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# A Real World prevalence study of cytomegalovirus infection and disease in allogeneic hematopoietic stem cell transplant recipients on Letermovir Prophylaxis

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## INTRODUCTION

Cytomegalovirus (CMV) remains the most common viral infection among recipients of allogeneic hematopoietic stem cell transplants (allo-HSCT). Untreated CMV infection and disease during the post-trasplant period are associated with high mortality rates.[1] The introduction of letermovir (LTV), antiviral agent approved as primary prophylaxis in CMV-seropositive recipients (CMV R+) has demostrated a safe and effective drug of preventing CMV reactivation, clinically significant CMV infection (CS-CMVi) and CMV disease, resulting in a reduction in mortality at 24 weeks post-transplant in comparison with placebo.[2]

Our aim was describe the prevalence of CMV reactivation, CS-CMVi and CMV disease between the beggining of LTV treatment and day +100 post-HSCT. We describe our real-world experience using LTV in allo-HSCT recipients.

## METHODS

**Definitions:** *CMV reactivation*: any DNAemia; *CS-CMVi*: CMV DNAemia leading to preemptive treatment; *high-risk CMV reactivation*: haploidentical or mismatched unrelated donor, cord blood transplantation, ex vivo T-cell depleted graft; and/or acute graft-versus-host disease (GVHD) that led to the use of prednisone ≥1 mg/kg; *lymphopenia*: lymphocytes count < 1 x$10^9$/L.[3]

**Study subjects:** this was a single-center cohort study of transplanted adult allo-HSCT patients in our institution between February 2020 and December 2022.
**Inclusion criteria:** (a) age >18 years old; (b) CMV R+; (c) first allo-HSCT.
**Exclusion criteria:** (a) death occurred within 30 days post-HSCT; (b) CMV R-; (c) cord blood transplant; (d) CMV disease 6 months previously transplant date; (e) active CMV DNAemia measured 7 days before transplant date; (f) exposure to antiviral treatment with (val)ganciclovir or foscarnet 7 days before transplant date. The study was approved by our Institutional Review Board, and study conducted consistent with principles in the Declaration of Helsinki. Statistical analysis was performed using SPSS v23.

**Antiviral prophylaxis and CMV preemptive therapy:** during the study period, LTV 240 mg PO once daily was administered from day + 7/8 to day +100 post-HSCT. CMV monitoring and preemptive therapy were performed per local protocol.

**CMV viral load (VL):** before 2021, CMV VL was performed using LightMix Human CMV Kit (TIB MolBiol GmbH, Berlin, Germany) with LoD of 20 copies/mL (1.3 $\log_{10}$) and LoQ of 200 copies/mL (2.3 $\log_{10}$). After 2021, the VL assay was replaced by CMV PCR kit 1.0 RealStar (Altona Diagnostics) with LoD of 100 IU/mL (2 $\log_{10}$) and LoQ of 1000 IU/mL (3 $\log_{10}$).

## RESULTS

Baseline characteristics of 28 patients who received LTV are shown in Table 1. 13 patients (46.43%) met the high-risk CMV reactivation criteria.

### LTV prophylaxis and CMV outcomes

All patients had negative baseline CMV VL 24 hours previously transplant date. Only one patient had delayed start treatment because lack of insurance coverage. Upon LTV initiation, 18 patients had an undetectable CMV VL, and 10 patients had an isolated detectable not quantifiable CMV VL. The prevalence of CMV reactivation was 35.71%. The risk factors among these ten patients are shown in Chart 1.

Start of CMV monitoring – median (IQR): 6 days (4 – 7)
Monitoring duration– median (IQR): 94 days (87.75 – 95.25)

Start of LTV – median (IQR): 7 days (7– 8.25)
Treatment duration– median (IQR): 93 days (86.5 – 93)
Dose reduction: 100% because cyclosporine A coadministration.

Treatment discontinuation – N (%): 5 (17.85)
• Inability to swallow due to mechanical ventilation: 4 (80)
• Other reasons: 1 (20)

### Follow-up

Acute GVHD – N (%): 12 (42.85)
Time to 1st acute GVHD episode – median (IQR): 41 days (30.75-48.5)

Lymphopenia: days +50 and +100 post-HSCT were taken as evaluations.
Day +50 – N (%): 23 (82.14)
Day +100 – N (%): 15 (53.57)

Death – N (%): 5 (17.85). No deaths were attributable to CMV.
• Relapse/disease progression: 1 (3.57)
• Other causes: 4 (14.28)

CMV reactivation – N (%): 10 (35.7)
CS-CMVi and CMV disease – N (%): 0 (0)

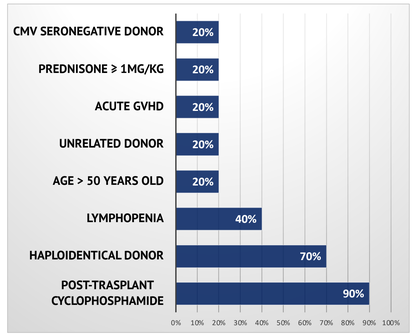



Chart 1. Risk factors distribution.

| Table 1. Baseline characteristics | Letermovir (N = 28) |
|---|---|
| **Median age, years (range)** | 43 (17-62) |
| **Male – N (%)** | 16 (57) |
| **Underlying diagnosis – N (%)** | |
| Acute myeloid leukemia | 11 (39.28) |
| Acute lymphocytic leukemia | 5 (17.85) |
| Myelodisplastic syndrome | 3 (10.71) |
| Multiple myeloma | 2 (7.14) |
| Aplastic anemia | 2 (7.14) |
| Myelodisplastic syndrome/Myeloproliferative neoplasm | 2 (7.14) |
| Other | 3 (10.71) |
| **Stem-cell source – N (%)** | |
| Peripheral blood | 26 (92.85) |
| Bone Marrow | 2 (7.14) |
| **Serological status – N (%)** | |
| D(+) – R(+) | 17 (60.71) |
| D(-) – R(+) | 11 (39.28) |
| **CD34⁺ cells infused (x$10^6$/Kg) – median (IQR)** | 5 (3.22 – 5.47) |
| **HLA matching and donor class – N (%)** | |
| Haploidentical donor | 12 (42.85) |
| Matched unrelated | 11 (39.28) |
| Matched related | 5 (17.85) |
| **Conditioning regimen – nro (%)** | |
| Myeloablative conditioning | 21 (75) |
| Reduced-Intensity conditioning | 7 (25) |
| **GVHD prophylaxis – N (%)** | |
| PTCy + CSA + MMF | 26 (92.85) |
| PTCy + MTX | 2 (7.14) |
| **Hospitalization days – median (IQR)** | 32 (29.25 – 36) |
| **Time to engraftment (days) – median (IQR)** | 19 (9 – 34) |

*Abbreviations*: N, number; D, donor; R, recipient; IQR, interquartile range; HLA, human leukocyte antigen; GVHD, Graft-Versus-Host disease; PTCy, Post-trasplantation cyclophosphamide; CSA, cyclosporine A; MMF, mycophenolate mofetil; MTX, methotrexate.

## CONCLUSIONS

This is the first report of Real-World experience with LTV in our hospital. Primary LTV prophylaxis was effective in preventing CMV infection and CMV disease in CMV R+ allo-HSCT patients. This drug was well tolerated. No discontinuations of LTV due to toxicity or intolerance.
There is limited data about who patients would be benefit from extended primary prophylaxis beyond 100 days post-trasplant.

## REFERENCES

1. Ljungman P, et al. A mortality analysis of LTV prophylaxis for Cytomegalovirus in CMV-seropositive recipients of allogeneic hematopoietic cell transplantation. Clinical Infectious Diseases. 2020;70(8):1525-1533.
2. Marty FM, et al. Letermovir prophylaxis for CMV in hematopoietic-cell transplantation. N Engl J Med. 2017;377:2433-2444.
3. Ljungman P, et al. Definitions of CMV infection and disease in transplant patients for use in clinical trials. Clinical Infectious Diseases. 2017;64(1).

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