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Letermovir prophylaxis for cytomegalovirus is associated with risk of post-transplant lymphoproliferative disorders after haploidentical stem cell transplantation

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Running title: CMV prophylaxis might increase risk of PTLD

Conflict of interest disclosure

The authors declare that they have no competing financial interests.

Authors' contribution

HXJ designed the study. PXY, HQ, LLJ and SHL collected and analyzed data. HXJ, PXY, HQ and CL wrote the manuscript. All authors provided patient data and gave final approval for the manuscript.

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Data sharing statement

The data that support the findings of this study are available upon reasonable request from the corresponding author.

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Cytomegalovirus (CMV) and Epstein-Barr virus (EBV) emerge as the most frequently reactivated opportunistic viruses after haploidentical stem cell transplantation (haplo-SCT).[1,2,3] As members of the herpes virus family, CMV and EBV are reported to be linked to causing clinical manifestations, resulting in a co-infection rates ranging from 10% to 32.7%.[4,5] Additionally, CMV treatment coincides with EBV reactivation, potentially affecting the progression of EBV reactivation and EBV associated diseases.[6,7] Letermovir (LMV) prophylaxis effectively reduces CMV infection after haplo-SCT.[8,9] However, its impact on EBV remains unclear. This study compared letermovir recipients (LMV group) to a control group receiving standard PCR-guided preemptive therapy (non-LMV group) in two independent cohorts. In both cohorts, letermovir significantly reduced clinically significant CMV infection and refractory CMV infection within 180 days post-transplant. While the incidence of EBV viremia was similar between groups, LMV recipients exhibited higher peak EBV titers and were associated with an increased risk of post-transplant lymphoproliferative disorder (PTLD) within the first 180 days. In both univariate and multivariate analyses, the use of letermovir was significantly linked to a higher risk of PTLD. These findings indicate that while letermovir prophylaxis is highly effective in preventing CMV after haplo-SCT, it may also be associated with an increased risk of PTLD, highlighting the need for caution and further research to explore this potential link in clinical practice.

Patients were divided into two cohorts based on transplant date. Cohort 1 (June 2022 to December 2022) included LMV-treated haplo-SCT patients where letermovir use depended on patient choice and drug availability. Cohort 2 (January 2023 to June 2023) included haplo-SCT patients who regularly received LMV and met our inclusion criteria as part of our registered clinical trial (clinicaltrials.gov NCT05656599). Non-LMV controls received PCR-guided therapy, matched 1:1 to LMV patients by gender, age, and disease via propensity score matching. Inclusion criteria were first haplo-SCT, age over 14, and LMV started within 28 days and

contined to 100 days post-transplant. Exclusions were patients with genetic metabolic disorders, bone marrow fibrosis and early death within 28 days. Patients who reactivated CMV or EBV before letermovir or within 7 days of letermovir administration were also excluded. The study received approval from the ethics committee of Peking University People's Hospital. Transplant protocols, including conditioning, stem cell mobilization, and acute graft-vesus-host-disease (aGVHD) prophylaxis were consistent with our previous studies. CMV and EBV were monitored by real-time quantitative polymerase chain (RT-qPCR) on plasma DNA twice weekly during hospitalization and at least once weekly post-discharge up to 180 days, or as needed. CMV >1000 copies/ml and EBV >500 copies/ml were the thresholds for positive results.[10,11,12] Clinically significant CMV (csCMV) infection was defined as CMV viremia requiring preemptive treatment or CMV disease.[8] Refractory CMV infection was defined as CMV viremia that persistent or increases after at least 2 weeks of antiviral therapy.[10,13] EBV-associated posttransplant lymphoproliferative disorders (PTLD) was diagnosed as as proven or probable based on published definition.[12] EBV-associated hemophagocytic syndrome (HLH) was difined by meeting HLH-2004 diagnostic criteria, active EBV infection, and excluding other causes.[14] Other herpesviruses not routinely monitored, and was performed on the suspicious patients with clinical manifestations.

In the LMV group, prophylaxis began after stable neutrophil engraftment. csCMV cases stopped LMV and received ganciclovir, foscarnet, and immunoglobulin if refractory; LMV resumed once CMV was controlled within 100 days. For EBV DNA >500 copies/ml for two consecutive tests with a rapid increase or when the patient presented clinical symptoms of EBV-related complications, rituximab therapy typically initiated within 24 hours, along with the reduction of immunosuppressive therapy if condition permits. EBV-specific T-cell therapy was also considered for high-risk or rituximab-refractory patients.[12] All haplo-SCT recipients received one-year acyclovir prophylaxis for herpersviruses (HSV), regardless of whether they were receiving letermovir. Statistical analyses were performed using R software.

The characteristics of patients are summarized in Table 1. In Cohort 1, 178 haplo-SCT patients (89 per group) were analyzed. LMV prophylaxis began at a median of 19 days post-SCT and lasted 84 days (range, 62-112 days) in LMV group. In Cohort 2, 464 haplo-SCT patients (232 per group) had similar baseline characteristics, with LMV starting at a median of 16 days post-SCT and lasting 84 days.

In Cohort 1 (Figure 1 A), the 180-day cumulative incidence of csCMV infection was lower in LMV group (39.7%, 95% CI 29.4-49.7%) than non-LMV group (80.9%, 95% CI 70.9-87.8%, $P < 0.001$). Similar results were observed in Cohort 2 (Figure 1B), with 21.4% (95% CI, 16.2-27.2%) in the LMV group vs. 78.4% (95% CI, 72.5-83.2%) in the non-LMV group ($P < 0.001$). Refractory CMV incidence was also lower in LMV groups in both cohorts (Figure 1 C-D). Delayed CMV reactivation and decreased CMV peak titer and duration are also notable benefits observed (Figure S1).

Despite a similar incidence of EBV viremia between LMV and non-LMV groups (Figure 1 E-F), the LMV group exhibited a higher peak EBV titer (5110 copies/mL) compared to the non-LMV group (1950 copies/mL, $P = 0.010$) (Figure S1). Importantly, LMV recipients showed an increased risk of PTLD (Table S1, Figure 1 G-H). In Cohort 1, 8 patients (5 proven, 3 probable) in the LMV group and 2 patients (2 probable) in the non-LMV group developed PTLD, resulting in cumulative incidences of 9.0% (95% CI, 4.2-16.1%) and 2.25% (95% CI, 0.4-7.1%), respectively ($P=0.049$, Figure 1 G), showing a significant difference. Cohort 2 provided further support for these findings, with 23 patients (9.9%, 12 proven, 11 probable) in the LMV group and 6 (2.6%, 2 proven, 4 probable) in the non-LMV group developing PTLD, leading cumulative incidences of 9.9% (95% CI, 6.5-14.2%) and 2.6% (95% CI, 1.1-5.3%), respectively ($P = 0.001$, Figure 1 H), highlighting the association between LMV prophylaxis and increased PTLD risk. To be note, 4 patients in the LMV group developed EBV-associated HLH, whereas none did in the non-LMV

group, resulting in a higher cumulative incidence of HLH in the LMV group (1.7% vs 0%, P=0.044).

Risk factors for PTLD after haplo-SCT were summarized in Table 2. In the univariate analysis of the entire group of 642 patients, LMV administration, EBV peak titer ≥ 2420 copies/ml (median), and EBV DNAemia duration time ≥ 10 days (median) emerged as significant risk factors for developing PTLD. Multivariate analysis identified LMV administration (hazard ratio [HR] 3.68, 95% CI 1.70-8.11, P = .001), EBV peak titer ≥ median 2420 copies/ml (HR 3.60, 95% CI 1.13-11.50, P = .031)), EBV DNAemia duration time ≥ 10 days (HR 123.12, 95% CI 13.62-1113.29, P < 0.001) remained the independent predictors for the development of PTLD. These associations were also confirmed in the prospective study of 464 patients (data not shown). Our data strongly indicate that LMV prophylaxis may contribute to an elevated risk of PTLD after haplo-SCT.

Transplant outcomes in LMV and non-LMV group showed comparable cumulative incidences (Figure S2). For grade 2-4 aGVHD at 100 days, Cohort 1 showed no difference (24.7% for both, P=0.953), and Cohort 2 results were similar (18.1% vs. 22.0%, P=0.312). Relapse incidence at 180 days was also comparable (Cohort 1: 4.5% for both, P=0.997; Cohort 2: 5.2% vs. 9.1%, P=0.111). Turning attention to treatment-related mortality (TRM), both Cohort 1 and Cohort 2 studies demonstrated a comparable cumulative incidence between the LMV and non-LMV groups (Cohort 1: 6.7% vs. 10.1%, P=0.414; Cohort 2: 6.3% vs. 3.9%, P=0.251). Infection-related mortality (IRM) showed no significant difference in either cohort (Cohort 1: 5.6% vs. 9.0%, P=0.380; Cohort 2: 6.0% vs. 2.6%, P=0.070). At 180 days, overall survival (OS) rates were comparable in both cohorts (Cohort 1: 93.9% vs. 89.8%, P=0.292; Cohort 2: 93.5% vs. 94.4%, P=0.694).

This study of two independent cohorts shows that LMV prophylaxis after haplo-SCT effectively reduces CMV complications but is unexpectedly linked to higher EBV-related disease risk, especially PTLD. This is the first study to suggest a

potential association between LMV and increased EBV-related diseases. Although the observed association between LMV and increased PTLD may be multifactorial, our data underscores the need for caution regarding this link. Despite increased PTLD cases, TRM, IRM, and OS remained unaffected. Given the clear benefit of LMV in reducing csCMV, LMV prophylaxis remains advisable for high-risk CMV patients. However, the increased PTLD risk needs careful monitoring, and further research is needed to explore the potential mechanisms.

Limitations of our study include its single-center design, lack of contemporaneous controls, missing data of some histologic confirmation of PTLD and the use of other anti-DNA virals. Prospective, multicenter studies are needed to assess clinical factors affecting outcomes and to confirm our findings. Additionally, our study focused on haplo-SCT with high-dose ATG, requiring validation in other transplant contexts. Immune reconstitution data were not collected; future studies should examine antiviral immune recovery.

In conclusion, while letermovir prophylaxis is highly effective in preventing CMV after haplo-SCT, it may also be associated with an increased risk of PTLD. Our results highlight the need for caution and further research to explore this potential link in clinical practice. Additional studies are essential to optimize post-transplant management and carefully balance the benefits and risks of letermovir use.

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1 **Table 1. Patients' characteristics**

Characteristics	Cohort 1				Cohort 2			
	Total (n=178)	LMV (n=89)	No LMV (n=89	P value	Total (n=464)	LMV (n=232)	No LMV (n=232)	P value
Median age at SCT (y, range)	42(14-66)	45 (16-66)	41 (14-61)	0.052	38 (14-70)	40 (14-70)	37 (14-64)	0.133
Age ≥40y ，n (%)	102 (57.3)	54 (60.7)	48 (53.9)	0.363	226 (48.7)	123 (49.8)	103 (41.7)	0.071
Sex (M/F)	94/84	49/40	45/44	0.548	290/204	144/103	146/101	0.855
Median follow up (d,range)	465 (33-573)	458 (33-568)	481 (66-573)	0.263	327 (28-728)	273 (28-352)	625 (28-728)	<0.001
Disease type, n (%)				0.965				0.103
AML	74 (41.6)	37 (41.6)	37 (41.6)		194 (41.8)	97 (41.8)	97 (41.8)	
ALL	64 (36.0)	33 (37.1)	31 (34.8)		127 (27.4)	54 (23.2)	73 (31.5)	
MDS	26 (14.6)	13 (14.6)	13 (14.6)		82 (17.7)	42 (18.1)	40 (17.2)	
AA	6 (3.4)	2 (2.2)	4 (4.5)		32 (6.9)	21 (9.1)	11 (4.7)	
Others	8 (4.5)	4 (4.5)	4 (4.5)		29 (6.3)	18 (7.8)	11 (4.7)	
Transplant regimen, n (%)				0.496				0.186

Bu/Cy/ATG	139 (78.1)	68 (76.5)	71 (79.8)		369 (79.5)	180 (77.6)	189 (81.5)	
Bu/Flu/Cy/ATG	6 (3.4)	2 (2.2)	4 (4.5)		32 (6.9)	21 (9.1)	11 (4.7)	
RIC-Bu/Flu/Cy/ATG	33 (18.5)	19 (21.3)	14 (15.7)		63 (13.6)	31 (13.4)	32 (13.8)	
Donor CMV serological status, n (%)								
D+	155 (87.1)	71 (79.8)	84 (94.4)	<0.001	443 (95.5)	221 (95.3)	222 (95.7)	0.999
D-	20 (11.2)	18 (20.2)	2 (2.2)		17 (3.7)	9 (3.9)	8 (3.4)	
Unknown	3 (1.7)	0 (0.0)	3 (3.4)		4 (0.9)	2 (0.9)	2 (0.9)	
Patient CMV serological status, n (%)				0.621				0.175
P+	174 (97.8)	88 (98.9)	86 (96.6)		455 (98.1)	225 (97.0)	230 (99.1)	
P-	4 (2.2)	1 (1.1)	2 (2.2)		9 (1.9)	7 (3.0)	2 (0.9)	
Donor EBV serological status, n (%)								0.345
D+	167 (93.8)	84 (94.4)	83 (93.3)	0.225	440 (94.8)	217 (93.5)	223 (96.1)	
D-	8 (4.5)	5 (5.6)	3 (3.4)		20 (4.3)	13 (5.6)	7 (3.0)	
Unknown	3 (1.7)	0 (0.0)	3 (3.4)		4 (0.9)	2 (0.9)	2 (0.9)	
Patient EBV serological status, n (%)				0.118				0.094
P+	171 (96.1)	88 (98.9)	83 (93.3)		440 (94.8)	224 (96.6)	216 (93.1)	

P-	7 (3.9)	1 (1.1)	6 (6.7)		24 (5.2)	8 (3.4)	16 (6.9)

Abbreviations: SCT, stem cell transplantation; M, male; F, female; AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia; MDS, myelodysplastic syndrome; AA, aplastic anemia; Bu, busulfan; Cy, cyclophosphamide; ATG, antithymocyte globulin; Flu, fludarabine; RIC, reduced intensity conditioning; CMV, cytomegalovirus; EBV, Epstein-Barr virus; P+, patient CMV or EBV-seropositive; P-, patient CMV or EBV--seronegative; D+, donor CMV or EBV-seropositive; D-, donor CMV or EBV--seronegative; LMV, letermovir

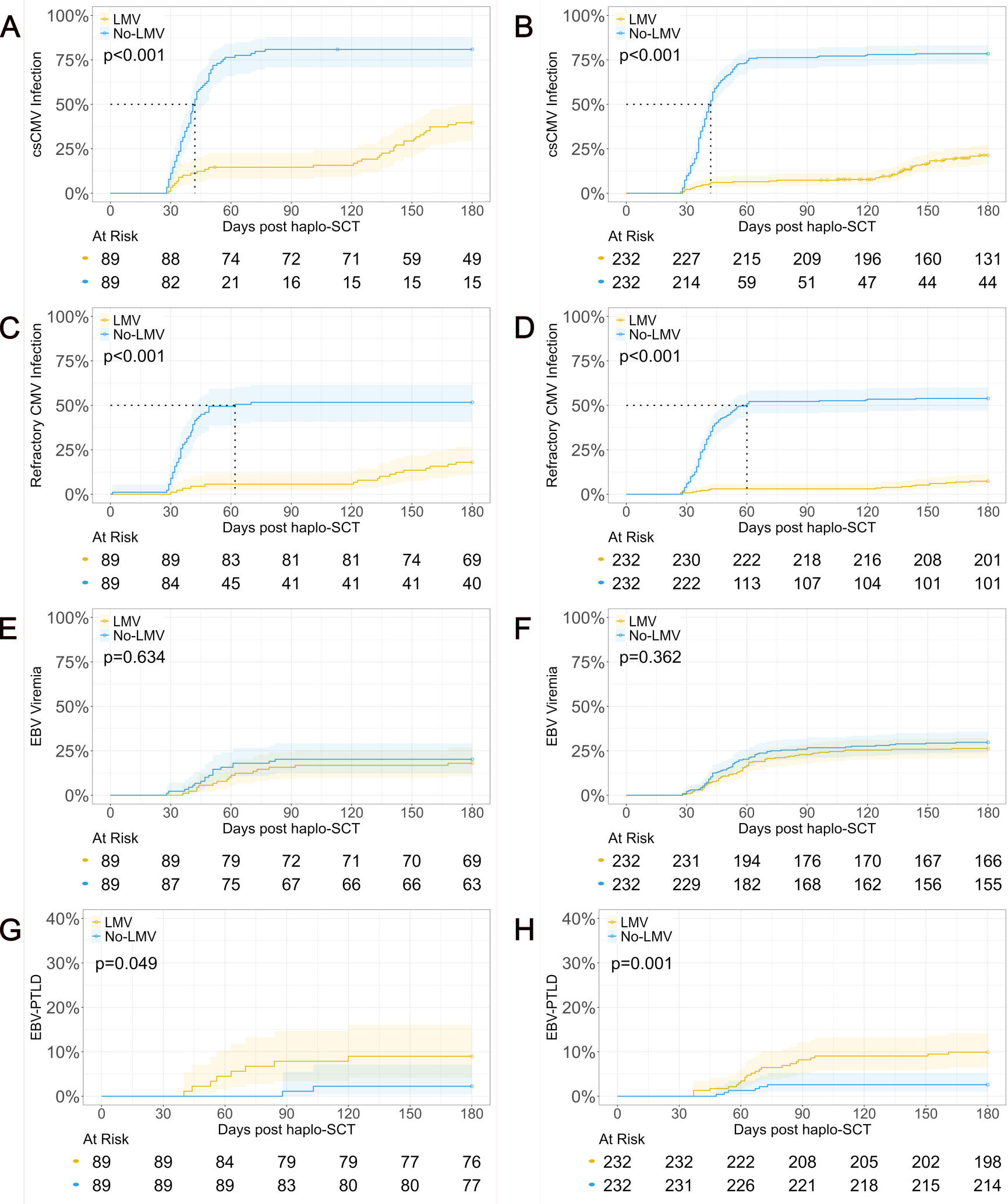
Table 2. Univariate analysis and multivariate analysis of risk factors for post-transplant lymphoproliferative disorder after haplo-SCT

Variable	Univariate Analysis		Multivariate Analysis	
	HR (95% CI)	**P Value**	**HR (95% CI)**	**P Value**
Patient sex (male vs female)	0.899 (0.471-1.719)	0.748		
Patient age at SCT (≥40 y vs <40 y)	0.938 (0.419-2.104)	0.877		
Underlying disease (acute leukemia vs not)	1.004 (0.500-2.017)	0.945		
Patient EBV serological status P+ vs P-)	1.590 (0.317-7.986)	0.573		
Donor EBV serological status (D+ vs others)	0.931 (0.258-3.362)	0.913		
aGVHD after SCT (grade 2-4vs grade 0-1)	1.819 (0.711-4.650)	0.212		
Steroid treatment(≥ 1mg/kg/d prednisone or its equivalent vs not)	1.290 (0.452-3.682)	0.634		
CMV DNAemia after SCT (yes vs no)	1.349 (0.615-2.961)	0.455		
EBV peak titer after SCT (≥2180 vs <2180)	3.384 (1.009-11.350)	**0.048**	3.598 (1.126-11.496)	**0.031**
EBV DNAemia duration days after SCT (≥10 vs <10)	136.791 (14.746-1268.936)	**<0.001**	123.124 (13.617-1113.285)	**<0.001**
Letermovir administration (yes vs no)	4.693 (1.905-11.558)	**<0.001**	3.679 (1.669-8.111)	**0.001**

Abbreviations: HR, hazard ratio; SCT, stem cell transplantation; vs, versus; CMV, cytomegalovirus; EBV, Epstein-Barr virus; D+, donor EBV-seropositive; D-, donor EBV-seronegative; P+, patientr EBV-seropositive; P-, patient EBV-seronegative

Figure Legends

Figure 1. CMV and EBV infection. Cumulative incidence of clinically significant CMV infection in Cohort 1 (A) and Cohort 2 (B), refractory CMV infection in Cohort 1 (C) and Cohort 2 (D), EBV viremia in Cohort 1 (E) and Cohort 2 (F), EBV-PTLD in Cohort 1 (G) and Cohort 2 (H). Abbreviations: CMV, cytomegalovirus; EBV, Epstein-Barr virus; haplo-SCT, haploidentical stem cell transplantation; PTLD, post-transplantation lymphoproliferative disorder.


A
csCMV Infection
LMV
No-LMV
p<0.001
100%
75%
50%
25%
0%
0
30
60
90
120
150
180
Days post haplo-SCT
At Risk
89 88 74 72 71 59 49
89 82 21 16 15 15 15
B
csCMV Infection
LMV
No-LMV
p<0.001
Days post haplo-SCT
At Risk
232 227 215 209 196 160 131
232 214 59 51 47 44 44
C
Refractory CMV Infection
LMV
No-LMV
p<0.001
Days post haplo-SCT
At Risk
89 89 83 81 81 74 69
89 84 45 41 41 41 40
D
Refractory CMV Infection
LMV
No-LMV
p<0.001
Days post haplo-SCT
At Risk
232 230 222 218 216 208 201
232 222 113 107 104 101 101
E
EBV Viremia
LMV
No-LMV
p=0.634
Days post haplo-SCT
At Risk
89 89 79 72 71 70 69
89 87 75 67 66 66 63
F
EBV Viremia
LMV
No-LMV
p=0.362
Days post haplo-SCT
At Risk
232 231 194 176 170 167 166
232 229 182 168 162 156 155
G
EBV-PTLD
40%
30%
20%
10%
0%
LMV
No-LMV
p=0.049
Days post haplo-SCT
At Risk
89 89 84 79 79 77 76
89 89 89 83 80 80 77
H
EBV-PTLD
LMV
No-LMV
p=0.001
Days post haplo-SCT
At Risk
232 232 222 208 205 202 198
232 231 226 221 218 215 214

Supplementary Data

Table S1. Characteristics and outcomes of diagnosed cases of EBV associated post-transplant lymphoproliferative disorder.

No	Cohort	Group	Disease	Age	Gender	EBV Peak Titer (Copy/ml)	PTLD Diagnosised Day post-SCT	Clinical Manifestations	Type of EBV-PTLD	Tissue Pathological Type	Total Rituximab doses	Outcomes
1	Cohort 1	LMV	ALL	55	Female	2950	161	Fever, lymphadenopathy,	Probable	/	3	Survival
2	Cohort 1	LMV	MDS	41	Female	7820	63	Fever, lymphadenopathy, hepatosplenomegaly	Proven	Polymorphic PTLD	4	Survival
3	Cohort 1	LMV	ALL	59	Male	168000	44	Fever, lymphadenopathy,	Probable	/	4	Survival
4	Cohort 1	LMV	ALL	17	Male	61500	56	Fever, lymphadenopathy,	Proven	Polymorphic PTLD	3	Survival
5	Cohort 1	LMV	ALL	25	Female	10000	84	Fever, lymphadenopathy,	Proven	Polymorphic PTLD	3	Survival
6	Cohort 1	LMV	ALL	16	Female	7760	40	Fever, lymphadenopathy,	Proven	Polymorphic PTLD	3	Survival
7	Cohort 1	LMV	AML	56	Female	82300	70	Fever, lymphadenopathy,	Probable	/	6	Die at 169 day
8	Cohort 1	LMV	AML	53	Female	42900	53	Fever, lymphadenopathy,	Proven	Monomorphic PTLD (DLBCL)	4	Survival
9	Cohort 2	LMV	ALL	59	Female	2440000	60	Fever, lymphadenopathy, HLH	Proven	Monomorphic PTLD (DLBCL)	2	Die at 75 day

10	Cohort 2	LMV	AML	55	Male	842000	96	Fever, lymphadenopathy,	Proven	Monomorphic PTLD (DLBCL)	4	Survival
11	Cohort 2	LMV	AML	16	Female	11500	62	Fever, lymphadenopathy,	Probable	/	4	Survival
12	Cohort 2	LMV	AML	40	Female	31100	84	Fever, lymphadenopathy,	Proven	Polymorphic PTLD	4	Survival
13	Cohort 2	LMV	AML	16	Male	2180	64	Fever, lymphadenopathy,	Probable	/	2	Survival
14	Cohort 2	LMV	AML	67	Male	174000	59	Fever, lymphadenopathy, hepatosplenomegaly, HLH	Probable	/	3	Die at 62 day
15	Cohort 2	LMV	MDS	41	Male	338000	80	Fever, lymphadenopathy, hepatosplenomegaly, HLH	Proven	Polymorphic PTLD	4	Die at 181 day
16	Cohort 2	LMV	MDS	41	Female	35400	65	Fever, lymphadenopathy, intracranial space-occupying lesion	Proven	Monomorphic PTLD (DLBCL)	4	Die at 173 day
17	Cohort 2	LMV	MDS	62	Male	67200	37	Fever, lymphadenopathy,	Probable	/	3	Survival
18	Cohort 2	LMV	ALL	19	Male	23940	88	Fever, lymphadenopathy, hepatosplenomegaly	Proven	Polymorphic PTLD	2	Die at 101 day
19	Cohort 2	LMV	AA	17	Male	1380	87	Fever, lymphadenopathy,	Proven	Polymorphic PTLD	4	Survival
20	Cohort 2	LMV	AML	62	Male	41000	59	Fever, lymphadenopathy,	Probable	/	4	Survival

21	Cohort 2	LMV	AML	30	Female	24900	70	Fever, lymphadenopathy, hypoxemia	Probable	/	2	Survival
22	Cohort 2	LMV	ALL	62	Female	1210	67	Fever, lymphadenopathy,	Probable	/	2	Survival
23	Cohort 2	LMV	AML	56	Male	20300	69	Fever, lymphadenopathy,	Probable	/	4	Survival
24	Cohort 2	LMV	AA	44	Male	15300	151	Fever, lymphadenopathy, hepatosplenomegaly	Proven	Monomorphic PTLD (T-cell neoplasma)	6	Survival
25	Cohort 2	LMV	MDS	61	Male	51740	54	Fever, lymphadenopathy,	Proven	Polymorphic PTLD	4	Survival
26	Cohort 2	LMV	ALL	49	Male	5450	58	Fever, lymphadenopathy,	Proven	Polymorphic PTLD	4	Survival
27	Cohort 2	LMV	ALL	18	Male	74500	63	Fever, lymphadenopathy,	Proven	Polymorphic PTLD	4	Survival
28	Cohort 2	LMV	AA	47	Male	500000	37	Fever, lymphadenopathy, hepatosplenomegaly, HLH	Proven	Monomorphic PTLD (DLBCL)	4	Die at 66 day
29	Cohort 2	LMV	AA	34	Male	2390	37	Fever, lymphadenopathy,	Probable	/	2	Survival
30	Cohort 2	LMV	ALL	29	Female	14700	45	Fever, lymphadenopathy,	Probable	/	2	Survival
31	Cohort 2	LMV	AML	60	Female	18600	62	Fever, lymphadenopathy,	Probable	/	4	Survival
32	Cohort 1	No-LMV	AML	57	Female	6210	103	Fever, lymphadenopathy,	Probable	/	3	Survival

33	Cohort 1	No-LMV	MDS	59	Male	6690	88	Fever, lymphadenopathy,	Probable	/	2	Survival
34	Cohort 2	No-LMV	MDS	38	Male	6330	48	Fever, lymphadenopathy, hypoxemia	Probable	/	2	Survival
35	Cohort 2	No-LMV	AML	35	Male	28600	69	Fever, lymphadenopathy,	Probable	/	4	Survival
36	Cohort 2	No-LMV	ALL	30	Male	7350	67	Fever, lymphadenopathy, tonsillar masses	Proven	Polymorphic PTLD	4	Survival
37	Cohort 2	No-LMV	AML	38	Female	51100	54	Fever, lymphadenopathy,	Proven	Polymorphic PTLD	4	Survival
38	Cohort 2	No-LMV	AML	60	Female	20700	52	Fever, lymphadenopathy,	Probable	/	4	Die at 246 day
39	Cohort 2	No-LMV	AML	32	Female	4800	73	Fever, lymphadenopathy,	Probable	/	4	Die at 221 day

Abbreviations: SCT, stem cell transplantation; AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia; MDS, myelodysplastic syndrome; AA, aplastic anemia; EBV, Epstein-Barr virus; PTLD, post-transplant lymphoproliferative disorder; DLBCL, diffuse large B-cell lymphoma.

Supplementary Figures

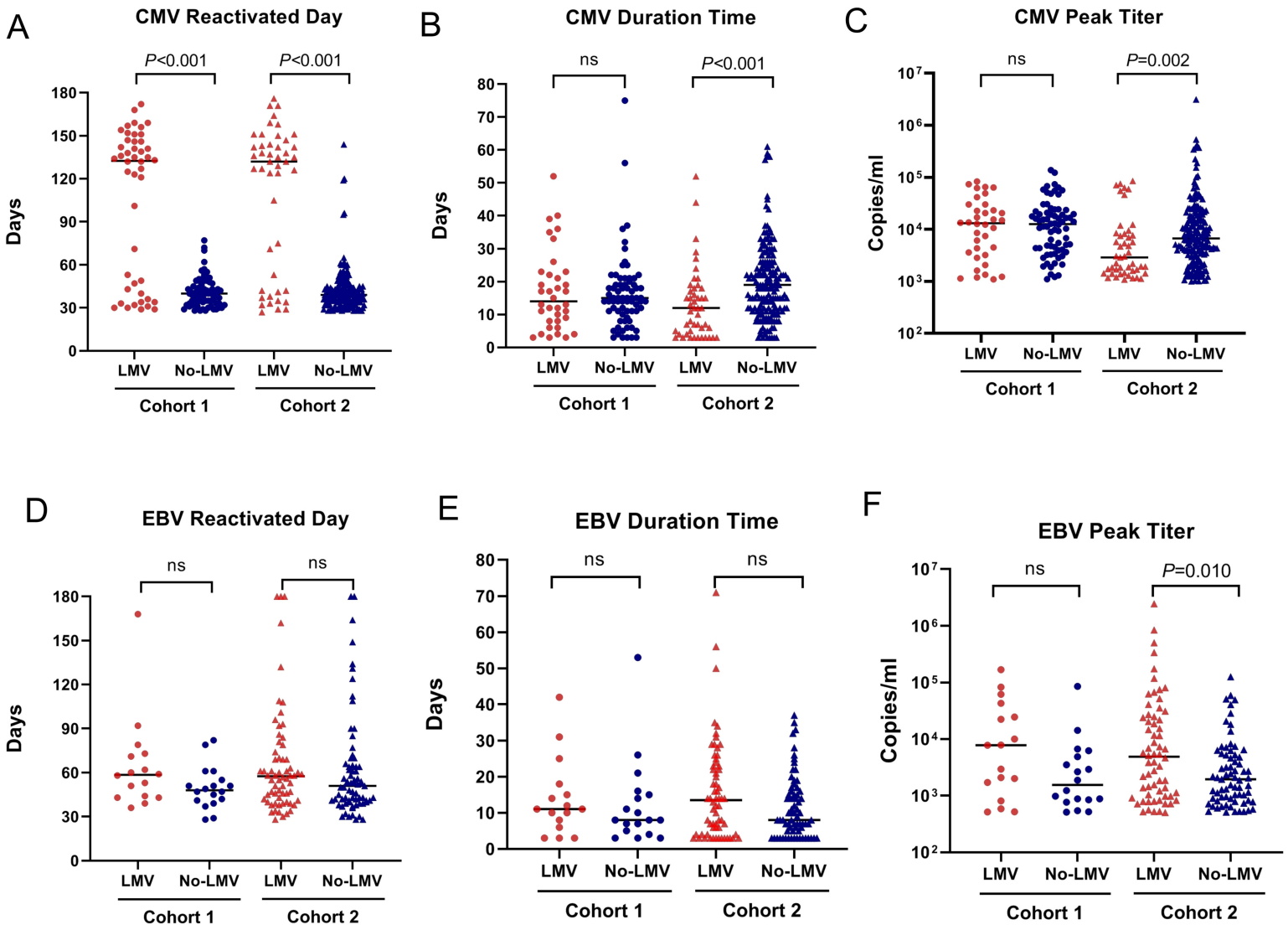


Figure S1. CMV and EBV infection. (A) CMV reactivated day, (B) CMV viremia duration time, (C) CMV peak titer, (D) EBV reactivated day, (E) EBV viremia duration time, (F) EBV peak titer. Abbreviations: CMV, cytomegalovirus; EBV, Epstein-Barr virus; LMV, letermovir.

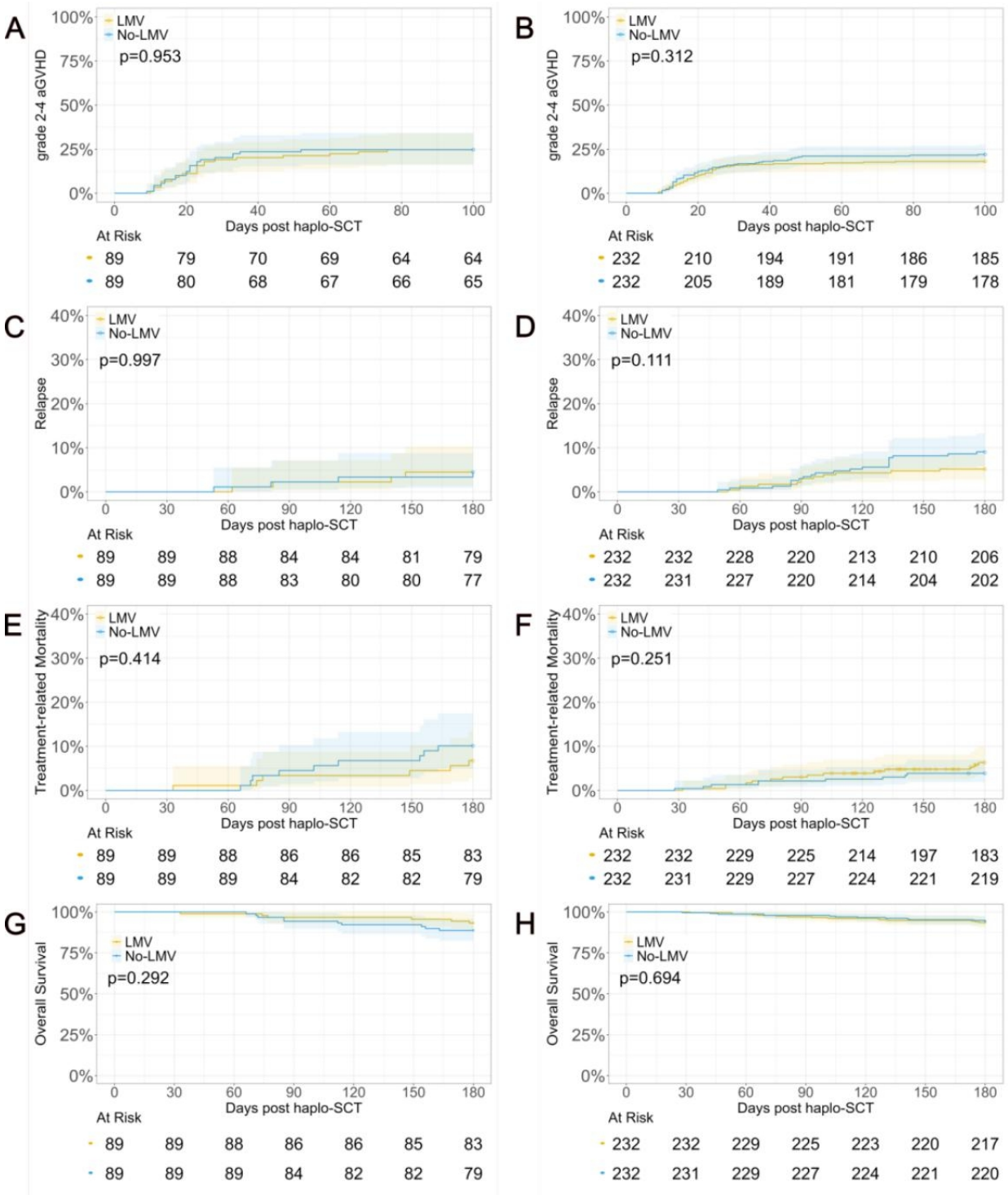


Figure S2. Transplant outcomes. Cumulative incidence of grade 2-4 aGVHD in Cohort 1 (A) and Cohort 2 (B), Relapse in Cohort 1 (C) and Cohort 2 (D), Treatment-related mortality in Cohort 1 (E) and Cohort 2 (F), Overall survival in Cohort 1 (G) and Cohort 2 (H). Abbreviations: aGVHD, acute graft-versus-host disease; TRM, treatment-related mortality; haplo-SCT, haploidentical stem cell transplantation.