Presentation Number: 207

Burden of Post-Transplant Neutropenia and Leukopenia among Kidney Transplant Recipients: A Multi-Institutional Real-World Observational Study

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Background

- Kidney transplant recipients (KTRs) are commonly prescribed valganciclovir/ganciclovir (V/G) to reduce the risk of cytomegalovirus (CMV) infection[1,2]
- Prolonged use of V/G increases the risk of myelosuppression, including post-transplant neutropenia (PTN) and post-transplant leukopenia (PTL) [1,2]
- Real-world evidence characterizing PTN/PTL and its associated consequences among KTRs is limited

Objective

- To determine the incidence of PTN and PTL among adult KTRs and examine the differences in the demographic, clinical, and medication-related characteristics among individuals with and without PTN and PTL

Methods

Study Design

- Retrospective observational cohort of KTRs who received KT between 2012 to 2020
- Database: Electronic Medical Records Database of TriNetX's Dataworks – USA Network, which provided access to electronic medical records from approximately 86 million patients across 54 healthcare organizations in the United States.

Study Periods and Definitions

- Index Date and Study Periods
  - Index date: date of first kidney transplant from Jan 1, 2012 - Sept 30, 2020
  - Follow-up period: index to 365 days post-index or censor date (e.g., mortality, last record)
  - Baseline period: from 365 days before index to the day before index

Inclusion Criteria

- First kidney transplant between Jan 1, 2012, and Sept 30, 2020
- Aged 18+ years old at time of index
- ≥1 record of V/G within 30 days post-transplant
- Availability of healthcare records for the entire duration of baseline and follow-up period
- ≥1 laboratory test result for ANC and WBC during the follow-up period

Exclusion Criteria

- Any solid organ transplant (other than kidney) on or prior to index
- Any kidney transplant rejection/graft failure on or prior to index
- Any record of letermovir prescription during the follow-up period

Primary Outcome

- Development of PTN and/or PTL during the follow-up period
  - PTN: ≥1 absolute neutrophil count (ANC) lab of <1,500 ANC/µL during the follow-up period
  - PTL: ≥1 white blood count (WBC) lab of <3,500 WBC/µL during the follow-up period

Statistical Analyses

- Incidence rates were calculated as the number of new cases of PTL and PTN during the follow-up period and reported as number of incident events per 100 person-days (PD)

Results

- 8,791 patients were included in the study
- Mean age was 52.8 years; 40.7% were females, 41.6% White, and 32.6% Black
- 3,383 patients (38.5%) developed PTN and 6,127 (69.7%) developed PTL
- Incidence rates for PTN and PTL were 0.15/100 PD and 0.51/100 PD, respectively
- G-CSF use was higher among KTR with PTN compared to those who did not (38.9% vs. 3.6%)
- Similarly, patients who developed PTL had higher G-CSF use compared to those who did not (22.8% vs 4.2%)
- PTN and PTL were significantly associated with increased risk of CMV infection, graft reject, and graft loss

Table 1. Clinical outcomes of kidney transplant recipients stratified by post-transplant neutropenia status

	PTN (N=3,383)	No PTN (N=5,408)
G-CSF use	1,316 (38.9%)	195 (3.6%)***
Graft rejection	1,002 (29.6%)	1,366 (25.3%)***
Graft loss	251 (7.4%)	260 (4.8%)***
Opportunistic Infections		
CMV infection	356 (10.5%)	195 (3.6%)***
Adenovirus	39 (1.2%)	51 (0.9%)
BK virus	365 (10.8%)	376 (7.0%)***
Varicella zoster virus	54 (1.6%)	47 (0.9%)**

** p-value<0.01; *** p-value<0.001

Table 2. Clinical outcomes of kidney transplant recipients stratified by post-transplant leukopenia status

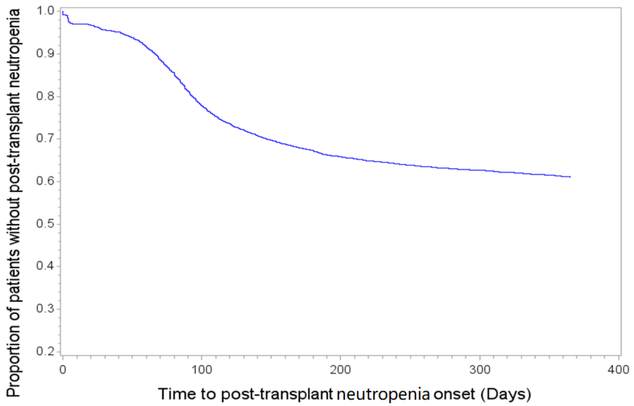
	PTL (N=6,127)	No PTL (N=2,664)
G-CSF use	1,398 (22.8%)	113 (4.2%)***
Graft rejection	1,776 (29.0%)	592 (22.2%)***
Graft loss	391 (6.4%)	120 (4.5%)***
Opportunistic Infections		
CMV infection	442 (7.2%)	109 (4.1%)***
Adenovirus	41 (0.7%)	49 (1.8%)***
BK virus	550 (9.0%)	191 (7.2%)**
Varicella zoster virus	86 (1.4%)	15 (0.6%)***

** p-value<0.01; *** p-value<0.001

1. Razonable RR, et al. Clin Transplant. 2019;33(9):e13512
2. Kotton CN, et al. Transplantation. 2018;102(6):900-931

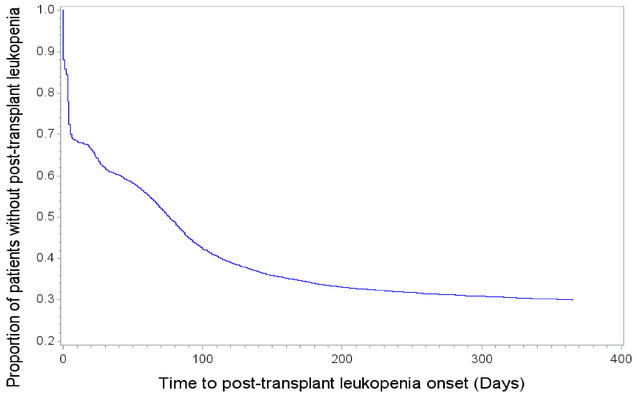
Time to Onset of Post-Transplant Neutropenia

Kaplan-Meier Curve - Time to onset of post-transplant neutropenia (ANC<1,500/mL)



Summary of Kaplan-Meier Curve	
Total Sample	8,791
Number of incident PTN	3,383
Person-days (PD) at risk	2,205,767
Incidence rate per 100 PD	0.15

Kaplan-Meier Curve - Time to onset of post-transplant leukopenia (WBC<3,500/mL)



Summary of Kaplan-Meier Curve	
Total Sample	8,791
Number of incident PTL	6,127
Person-days (PD) at risk	1,209,655
Incidence rate per 100 PD	0.51

Conclusions

- **In this multi-center study of 8,791 kidney transplant recipients, we observed a large burden of neutropenia and leukopenia within a year of transplantation**
  - **Two-thirds of kidney transplant recipients who received valganciclovir or ganciclovir developed post-transplant leukopenia and one-third developed post-transplant neutropenia**
  - **Post-transplant neutropenia and post-transplant leukopenia were associated with higher rates of adverse graft outcomes, opportunistic infection, and increased use of G-CSF**
- **Future studies with longer follow-up period are needed to understand if PTL/PTN in these KTRs are associated with additional morbidity and mortality**

IDWeek2022, October 19, 2022 – October 23, 2022, Washington, D.C.