Methods. A patient was admitted on 3/21/21 from a group home. He developed abdominal pain, diarrhea and vomiting on 4/15, with elevated liver function tests (LFT). He was transferred to Medicine on 4/17 and HAV IgM and IgG resulted positive on 4/18. Visitation to the unit has been halted for over a year, and no outside food has been allowed. The patient has not been observed to have any sexual exposure to others.

Investigation. Exposure window: 15 days prior to start of symptoms. Patients in the unit were screened for symptoms, tested for HAV IgM/IgG, LFTs. Discharged patients were contacted and referred straight for vaccination (difficult to have multiple visits). Staff members with contact to the unit were screened, via email and phone calls. If no previous vaccination and there was presence of exposure or symptoms, staff were referred to Occupational Health Services (OHS). Other Measures: The unit was terminally cleaned and daily enhanced cleaning with bleach ensued. Daily assessment of patients and staff for symptoms. Admissions were held for 2 days until all the patients were tested and given vaccine. Further admissions were screened for HAV.

Results. 32 inpatients screened. One patient was positive for HAV IgM, but was asymptomatic with normal LFTs. On investigation, patient had acute hepatitis in February 2021. Patients with no immunity were vaccinated. Two immunocompromised patients were also given HAV immunoglobulin. On chart review, 6 out of 29 discharged patients had evidence of immunity. 133 staff were screened and 54 referred to OHS (see table).

Exposure Investigation

	Total	IgM pos	IgG pos	IgG Neg	Normal LFTs	Vaccinated by OHS	HAV immunoglob
Inpatients	32	1	24 (75%)	8 (25%)	31	8	2
Discharged patients	29	N/A	6	N/A	N/A	N/A	
Staff screened	133						
Vaccinated or no exposure	79						
Staff referred to OHS	54						
Seen by OHS	36	0	23 (64%)	14(36%)	35 (97%)	6/14 (43%)	1
No show OHS	18						
Symptoms	8	0	2	5	7	3	

Conclusion. As evident with numerous COVID outbreaks in inpatient Psychiatry units, communicable diseases are difficult to control. Patients are in an interactive communal setting and participate in group sessions. For better care and safety of patients and staff, our unit will screen and offer HAV vaccine to new admissions.

Disclosures. **Gregory Weston, MD MSCR**, **Allergan** (Grant/Research Support) **Inessa Gendlina**, Nothing to disclose

922. The Impact of Clinically Significant CMV Infections on Other Viral Infections in the Era of Letermovir Primary Prophylaxis

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Session: P-53. Infections in Immunocompromised Individuals

Background. Cytomegalovirus (CMV) is a frequent complication after hematopoietic cell transplant (HCT) and may increase the risk of other viral infections through its immunomodulatory effects. Letermovir, a novel antiviral targeting the viral terminase complex, was approved for primary prophylaxis in CMV-seropositive adult recipients after allogeneic HCT (allo-HCT). Because of its efficacy and safety, letermovir has become the standard of care for primary prophylaxis against CMV during the first 100 days post-transplant. However, its impact on the frequency of other viral infections and non-relapse mortality (NRM), through its reduction in clinically significant CMV infections (CS-CMVi), is not known.

Methods. This is a single-center, retrospective cohort study of 150 allo-HCT recipients, including controls that were matched by the transplant type (match-unrelated, matched-related, cord, and haploidentical), cared for at our institution between March 2016 and December 2018. Baseline demographics, transplant characteristics, prophylaxis, CMV and other viral infections, and outcomes were collected (Table 1) and analyzed on IBM® SPSS version 26 using a binary logistic regression model for multivariate analysis. For univariate analysis, we used Chi-square and Fischer's Exact Test.

Table 1. Baseline patient characteristics

Characteristic	No CS-CMVi (n = 91)	CS-CMVi (n = 59)	Total (n = 150)	p-value
Age, median (range)	55 (22-73)	53 (18-77)	55 (18-77)	.80
Letermovir primary ppx	40 (44)	10 (17)	50 (33)	.001
Gender				.98
Female	43 (47)	28 (48)	71 (47)	
Male	48 (53)	31 (52)	79 (53)	
Race				.55
Asian	5 (6)	3 (5)	8 (5)	
African American	5 (6)	4 (7)	9 (6)	
Hispanic/Latino	13 (14)	11 (19)	24 (16)	
Middle Eastern	5 (6)	3 (5)	8 (5)	
White	63 (69)	36 (61)	99 (66)	
Other	0 (0)	2 (3)	2 (1)	
Cancer				.77
ALL	15 (17)	13 (22)	28 (19)	
AML	42 (46)	28 (48)	70 (47)	
Acute bi-phenotypic leukemia	2 (2)	0 (0)	2 (1)	
Aplastic anemia	1 (1)	0 (0)	1 (1)	
CLL/SLL	5 (6)	2 (3)	7 (5)	
CML	3 (3)	2 (3)	5 (3)	
CMML	2 (2)	2 (3)	4 (3)	
MDS	7 (8)	4 (7)	11 (7)	
MF	7 (8)	1 (2)	8 (5)	
NHL	3 (3)	4 (7)	7 (5)	
Other	4 (4)	3 (5)	7 (5)	
HCT Type				.007
MRD*	48 (53)	15 (25)	63 (42)	
MUD	31 (34)	29 (49)	60 (40)	
Haploidentical*	10 (11)	14 (24)	24 (16)	
Cord	2 (2)	1 (2)	3 (2)	
HCT Source				.21
Marrow	14 (15)	16 (27)	30 (20)	
Peripheral	75 (82)	42 (71)	117 (78)	
Cord	2 (2)	1 (2)	3 (2)	
Time to engraftment in days, median (range)	13 (7-34)	14 (8-33)	13 (7-34)	.60
Donor CMV seropositivity	56 (62)	24 (41)	80 (53)	.01
ATG	11 (12)	19 (32)	30 (20)	.003
Post-Cy	39 (43)	26 (44)	65 (43)	.88
GVHD	43 (47)	29 (49)	72 (48)	.82
GVHD at D100	42 (46)	27 (46)	69 (46)	.96
Other CMV ppx				.12
Lead in GCV	13 (14)	16 (27)	29 (19)	
FOS into HCT	1 (1)	0 (0)	1 (1)	
No ppx	77 (85)	43 (73)	120 (80)	

Abbreviations. CS-CMVi, clinically significant cytomegalovirus infection; ppx, prophylaxis; AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia; CLL/SLL, chronic lymphocytic leukemia and small lymphocytic lymphoma; CML, chronic myelogenous leukemia; CMML, chronic myelomonocytic leukemia; MDS, myelodysplastic syndrome; NHL, Non-Hodgkin Lymphoma; MF, myelofibrosis; HCT, hematopoietic cell transplant; MRD, matched related donor; MUD, matched unrelated donor; GVHD, graft-versus-host-disease; ATG, anti-thymocyte globulin; Cyc, cyclophosphamide; FOS, foscarnet.
* Denotes statistically significant differences between the two groups.

Results. In our 2:1 matched cohort analysis, 50 patients received letermovir for primary prophylaxis during the first 100 days post-HCT, and 100 did not. In a univariate analysis with CS-CMVi as the outcome, there was a statistically significant difference in NRM at 24 and 48 weeks. Our data indicated a trend towards a decrease in other viral infections for those without CS-CMVi (Table 2). However, in a multivariate analysis accounting for primary prophylaxis with letermovir as an effect modulator, CS-CMVi did not demonstrate a significant impact on the frequency of other viral infections but was associated with NRM at week 24 and 48 (Table 3). Interestingly, having ALL and donor CMV seropositivity were protective factors against other viral infections (*Herpesviridae*).

Table 2. Infections and outcomes by CS-CMVi (univariate)

	No CS-CMVi (n=91)	CS-CMVi (n=59)	Total (n=150)	*P*-value
Non-CMV infections*	52 (57%)	42 (71%)	94 (63%)	.08
Non-CMV/non-RVI infections**	37 (41%)	33 (56%)	70 (47%)	.07
Non-CMV Herpesviridae infections***	18 (20%)	19 (32%)	37 (25%)	.09
Respiratory viral infection	30 (33%)	28 (48%)	58 (39%)	.08
HSV	3 (3%)	4 (7%)	7 (5%)	.43
VZV	1 (1%)	0 (0)	1 (1%)	>.99
HHV-6	12 (13%)	15 (25%)	27 (18%)	.06
EBV	6 (7%)	5 (8%)	11 (7%)	.75
ADV	4 (4%)	5 (8%)	9 (6%)	.32
BKV	22 (24%)	20 (34%)	42 (28%)	.20
Non-relapse mortality at day 100	6 (7%)	9 (15%)	15 (10%)	.08
Non-relapse mortality by 24 weeks	6 (7%)	13 (22%)	19 (13%)	.005
Non-relapse mortality by 48 weeks	8 (9%)	17 (29%)	25 (17%)	.001

Abbreviations. CS-CMVi, clinically significant cytomegalovirus infection; CMV, cytomegalovirus; RVI, respiratory viral infection. HSV, herpes simplex virus 1-2; VZV, varicella zoster virus; HHV-6, human herpes virus-6; EBV, Epstein-Barr virus; ADV, adenovirus (non-RVI); BKV, BK virus.
*Non-CMV infections include HSV, VZV, HHV-6, Adenovirus (non-RVI), EBV, BK, and RVI.
**Non-CMV/non-RVI infections include HSV, VZV, HHV-6, Adenovirus (non-RVI), EBV, and BK.
***Non-CMV Herpesviridae infections include HSV, VZV, HHV-6, and EBV.

Table 3. Logistic Regression Analysis of Outcomes Using CS-CMVi as Exposure

Risk Factor	OR	95% CI	p-value
A. Logistic Regression – Herpesviridae			
Letermovir primary ppx	1.24	0.34-4.5	.74
CS-CMVi	0.94	0.31-2.8	.90
ALL as primary malignancy	0.19	0.05-0.76	.02
Donor CMV seropositivity	0.24	0.07-0.84	.03
B. Logistic Regression – Non-CMV/Non-RVI			
Letermovir primary ppx	0.77	0.30-1.98	.60
CS-CMVi	0.94	0.39-2.25	.89
C. Logistic Regression – All Non-CMV			
Letermovir primary ppx	2.61	0.96-7.1	.06
CS-CMVi	1.44	0.55-3.72	.46
D. Logistic Regression – HHV-6			
Letermovir primary ppx	4.66	0.35-7.82	.52
CS-CMVi	1.67	0.48-5.88	.42
ALL as primary malignancy	0.17	0.03-0.84	.03
E. Logistic Regression – BKV			
Letermovir primary ppx	0.95	0.36-2.48	.91
CS-CMVi	1.31	0.54-3.14	.55
F. Logistic Regression – RVI			
Letermovir primary ppx	2.81	1.11-7.12	.03
CS-CMVi	2.07	0.85-5.04	.11
G. Logistic Regression – NRM Day 100			
Letermovir primary ppx	0.68	0.12-3.91	.67
CS-CMVi	1.90	0.41-8.88	.42
HCT source - Marrow	16.5	1.36-200	.03
H. Logistic Regression – NRM Week 24			
Letermovir primary ppx	0.55	0.11-2.8	.47
CS-CMVi	4.83	1.14-20.4	.03
HCT source - Marrow	39.1	3.24-471	.004
I. Logistic Regression – NRM Week 48			
Letermovir primary ppx	0.61	0.15-2.43	.48
CS-CMVi	5.30	1.44-19.4	.01
HCT source - Marrow	16.71	2.70-103.3	.002
Time to engraftment	1.16	1.02-1.33	.03

Abbreviations. OR. odds ratio; CL, confidence interval; ppx, prophylaxis; CS-CMVi, clinically significant cytomegalovirus infection; CMV, cytomegalovirus; RVI, respiratory viral infection; ALL, acute lymphoblastic leukemia; HHV-6, human herpes virus-6; BKV, BK virus; NRM, non-relapse mortality; HCT, hematopoietic cell transplant.

Conclusion. Our study showed that CS-CMVi is associated with higher 24- and 48-week non-relapse mortality but with no increase in the incidence of other non-respiratory viral infections in this matched cohort of allo-HCT recipients.

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923. Respiratory Syncytial and Parainfluenza Virus Infection Increase the Risk of Cytomegalovirus Reactivation in Allogeneic Hematopoietic Cell Transplant Recipients

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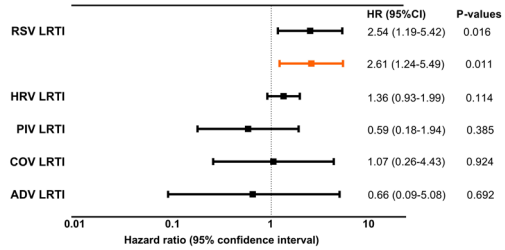
Session: P-53. Infections in Immunocompromised Individuals

Background. Respiratory virus infections are associated with significant and specific local and systemic inflammatory response patterns, which may lead to reactivation of latent viruses. We examined whether viral upper (URTI) or lower respiratory tract infection (LRTI) with common respiratory viruses increased the risk of CMV viremia after allogeneic hematopoietic cell transplantation (HCT).

Methods. We retrospectively analyzed patients undergoing allogeneic HCT between 4/2008 and 9/2018. CMV surveillance was performed weekly and the presence of upper and lower respiratory symptoms were evaluated by multiplex respiratory viral PCR. We used Cox proportional hazards models to evaluate risk factors for development of any CMV viremia or high level CMV viremia in the first 100 days post-HCT. Each respiratory virus infection episode was considered positive for 30 days beginning the day of diagnosis.

Results. Among 2,545 patients (404 children, 2141 adults), 1,221 and 247 developed CMV viremia and high level CMV viremia, respectively, in the first 100 days post-HCT. Infections due to human rhinoviruses (HRV, N=476) were most frequent, followed by parainfluenza viruses 1-4 (PIV, N=139), seasonal human coronaviruses (COV, N=134), respiratory syncytial virus (RSV, N=77), influenza A/B (FLU, N=35), human metapneumovirus (MPV, N=37), and adenovirus (ADV, N=61). In adjusted models, RSV LRTI was associated with increased risk of developing CMV viremia at all levels (**Figures 1** and **2**), and PIV or RSV URTI increased the risk of high level CMV viremia; all other viruses showed no association in univariable models.

Model estimates for associations between LRTI and development of any CMV viremia‡



‡ Models were not performed with other viruses given limited number of outcome events. P values of LRTI with <0.05 in univariable models were included multivariable moddels.

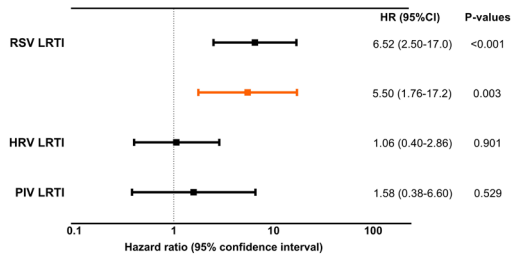
In univariable models

Adjusted for pre- and post-transplant factors if p<0.05 in univariable models. Adjustment factors: Pretransplant factors (age, sex, race, body habitus, donor type, stem cell source, CMV serostatus) + post-transplant factors (subsequent transplantation, lymphopenia and acute severe GVHD as time dependent covariates).

Abbreviation: LRTI = lower respiratory tract infection, CMV = cytomegalovirus, RSV = respiratory syncytial virus, HRV = human rhinovirus, PIV = parainfluenza virus, COV = seasonal human coronavirus, ADV = adenovirus, HR = hazard ratio, CI = confidence interval, GVHD = graft-versus-host disease.

Figure 1. Model estimates for associations between LRTI and development of any CMV viremia

Model estimates for associations between LRTI and development of high level CMV viremia‡



‡ Models were not performed with other viruses given limited number of outcome events. P values of LRTI with <0.05 in univariable models were included multivariable moddels. High level CMV viremia was defined as viral load >1,000 IU/ml (PCR).

In univariable models

Adjusted for pre- and post-transplant factors if p<0.05 in univariable models.Adjustment factors: Pretransplant factors (race, body habitus, stem cell source, CMV serostatus, and year of transplantation) + post-transplant factors (lymphopenia and acute severe GVHD as time dependent covariates).

Abbreviation: LRTI = lower respiratory tract infection, CMV = cytomegalovirus, RSV = respiratory syncytial virus, HRV = human rhinovirus, PIV = parainfluenza virus, HR = hazard ratio, CI = confidence interval, GVHD = graft-versus-host disease.

Figure 2. Model estimates for associations between LRTI and development of high level CMV viremia

Conclusion. We demonstrated that RSV and PIV infections are associated with an increased risk for development of CMV viremia after allogeneic HCT. This novel association provides the rationale to explore virus-specific inflammatory pathways that may trigger CMV reactivation. CMV viremia may also serve as an endpoint in clinical trials that assess new preventative or therapeutic interventions of RSV or PIV infection.

Disclosures. **Alpana Waghmare, MD**, **Allovir** (Scientific Research Study Investigator)**Ansun Biopharma** (Scientific Research Study Investigator)**Kyorin Pharmaceutical** (Advisor or Review Panel member) **Janet A. Englund, MD**, **AstraZeneca** (Consultant, Grant/Research Support)**GlaxoSmithKline** (Research Grant or Support)**Meissa Vaccines** (Consultant)**Pfizer** (Research Grant or Support)**Sanofi Pasteur** (Consultant)**Teva Pharmaceuticals** (Consultant) **Michael Boeckh, MD PhD**, **AlloVir** (Consultant)**Ansun Biopharma** (Grant/Research Support)**Astellas** (Grant/Research Support)**EvrysBio** (Consultant, Other Financial or Material Support, Options to acquire equity, but have not exercised them)**Gilead Sciences** (Consultant, Grant/Research Support)**GlaxoSmithKline** (Consultant)**Helocyte** (Consultant, Other Financial or Material Support, Options to acquire equity, but have not exercised them)-**Janssen** (Grant/Research Support)**Kyorin** (Consultant)**Merck** (Consultant, Grant/Research Support)**Moderna** (Consultant)**Symbio** (Consultant)**Takeda (formerly known as Shire)** (Consultant, Grant/Research Support)**VirBio** (Consultant, Grant/Research Support)

924. Cytomegalovirus (CMV) Retinitis during Maintenance Chemotherapy for Acute Lymphoblastic Leukemia

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