	% of Cohort	P-Value
1	Age	Current Age	59.1 +/- 17.7	199	100%	0.946
2			59.2 +/- 16.5	199	100%	
1	AI	Age at Index	53.8 +/- 17.5	199	100%	0.979
2			53.8 +/- 16.6	199	100%	
1	2106-3	White		153	76.9%	0.718
2				156	78.4%	
1	UNK	Unknown Race		10	5.0%	1
2				10	5.0%	
1	F	Female		82	41.2%	0.539
2				76	38.2%	
1	2054-5	Black or African American		21	10.6%	0.869
2				20	10.1%	
1	M	Male		117	58.8%	0.539
2				123	61.8%	
1	2131-1	Other Race		10	5.0%	1
2				10	5.0%	
1	2028-9	Asian		10	5.0%	1
2				10	5.0%	

Results

- CNI-free prophylaxis was associated with a significant reduction in GVHD incidence (HR 0.592, p=0.000).
- Neutropenia rates were lower in the CNI-free group (HR 0.767, p=0.004).
- Patients receiving CNI-free prophylaxis had fewer emergency department visits (HR 0.615, p=0.027).
- Renal toxicity was significantly reduced with CNI-free regimens (HR 0.441, p=0.000).
- All-cause mortality was higher in the CNI-free arm (HR 1.390, p=0.045).
- Febrile neutropenia occurred more frequently in the CNI-free group (HR 1.619, p=0.002).
- No significant differences were observed for relapse, pneumonia, sepsis, anaemia, pleural effusion, ventilation, or hospital dependence.

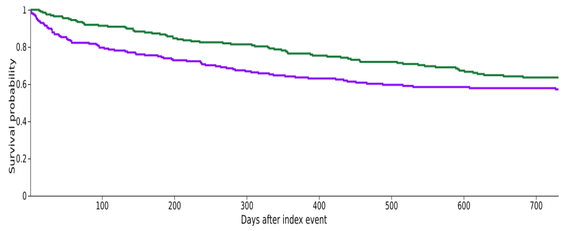


Figure 1. Kaplan–Meier overall survival analysis: CNI-free prophylaxis was associated with higher all-cause mortality compared to CNI-based prophylaxis (HR 1.39, 95% CI 1.01–1.92, p=0.045).

Summary

- CNI-free GVHD prophylaxis post-allo-HCT demonstrated lower GaVHD incidence and improved renal safety but was associated with higher mortality and febrile neutropenia.
- These findings suggest that while CNI-free regimens offer certain advantages, careful patient selection and infection surveillance are critical.

Discussion

- CNI-free prophylaxis significantly reduced GVHD, nephrotoxicity, and healthcare burden, highlighting potential benefits for patient quality of life and long-term renal safety (2).
- However, the observed increase in mortality and febrile neutropenia underscores critical safety concerns, likely related to immune dysregulation and infection risk. (3)
- These findings suggest that patient selection, infection surveillance, and supportive care are crucial when considering CNI-free approaches.
- Current evidence supports cautious adoption while awaiting results from prospective randomized trials.

References

1. Zeiser & Blazar et al. NEJM 2017
2. Kanakry et al., Blood 2014
3. Luznik et al., Seminars in Oncology. 2012

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