(PB4016) ERAVACYCLINE IN ALLOGENEIC STEM CELL TRANSPLANT RECIPIENTS: A REAL-WORLD STUDY OF DRUG-DRUG INTERACTIONS WITH CYCLOSPORINE/TACROLIMUS AND ANTI-INFECTIVE EFFICACY

Topic: 23. Stem cell transplantation - Clinical

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Background

Calcineurin inhibitors (CNIs) are standard prophylaxis for acute graft-versus-host disease (aGVHD) after allogeneic hematopoietic stem cell transplantation (allo-HSCT). Given their narrow therapeutic window and variable bioavailability, rigorous therapeutic drug monitoring is mandatory, particularly during serious infections. Eravacycline, a novel synthetic tetracycline, shares the CYP3A4 metabolic pathway with CNIs, yet comprehensive data on their potential pharmacokinetic interactions are scarce.

Aims

This study aimed to evaluate the drug-drug interactions between eravacycline and CNIs, as well as its anti-infective efficacy and safety in allo-HSCT.

Methods

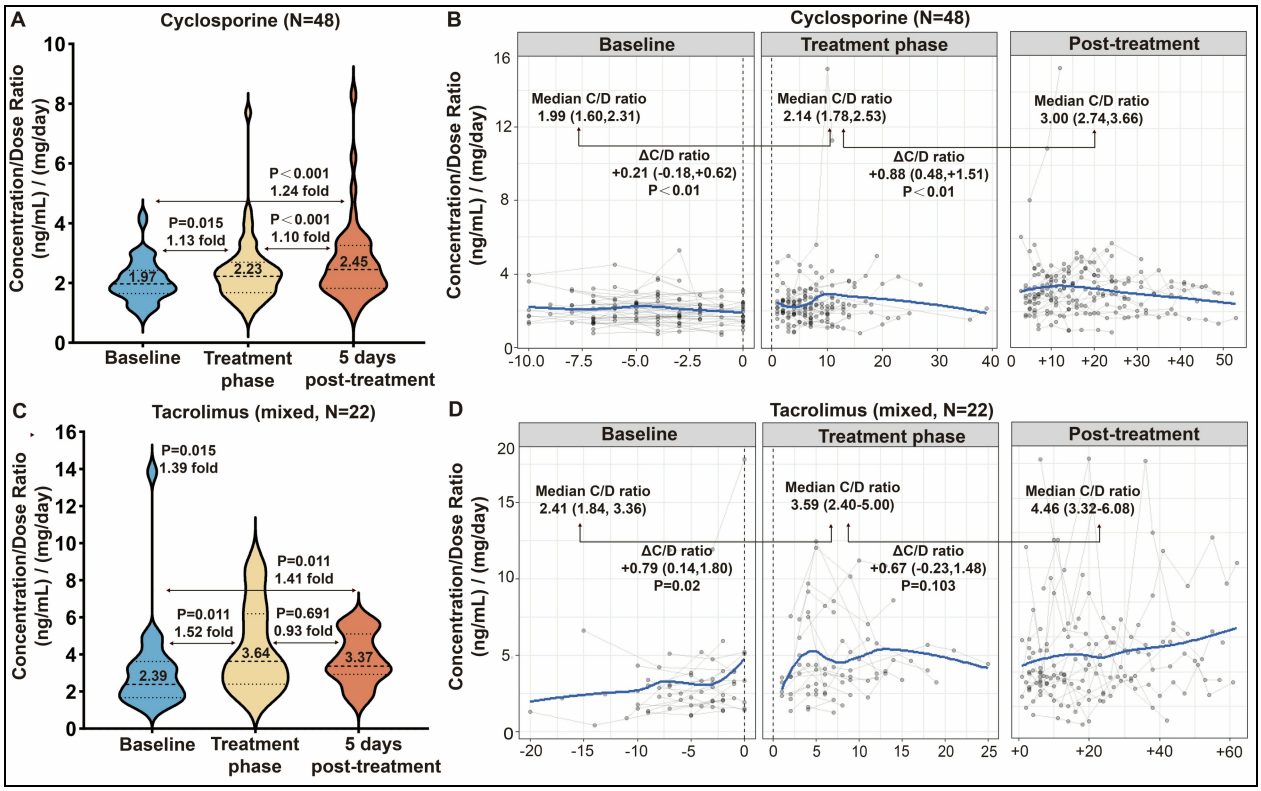
This single-center, retrospective study was conducted at the Institute of Hematology & Blood Diseases Hospital from August 2023 to December 2025, enrolling allo-HSCT recipients who received CNIs and eravacycline (50 mg q12h). CNI concentration-to-dose (C/D) ratios were monitored at a median interval of every 3 days before, during, and after eravacycline administration, with mean C/D ratios calculated for each phase. The Wilcoxon signed-rank test and LOWESS regression were used to analyze trends over time.

Results

A total of 70 patients were included, comprising 48 receiving cyclosporine and 22 receiving tacrolimus. Eravacycline was initiated at a median of 10 (IQR 4–17.3) days post-transplant; 64.3% received therapy during neutropenia phase and 8.6% during aGVHD phase. The median treatment duration was 11 (IQR 7–15) days . Pulmonary (41.4%) and bloodstream (38.6%) infections predominated, with *Stenotrophomonas maltophilia* (38.6%) as the leading pathogen.
In the cyclosporine group, co-administration with eravacycline increased the C/D ratio by 13.2% (P=0.015), requiring a mean 10% dose reduction to maintain therapeutic concentrations. Within five half-lives after discontinuation, C/D ratios increased by an additional 9.9% (P<0.01), necessitating a further 11% dose reduction. In the tacrolimus group, C/D ratios increased by 52.3% during co-administration (P=0.011), prompting dose reductions of 33.3%–36.5%, with no significant change after discontinuation (P=0.691). These trends persisted in patients receiving concomitant azoles/ letermovir and in those with non-terminal status and grade 0–2 liver and kidney function. Patients with aGVHD exhibited higher and more variable C/D ratios. Despite increased exposure, the rate of supratherapeutic concentrations remained low (5.0 %).
After excluding patients with end-stage multi-organ failure, grade 3 adverse events occurred in 3.5% during treatment and 2.6% within five half-lives post-discontinuation. Clinically, the remission rate was 81.4%. The 28-day all-cause and infection-related mortality rates were 18.6% and 4.3%, respectively. One-year overall survival was 52.3% (95% CI 41.1%–66.7%).

Summary/Conclusion

This study provided the first clinical evidence of a pharmacokinetic interaction between eravacycline and CNIs in allo-HSCT recipients. Eravacycline increased CNI exposure during co-administration and induced a transient post-discontinuation elevation that resolved within approximately two weeks. Although the magnitude of the interaction was moderate, intensified therapeutic drug monitoring and stepwise dose adjustments were recommended during and shortly after eravacycline therapy, particularly with tacrolimus. In the post-transplant setting, eravacycline demonstrated robust anti-infective efficacy with an acceptable safety profile.



Changes in CNI concentration-to-dose (C/D) Before and After Eravacycline Coadministration