IDSA # 571

# "Real-World" Impact of Letermovir Prophylaxis for Cytomegalovirus in Allogeneic Hematopoietic-Cell Transplantation

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## Background

- Letermovir was FDA-approved in November 2017 for cytomegalovirus (CMV) prophylaxis in allogeneic hematopoietic cell transplant (HCT) patients
- We evaluated the "real-world" impact of letermovir in adult HCT recipients at the Mount Sinai Hospital in New York following addition of letermovir to our formulary in June 2018

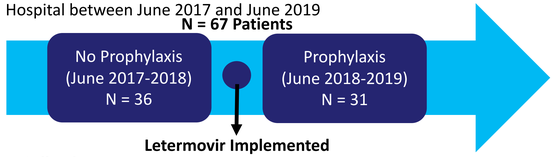
## Objectives

- To evaluate the impact of letermovir prophylaxis on incidence of CMV infection after HCT
- To evaluate the impact of letermovir on mortality, GVHD, and antiviral usage

## Methods

**Study Population:**

- Allogeneic HCT patients who underwent transplantation at The Mount Sinai Hospital between June 2017 and June 2019




**Data Collection:**

- Single-center, retrospective chart review
- All demographic, clinical, and laboratory data were abstracted from the existing medical record
- Data points for each patient were collected for 6 months following transplantation

**Inclusion Criteria:**

Adult patients who were CMV seropositive and received their first HCT at The Mount Sinai Hospital between June 2017 and June 2019 were included.

**Definitions:**

- Clinically significant CMV infection (CS-CMV) – CMV infection which required the use of anti-CMV antiviral therapy
- CMV disease – CMV infection resulting in end organ involvement

**Outcomes:**

| Primary Endpoints | Secondary Endpoints |
|---|---|
| • CS-CMV at 6 months post-transplant | • Mortality<br>• Occurrence of CMV disease<br>• GVHD Disease<br>• Subsequent hospital admissions required for CMV infection |

**Statistical Analysis:**

- Univariable analysis was conducted using chi-square and Fisher's exact tests, as appropriate, for categorical variables and Wilcoxon rank-sum test for continuous variables.
- For determining factors independently associated with CMV infection, logistic regression was used. Variables with a p-value ≤ 0.2 on univariable analysis were entered into the multivariable model.
- Kaplan-Meier plots were used for time-to-event analyses
- Log-rank test was used to compare CMV infection between patients who did and did not receive prophylaxis.

## Results

**Table 1: Baseline Characteristics**

| | No Prophylaxis (N = 36) | Prophylaxis (N = 31) | P Value |
|---|---|---|---|
| Median age at HCT (IQR) | 52 (43.8 – 58.5) | 58 (32.5 – 63.5) | 0.47 |
| Male, N (%) | 20 (55.6) | 17 (54.8) | 0.95 |
| Race, N (%) | | | 0.06 |
| White | 14 (38.9) | 21 (67.7) | |
| Black | 10 (27.8) | 6 (19.4) | |
| Asian | 8 (22.2) | 4 (12.9) | |
| Unknown | 4 (11.1) | 0 (0) | |
| Ethnicity, N (%) | | | 0.37 |
| Hispanic | 13 (36.1) | 9 (29.0) | |
| Non-hispanic | 23 (63.9) | 22 (71.0) | |
| Karnofsky Score, N (%) | | | < 0.001 |
| 100 | 0 (0) | 8 (25.8) | |
| 90 | 7 (19.4) | 13 (41.9) | |
| 80 | 15 (41.7) | 5 (16.1) | |
| ≤ 70 | 14 (38.9) | 5 (16.1) | |
| HCT Comorbidity Index, N (%) | | | 0.39 |
| Low | 5 (13.9) | 8 (25.8) | |
| Intermediate | 11 (30.6) | 10 (32.3) | |
| High | 20 (55.6) | 13 (41.9) | |
| Transplant Type, N (%) | | | 0.67 |
| Matched | 22 (61.1) | 18 (58.0) | |
| Mismatched | 1 (2.8) | 0 (0) | |
| Haploidentical | 6 (16.7) | 3 (9.7) | |
| Cord | 7 (19.4) | 10 (32.3) | |
| Source of Stem Cells, N (%) | | | 0.48 |
| Peripheral Blood | 16 (44.4) | 12 (38.7) | |
| Bone Marrow | 13 (36.1) | 9 (29.0) | |
| Cord Blood | 7 (19.4) | 10 (32.3) | |
| Conditioning Regimen, N (%) | | | 0.23 |
| Myeloablative (MAC) | 13 (36.1) | 7 (22.6) | |
| Reduced Intensity (RIC) | 23 (63.9) | 24 (77.4) | |
| Thymoglobulin, N (%) | 4 (11.1) | 2 (6.5) | 0.77 |
| Median days letermovir (IQR) | N/A | 96 (66 – 116) | - |

**Table 2: Comparison of HCT recipients receiving letermovir prophylaxis who did and did not develop clinically significant CMV**

| | Patients with CS-CMV, n=9 (%) | Patients without CS-CMV, n=22 (%) | P-value |
|---|---|---|---|
| Median age at transplant (range) | 58 (27 – 65) | 55.5 (23 – 73) | 0.50 |
| Female | 2 (22) | 12 (55) | 0.10 |
| Karnofsky score | | | 0.30 |
| 90-100 | 5 (56) | 16 (73) | |
| ≤80 | 4 (44) | 6 (27) | |
| Transplant Type | | | 0.72 |
| Haploidentical | 0 | 3 (14) | |
| Umbilical cord | 3 (33) | 7 (32) | |
| Other | 6 (67) | 12 (55) | |
| Stem cell source | | | 1.00 |
| Peripheral blood | 3 (33) | 9 (41) | |
| Bone marrow | 3 (33) | 6 (27) | |
| Cord blood | 3 (33) | 7 (32) | |
| Conditioning regimen | | | 1.00 |
| Reduced intensity | 7 (78) | 17 (78) | |
| Myeloablative | 2 (22) | 5 (23) | |
| Donor CMV IgG negative | 4 (44) | 8 (36) | 0.49 |
| Donor CMV IgG positive | 5 (56) | 14 (64) | |
| GVHD requiring systemic therapy | 4 (44) | 6 (27) | 0.42 |
| Thymoglobulin | 1 (11) | 1 (5) | 0.50 |

**Figure 1: Primary Outcome**

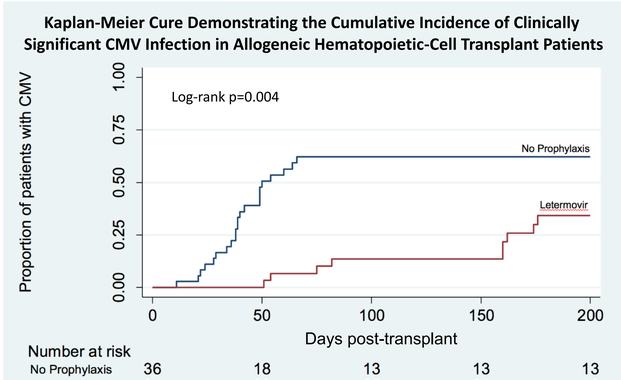



**Table 3: Secondary Outcomes**

| | No Prophylaxis (N = 36) | Prophylaxis (N = 31) | OR | 95% CI | P-value |
|---|---|---|---|---|---|
| Peak CMV viral load among patients requiring antiviral therapy (IU/mL), median (IQR) | 1674 (557 – 7780) | 353 (136 – 447) | - | - | 0.01 |
| Time from HCT to CS-CMV (days), median (IQR) | 39 (29 – 49) | 160 (75 – 162) | - | - | < 0.01 |
| Time from HCT to any detectable CMV (days), median (IQR) | 21 (14 - 33) | 19 (14 - 67) | - | - | 0.28 |
| Duration of anti-CMV antiviral therapy (days), median (IQR) | 70 (50 – 112) | 39 (25-57) | - | - | < 0.01 |
| CMV Disease, N (%) | 5 (13.9) | 1 (3.2) | 0.21 | 0.02 – 1.87 | 0.21 |
| GVHD Requiring Systemic Treatment, N (%) | 15 (41.7) | 10 (32.3) | 0.67 | 0.24 – 1.82 | 0.43 |
| Time from HCT to GVHD diagnosis (days), median (IQR) | 27 (21 - 29) | 63 (32 - 79) | - | - | 0.02 |
| Steroid Refractory GVHD, N (%) | 6 (16.7) | 3 (9.7) | 0.54 | 0.12 – 2.35 | 0.49 |
| Subsequent Admissions, N (%) | | | 1.05 | 0.38 – 2.9 | 1.00 |
| 0 | 12 (33.3) | 10 (32.3) | | | |
| ≥ 1 | 24 (66.7) | 21 (67.7) | | | |
| Subsequent Admissions for CMV, N (%) | | | 0.17 | 0.02 – 1.45 | 0.11 |
| 0 | 30 (83.3) | 30 (96.8) | | | |
| ≥ 1 | 6 (16.7) | 1 (3.2) | | | |
| All-Cause Mortality, N (%) | 5 (13.9) | 8 (25.8) | 2.16 | 0.62 – 7.46 | 0.35 |
| Time from HCT to Death (days), median (IQR) | 127 (106 – 169) | 106 (78 – 126) | - | - | 0.19 |

## Results

**Table 4: Factors Associated with CS-CMV at Day + 200**

| | CS-CMV N = 31 | No CS-CMV N = 36 | Multivariate OR | Multivariate 95% CI | Multivariate P-value |
|---|---|---|---|---|---|
| **Letermovir** | **9 (29.0)** | **22 (61.1)** | **0.29** | **0.08 – 0.99** | **0.05** |
| Bone Marrow Source | 12 (38.7) | 10 (27.8) | 2.94 | 0.74 – 11.7 | 0.12 |
| Umbilical Cord Blood Source | 10 (32.3) | 7 (19.4) | 6.16 | 0.62 - 61.1 | 0.12 |
| Karnofsky Score 90 or 100 | 9 (29.0) | 19 (52.8) | 0.39 | 0.10 – 1.46 | 0.16 |
| Haploidentical or Umbilical Cord Transplant | 15 (48.4) | 11 (30.1) | 1.07 | 0.19 – 6.06 | 0.94 |

## Conclusions

- In real-world practice, letermovir is associated with a decreased risk of CMV infection
- Risk factors for CS-CMV among patients who receive prophylaxis with letermovir warrant future study
- Future studies should also evaluate the impact of letermovir on antiviral drug usage, GVHD, and other transplant-related outcomes in this population

## Limitations

- Single-center study with a small sample size
- Inability to assess adherence to letermovir
- Reliance on retrospective chart review – not all endpoints may have been recorded properly in progress notes

## 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.*

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