A Clinical Experience of CMV T-cell Immunity in Lung Transplant Recipients

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Background

- **Cytomegalovirus infections (CMV)** is a common complication in solid organ transplant recipients. Per Keck's protocol, **CMV prophylaxis** consists of **valganciclovir** (adjusted for renal function) or **letermovir** lung transplant recipients for 12 months.
- The optimal duration of antiviral prophylaxis in lung transplant recipients is uncertain, and **deficiencies in T-cell immunity post-transplant increase the risk of CMV-associated complications.**
- Despite antiviral prophylaxis, patients may still develop CMV infection following discontinuation of prophylaxis.
- The **CMV T-cell Immunity Panel** is a commercially available assay for measuring CMV-specific cell mediated immunity, however there is a **paucity of information in the lung transplant population of the test's ability to predict CMV events**.

Objectives

- **Primary objective**: Investigate the onset of developing CMV T-cell immunity for letermovir and valganciclovir.
- **Secondary objective**: Evaluate whether lung transplant patients who previously developed CMV T-cell immunity develop CMV infections/viremia and the timing (onset) of such reactivation.
- **Hypothesis:** With the recent placement of letermovir as the preferred prophylaxis treatment in lung transplant patients for CMV prevention, if letermovir is noninferior to valganciclovir, then **letermovir will be no worse than valganciclovir in the duration of developing T-cell immunity.**

Methods

Inclusion Criteria

- Adults ≥ 18 years old
- Lung transplant recipients between 2018-2024
- Patients with history of letermovir or valganciclovir prophylaxis treatment therapy post-transplant
- CMV T-cell immunity panel assay performed

Exclusion Criteria

- Received other solid organ transplants, hematopoietic stem cell, or multi-organ transplants
- Lung transplant recipients (D-/R-) pre-transplant
- Patients on acyclovir or valacyclovir
- Patients with no T-cell immunity assays completed
- T-cell immunity not yet reached by February 2024
- Suspected or known hypersensitivity to letermovir or valganciclovir
- Deceased as of February 2024

Data collection

- Subject records identified by retrospective review of the electronic health record.
- Patient identifiers removed and coded during data collection.
- Prophylaxis and duration, date of CMV detection, neutropenia, date of T-cell immunity, and immunosuppressant drugs received were collected.

Methods

Figure 1. Study Eligibility Criteria

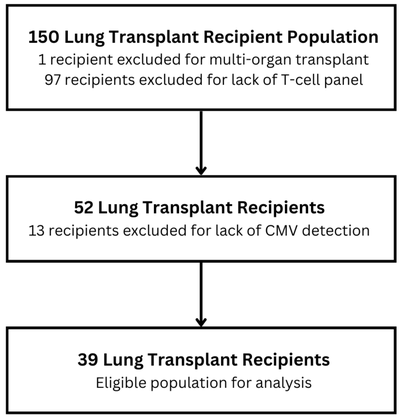

Figure 2. Baseline Patient Characteristics

Patient Characteristics (n = 39)		
Transplant Type	Bilateral	32 (82.1%)
	Left Lung	6 (15.4%)
	Right Lung	1 (2.6%)
Prophylactic Drug	Valganciclovir	25 (64.1%)
	Letermovir	14 (35.9%)
Immunosuppressants	Mycophenolate mofetil	36 (92.3%)
	Azathioprine	1 (2.6%)
	Neither mycophenolate mofetil or azathioprine	2 (5.1%)
	Tacrolimus	38 (97.4%)
	Cyclosporine	1 (2.6%)
Other Drugs	Methylprednisolone/ Prednisone	39 (100%)
	Linezolid	4 (10.3%)
	Colony stimulating factor	21 (53.9%)
	Thymoglobulin	9 (23.1%)
	Dapsone	1 (2.6%)
	Atovaquone	2 (5.1%)
	Bactrim	36 (92.3%)

Results

Figure 3. Mean Duration to T-cell Immunity of Letermovir vs. Valganciclovir Recipients

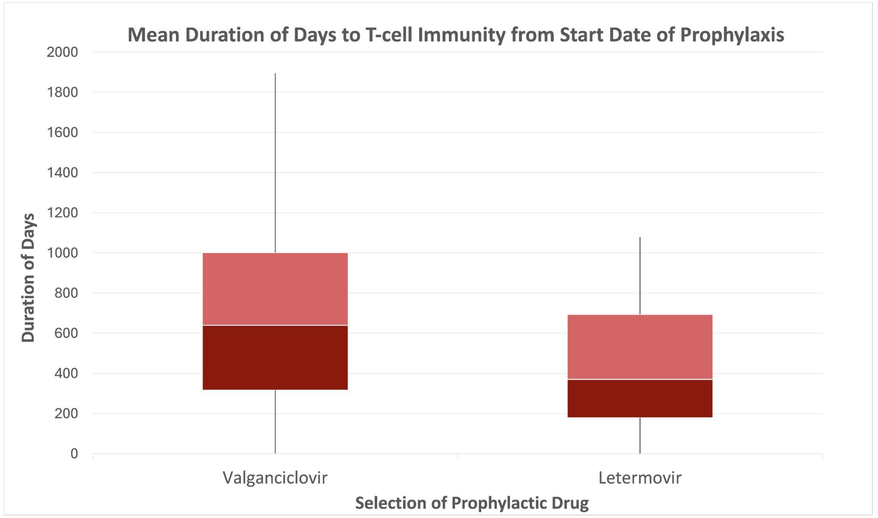

Figure 4. Recurrence of CMV after T-cell immunity and Mean Duration of Days to Recurrence of CMV in Valganciclovir vs. Letermovir

Drug	Incidence of CMV after T-cell immunity	Mean Duration of Days of Incidence of CMV after T-cell immunity
Valganciclovir	3/39 (7.7%)	235 Days
Letermovir	1/39 (2.6%)	194 Days

Figure 5. Incidence of Neutropenia in Valganciclovir vs Letermovir

Drug	Incidence of Neutropenia	Incidence of Colony Stimulating Factor Use	Incidence of Thymoglobulin Use
Valganciclovir	7/39 (17.9%)	17/39 (43.6%)	7/39 (17.9%)
Letermovir	2/39 (5.1%)	3/39 (7.7%)	2/39 (5.1%)

Limitations

- The lung transplant population is small and niche group limited to one institution.
- The retrospective study is limited to date of revision from 2021 due to the lack of T-cell panels obtained from lung transplant recipients in 2018 to 2020.
- There is currently limited literature regarding T-cell immunity and CMV prophylaxis in transplants.
- Select patients were switched from their original prophylactic treatment to other prophylactic agents during their time of therapy.
- In many cases, the T-cell immunity panel was not consistently reported in which the routine panel was collected from the prophylaxis start date.
- Due to protocol revision in June 2023, there is a larger observation of transplant recipients who were initiated on valganciclovir compared to letermovir.

Discussion & Conclusion

- New insight into association between T-cell immunity and CMV prophylaxis with sample size maximized to include T-cell immunity and CMV prophylaxis protocol change
- The **duration to T-cell immunity and CMV recurrence** was **shorter with letermovir** than with valganciclovir.
- **CMV recurrence after T-cell immunity development** was **observed less with letermovir** than with valganciclovir.
- **Letermovir** was observed to have a **decreased incidence of neutropenia and decreased administration of colony stimulating factors and thymoglobulin** than in those who received valganciclovir.
- Due to lack of consistency in obtaining a T-cell immunity panel with regards to the prophylaxis start date, it is difficult to compare the efficacy of the two drugs in reaching T-cell immunity.
- Another study may re-evaluate our findings in the future once T-cell immunity panels are well established.

References

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