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malignancies who received CMV prophylaxis with letemovir. Baseline demographics, cancer characteristics, CMV infections, treatment and mortality data were collected from the electronic medical record. The primary outcome is the occurrence of CS-CMVi while on letemovir. Data was analyzed on IBM® SPSS version 24.

Results: We identified 37 patients with relapsed or refractory HM who received letemovir; 23 as primary prophylaxis and 14 as secondary prophylaxis. Only 5 patients developed CS-CMVi while on letemovir for primary prophylaxis with 3 progressing to CMV end organ disease. None of the 9 patients who received CART cell therapy developed CS-CMVi while on letemovir. There is no significant difference in outcomes between patients with leukemia and patients with lymphoma or myeloma. Letemovir was well tolerated and was discontinued in 1 patient who developed thrombocytopenia.

Conclusion: The use of letemovir for prevention of CMV infections in patients with relapsed or refractory hematological malignancies, including CAR T cell recipients, should be determined in future trials.

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Dosing of Cidofovir in Pediatric Stem Cell Transplant Patients Requiring Continuous Renal Replacement Therapy (CRRT)

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Background: Cidofovir is an antiviral agent commonly utilized in the treatment of adenoviral and BK viral infections. In patients following bone marrow transplant who are critically ill, renal failure is common and can be compounded by the nephrotoxicity associated with cidofovir utilization. In patients requiring CRRT, there is a lack of information to guide optimal dosing of cidofovir.

Objective: The primary objective of this research is to describe cidofovir dosing for patients requiring CRRT at Children's National Hospital. Secondary objectives include an evaluation of viral clearance and toxicities associated with cidofovir use in CRRT, and to determine optimal cidofovir dosing in CRRT.

Table 1

| Patient ID | 4 | 7 | 10 | 9 | 6 | 5 | 8 | 11 | Median (QR) |
|------------|---|---|----|---|---|---|---|---|-------------|
| Age (yr)   | 1 | 8 | 0.66 | 16 | 16 | 17 | 17 | 16 | 16 (13.5)   |
| Weight (kg)| 9.7| 41.7| 7.4 | 68 | 66 | 57 | 50 | 40 | 41.7 (47.2) |
| Sex        | M | F | M | M | F | M | F | M | 55% (M)      |
| Indication for transplant | SDS | ALL | MHC | HD | AML | MHC | ALL | MHC | Adeno + BK |
| Virus Being Treated | Adeno | Adeno | Adeno | Adeno | BK | Adeno + BK | Adeno + BK | Adeno + BK | Adeno + BK |
| Prep Regimen | FLU/ME/ ALEM | TBI/FLU/ CY | BU/FLU | BU/FLU/ THIO/TBI | BU/CY | TBI/FLU/ CY | TBI/THIO/ CY | FLU/ME/ ALEM |
| GVHD       | N | N | N | N | N | N | N | N | N           |
| VOD        | N | Y | Y | N | Y | N | Y | N | N           |
| Concomitant infection identified | Y | Y | Y | Y | Y | Y | Y | Y | Y           |
| Cidofovir (mg/kg) Regimen | Received majority of treatment days | 1-3 wk | 1-1.5 MWF | 3-5.5 wk | 3-5.5 wk | 1-3 wk | 1-3 wk | 1-1.5 MWF | 1.5 MWF |
| Duration cidofovir treatment (days) | 34 | 54 | 22 | 34 | 30 | 65 | 65 | 17 | 34           |
| Days of hypok N (%) | 10 (30) | 4 (7) | 9 (181) | 9 (26) | 15 (50) | 4 (6) | 8 (12) | 7 (41) | 8.5 (22) |
| Days of hypomg N (%) | 21 (62) | 0 | 6 (27) | 12 (35) | 1 (3) | 4 (6) | 8 (12) | 7 (41) | 3.5 (9.5) |
| Days of Neutropenia | N, grade (%) | 30; 4 (88) | 24; 5 (44) | 11; 4 (50) | 17; 4 (50) | 7; 23 | 58; 4 (89) | 16; 4 (25) | 8; 3 (47) |
| Days of thrombocytopenia N, Grade (%) | 30; 4 (88) | 18; 4 (33) | 17; 4 (77) | 18; 4 (53) | 28; 3 (93) | 64; 4 (98) | 19; 4 (28) | 17; 3 (100) | 18.5 (82.5) |

Methods: A single center, retrospective review of pediatric bone marrow transplant patients from January 1, 2012 through August 31, 2019 was conducted.

Results: Patients’ baseline characteristics and treatment details are described in Table 1. Eight children with adenovirus, BK virus, or both following allogeneic stem cell transplant were treated with CRRT and cidofovir during the study period. The most common dosing regimens utilized included 1–1.5 mg/kg administered intravenously (IV) on Monday, Wednesday, Friday and 3.5–5 mg/kg administered IV once weekly. Stable or downtrending PCR values were seen in patients receiving the 3.5–5 mg/kg administered IV once weekly and in the patient who received 1.5 mg/kg every IV 48 hours. Adverse events did not correlate with dosing regimen received.

Conclusions: Higher dosing regimens, such as 3.5–5 mg/kg administered IV weekly and 1.5 mg/kg IV every 48 hours should be utilized for patients receiving CRRT and cidofovir. These patients saw downtrending or stable viral PCRs with no increase in adverse effects. Further randomized trials are needed to determine the best dosing for pediatric patients requiring cidofovir and CRRT.

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Allogeneic, Off-the-Shelf, Sars-Cov-2-Specific T Cells to Treat High-Risk Patients with COVID-19

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The impact of COVID-19, caused by SARS-CoV-2, has been tremendous, with >33,000,000 confirmed cases worldwide. Older age, comorbidities (e.g. obesity, hypertension, diabetes), and immune deficits have been unequivocally associated with severe disease and unfavorable outcomes. For example, in immunocompromised H SCT recipients mortality rates as
high as 20% have been reported (www.cibmtr.org/COVID19). Notably, >80% of patients with COVID-19 are lymphopenic. Given the limited antiviral options, the lymphopenia seen in severely afflicted individuals, and our data demonstrating that allogeneic, off-the-shelf virus-specific T cells (VSTs) can safely and effectively treat viral infections/disease caused by EBV, CMV, BKV, HHV6 and AdV in allo-HSCT recipients, we sought to explore the feasibility of extending this therapy to COVID-19 by developing banked, SARS-CoV-2–specific VSTs.

To first identify immunogenic SARS-CoV-2 target antigens we exposed PBMCs from convalescent individuals to a cocktail of pepmixes spanning 17 structural and non-structural proteins (Nsps). Of these a number of structural and non-structural proteins were identified as immunodominant and advanced for VST generation using our manufacturing platform of PBMC stimulation in a G-Rex using cytokine-supplemented medium. We achieved a mean 9.3±1.1 fold expansion (mean±SEM; n=8) of cells with a single stimulation. These cells were comprised almost exclusively of CD3+ T cells (97±0.5%), with a mixture of cytotoxic (CD8+) and helper (CD4+) T cells that expressed the activation markers CD69 and CD28 as well as central (CD45RO+/CD62L+) and effector memory markers (CD45RO+/CD62L−), with minimal PD1 or Tim3. The anti-viral activity of our expanded cells was tested in an IFN-γ ELIspot using each of the individual stimulating antigens as an immunogen and all lines proved to be reactive against the target antigens. The VSTs were Th1-polarized and polyfunctional, producing TNF-α, GM-CSF and Granzyme B, as assessed by single-cell protein analysis. Finally, the cells were able to kill viral pepmix-loaded autologous PHA blasts with no evidence of auto- or alloreactivity, attesting to both their selectivity and their safety for clinical use in high risk COVID-19 patients (Fig. 1).

In conclusion, we have shown that it is feasible to generate polyclonal SARS-CoV-2–target antigens we exposed PBMCs from convalescent individuals to a cocktail of pepmixes spanning 17 structural and non-structural proteins (Nsps). Of these a number of structural and non-structural proteins were identified as immunodominant and advanced for VST generation using our manufacturing platform of PBMC stimulation in a G-Rex using cytokine-supplemented medium. We achieved a mean 9.3±1.1 fold expansion (mean±SEM; n=8) of cells with a single stimulation. These cells were comprised almost exclusively of CD3+ T cells (97±0.5%), with a mixture of cytotoxic (CD8+) and helper (CD4+) T cells that expressed the activation markers CD69 and CD28 as well as central (CD45RO+/CD62L+) and effector memory markers (CD45RO+/CD62L−), with minimal PD1 or Tim3. The anti-viral activity of our expanded cells was tested in an IFN-γ ELIspot using each of the individual stimulating antigens as an immunogen and all lines proved to be reactive against the target antigens. The VSTs were Th1-polarized and polyfunctional, producing TNF-α, GM-CSF and Granzyme B, as assessed by single-cell protein analysis. Finally, the cells were able to kill viral pepmix-loaded autologous PHA blasts with no evidence of auto- or alloreactivity, attesting to both their selectivity and their safety for clinical use in high risk COVID-19 patients (Fig. 1).

In conclusion, we have shown that it is feasible to generate polyclonal SARS-CoV-2–VSTs from convalescent individuals using GMP-compliant manufacturing methodologies. We are rapidly advancing this product to the clinic for administration in a randomized clinical trial (VSTs+SOC vs SOC) to prevent the development of severe disease in hospitalized high-risk patients with COVID-19, including allo-HSCT recipients (NCT04401410).

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### Real-World Experience Using Letermovir for CMV Prophylaxis in High-Risk Allogeneic Hematopoietic Stem Cell Patients in the Setting of Using T-Cell Depletion As GVHD Prophylaxis and the Impact on CMV Reactivation, 1-Year Overall Survival, and 1-Year GVHD-Free-Relapse-Free Survival

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### Introduction/ Objectives

Cytomegalovirus (CMV) is a major cause of morbidity in allogeneic hematopoietic stem cell transplant (HSCT) patients. Marty et al. 2017 showed that lettermovir is effective in preventing CMV reactivation in high-risk HSCT patients, though only 16% were haplo-identical. Recently, Karam et al. 2019 showed decreased rates of CMV reactivation in haplo-identical HSCT using letermovir in unselected high-risk patients. This study evaluates the effects of letermovir on other transplant-related outcomes including overall survival (OS), relapse free survival (RFS), and Graft-versus-host-disease (GVHD)-free-relapse-free survival (GRFS) as they are not as well-known.

### Methods

We retrospectively analyzed adult patients at USC Norris Cancer Hospital who received allo-HSCT from 2018 to 2020. Recipients who were CMV positive, received T-cell depleting therapies such as PTCy for GVHD prophylaxis and/or ATG in the conditioning regimen, and those who fulfilled the criteria in Marty et al. 2017 were categorized as “high-risk”. Patients were considered to have CMV reactivation if they had clinically significant serum CMV viremia or organ involvement by day+100. The primary end-point assessed was day+100 CMV reactivation. Secondary end-points included 1-year OS, 1-year RFS, 1-year transplant-related mortality (TRM), and 1-year GRFS.

### Results

A total of 116 adult HSCT recipients were reviewed. 61% of patients received letermovir prophylaxis (n=71), all high-risk, and 38% did not (n=45). 13 high-risk patients did not receive letermovir due to insurance limitations and were included in the non-letermovir group. 90% (n=64) were CMV positive in the letermovir group and 64% (n= 29) were positive in the non-letermovir group. CMV reactivation in the letermovir group was 32% compared to 29% in the non-letermovir group. In a subset analysis of all high-risk patients, CMV reactivation

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### Table 1. Patient Characteristics

| Letermovir (n=71) | No Letermovir (n=45) | Risk factor for CMV Reactivation p-value |
|------------------|---------------------|----------------------------------------|
| **Gender**       |                     |                                        |
| Female           | 38 (53.5%)          | 19 (42.1%)                             | p = 0.114                                  |
| Male             | 33 (46.5%)          | 26 (57.8%)                             |                                        |
| **Diagnosis**    |                     |                                        |
| AML              | 29 (40.8%)          | 15 (31.3%)                             |                                        |
| ALI              | 22 (31.0%)          | 22 (48.9%)                             |                                        |
| MDS              | 5 (7.0%)            | 4 (8.9%)                               |                                        |
| Other            | 15 (21.1%)          | 4 (8.9%)                               |                                        |
| **Disease Status at time of transplant** | | p = 0.524 | |
| CR1              | 38 (53.5%)          | 25 (55.6%)                             |                                        |
| SG               | 6 (8.3%)            | 4 (8.3%)                               |                                        |
| Other            | 37 (52.1%)          | 16 (35.6%)                             |                                        |
| **Donor Type**   |                     |                                        |
| Match Related    | 17 (23.9%)          | 14 (31.3%)                             |                                        |
| Match Unrelated  | 17 (23.9%)          | 16 (35.6%)                             | p = 0.392                                |
| **Conditioning Regimen** | | p = 0.054 | |
| Myeloablative    | 44 (62.0%)          | 30 (66.7%)                             |                                        |
| Reduced intensity | 27 (38.0%)          | 15 (33.3%)                             |                                        |
| **T-Cell Depleting** | | p = 0.003 | |
| Yes              | 60 (85%)            | 23 (51%)                               |                                        |
| None             | 15 (21%)            | 22 (48%)                               |                                        |
| **Stem Cell Source** | | p = 1.00 | |
| Peripheral Blood | 64 (90.1%)          | 43 (95.6%)                             |                                        |
| Bone Marrow      | 7 (9.9%)            | 2 (4.4%)                               |                                        |
| **Mean CD34 dose (cells/kg)** | | p = 0.024 | |
| Total Acute      | 32 (45%)            | 22 (49%)                               |                                        |
| Grade 3-4 Acute  | 3 (4.2%)            | 2 (4.4%)                               |                                        |
| Chronic          | 13 (18.3%)          | 8 (17.8%)                              |                                        |
| **CMV Status of Recipient** | | p = 0.017 | |
| Positive         | 64 (90%)            | 29 (66%)                               |                                        |
| Negative         | 7 (10%)             | 16 (36%)                               |                                        |
| **Risk for CMV Reactivation** | | | |