Assessing the Safety and Efficacy of Valganciclovir Dosing for Cytomegalovirus Prophylaxis in Solid Organ Transplant Recipients on Hemodialysis

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Background

- Cytomegalovirus (CMV) infection is one of the most common infections in solid organ transplant (SOT) recipients that causes significant morbidity and mortality. Valganciclovir has been the standard of care used for the prevention of CMV infections.
- Currently there is minimal guidance for prophylaxis dosing in SOT recipients undergoing intermittent hemodialysis (IHD).
- At Mount Sinai Hospital (MSH), the current practice for CMV prophylaxis in SOT recipients on IHD is to prescribe valganciclovir 450 mg every other day or three-times weekly.

Objectives

Primary objective:

1. To determine the safety of using valganciclovir 450 mg every other day or three-times weekly for CMV prophylaxis
    a) To identify the incidence of leukopenia (WBC < 4 x 10^3/uL), thrombocytopenia (Plts < 50 x 10^3/uL), and the administration of growth colony stimulating factor (GCSF

Secondary objective:

1. To identify the incidence of CMV viremia and/or CMV disease on valganciclovir 450 mg every other day vs three-times weekly for CMV prophylaxis

Methods

- **Study Design:** Single center, retrospective chart review study from 1/1/2018 to 12/31/2018
- **Inclusion Criteria:**
    - SOT transplant recipients (kidney, liver, heart, pancreas and/or small bowel)
    - Receiving valganciclovir 450 mg every other day or three-times weekly for CMV prophylaxis
    - Undergoing IHD for at least 30 days
- **Data Analysis**
    - Data was analyzed using descriptive statistics.

Results

Figure 1: Patient Eligibility.

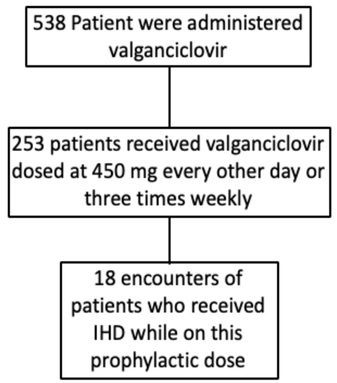

Table 1. Baseline Characteristic	Patients (N = 18)
Mean age at transplantation, years ± SD	51 ± 6
Male, n (%) Female, n (%)	8 (44.4%) 10 (55.5%)
Type of transplant, n (%) Kidney Liver Heart Kidney/Liver Kidney/Pancreas	 5 (27.8%) 7 (38.9%) 2 (11.1%) 2 (11.1%) 2 (11.1%)
Deceased donor, n (%)	14 (77.8%)
Median Length of Transplant Admission, days ± SD	37 ± 64
CMV serostatus (D/R), n (%) High Risk (+/-) Moderate Risk (+/+, -/+) Low risk (-/-) Not available	 2 (11.1%) 13 (72.2%) 2 (11.1%) 1 (5.6%)
IHD mean duration, days ± SD	254 ± 246
Prophylaxis Dose, n (%) 450 mg every other day (Q48H) 450 mg three times weekly (TIW)	 13 (72.2%) 5 (27.8%)
Induction Therapy, n (%) Steroids Thymoglobulin Thymoglobulin + IVIG Not available	 10 (55.6%) 5 (27.8%) 1 (5.6%) 2 (11.1%)

Table 2. Primary Outcomes (N = 18)	Q48H Regimen (n = 13)	TIW Regimen (n = 5)
Lowest Platelet Count (10^3/uL) while on Prophylaxis Mean, n ± SD Median, n ± SD	 131 ± 93 102 ± 93	 161 ± 115 116 ± 115
Thrombocytopenia, n (%)	3 (23.1%)	0 (0.0%)
Lowest White Blood Cell Count (10^3/uL) while on Prophylaxis Mean, n ± SD Median, n ± SD	 3.4 ± 2.5 3.3 ± 2.5	 5.1 ± 3.8 3.2 ± 3.8
Leukopenia, n (%)	9 (69.2%)	3 (60.0%)
Mean Lowest White Blood Cell Count, n (%) n > 4 4 > n ≥ 3 3 > n ≥ 2 2 > n ≥ 1 1 > n ≥ 0	 4 (30.8%) 3 (23.1%) 1 (7.7%) 3 (23.1%) 2 (15.4%)	 2 (40.0%) 1 (20.0%) 1 (20.0%) 1 (20.0%) 0 (0.0%)
Requiring GCSF, n (%)	4 (30.8%)	0 (0.0%)

Table 3. Secondary Outcomes	Patients N=18
Breakthrough CMV viremia*, n (%)	0 (0.0%)
Late-onset CMV viremia, n (%)	3 (16.6%)
CMV disease⁺, n (%)	2 (11.1%)

*CMV viremia was defined as a CMV detectable PCR level greater than 37 units/liter.
⁺CMV disease was defined as CMV viral load greater than 37 units/liter and documentation of CMV associated signs and/or symptoms.

Discussion

- The TIW dosing regimen had higher platelet and white blood cell count nadirs with fewer associated incidences of thrombocytopenia and leukopenia.
- Of the three patients who developed late-onset CMV viremia, two of the patients had discontinued prophylaxis after 2-3 months due to leukopenia and thrombocytopenia.
- Limitations
    - Small, retrospective study dependent on accuracy of documentation
    - Timing of valganciclovir administrations as valganciclovir is dialyzable

Conclusion

- Valganciclovir 450 mg TIW may be safer than and as efficacious as Q48H dosing for prophylaxis in SOT recipients on chronic IHD. There is a possible trend towards safer outcomes as TIW dosing was associated with fewer incidences of thrombocytopenia, leukopenia, and requiring GCSF. This data supports the use of TIW dosing as standardized practice at The Mount Sinai Hospital, however more data is necessary to determine a conclusive result.

References

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Disclosures

Authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation.