Characterization of Cytomegalovirus Viremia in Renal Transplant Recipients

Ishan Chaudhari, B.Sc. (Pharm), Marianna Leung, B.Sc. (Pharm), Pharm.D, ACPR, Bita Bateni, B.Sc.(Pharm), M.Sc.(Pharm), ACPR

Background

- Cytomegalovirus (CMV) is highly prevalent in the general population and may reactivate in immunocompromised patients, including kidney transplant recipients (KTRs)
- CMV can cause serious disease and result in organ dysfunction, allograft rejection and death
- Risk factors include age, CMV serostatus, deceased donors and others
- Immunosuppressants, such as anti-thymoglobulin (ATG), tacrolimus, mycophenolate mofetil (MMF), have also been implicated with a higher incidence of CMV viremia
- In order to prevent CMV viremia post-transplant, patients may be given an antiviral medication, valganciclovir
- A key clinical objective is to ensure adequate duration of valganciclovir prophylaxis in high risk patients

Objectives

In a cohort of contemporary KTRs, identify whether CMV viremia is associated with:

- Certain demographic characteristics
- Choice and dosing of immunosuppressants (induction and maintenance)
- Duration of CMV prophylaxis with valganciclovir

Methods

Retrospective case control study

- All kidney-only transplant recipients at St. Paul's Hospital from 2012 to 2016 with minimum 1 year follow-up
- Viremia defined as serum CMV >1000 IU/mL

Incidence of viremia, patient demographics and drug exposure data were extracted from PROMIS (provincial renal database)

For the univariate analysis, categorical variables were reported as counts and percentages; quantitative variables were reported as means ± standard deviations

Statistical analysis performed using Chi-squared and Student's t-test, where appropriate

Multivariate analysis pending

Results

Table 1- Demographic Characteristics

Parameter	no CMV n=492 (75%)	CMV n=161 (25%)	p-value
Age (yrs)	**53 ± 13.4**	**55 ± 13.4**	0.0375
Sex			0.0533
Male	311 (63%)	88 (55%)	
Female	181 (37%)	73 (45%)	
Weight (kg)	**79 ± 17.7**	**75 ± 17.4**	0.0146
Race			<0.0001
White	349 (71%)	83 (52%)	
Asian	**104 (21%)**	**64 (40%)**	
North American Indian	17 (3%)	6 (4%)	
Hispanic	6 (1%)	3 (2%)	
Black	4 (1%)	4 (2%)	
Other/Multiracial	12 (2%)	1 (1%)	
D/R serostatus			<0.0001
+/-	**70 (14%)**	**47 (29%)**	
+/+	**177 (36%)**	**71 (44%)**	
-/+	122 (25%)	38 (24%)	
-/-	110 (22%)	1 (1%)	
Donor type			<0.0001
LD	257 (52%)	53 (33%)	
SCD	147 (30%)	44 (27%)	
ECD	**47 (10%)**	**33 (20%)**	
DCD	**41 (8%)**	**31 (19%)**	
Dialysis (Y)	**379 (77%)**	**141 (88%)**	0.0039
Dialysis vintage			0.0033
1 year or less	58 (12%)	14 (9%)	
1 to 5 years	242 (49%)	78 (48%)	
5+ years	**79 (16%)**	**49 (30%)**	
PRA percentage			0.0046
n=	258 (52%)	96 (61%)	
0-19	202 (41%)	60 (37%)	
20-80	**35 (7%)**	**18 (11%)**	
>80	**21 (4%)**	**18 (11%)**	

LD=living donor, SCD=standard criteria donor, ECD=expanded criteria donor, DCD=donation after cardiac death, PRA=panel reactive antibody

Table 2- Induction Agents

Parameter	no CMV (n=492)	CMV (n=161)	p-value
ATG	**138 (28%)**	**80 (50%)**	<0.0001
Basiliximab	347 (71%)	78 (48%)	
Cumulative ATG (mg/kg)	**4.1 ± 1.45**	**4.5 ± 1.65**	0.0376

Figure 1- ATG Dosing

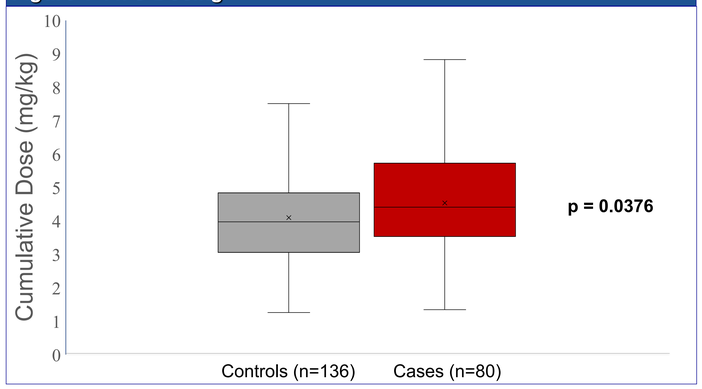


Figure 2- Maintenance Therapy

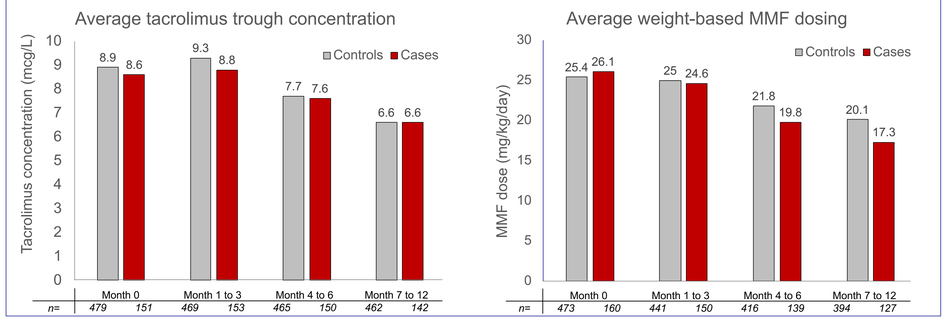
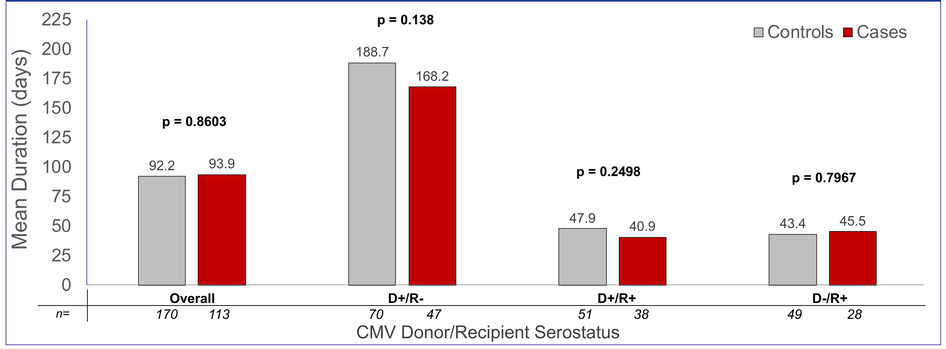


Figure 3- Valganciclovir Prophylaxis



Limitations

- Retrospective analysis (cannot account for errors or missing data in charting and significant potential for confounding)
- Viremia is not the final clinical endpoint
- Drug exposure data was reported as a discrete variable
- Potential sample size limitations

Conclusion

In the univariate analysis, CMV viremia in KTRs was associated with:

- Recipients of older age, female, lower body weight, or Asian decent
- CMV serostatus (D+/R-, D+/R+), deceased donors (ECD or DCD), higher PRA percentage, longer dialysis vintage pre-transplant
- Higher ATG usage or cumulative weight-based ATG dosing

No statistically significant difference found with tacrolimus trough concentrations, weight-based MMF dosing or valganciclovir duration

Multivariate analysis pending