Real-World Experience of Letermovir Use at an Academic Transplant Center

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Background

- Letermovir (LMV) is FDA-approved for primary prophylaxis of cytomegalovirus (CMV) infection and disease in adult CMV-seropositive recipients of an allogeneic hematopoietic stem cell transplant (alloSCT)[1]
- LMV use currently restricted to high-risk patient groups to maximize cost/benefit[2]

Letermovir Restriction Criteria

CMV+ alloSCT adults with any 1 of the following:

- Donor is CMV negative (R+/D-)
- Cord-blood or haploidentical SCT
- T-cell depleted allografts
- Receiving alemtuzumab or antithymoglobulin
- Receiving >1mg/kg/day of prednisone
- Pre-SCT CMV infection or disease

- LMV ranked amongst the institution's top 50 drug expenditures
- OHSU is a 576-bed academic transplant center and performed 187 alloSCTs in 2021

Objective

To evaluate the use of letermovir and identify the clinical parameters, circumstances, or other rationale that may have necessitated use outside the institutional restriction criteria

Methods

Study Design

Single-center, retrospective, descriptive (IRB-approved)

Patient Eligibility

Any hospitalized patient who received ≥1 dose of LMV between 08/2021 and 01/2022

Study Outcomes

- Incidence of LMV use outside restriction criteria
- Drug expenditure for non-criteria uses over study period

Data Collected

- Administration data
- Transplant status
- ID consultation
- Rationale for non-criteria uses
- Age
- Length of stay
- Drug cost

Results

388 doses given

31 unique patients

41 admissions

Table 1. Cohort Characteristics

Mean age, in years (range)	54.9 (15-75)
Median days of LMV (IQR)	9 (4-13)
Median LOS in days (IQR)	21 (9-25)
AlloSCT recipients (n, %)	27/31 (87%)

LMV, letermovir; IQR, interquartile range; LOS, length of stay; AlloSCT, allogeneic hematopoietic stem cell transplant

Non-criteria uses occurred in 12/41 admissions (31.7%)*

Including use in 4 non-alloSCT patients: autologous SCT recipient (n=1), solid organ transplant recipients (n=2), CAR-T patient (n=1)

Non-criteria uses accounted for $20 414 in drug cost over 6 months, 29% total expenditure for all LMV uses**

*only 6 of 12 non-criteria uses (50%) had an ID consultation
**cost calculated based on number of doses for inpatient usage

Results (continued)

Table 2. Rationale for Non-Criteria Use	# of Admissions
Primary prophylaxis	4[a]
Pre-emptive therapy[b]	2
Step-down therapy following initial CMV treatment (e.g., foscarnet)	6[c]

Notes:
[a]Includes 1 heart transplant patient given LMV to avoid ganciclovir toxicity and 3 alloSCT patients who did not meet criteria: 1 continued beyond D+100 d/t use of low dose steroids (<1mg/kg/d), 1 without high risk for CMV, and 1 unintentionally continued beyond D+100
[b]Refers to LMV start as the initial therapy for CMV reactivation
[c]Includes 4 unique patients as 2 patients were admitted twice

Conclusions

- Real-world use of LMV often differs from patient types enrolled in the phase 3 trials
- Desire to avoid drug toxicities with other CMV agents likely drives LMV use outside of restriction criteria[3]
- Use outside of institutional restriction criteria was frequent and incurred a nontrivial cost
- ID consultation for all non-criteria use may decrease off-label usage of LMV

References

1. Letermovir (Prevymis™) [package insert]. Whitehouse Station, NJ: Merck & Co., Inc. 2021.
2. Hakki M et al. *Transplant Cell Ther.* 2021;27(9):707-719.
3. Linder KA et al. *Transpl Infect Dis.* 2021;23(4):e13687.