Not for publication or presentation

A G E N D A
CIBMTR WORKING COMMITTEE FOR INFECTION AND IMMUNE RECONSTITUTION
Salt Lake City, UT
Thursday, February 5, 2026, 1:00 – 3:00 PM (MT)

Co-Chair:	**Hemant Murthy, MD; Mayo Clinic, Jacksonville, FL; Telephone: 352-273-7822; E-mail: Murthy.hemant@mayo.edu**
Co-Chair:	**Christine Ebens, MD, MPH; University of Minnesota, Minneapolis, MN; Telephone: 612-626-8094; E-mail: ebens012@umn.edu**
Co-Chair:	**Joshua Hill, MD; Fred Hutchinson Cancer Center, Seattle, WA; Telephone: 206-667-6504; E-mail: jahill3@fredhutch.org**
Scientific Director:	**Anna Huppler; CIBMTR® (Center for International Blood and Marrow Transplant Research), Milwaukee, WI; Telephone: 414-337-7070; E-mail: ahuppler@mcw.edu**
Statistical Director:	**Michael Martens, PhD; CIBMTR® (Center for International Blood and Marrow Transplant Research), Milwaukee, WI; Telephone: 414-955-8674; E-mail: mmartens@mcw.edu**
Statistician:	**Qiran (Lexie) Ye, MPH; CIBMTR® (Center for International Blood and Marrow Transplant Research), Milwaukee, WI; Telephone: 414-955-3693; E-mail: qye@mcw.edu**
Page Scholar:	**Sanghee Hong, MD, BS; Cleveland Clinic Foundation, Cleveland, OH; Telephone: 216-387-0855; E-mail: sangheesanghee@gmail.com**

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1. **Introduction**
    a. Minutes from February 2025 (**Attachment 1**)

2. **Accrual summary** (**Attachment 2**)

3. **Presentations, Publications or Submitted papers**
    a. **IN19-01** Perales MA, Riches M, He N, Martens MJ, Chemaly RF, Dandoy CE, Hill JA, Díaz MA, Hashmi S, Prockop S, Lazarus HM, Beitinjaneh AM, Hildebrandt GC, Auletta JJ, Szabolcs P. Delayed T cell recovery after hematopoietic cell transplantation is associated with decreased overall survival in adults. **Blood Advances. 2025 Jul 10; 9(14):3502-3517. doi:10.1182/bloodadvances.2024015288. Epub 2025 Apr 18. PMC12274672.**
    b. **IN20-01a** Wudhikarn K, Herr MM, Chen M, Martens MJ, Baird JH, Gowda L, Rangarajan HG, Bilal AM, Kharfan-Dabaja MA, Williams KM, Ganguly S, Young JH, Sharma A, Fatobene G, Jain T, Kanakry CH, Modi D, Grover NS, Salem B, Batista MV, Vergidis P, Yin DE, Beitinjaneh AM, Kelkar AH, Nishihori T, Holter-Chakrabarty J, Gergis U, Smith M, El Boghdadly Z, Dandoy CE, Huppler AH, Murthy H, Perales MA, Chemaly RF, Hill JA, Riches M, Auletta JJ. Infection after CD19 chimeric antigen receptor T cell therapy for large B cell lymphoma: Real-world analysis from CIBMTR. **Blood Advances. doi:10.1182/bloodadvances.2025016141. Epub 2025 May 28. PMC12607006.**
    c. **IN20-01b** Rangarajan HG, Satwani P, Herr MM, Chen M, Martens MJ, Wudhikarn K, John S, Fabrizio VA, Hsieh EM, Kelkar AH, Doherty E, Marks DI, Ringden O, Friend BD, Kelly MS,

Farhadfar N, Prestidge T, Hossain NM, Liu H, Hashmi S, Modi D, Winestone LE, El Boghdadly Z, Murthy HS, Perales MA, Chemaly RF, Dandoy CE, Hill JA, Huppler AR, Riches M, Auletta JJ. Real-world outcomes of infections following Tisagenlecleucel in patients with B-cell ALL: A CIBMTR analysis. **Blood Advances. 2025 Nov 11; 9(21):5489-5500. doi:10.1182/bloodadvances.2025016149. Epub 2025 Jul 30. PMC12607035.**

d. **IN23-01** Infectious complications in patients with relapsed/refractory multiple myeloma receiving idecabtagene vicleucel (ide-cel), a B-cell maturation antigen (BCMA) targeted chimeric antigen receptor (CAR) T cell (K Wudhikarn/ M Angel Perales/ S Devarakonda/ Y Efebera/ A-S Mirza/ L Gowda/ M B Abid). ***Oral Presentation, ASH 2025.***

4. Studies in progress (Attachment 3)

a. **IN19-02** Impact of Antibiotic Prophylaxis in Patients Undergoing Allogeneic Hematopoietic Cell Transplantation in the Current Era (C Dandoy/ C Alonso/Z El Boghdadly). **Protocol Development.**
b. **IN22-01** Viral Hepatitis after allogeneic hematopoietic cell transplant using post-transplant cyclophosphamide for graft versus host disease prophylaxis (K Wudhikarn/ M Perales). **Protocol Development.**
c. **IN23-01** Infectious complications in patients with relapsed/refractory multiple myeloma receiving B-cell maturation antigen targeted chimeric antigen receptor T cells (K Wudhikarn/ MA Perales/ A Mirza/ L Gowda/ MB Abid/ S Devarakonda/ Y Efebera). **Manuscript Preparation.**
d. **IN24-01** Evaluating infection rates in autologous hematopoietic stem cell transplants for primary solid tumors and lymphoma (J Koo/ C Dandoy). **Protocol Development.**
e. **IN25-01** Risk Stratification and Letermovir Prophylaxis for CMV Infections in Allogeneic Hematopoietic Cell Transplant Recipients: A Focus on the Incidence of Late CMV Infections, All-Cause Mortality, and Mismatched Donor–Recipient CMV Serostatus in the Era of Cyclophosphamide Prophylaxis. (R Chemaly/ M Batista/ J Tossey/ J Sen/ Z Shahid/ H Murthy). **Protocol Pending.**

5. Future/proposed studies

a. **PROP 2509-36** Incidence of Pneumocystis jirovecii Pneumonia (PJP) after Allogeneic Hematopoietic Stem Cell Transplant: Comparison of Trimethoprim-Sulfamethoxazole versus Non–Trimethoprim-Sulfamethoxazole Prophylaxis (M A Mendoza/ H N Imlay). (**Attachment 4**)
b. **PROP 2509-37** Incidence and Outcomes of Respiratory Virus Infections in Allogeneic HSCT Recipients Receiving Post-Transplant Cyclophosphamide (PTCy) for GVHD Prophylaxis (M A Mendoza/ H N Imlay). (**Attachment 5**)
c. **PROP 2509-102** The Impact of HLA-B*35 Expression on CMV Viremia and Clinically Significant CMV Infection following PTCy-based Hematopoietic Cell Transplantation (J Little/ S Prockop). (**Attachment 6**)
d. **PROP 2509-117** Retrospective study of the impact of mammalian target of rapamycin inhibitors (mTORi) in the incidence of virus-associated complications after allogeneic hematopoietic cell transplantation (HCT) (P Beale/ K Rechache). (**Attachment 7**)
e. **PROP 2509-148** Impact of Early Natural Killer Cell Reconstitution on Relapse and Survival after Allogeneic HCT in the PTCy Era (J Clara). (**Attachment 8**)

Proposed studies; not accepted for consideration at this time

f. **PROP 2411-02** Early Post-Transplant Vitamin D Level Correlates with Reduced Infection Risk Through Enhanced NK Cell Activity (Y Choi). ***Dropped due to need of supplemental data.***
g. **PROP 2505-03** Identifying the prevalence of Epstein-Barr Virus Seronegative status among donors and recipients (V Potluri). ***Dropped due to need of supplemental data.***

h. **PROP 2509-29** Validation of CAR-Hematox for prognosis of infections and outcomes in non-DLBCL patients undergoing CAR T-cell therapy - expanding the application of a predictive tool (C Nichols/ N Hossain) ***Dropped due to overlap with current study/publication.***
i. **2509-59** Validation of CAR-Hematox for prognosis of infections and outcomes in non-DLBCL patients undergoing CAR T-cell therapy - expanding the application of a predictive tool (C Nichols/ N Hossain) ***Dropped due to overlap with current study/publication.***
j. **2509-131** – Association Between Pre-Transplant Herpes Simplex Virus Serostatus and 1-Year Survival Among Adult Allogeneic Hematopoietic Cell Transplant Recipients (S Pergam/ C Johnston). ***Dropped due to need of supplemental data.***
k. **PROP 2509-143** Management of Adenovirus Infection in Pediatric Stem Cell Recipients Both Autologous and Allogeneic in the Modern Era (M Ali/ M Foca). ***Dropped due to need of supplemental data.***
l. **2509-173** – ImmunoAI-CMV: Dynamic Immune Recovery Modeling, Causal AI, and Calibration-First Evaluation for Precision CMV Prevention in Pediatric Allogeneic Hematopoietic Cell Transplantation (E Elsabbagh/ A Dulanto Chiang). ***Dropped due to need of supplemental data.***

6. Other business

a. Form revisions and data availability updates

MINUTES
CIBMTR WORKING COMMITTEE FOR INFECTION AND IMMUNE RECONSTITUTION
Honolulu, HI
Thursday, February 13, 2025, 1:00 – 3:00 PM HST

Co-Chair:	**Hemant Murthy, MD; Mayo Clinic, Jacksonville, FL; Telephone: 352-273-7822; E-mail: Murthy.hemant@mayo.edu**
Co-Chair:	**Christopher Dandoy, MD, MS; Cincinnati Children's Hospital Medical Center, Cincinnati, OH; Telephone: 801-209-3843; E-mail: christopher.dandoy@cchmc.org**
Co-Chair:	**Joshua Hill, MD; Fred Hutchinson Cancer Center, Seattle, WA; Telephone: 206-667-6504; E-mail: jahill3@fredhutch.org**
Page Scholar:	**Zeinab El Boghdadly, Ohio State University, Columbus , OH; Email: zeinab.elboghdadly@osumc.edu**
Scientific Director:	**Jeffery Auletta, MD; CIBMTR® (Center for International Blood and Marrow Transplant Research), Minneapolis, MN; E-mail: jaulett3@nmdp.org**
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Statistician:	**Qiran (Lexie) Ye, MPH; CIBMTR® (Center for International Blood and Marrow Transplant Research), Milwaukee, WI; E-mail: qye@mcw.edu**

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1. **Introduction**
   a. Minutes from February 2024 (Attachment 1)

2. **Accrual summary** (Attachment 2)

3. **Presentations, Publications or Submitted papers**
   a. **IN19-01** Delayed T cell recovery after hematopoietic cell transplantation is associated with decreased overall survival in adults (M-A Perales). ***Submitted.***
   b. **IN20-01a** Infectious complications in patients with B-Lymphoid hematologic malignancy (Lymphoma cohort) treated with CD19 chimeric antigen receptor T cell therapy. (K Wudhikarn/ M McGhee/ J Hill/ M Herr/ H Rangarajan/ P Satwani/ J Baird/ E McGehee/ L Gowda/ G Fatobene). ***Submitted***.
   c. **IN20-01b** Infectious complications in patients with B-Lymphoid hematologic malignancy (ALL cohort) treated with CD19 chimeric antigen receptor T cell therapy. (K Wudhikarn/ M McGhee/ J Hill/ M Herr/ H Rangarajan/ P Satwani/ J Baird/ E McGehee/ L Gowda/ G Fatobene). ***Submitted***.

4. **Studies in progress** (Attachment 3)
   a. **IN19-02** Impact of Antibiotic Prophylaxis in Patients Undergoing Allogeneic Hematopoietic Cell Transplantation in the Current Era (C Dandoy/ C Alonso/Z El Boghdadly). **Protocol Development.**

b. **IN22-01** Viral Hepatitis after allogeneic hematopoietic cell transplant using post-transplant cyclophosphamide for graft versus host disease prophylaxis (K Wudhikarn/ M Perales). **Protocol Received.**
c. **IN23-01** Infectious complications in patients with relapsed/refractory multiple myeloma receiving B-cell maturation antigen targeted chimeric antigen receptor T cells (K Wudhikarn/ MA Perales/ A Mirza/ L Gowda/ MB Abid/ S Devarakonda/ Y Efebera). **Datafile Preparation.**
d. **IN24-01** Evaluating infection rates in autologous hematopoietic stem cell transplants for primary solid tumors and lymphoma (J Koo/ C Dandoy). **Protocol Received.**

5. Future/proposed studies

a. **PROP 2410-45; 2410-206** Risk Stratification and Letermovir Prophylaxis Strategies for Cytomegalovirus in Hematopoietic Cell Transplantation: A Focus on Late CMV Infections, All-Cause Mortality, and Mismatched Donor-Recipient Serostatus (R Chemaly/ M Batista/ J Tossey/ J Sen). (Attachment 4)

Dr. Batista from Sao Paulo presented.

Presentation Summary:

- *Focus: Risk stratification and Letermovir prophylaxis strategies for CMV in transplant recipients, particularly late CMV infections, all-cause mortality, and mismatched donor-recipient serostatus.*
- *Hypothesis: Risk factors for late CMV infection with or without Letermovir prophylaxis could help stratify patients at higher risk of CMV infection and all-cause mortality.*
- *Study Design: Retrospective study using data from the CIBMTR research database, including variables such as recipient/donor pre-transplant status, disease/transplant-related factors, and immune recovery at day 100.*
- *Objectives:*
  - *Primary Objectives:*
    - *Define risk factors for late CMV infection with or without letermovir prophylaxis.*
    - *Assess cumulative incidence of late CMV infections with or without Letermovir prophylaxis.*
  - *Secondary Objectives:*
    - *Evaluate survival, non-relapse mortality, and incidence of other infections post-transplant.*
- *Significance and impact of the expected research contribution:*
  - *Investigate preliminary findings on incidence of late CMV infection in a larger multicenter population and identify at risk populations*
  - *Facilitate additional studies within the CIMBTR and potentially inform future interventional studies*
  - *Stratify patients who are at higher risk of CMV infection and all-cause mortality to optimize therapeutic interventions, including prolonged prophylactic measures.*
- *Limitations: retrospective data, not all risk factors are collected, duration of Letermovir prophylaxis is not consistently available.*
- *Strengths: Large cohort (4499 patients), multiple comparisons by D/R CMV status and letermovir status, robust outcome measures*

Discussion:

- *Concerns about variability in the duration of Letermovir prophylaxis and alternative approaches to CMV prophylaxis.*
- *Defining incidence of late CMV infection is important- note recent manuscript in Blood Advances on late CMV*
- *Questions about the impact of the timing of the late CMV infection*
- *Importance of defining the impact of CMV viremia versus disease post-day 100.*
- *Potential gaps in data regarding CMV-specific T-cell immunity at day 100.*
- *Unknown which timepoint is most impactful for immune reconstitution- day 30 versus day 100.*

b. **PROP 2410-55** Peri-transplant Norovirus infection as a risk factor for allogeneic HSCT outcomes (K Lind/ L McLaughlin). (Attachment 5)

Dr. Lind from Children's Hospital, Colorado presented.

Presentation Summary:

- *Focus: Impact of norovirus infection on HCT outcomes among allogeneic transplant patients with larger cohort and longer follow-up than available in current literature.*
- *Hypothesis: Allogeneic transplant patients who develop norovirus infection within 100 days of HCT have inferior overall survival compared to recipients without norovirus infection*
- *Study Design: Retrospective case-control cohort study with primary outcome of overall survival at one year with matching of pediatric vs adult, indication for transplant, conditioning intensity, stem cell source, and GVHD prophylaxis.*
- *Objectives:*
    - *Primary Objective:*
        - *Identify incidence and impact of norovirus infection on overall survival amongst allogeneic HCT patients.*
    - *Secondary Objectives:*
        - *Assess non-relapse mortality, relapse, total inpatient days, recipient weight change, renal impairment, aGvHD and cGvHD, immune reconstitution, and prevalence of outbreaks.*
- *Significance and impact of the expected research contribution:*
    - *Current surge of norovirus infections and outbreaks in US*
    - *Previously published cohort only 19 patients*
    - *Inform prognosis of patients with norovirus infection and prioritize development of effective treatment and outbreak prevention*
- *Feasibility: Data available for 136 patients, with a mix of pediatric and adult patients, and various indications for transplant.*

Discussion:

- Challenges in accurately classifying cases and controls due to variability in diagnostic approaches, expected prolonged shedding after acute infection (particularly in young children), and multifactorial etiologies of diarrhea in HCT population (active viral infection versus C diff versus GVHD).

- Suggestions to match controls from the same centers to control for the diagnostic approach and consider a cohort study design.
- Note the outcome of relapse will not apply for the patients with non-malignant indications for transplant.

c. **PROP 2410-61** The Incidence and Impact of Clostridioides Difficile Infection on CAR-T Cell Therapy Outcomes – A CIBMTR Study (M Bilal Abid/ M Aljurf). Attachment 6)

Dr. Bilal Abid presented remotely.

Presentation Summary:

- *Focus: Clostridioides difficile infection (CDI) is the most common healthcare-associated infection in the US, but the incidence, risk factors, and impact of CDI on CAR T-cell therapy outcomes has not been examined.*
- *Hypothesis: CDI in CAR T patients confers inferior overall survival, infectious complications due to CDI will vary based on underlying disease and target antigen, CDI infectious complications will vary in different post-CAR-T periods, and the pattern of infection after CAR-T has evolved over time.*
- *Study Design: Case-control analysis of CDI burden, risk factors, and impact on clinical outcomes, stratified by target antigen and underlying disease.*
- *Objectives:*
  - *Primary Objective:*
    - *Estimate cumulative incidence, infection density, patterns, and mortality due to CDI in patients receiving CAR-T therapy*
  - *Secondary Objective:*
    - *Identify risk factors for CDI in patients treated with CAR-T therapy*
    - *Explore impact of CDI on short-term and long-term clinical outcomes following CAR-T therapy.*
- *Significance and impact:*
  - *The burden, risk factors for CDI in CAR-T and its impact on survival outcomes*
- *Limitations: Retrospective nature, note of antibiotic prophylaxis data back to March 2017, reliance on center-reported CDI without further specifics on the presence of compatible symptoms. Plan to identify controls from the same centers to control for center-specific factors on diagnosis and antibiotic prophylaxis.*
- *Strengths: data available for 202 CDI after CD19-targeted CAR-T and 32 CDI after BCMA-targeted CAR-T*

Discussion:

- *Question about what makes this study different from the recent CAR-T cell therapy and infection manuscript. Note that BCMA-targeted CAR-T cells were not included in that paper (20 patients in this cohort to date).*
- *Differences in CDI burden between pediatric and adult cohorts.*
- *Importance of considering pre-CAR T CDI as a variable in the analysis.*

d. **PROP 2410-137** Impact of Letermovir Prophylaxis on the Epidemiology of CMV Infection Among Allogenic Hematopoietic Cellular Therapy Recipients Receiving Post-Transplant Cyclophosphamide (Z Shahid/ H Murthy). (Attachment 7)

Dr. Shahid from MSK Cancer Center presented.

Presentation Summary:

- *Focus: Impact of Letermovir prophylaxis on CMV infection in recipients receiving post-transplant cyclophosphamide (PTCy).*
- *Hypothesis: Letermovir prophylaxis is associated with decreased rate of CMV reactivation among CMV seropositive recipients receiving PTCy, with a positive impact on short and long-term outcomes.*
- *Study Design: Analysis of CMV infection rates, risk factors, and clinical outcomes in PTCy recipients with and without Letermovir prophylaxis.*
- *Objectives:*
    - *Primary Objective:*
        - *Assess cumulative incidence of CMV infection among CMV R+ HCT recipients receiving post-Tx Cy in the presence and absence of CMV prophylaxis*
    - *Secondary Objectives:*
        - *Evaluate early and late CMV infection patterns and risk factors in the presence and absence of CMV prophylaxis*
        - *Assess differences in the epidemiology of other viral reactivations in the two comparator groups.*
        - *Measure the impact of CMV infection on non-infectious clinical outcomes*
    - *Study epidemiology of other viral reactivations and impact on clinical outcomes.*
- *Significance and impact:*
    - *Understand the impact of CMV prophylaxis in contemporary cohort among HCT recipients receiving PTCy, potentially guide future CMV prophylaxis strategies or support advocacy for insurance coverage*
- *Limitations: retrospective study, sample size, delayed CMV reactivation might be missed*
- *Strengths: Data available for 458 patients (CMV R+, received post-tx Cy) who received letermovir prophylaxis and 160 without prophylaxis.*

Discussion:

- *Questions about whether PT-Cy population will be different than other GVHD prophylaxis but note that PT-Cy use is prevalent and should be specifically studied.*
- *Importance of understanding the impact of prophylaxis in the PTCy setting, including kinetics of reactivation and relationship with GVHD patterns.*
- *Impact of PT-Cy on T cells may change late onset CMV risk*
- *Concern expressed about accuracy of the data for late CMV and center definitions of "CMV R+"*

e. **PROP 2410-141** Epidemiology of Respiratory Virus Infections among Hematopoietic Cellular Therapy and Chimeric Antigen Receptor T-cell Therapy Recipients in the Post COVID-19 and Respiratory Syncytial Virus Vaccine Era (Z Shahid/ H Murthy). (Attachment 8)

Dr. Shahid from MSK Cancer Center presented.

Presentation Summary:

- *Focus: Changing landscape of respiratory viral infections (RVIs) in the post-pandemic era, particularly with the introduction of RSV vaccines.*
- *Hypothesis: The epidemiology of RVIs among HCT and CAR-T cell therapy recipients has changed since the pandemic.*
- *Study Design: Analysis of incidence rates, severity, and outcomes of RVIs in HCT and CAR T recipients.*
- *Objectives:*
  - *Primary Objective:*
    - *Assess incidence rate of RVIs during the first-year post-HCT and CAR T-cell therapy*
  - *Secondary Objectives:*
    - *Measure severity, timing, and outcomes of RVIs*
    - *Assess for risk factors associated with RVIs*
    - *Describe incidence and risk factors associated with recurrent infections*
    - *Determine correlates of immune protection against severe RVIs*
- *Significance and impact:*
  - *Understanding the evolving epidemiology of RVIs and their burden will help us understand the changing landscape of RVIs in HCT and CAR-T cell therapy recipients to guide clinical practice, highlight high-risk populations, and identify targets for vaccination strategies*
- *Limitations: retrospective study, potential missing mild RVIs due to lack of testing, autologous HCT patients' numbers are low*
- *Strengths: Data available for 109 HCT and 106 CAR-T patients with RVIs, outcome data on Form 2149 and 2100*

Discussion:

- *Importance of including pediatric patients and controlling for IVIG exposure.*
- *Potential need to look at infection-related mortality and vaccination status (patient and family/community).*
- *Include viruses like parainfluenza with no vaccine, nosocomial and community-acquired RVIs*
- *Include the 2 years pre-COVID, may need additional post-COVID time to accrue sufficient sample size*

Proposed studies; not accepted for consideration at this time

f. **PROP 2408-08** Comparing Levofloxacin with Ciprofloxacin in the area of Hematopoietic Stem Cell Transplantation (M Pamukcuoglu). ***Dropped due to overlap with current study/publication.***
g. **PROP 2409-27** Impact of Chimeric Antigen Receptor Therapy (CART) followed by AlloSCT on post-transplant infection risk in Lymphoid Malignancies – A CIBMTR Analysis (N Hossain, P Munshi). ***Dropped due to overlap with current study/publication.***
h. **PROP 2409-29** Impact of Granulocyte Infusions on Outcomes for Allogeneic Stem Cell Transplant patients prior to initial engraftment - A CIBMTR Analysis (N Hossain). ***Dropped due to small sample size.***
i. **PROP 2409-31** Characterization of infectious complications post-CAR T Cell therapy (L Liu/ M Janakiram). ***Dropped due to overlap with current study/publication.***

j. **PROP 2410-01** Impact of post-transplant G-CSF in allogeneic transplant in the post-transplant cyclophosphamide era (N Agarwal/ L Metheny). ***Dropped due to overlap with current study/publication.***
k. **PROP 2410-18** Impact of HLA disparity on infection-related complications in patients undergoing allogeneic HSCT with post-transplant cyclophosphamide GVHD prophylaxis (K Wudhikarn/ M Perales). ***Dropped due to overlap with current study/publication.***
l. **PROP 2410-32** Infections and Immune Reconstitution in Adults with B-Cell Acute Lymphoblastic Leukemia Who Received CAR-T Therapy Prior to Allogeneic Hematopoietic Stem Cell Transplantation (H De Sa/ B Hayes-Lattin). ***Dropped due to overlap with current study/publication.***
m. **PROP 2410-38** Infectious Complications in patients with Hematologic Malignancies Receiving CD19 vs. BCMA-targeted CAR-T Therapy (M Bilal Abid). ***Dropped due to overlap with current study/publication.***
n. **PROP 2410-63** Potential for granulocyte-colony stimulating factor in preventing infections in CAR-T recipients without worsening immune-related toxicities (M Bilal Abid/ M Aljurf). ***Dropped due to overlap with current study/publication.***
o. **PROP 2410-75** Donor Selection in Cytomegalovirus Seronegative Patients Undergoing HCT with Post-Transplant Cyclophosphamide-based Graft-versus-Host Disease Prophylaxis (R Mehta). ***Dropped due to small sample size.***
p. **PROP 2410-128** Outcomes of CD34-selected stem cell boost following allogeneic hematopoietic stem cell transplantation in the contemporary era (X Bi/ U Gergis). ***Dropped due to small sample size.***
q. **PROP 2410-135** Impact of Granulocyte Stimulating Factor on Infectious Complications, Treatment Response and Outcomes after CAR T-cell therapy (S Bowden/ P Bindal). ***Dropped due to small sample size.***
r. **PROP 2410-144** Safety and Efficacy of BCMA-directed CAR T-cell Therapy in the Treatment of Relapsed/Refractory Multiple Myeloma in Patients with HIV Infection (P Bindal/ C Reimonn). ***Dropped due to supplemental data needed.***
s. **PROP 2410-186** Real world analysis of non-respiratory viral diseases in BCMA and CD 19 CART cell therapy recipients (N Vojjala/ N Ahmed). ***Dropped due to overlap with current study/publication.***
t. **PROP 2410-245** Real World Evidence of Infectious Complications, HIV Disease Control, and Outcome among Patients with HIV who Receive Hematopoietic Stem Cell Transplant or Chimeric Antigen Receptor T cell therapy (L Gowda/ B Emu). ***Dropped due to supplemental data needed.***
u. **PROP 2410-253** Incidence of severe infections (BMTCTN grade 3) early after HCT (100 days) and its impact on survival (OS) and non-relapse mortality (NRM) - development of a composite endpoint: GVHD-free, relapse-free, and infection-free survival (GRIFS) (R Nakamura). ***Dropped due to overlap with current study/publication.***

6. Other business

INWC accrual table

Characteristic	Allogeneic	Autologous
Number of patients, no. (%)		
1	55223 (100)	20579 (100)
Infection		
Donor/receipient CMV status, no. (%)		
-/-	11501 (20.8)	0 (0.0)
+/-	5793 (10.5)	0 (0.0)
-/+	13002 (23.5)	0 (0.0)
+/+	20141 (36.5)	2 (0.0)
Missing/not tested	4786 (8.7)	20577 (100)
Donor/recipient hepatitis B status, no. (%)		
-/-	10855 (19.7)	15145 (73.6)
+/-	337 (0.6)	0 (0.0)
-/+	3185 (5.8)	0 (0.0)
+/+	295 (0.5)	1942 (9.4)
-/?	248 (0.4)	0 (0.0)
+/?	7 (0.0)	0 (0.0)
?/-	20083 (36.4)	0 (0.0)
?/+	6917 (12.5)	0 (0.0)
Missing/not tested	13296 (24.1)	3492 (17.0)
Donor/recipient hepatitis C status, no. (%)		
-/-	13737 (24.9)	16083 (78.2)
+/-	93 (0.2)	0 (0.0)
-/+	152 (0.3)	0 (0.0)
+/+	9 (0.0)	276 (1.3)
-/?	107 (0.2)	0 (0.0)
?/-	23764 (43.0)	0 (0.0)
?/+	388 (0.7)	0 (0.0)
Missing/not tested	16973 (30.7)	4220 (20.5)
Fungal infection history, no. (%)		
No	51380 (93.0)	20350 (98.9)
Yes	3774 (6.8)	223 (1.1)
Not reported	69 (0.1)	6 (0.0)
Fungal infection after starting of conditioning, no. (%)		
No	46777 (84.7)	19532 (94.9)
Yes	8326 (15.1)	1035 (5.0)
Not reported	120 (0.2)	12 (0.1)
Immune Reconstitution		

Characteristic	Allogeneic	Autologous
IgG at 100 day, no. (%)		
Data not available	20068 (36.3)	7774 (37.8)
Data available	35155 (63.7)	12805 (62.2)
IgM at 100 day, no. (%)		
Data not available	37084 (67.2)	9269 (45.0)
Data available	18139 (32.8)	11310 (55.0)
IgA at 100 day, no. (%)		
Data not available	37068 (67.1)	9172 (44.6)
Data available	18155 (32.9)	11407 (55.4)
CD3 at 100 day, no. (%)		
Lymphocyte analyses wre not performed	48617 (88.0)	20199 (98.2)
Data not available	548 (1.0)	114 (0.6)
Data available	6058 (11.0)	266 (1.3)
CD4 at 100 day, no. (%)		
Lymphocyte analyses wre not performed	48617 (88.0)	20199 (98.2)
Data not available	409 (0.7)	89 (0.4)
Data available	6197 (11.2)	291 (1.4)
CD8 at 100 day, no. (%)		
Lymphocyte analyses wre not performed	48617 (88.0)	20199 (98.2)
Data not available	580 (1.1)	122 (0.6)
Data available	6026 (10.9)	258 (1.3)
CD20 at 100 day, no. (%)		
Lymphocyte analyses wre not performed	48617 (88.0)	20199 (98.2)
Data not available	5654 (10.2)	344 (1.7)
Data available	952 (1.7)	36 (0.2)
CD56 at 100 day, no. (%)		
Lymphocyte analyses wre not performed	48617 (88.0)	20199 (98.2)
Data not available	2198 (4.0)	224 (1.1)
Data available	4408 (8.0)	156 (0.8)
Infection Prophylaxis		
Infection prophylaxis, no. (%)		
No	361 (0.7)	58 (0.3)
Yes	53659 (97.2)	19706 (95.8)
Not reported	1203 (2.2)	815 (4.0)
Antibacterial Prophylaxis, no. (%)		
No	2605 (4.7)	468 (2.3)
Yes	20205 (36.6)	7632 (37.1)
Not reported	32413 (58.7)	12479 (60.6)
Antiviral Prophylaxis, no. (%)		
No	1313 (2.4)	338 (1.6)

Characteristic	Allogeneic	Autologous
Yes	51922 (94.0)	19226 (93.4)
Not reported	1988 (3.6)	1015 (4.9)
Antifungal Prophylaxis, no. (%)		
No	1564 (2.8)	949 (4.6)
Yes	50729 (91.9)	17276 (83.9)
Not reported	2930 (5.3)	2354 (11.4)
First antibacterial drug given as prophylaxis - Amoxicillin clavulanate oral, no. (%)		
No	22442 (40.6)	8015 (38.9)
Yes	387 (0.7)	91 (0.4)
Not reported	32394 (58.7)	12473 (60.6)
First antibacterial drug given as prophylaxis - Moxifloxacin IV or oral, no. (%)		
No	22430 (40.6)	8029 (39.0)
Yes	398 (0.7)	78 (0.4)
Not reported	32395 (58.7)	12472 (60.6)
First antibacterial drug given as prophylaxis - Ciprofloxacin IV or oral, no. (%)		
No	19276 (34.9)	6618 (32.2)
Yes	3552 (6.4)	1489 (7.2)
Not reported	32395 (58.7)	12472 (60.6)
First antibacterial drug given as prophylaxis - Levofloxacin IV or oral, no. (%)		
No	12257 (22.2)	2968 (14.4)
Yes	10569 (19.1)	5140 (25.0)
Not reported	32397 (58.7)	12471 (60.6)
First antibacterial drug given as prophylaxis - Other antibacterial drug, no. (%)		
No	18218 (33.0)	6988 (34.0)
Yes	4608 (8.3)	1118 (5.4)
Not reported	32397 (58.7)	12473 (60.6)
First antibacterial drug given as prophylaxis - Cefdinir oral, no. (%)		
No	22673 (41.1)	8025 (39.0)
Yes	156 (0.3)	82 (0.4)
Not reported	32394 (58.7)	12472 (60.6)
First antibacterial drug given as prophylaxis - Penicillin, no. (%)		
No	11395 (20.6)	2739 (13.3)
Yes	366 (0.7)	43 (0.2)
Not reported	43462 (78.7)	17797 (86.5)
First antibacterial drug given as prophylaxis - Cefpodoxime oral, no. (%)		
No	22634 (41.0)	8071 (39.2)
Yes	195 (0.4)	36 (0.2)
Not reported	32394 (58.7)	12472 (60.6)
Was vancomycin IV also given as prophylaxis?, no. (%)		
No	20030 (36.3)	7566 (36.8)

Characteristic	Allogeneic	Autologous
Yes	2104 (3.8)	481 (2.3)
Not reported	33089 (59.9)	12532 (60.9)
First antiviral drug given as prophylaxis - Acyclovir, no. (%)		
No	12705 (23.0)	4049 (19.7)
Yes	41756 (75.6)	16011 (77.8)
Not reported	762 (1.4)	519 (2.5)
Was letermovir (Prevymis) given as prophylaxis?, no. (%)		
No	22692 (41.1)	9083 (44.1)
Yes	3966 (7.2)	9 (0.0)
Not reported	28565 (51.7)	11487 (55.8)
First antiviral drug given as prophylaxis - Famciclovir (Famvir), no. (%)		
No	26426 (47.9)	9073 (44.1)
Yes	227 (0.4)	18 (0.1)
Not reported	28570 (51.7)	11488 (55.8)
First antiviral drug given as prophylaxis - Ganciclovir, no. (%)		
No	51820 (93.8)	20002 (97.2)
Yes	2641 (4.8)	58 (0.3)
Not reported	762 (1.4)	519 (2.5)
First antiviral drug given as prophylaxis - Other antiviral drug, no. (%)		
No	53030 (96.0)	19837 (96.4)
Yes	1430 (2.6)	223 (1.1)
Not reported	763 (1.4)	519 (2.5)
First antiviral drug given as prophylaxis - Valacyclovir (Valtrex), no. (%)		
No	42529 (77.0)	15865 (77.1)
Yes	11932 (21.6)	4195 (20.4)
Not reported	762 (1.4)	519 (2.5)
First antiviral drug given as prophylaxis - Valganciclovir (Valcyte), no. (%)		
No	51373 (93.0)	19891 (96.7)
Yes	3085 (5.6)	169 (0.8)
Not reported	765 (1.4)	519 (2.5)
First antifungal drug given as prophylaxis - Amphotericin products, no. (%)		
No	52201 (94.5)	19957 (97.0)
Yes	2243 (4.1)	90 (0.4)
Not reported	779 (1.4)	532 (2.6)
First antifungal drug given as prophylaxis - Caspofungin (Cancidas), no. (%)		
No	51083 (92.5)	19864 (96.5)
Yes	3361 (6.1)	183 (0.9)
Not reported	779 (1.4)	532 (2.6)
First antifungal drug given as prophylaxis - Isavuconazole (Cresemba), no. (%)		
No	26154 (47.4)	9074 (44.1)

Characteristic	Allogeneic	Autologous
Yes	482 (0.9)	5 (0.0)
Not reported	28587 (51.8)	11500 (55.9)
First antifungal drug given as prophylaxis - Anidulafungin (Eraxis), no. (%)		
No	26506 (48.0)	9075 (44.1)
Yes	130 (0.2)	4 (0.0)
Not reported	28587 (51.8)	11500 (55.9)
First antifungal drug given as prophylaxis - Fluconazole (Diflucan), no. (%)		
No	27883 (50.5)	3673 (17.8)
Yes	26560 (48.1)	16374 (79.6)
Not reported	780 (1.4)	532 (2.6)
First antifungal drug given as prophylaxis - Itraconazole, no. (%)		
No	53377 (96.7)	19948 (96.9)
Yes	1067 (1.9)	99 (0.5)
Not reported	779 (1.4)	532 (2.6)
First antifungal drug given as prophylaxis - Micafungin (Mycamine), no. (%)		
No	43538 (78.8)	19466 (94.6)
Yes	10906 (19.7)	581 (2.8)
Not reported	779 (1.4)	532 (2.6)
First antifungal drug given as prophylaxis - Other antifungal drug, no. (%)		
No	53033 (96.0)	19795 (96.2)
Yes	1410 (2.6)	252 (1.2)
Not reported	780 (1.4)	532 (2.6)
First antifungal drug given as prophylaxis - Posaconazole (Noxafil), no. (%)		
No	46140 (83.6)	19927 (96.8)
Yes	8303 (15.0)	120 (0.6)
Not reported	780 (1.4)	532 (2.6)
First antifungal drug given as prophylaxis - Voriconazole (Vfend), no. (%)		
No	41546 (75.2)	19587 (95.2)
Yes	12897 (23.4)	460 (2.2)
Not reported	780 (1.4)	532 (2.6)
Patient related		
Disease Grouping, no. (%)		
MM/PCD	727 (1.3)	12569 (61.1)
AML	15165 (27.5)	185 (0.9)
ALL	6059 (11.0)	16 (0.1)
CML	1217 (2.2)	0 (0.0)
Other Leukemias	488 (0.9)	2 (0.0)
NHL	3083 (5.6)	4084 (19.8)
HD	1339 (2.4)	1394 (6.8)
MDS/MPN	13174 (23.9)	2 (0.0)

Characteristic	Allogeneic	Autologous
CLL	1029 (1.9)	16 (0.1)
Acquired Aplastic Anemia	4308 (7.8)	2 (0.0)
Congenital Bone Marrow Failure Syndrome	1101 (2.0)	2 (0.0)
Hemoglobinopathies	3972 (7.2)	161 (0.8)
Primary Immune Deficiency	2046 (3.7)	79 (0.4)
Histiocytic Disorder	489 (0.9)	3 (0.0)
Platelet Disorders	59 (0.1)	0 (0.0)
Inherited Disorders of Metabolism	785 (1.4)	24 (0.1)
Autoimmune Disease	36 (0.1)	77 (0.4)
Solid tumors	34 (0.1)	1950 (9.5)
Other Diseases	54 (0.1)	9 (0.0)
Not reported	58 (0.1)	4 (0.0)
Year of current transplant, no. (%)		
2008	4371 (7.9)	2656 (12.9)
2009	3963 (7.2)	1272 (6.2)
2010	2437 (4.4)	579 (2.8)
2011	1792 (3.2)	691 (3.4)
2012	1865 (3.4)	726 (3.5)
2013	3318 (6.0)	1462 (7.1)
2014	4177 (7.6)	1467 (7.1)
2015	4182 (7.6)	1684 (8.2)
2016	3980 (7.2)	1753 (8.5)
2017	3812 (6.9)	1646 (8.0)
2018	3793 (6.9)	2258 (11.0)
2019	3580 (6.5)	1356 (6.6)
2020	2312 (4.2)	376 (1.8)
2021	2470 (4.5)	320 (1.6)
2022	2533 (4.6)	678 (3.3)
2023	2823 (5.1)	687 (3.3)
2024	2887 (5.2)	744 (3.6)
2025	928 (1.7)	224 (1.1)

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A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

TO: Infection and Immune Reconstitution Working Committee Members

FROM: Anna Huppler, MD; Scientific Director for the Infection and Immune Reconstitution Working Committee

RE: 2025-2026 Studies in Progress Summary

IN19-02 Impact of Antibiotic Prophylaxis in Patients Undergoing Allogeneic Hematopoietic Cell Transplantation in the Current Era (C Dandoy/ C Alonso/Z El Boghdadly). Antibiotic prophylaxis in patients undergoing allogenic HSCT has been the standard of practice for decades. However, there are some collateral consequences of this practice such as early microbiome disruption, acute GVHD, emergence of resistant bacterial infections and increased risk for Clostridioides difficile infection (CDI). This study will assess the efficacy of antibiotic prophylaxis in the modern era and results will have implications on current clinical practice.

Status: **Protocol Development**

IN22-01 Viral Hepatitis after allogeneic hematopoietic cell transplant using post-transplant cyclophosphamide for graft versus host disease prophylaxis (K Wudhikarn/ M Perales). The study hypothesizes that patients undergoing allogeneic HCT with post-transplant cyclophosphamide (PTCy) have a higher incidence of viral hepatitis reactivation compared to those without PTCy. It aims to assess the rate and risk factors of viral hepatitis reactivation, compare reactivation rates between PTCy and non-PTCy platforms, and evaluate the impact of chronic viral hepatitis on hepatic complications and survival. The study will provide critical insights into the incidence, patterns, and predisposing factors of hepatitis B and C reactivation, as well as the proper approach to antimicrobial prophylaxis in these patients.

Status: **Protocol Development**

IN23-01 Infectious complications in patients with relapsed/refractory multiple myeloma receiving B-cell maturation antigen targeted chimeric antigen receptor T cells (K Wudhikarn/ MA Perales/ A Mirza/ L Gowda/ MB Abid/ S Devarakonda/ Y Efebera). The study hypothesizes that infectious complications after idecabtagene vicleucel are common and likely higher in real-world settings compared to clinical trials, associated with specific disease, host, and CAR T-cell characteristics, and linked to poorer outcomes. It aims to describe the incidence, patterns, and mortality of infections, identify risk factors, and explore the impact on clinical outcomes. This research will provide critical insights into infection prevention strategies and improve patient care for those treated with BCMA CAR T-cells.

Status: **Manuscript Preparation**

IN24-01 Evaluating infection rates in autologous hematopoietic stem cell transplants for primary solid tumors and lymphoma (J Koo/ C Dandoy). There are limited data on the diversity of approaches to prevent infection and the incidence of clinically significant infections in solid tumor or lymphoma autologous HSCT recipients. This observational, cross-sectional study will examine the primary endpoint of the incidence of clinically significant bacterial, viral and fungal infections during the first 100 days following auto-HSCT for patients with solid tumors and lymphomas.

Status: **Protocol Development**

IN25-01 Risk Stratification and Letermovir Prophylaxis for CMV Infections in Allogeneic Hematopoietic Cell Transplant Recipients: A Focus on the Incidence of Late CMV Infections, All-Cause Mortality, and Mismatched Donor–Recipient CMV Serostatus in the Era of Cyclophosphamide Prophylaxis. (R Chemaly/ M Batista/ J Tossey/ J Sen/ Z Shahid/ H Murthy). Letermovir prophylaxis has reduced early cytomegalovirus (CMV) infection after allogeneic hematopoietic cell transplantation (allo-HCT), yet late clinically significant CMV infection remains frequent following prophylaxis discontinuation, particularly in high-risk patients. The study will determine risk factors for late CMVi in patients with or without letermovir prophylaxis, including receipt of PTCy.

Status: **Protocol Pending**

Field	Response
Proposal Number	2509-36-MENDOZA
Proposal Title	Incidence of Pneumocystis jirovecii Pneumonia (PJP) after Allogeneic Hematopoietic Stem Cell Transplant: Comparison of Trimethoprim-Sulfamethoxazole versus Non Trimethoprim-Sulfamethoxazole Prophylaxis
Key Words	Pneumocystis jirovecii Pneumonia, Allogeneic Hematopoietic Stem Cell Transplant, Trimethoprim-Sulfamethoxazole, dapsone, atovaquone, pentamidine
Principal Investigator #1: - First and last name, degree(s)	Maria Alejandra Mendoza
Principal Investigator #1: - Email address	alejandra.mendoza@hsc.utah.edu
Principal Investigator #1: - Institution name	University of Utah
Principal Investigator #1: - Academic rank	Assistant professor
Junior investigator status (defined as 㑊、5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	Yes
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Hannah N. Imlay
Principal Investigator #2 (If applicable): - Email address:)	hannah.imlay@hsc.utah.edu
Principal Investigator #2 (If applicable): - Institution name:	University of Utah
Principal Investigator #2 (If applicable): - Academic rank:	Associate Professor
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	Hannah Imlay
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	na
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Infection and Immune Reconstitution
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	No

Field	Response
RESEARCH QUESTION:	What is the incidence of Pneumocystis jirovecii pneumonia (PJP) within 1 year after allogeneic hematopoietic stem cell transplant, and how does it compare between recipients receiving trimethoprim-sulfamethoxazole versus non trimethoprim-sulfamethoxazole prophylaxis?
RESEARCH HYPOTHESIS:	We hypothesize that the incidence of Pneumocystis jirovecii pneumonia (PJP) will not significantly differ between allogeneic HSCT recipients receiving trimethoprim-sulfamethoxazole prophylaxis and those receiving alternative non trimethoprim-sulfamethoxazole regimens. Although trimethoprim-sulfamethoxazole is considered the most effective agent for PJP prophylaxis, based largely on data extrapolated from HIV populations, its association with myelosuppression, cytopenias, electrolyte abnormalities, and renal dysfunction may limit tolerability in the early post-HSCT period, along with perceived or real issues with tolerance. We further hypothesize that patients on non trimethoprim-sulfamethoxazole prophylaxis will have a similar incidence of PJP but may demonstrate improved hematologic recovery.

Field	Response
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary Aim: 1.Determine the incidence of PJP infection among allogeneic HSCT recipients, within the first year post-transplant, receiving trimethoprim-sulfamethoxazole versus non trimethoprim-sulfamethoxazole primary prophylaxis. Secondary Aims: 1. Compare hematologic outcomes (time to neutrophil and platelet recovery, frequency of cytopenias) between recipients receiving trimethoprim-sulfamethoxazole versus non trimethoprim-sulfamethoxazole prophylaxis. 2. Assess the impact of prophylaxis choice on transplant outcomes including relapse, non-relapse mortality (NRM), bacterial/fungal infections, graft-versus-host disease (GVHD), and overall survival. 3. Describe practice patterns across centers in the use of trimethoprim-sulfamethoxazole versus alternative prophylactic regimens after HSCT. 4. Determine the incidence of PJP infection among allogeneic HSCT recipients receiving trimethoprim-sulfamethoxazole versus non trimethoprim-sulfamethoxazole secondary prophylaxis. 5. Evaluate absolute lymphocyte count as a predictor of PJP within the first year post HSCT
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	Trimethoprim-sulfamethoxazole is widely regarded as the most effective agent for prevention of PJP, but its hematologic toxicity poses a particular challenge in the immediate post-transplant setting. Alternatives such as atovaquone, dapsone, or pentamidine are commonly used but less well studied in HSCT recipients. This study will provide important real-world data on the comparative effectiveness of trimethoprim-sulfamethoxazole versus non trimethoprim-sulfamethoxazole prophylaxis, inform practice guidelines, and guide individualized prophylaxis strategies balancing efficacy and tolerability in transplant recipients.

Field	Response
SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.	PJP is a life-threatening infection in immunocompromised hosts. In HIV populations, trimethoprim-sulfamethoxazole has demonstrated superior protection and remains the gold-standard prophylaxis (1,2). In HSCT recipients, however, its use is limited by drug-induced myelosuppression and cytopenias (3). Alternative agents (e.g., atovaquone, dapsone, aerosolized or intravenous pentamidine) are frequently substituted, but comparative data in the HSCT setting are scarce (4,5). A large CIBMTR analysis quantified the incidence and timing of PJP following HSCT and described prophylaxis regimens used across transplant centers, demonstrating that breakthrough infections occur despite prophylaxis and that non trimethoprim-sulfamethoxazole strategies are common in clinical practice (6). Additional single-center studies support the feasibility of these alternatives, with dapsone showing similar efficacy to trimethoprim-sulfamethoxazole in allo-HSCT recipients (7) and large institutional cohorts reporting no PJP cases among hundreds of patients receiving intravenous pentamidine prophylaxis (8). International guidelines continue to recommend trimethoprim-sulfamethoxazole as first-line prophylaxis (A-I), with alternatives reserved for intolerance or cytopenias (9). Current CIBMTR forms capture anti-PJP prophylaxis and infection outcomes, offering a unique opportunity to examine prophylaxis strategies and their relationship to PJP incidence and post-transplant outcomes at scale. Notably, the prior CIBMTR (6) analysis was limited by incomplete prophylaxis data, relied on cohorts transplanted between 1995 2005, and predated the widespread adoption of PTCy, underscoring the need for contemporary data to reassess PJP prophylaxis strategies in the modern HSCT era. Our study will address this evidence gap and inform whether non trimethoprim-sulfamethoxazole prophylaxis can provide equivalent protection against PJP without compromising hematologic recovery.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion Criteria: First allogeneic HCTs All graft sources All donor relationships, conditioning regimens/intensities Age 18 years or older at the time of transplant Exclusion Criteria: Two or more allogeneic HCTs Pediatric patients

Field	Response
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	This study excludes pediatric patients because their immune reconstitution, prophylaxis practices, and risk factors for PJP differ substantially from adults, limiting the validity and generalizability of pooled analyses.
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Outline any supplementary data required.	Infectious Disease Markers (Form 2004) Pre-Transplant Essential Data (Form 2400) Post-Transplant Essential Data (Form 2450) Pre-Cellular Therapy Essential Data (Form 4000) Post-HCT Follow-up Data (Form 2100) Cellular Therapy Product (Form 4003) Cellular Therapy Infusion (Form 4006) Cellular Therapy Essential Data Follow-Up (Form 4100) Fungal Infection Post-HSCT (Form 2146) Recipient death data (Form 2900) Laboratory studies (Form 3502)
Types of cellular therapy data this proposal includes:	Hematopoietic Cell Transplantation (HCT)
PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis speci	na
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	na
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	na
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	na

Field	Response
REFERENCES:	1. Schneider MM, et al. A controlled trial of aerosolized pentamidine or trimethoprim-sulfamethoxazole for primary prophylaxis of PCP in HIV. N Engl J Med. 1992;327:1836 1841. PMID: 1360145. 2. May T, et al. Trimethoprim-sulfamethoxazole versus aerosolized pentamidine for primary PCP prophylaxis in HIV: randomized multicenter trial. Infection. 1994;22(6):410 415. PMID: 8158539. 3. Schey SA, Kay HEM. Myelosuppression complicating co-trimoxazole prophylaxis after bone marrow transplantation. Br J Haematol. 1984;56(1):179 180. PMID: 6367807. 4. Stern A, et al. Prophylaxis for Pneumocystis pneumonia in non-HIV immunocompromised patients: Cochrane review. Cochrane Database Syst Rev. 2014;(10):CD005590. PMID: 25269391. 5. Green H, et al. Prophylaxis of Pneumocystis pneumonia in immunocompromised non-HIV patients: systematic review & meta-analysis of RCTs. Mayo Clin Proc. 2007;82(9):1052 1059. PMID: 17803871. 6. Williams KM, et al. The incidence, mortality and timing of PJP after hematopoietic cell transplantation: a CIBMTR analysis. Bone Marrow Transplant. 2016;51(4):573 580. PMID: 26726945 (PMCID: PMC4823157). 7. Sangiolo D, et al. Toxicity and efficacy of daily dapsone as PJP prophylaxis after HSCT: case-control study. Biol Blood Marrow Transplant. 2005;11(7):521 529. PMID: 15983552. 8. McCollam S, et al. PJP prophylaxis with once-monthly IV pentamidine in adult allo-HSCT. Antimicrob Agents Chemother. 2022;66(12):e01207-22. PMID: 36214573. 9. Maertens J, et al. ECIL guidelines for preventing PJP in hematologic malignancies and HSCT. J Antimicrob Chemother. 2016;71(9):2397 2404. PMID: 27550992.
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	No, I do not have any conflicts of interest pertinent to this proposal

PROP2509-36 Incidence of Pneumocystis jirovecii Pneumonia (PJP) after Allogeneic Hematopoietic Stem Cell Transplant: Comparison of Trimethoprim-Sulfamethoxazole versus Non-Trimethoprim-Sulfamethoxazole Prophylaxis

Characteristics of U.S. adult patients underwent first allo transplant after 2018

Characteristic	Trimethoprim/sulfamethoxazole (bactrim, septra)	Other PJP drug	None or missing PJP drug
Number of patients	7098	4510	1902
No. of centers	140	153	115
Patient related			
Age by deciles - no. (%)			
Median (min-max)	60.2 (18.0-81.8)	60.6 (18.0-87.8)	61.7 (18.2-82.7)
18-29	796 (11.2)	594 (13.2)	162 (8.5)
30-39	622 (8.8)	328 (7.3)	128 (6.7)
40-49	732 (10.3)	457 (10.1)	219 (11.5)
50-59	1373 (19.3)	784 (17.4)	357 (18.8)
60-69	2603 (36.7)	1723 (38.2)	732 (38.5)
70+	972 (13.7)	624 (13.8)	304 (16.0)
Sex - no. (%)			
Male	4249 (59.9)	2541 (56.3)	1091 (57.4)
Female	2849 (40.1)	1969 (43.7)	811 (42.6)
Karnofsky score prior to HCT - no. (%)			
90-100	3785 (53.3)	2290 (50.8)	841 (44.2)
80	2061 (29.0)	1414 (31.4)	593 (31.2)
< 80	1198 (16.9)	754 (16.7)	418 (22.0)
Not reported	54 (0.8)	52 (1.2)	50 (2.6)
Race - no. (%)			
White	5495 (77.4)	3508 (77.8)	1500 (78.9)
Black or African American	729 (10.3)	527 (11.7)	215 (11.3)
Asian	431 (6.1)	213 (4.7)	79 (4.2)
Native Hawaiian or other Pacific Islander	27 (0.4)	14 (0.3)	5 (0.3)
American Indian or Alaska Native	49 (0.7)	17 (0.4)	8 (0.4)
More than one race	58 (0.8)	40 (0.9)	14 (0.7)
Not reported	309 (4.4)	191 (4.2)	81 (4.3)
Ethnicity - no. (%)			
Hispanic or Latino	723 (10.2)	491 (10.9)	199 (10.5)
Non Hispanic or non-Latino	6171 (86.9)	3862 (85.6)	1644 (86.4)
Non-resident of the U.S.	33 (0.5)	22 (0.5)	6 (0.3)
Not reported	171 (2.4)	135 (3.0)	53 (2.8)

Characteristic	Trimethoprim/sulfamethoxazole (bactrim, septra)	Other PJP drug	None or missing PJP drug
Disease related			
Primary disease - no. (%)			
Acute myelogenous leukemia or ANLL	1945 (27.4)	995 (22.1)	483 (25.4)
Acute lymphoblastic leukemia	651 (9.2)	432 (9.6)	136 (7.2)
Other leukemia	90 (1.3)	46 (1.0)	33 (1.7)
Chronic myelogenous leukemia	112 (1.6)	57 (1.3)	18 (0.9)
Myelodysplastic/myeloproliferative disorders (please classify all preleukemia)	1445 (20.4)	873 (19.4)	422 (22.2)
Other acute leukemia	69 (1.0)	25 (0.6)	8 (0.4)
Non-Hodgkin lymphoma	385 (5.4)	239 (5.3)	127 (6.7)
Hodgkin lymphoma	281 (4.0)	154 (3.4)	89 (4.7)
Plasma cell disorder/Multiple Myeloma	106 (1.5)	35 (0.8)	33 (1.7)
Other Malignancies	1 (0.0)	0 (0.0)	1 (0.1)
Severe aplastic anemia	444 (6.3)	363 (8.0)	131 (6.9)
Inherited bone marrow failure syndromes	25 (0.4)	23 (0.5)	1 (0.1)
Hemoglobinopathies	129 (1.8)	122 (2.7)	24 (1.3)
Paroxysmal nocturnal hemoglobinuria	8 (0.1)	11 (0.2)	0 (0.0)
SCID and other immune system disorders	22 (0.3)	12 (0.3)	3 (0.2)
Inherited abnormalities of platelets	0 (0.0)	1 (0.0)	0 (0.0)
Inherited disorders of metabolism	3 (0.0)	3 (0.1)	1 (0.1)
Histiocytic disorders	6 (0.1)	3 (0.1)	0 (0.0)
Autoimmune Diseases	0 (0.0)	3 (0.1)	0 (0.0)
Other, specify	2 (0.0)	3 (0.1)	0 (0.0)
Tolerance induction associated with solid organ transplant	1 (0.0)	1 (0.0)	0 (0.0)
Myeloproliferative Neoplasms	1373 (19.3)	1109 (24.6)	392 (20.6)
Transplant related			
Stem cell source - no. (%)			
Bone Marrow	1077 (15.2)	713 (15.8)	250 (13.1)
Peripheral Blood	5692 (80.2)	3656 (81.1)	1594 (83.8)
Cord Blood	328 (4.6)	141 (3.1)	58 (3.0)
Missing or Other	1 (0.0)	0 (0.0)	0 (0.0)
Classify the recipient's prescribed preparative regimen - no. (%)			
Myeloablative	2362 (33.3)	1478 (32.8)	637 (33.5)
Non-myeloablative (NST)	1156 (16.3)	790 (17.5)	328 (17.2)

Characteristic	Trimethoprim/sulfamethoxazole (bactrim, septra)	Other PJP drug	None or missing PJP drug
Reduced intensity (RIC)	3563 (50.2)	2237 (49.6)	934 (49.1)
Not reported	17 (0.2)	5 (0.1)	3 (0.2)
GVHD prophylaxis - no. (%)			
None	173 (2.4)	73 (1.6)	76 (4.0)
Ex-vivo T-cell depletion	40 (0.6)	18 (0.4)	8 (0.4)
CD34 selection	174 (2.5)	71 (1.6)	17 (0.9)
Post-CY + other(s)	2780 (39.2)	2074 (46.0)	858 (45.1)
Post-CY alone	46 (0.6)	23 (0.5)	11 (0.6)
CNI (TAC/CSA) + MMF +/- Other(except post-CY)	929 (13.1)	564 (12.5)	271 (14.2)
CNI (TAC/CSA) + MTX +/- Other(except MMF, post-CY)	2486 (35.0)	1325 (29.4)	493 (25.9)
CNI (TAC/CSA) +/- Other (except MMF, MTX, post-CY)	268 (3.8)	194 (4.3)	84 (4.4)
TAC alone	125 (1.8)	83 (1.8)	49 (2.6)
CSA alone	7 (0.1)	7 (0.2)	1 (0.1)
Others	70 (1.0)	76 (1.7)	34 (1.8)
Missing	0 (0.0)	2 (0.0)	0 (0.0)
Year of current transplant - no. (%)			
2017	1220 (17.2)	619 (13.7)	381 (20.0)
2018	1166 (16.4)	681 (15.1)	334 (17.6)
2019	1060 (14.9)	726 (16.1)	270 (14.2)
2020	750 (10.6)	468 (10.4)	196 (10.3)
2021	761 (10.7)	476 (10.6)	163 (8.6)
2022	628 (8.8)	461 (10.2)	151 (7.9)
2023	681 (9.6)	439 (9.7)	204 (10.7)
2024	745 (10.5)	575 (12.7)	170 (8.9)
2025	87 (1.2)	65 (1.4)	33 (1.7)
Infection prophylaxis			
First anti-pneumocystis(PJP) drug given as prophylaxis [Not mutually exclusive] - no. (%)			
Trimethoprim/Sulfamethoxazole (Bactrim, Septra)	7098 (100)	0 (0.0)	0 (0.0)
Atovaquone (Mepron)	0 (0.0)	1125 (24.9)	0 (0.0)
Dapsone (Aczone)	0 (0.0)	551 (12.2)	0 (0.0)
Other specified anti-pneumocystis	0 (0.0)	26 (0.6)	0 (0.0)
Pentamidine inhaled	0 (0.0)	1623 (36.0)	0 (0.0)
Pentamidine IV	0 (0.0)	1188 (26.3)	0 (0.0)

Characteristic	Trimethoprim/sulfamethoxazole (bactrim, septra)	Other PJP drug	None or missing PJP drug
No anti-pneumocystis (PJP) drug given as prophylaxis	0 (0.0)	0 (0.0)	1694 (89.1)
Infection related			
Pneumocystis infection in 1 year post transplant - no. (%)			
Yes	31 (0.4)	26 (0.6)	12 (0.6)
No	7067 (99.6)	4484 (99.4)	1890 (99.4)
Follow-up of survivors, months - median (range)	48.3 (2.3-99.7)	47.3 (0.8-101.4)	48.2 (0.3-99.8)

Field	Response
Proposal Number	2509-37-MENDOZA
Proposal Title	Incidence and Outcomes of Respiratory Virus Infections in Allogeneic HSCT Recipients Receiving Post-Transplant Cyclophosphamide (PTCy) for GVHD Prophylaxis
Key Words	respiratory viruses, cyclophosphamide, GVHD, coronavirus, influenza, RSV, COVID
Principal Investigator #1: - First and last name, degree(s)	Maria Alejandra Mendoza
Principal Investigator #1: - Email address	alejandra.mendoza@hsc.utah.edu
Principal Investigator #1: - Institution name	University of Utah
Principal Investigator #1: - Academic rank	Assistant professor
Junior investigator status (defined as 㸱、5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	Yes
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Hannah Imlay
Principal Investigator #2 (If applicable): - Email address:)	hannah.imlay@hsc.utah.edu
Principal Investigator #2 (If applicable): - Institution name:	University of Utah
Principal Investigator #2 (If applicable): - Academic rank:	Assistant Professor
Junior investigator status (defined as 㸱、5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	na
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Infection and Immune Reconstitution
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	No
RESEARCH QUESTION:	What is the incidence and what are the outcomes of respiratory virus infections within 1 year after allogeneic hematopoietic stem cell transplant in recipients receiving post-transplant cyclophosphamide (PTCy) for GVHD prophylaxis?

Field	Response
RESEARCH HYPOTHESIS:	We hypothesize that use of PTCy for GVHD prophylaxis is associated with an increased incidence of respiratory virus infections within the first year post-transplant, compared to recipients receiving other GVHD prophylaxis regimens. We further hypothesize that respiratory virus infections in the context of PTCy use are associated with higher risks of downstream complications including bacterial/fungal superinfections, GVHD, and increased non-relapse mortality.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary Aim: 1.Define the incidence of respiratory virus infections within the first year post-HSCT among recipients receiving PTCy versus those receiving other GVHD prophylaxis regimens. Secondary Aims: 1. Identify risk factors for respiratory virus infections after HSCT, including GVHD prophylaxis type, donor source, conditioning regimen, graft source, and patient-related factors (e.g., age, underlying disease). 2. Assess the impact of respiratory virus infections on transplant outcomes including hematologic recovery, bacterial and fungal superinfections, acute and chronic GVHD, relapse, non-relapse mortality (NRM), disease-free survival (DFS), and overall survival. 3. Describe patterns of antiviral therapy and supportive care used for respiratory virus infections in this population. 4. Describe vaccination patters 5. Identify absolute lymphocyte count as a predictor of outcomes in respiratory viral infections
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	Respiratory virus infections (e.g., RSV, influenza, parainfluenza, metapneumovirus, rhinovirus, adenovirus, and coronaviruses [including SARS-CoV-2]) are a leading cause of morbidity and mortality after HSCT. PTCy has rapidly emerged as a standard GVHD prophylaxis platform across donor types, yet its effects on susceptibility to respiratory viruses remain incompletely understood. This study will leverage large-scale registry data to define the burden of respiratory virus infections after PTCy, inform risk stratification, and guide prevention and management strategies in this expanding population.

Field	Response
SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.	Respiratory viral infections are common after allogeneic HSCT and are associated with substantial morbidity and mortality. Community-acquired respiratory viruses (CARVs) including RSV, influenza, parainfluenza, human metapneumovirus, rhinovirus/enterovirus, adenovirus, and coronaviruses pose a persistent risk of severe lower respiratory tract disease, hospitalization, and death in this population (1,2). The adoption of post-transplant cyclophosphamide (PTCy) across donor types has transformed GVHD prophylaxis but is associated with early, profound immunosuppression and delayed immune reconstitution, which may increase susceptibility to viral infections (3). Emerging evidence suggests that recipients receiving PTCy for GVHD prophylaxis have delayed immune recovery and a higher burden of infectious complications overall, including signals of increased respiratory viral infection risk (3,4). Broader literature consistently shows that CARV lower respiratory tract disease carries high short-term mortality in HSCT cohorts, underscoring the clinical importance of prevention and early treatment (4,5). Contemporary guideline updates emphasize vigilant testing and supportive/antiviral strategies in HSCT populations, while acknowledging ongoing evidence gaps regarding regimen-specific risk precisely the space where a PTCy-focused incidence study can add value.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion Criteria: First allogeneic HCTs All graft sources All donor relationships, conditioning regimens/intensities Age 18 years or older at time of transplant Exclusion Criteria: Two or more allogeneic HCTs Pediatric patients
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	This study excludes pediatric patients because their immune reconstitution, prophylaxis strategies, and clinical outcomes differ substantially from adults, and they also have distinct patterns of viral exposures (e.g., school and daycare settings), which would limit the validity and generalizability of pooled analyses.

Field	Response
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Outline any supplementary data required.	Respiratory Virus Post-Infusion (Form 2149) Infectious Disease Markers (Form 2004) Pre-Transplant Essential Data (Form 2400) Post-Transplant Essential Data (Form 2450) Pre-Cellular Therapy Essential Data (Form 4000) Post-HCT Follow-up Data (Form 2100) Cellular Therapy Product (Form 4003) Cellular Therapy Infusion (Form 4006) Cellular Therapy Essential Data Follow-Up (Form 4100) Fungal Infection Post-HSCT (Form 2146) Laboratory studies (Form 3502) Recipient death data (Form 2900)
Types of cellular therapy data this proposal includes:	Hematopoietic Cell Transplantation (HCT)
PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis speci	na
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	na
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	na
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	na

Field	Response
REFERENCES:	1. Sim SA, Leung VKY, Ritchie D, Slavin MA, Sullivan SG, Teh BW. Viral Respiratory Tract Infections in Allogeneic Hematopoietic Stem Cell Transplantation Recipients in the Era of Molecular Testing. Biol Blood Marrow Transplant. 2018 Jul;24(7):1490-1496. doi: 10.1016/j.bbmt.2018.03.004. Epub 2018 Mar 9. PMID: 29530766; PMCID: PMC7110577. 2. Ogimi C, Xie H, Waghmare A, Jerome KR, Leisenring WM, Ueda Oshima M, Carpenter PA, Englund JA, Boeckh M. Novel factors to predict respiratory viral disease progression in allogeneic hematopoietic cell transplant recipients. Bone Marrow Transplant. 2022 Apr;57(4):649-657. doi: 10.1038/s41409-022-01575-z. Epub 2022 Feb 16. Erratum in: Bone Marrow Transplant. 2024 Dec;59(12):1790. doi: 10.1038/s41409-024-02418-9. PMID: 35173288; PMCID: PMC8853301. 3. Mikulska M, Bartalucci C, Raiola AM, Oltolini C. Does PTCY increase the risk of infections? Blood Rev. 2023 Nov;62:101092. doi: 10.1016/j.blre.2023.101092. Epub 2023 Apr 20. PMID: 37120352. 4. Meyer T, Maas-Bauer K, W sch R, Duyster J, Zeiser R, Finke J, Wehr C. Immunological reconstitution and infections after alloHCT - a comparison between post-transplantation cyclophosphamide, ATLG and non-ATLG based GvHD prophylaxis. Bone Marrow Transplant. 2025 Mar;60(3):286-296. doi: 10.1038/s41409-024-02474-1. Epub 2024 Nov 19. PMID: 39562716; PMCID: PMC11893447. 5. Merch n-Mu oz B, Su rez-Lled M, Rodr guez-Lobato LG, Aiello TF, Gallardo-Pizarro A, Charry P, Cid J, Lozano M, Pedraza A, Mart nez-Roca A, Guardia A, Guardia L, Moreno C, Carreras E, Rosi ol L, Garc a-Vidal C, Fern ndez-Avil s F, Mart nez C, Rovira M, Salas MQ. Post-Transplant Cyclophosphamide-Based Prophylaxis and Its Impact on Infectious Complications and Immune Reconstitution According to Donor Type. Cancers (Basel). 2025 Mar 26;17(7):1109. doi: 10.3390/cancers17071109. PMID: 40227629; PMCID: PMC11987969.
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	No, I do not have any conflicts of interest pertinent to this proposal
If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.	na

PROP2509-37 Incidence and Outcomes of Respiratory Virus Infections in Allogeneic HSCT Recipients Receiving Post-Transplant Cyclophosphamide (PTCy) for GVHD Prophylaxis

Characteristics of U.S. adult patients underwent first allo transplant after 2018

Characteristic	PTCY (alone or with others)	Other GVHD prophylaxis
Number of patients	5175	5817
No. of centers	150	150
Patient related		
Age by deciles - no. (%)		
Median (min-max)	60.5 (18.0-82.2)	60.9 (18.0-82.7)
18-29	586 (11.3)	729 (12.5)
30-39	459 (8.9)	424 (7.3)
40-49	544 (10.5)	550 (9.5)
50-59	941 (18.2)	1060 (18.2)
60-69	1903 (36.8)	2190 (37.6)
70+	742 (14.3)	864 (14.9)
Sex - no. (%)		
Male	3021 (58.4)	3402 (58.5)
Female	2154 (41.6)	2415 (41.5)
Karnofsky score prior to HCT - no. (%)		
90-100	2647 (51.1)	2939 (50.5)
80	1543 (29.8)	1766 (30.4)
< 80	925 (17.9)	1043 (17.9)
Not reported	60 (1.2)	69 (1.2)
Race - no. (%)		
White	3809 (73.6)	4717 (81.1)
Black or African American	743 (14.4)	466 (8.0)
Asian	259 (5.0)	324 (5.6)
Native Hawaiian or other Pacific Islander	19 (0.4)	19 (0.3)
American Indian or Alaska Native	34 (0.7)	23 (0.4)
More than one race	42 (0.8)	51 (0.9)
Not reported	269 (5.2)	217 (3.7)
Ethnicity - no. (%)		
Hispanic or Latino	659 (12.7)	521 (9.0)
Non-Hispanic or non-Latino	4349 (84.0)	5126 (88.1)
Non-resident of the U.S.	21 (0.4)	17 (0.3)
Not reported	146 (2.8)	153 (2.6)
Disease related		
Primary disease - no. (%)		

Characteristic	PTCY (alone or with others)	Other GVHD prophylaxis
Acute myelogenous leukemia or ANLL	1434 (27.7)	1328 (22.8)
Acute lymphoblastic leukemia	490 (9.5)	504 (8.7)
Other leukemia	52 (1.0)	54 (0.9)
Chronic myelogenous leukemia	81 (1.6)	72 (1.2)
Myelodysplastic/myeloproliferative disorders (please classify all preleukemia)	896 (17.3)	1145 (19.7)
Other acute leukemia	38 (0.7)	43 (0.7)
Non-Hodgkin lymphoma	314 (6.1)	268 (4.6)
Hodgkin lymphoma	302 (5.8)	143 (2.5)
Plasma cell disorder/Multiple Myeloma	40 (0.8)	82 (1.4)
Other Malignancies	1 (0.0)	0 (0.0)
Severe aplastic anemia	321 (6.2)	508 (8.7)
Inherited bone marrow failure syndromes	10 (0.2)	31 (0.5)
Hemoglobinopathies	118 (2.3)	125 (2.1)
Paroxysmal nocturnal hemoglobinuria	8 (0.2)	11 (0.2)
SCID and other immune system disorders	8 (0.2)	19 (0.3)
Inherited abnormalities of platelets	1 (0.0)	0 (0.0)
Inherited disorders of metabolism	2 (0.0)	4 (0.1)
Histiocytic disorders	5 (0.1)	1 (0.0)
Autoimmune Diseases	1 (0.0)	2 (0.0)
Other, specify	3 (0.1)	1 (0.0)
Tolerance induction associated with solid organ transplant	0 (0.0)	2 (0.0)
Myeloproliferative Neoplasms	1050 (20.3)	1474 (25.3)
Stem cell source - no. (%)		
Bone Marrow	757 (14.6)	823 (14.1)
Peripheral Blood	4418 (85.4)	4672 (80.3)
Cord Blood	0 (0.0)	322 (5.5)
Donor type - no. (%)		
HLA-identical sibling	387 (7.5)	1342 (23.1)
Twin	0 (0.0)	5 (0.1)
1 Ag/allele	78 (1.5)	13 (0.2)
>=2 Ag/allele	1987 (38.4)	150 (2.6)
Other related(matching TBD)	58 (1.1)	64 (1.1)
Well-matched unrelated (8/8)	1434 (27.7)	3354 (57.7)
Partially-matched unrelated (7/8)	968 (18.7)	316 (5.4)
Mis-matched unrelated (<=6/8)	137 (2.6)	17 (0.3)
Multi-donor	29 (0.6)	37 (0.6)
Unrelated (matching TBD)	97 (1.9)	197 (3.4)
Cord blood	0 (0.0)	322 (5.5)

Characteristic	PTCY (alone or with others)	Other GVHD prophylaxis
Classify the recipient's prescribed preparative regimen - no. (%)		
Myeloablative	1461 (28.2)	2017 (34.7)
Non-myeloablative (NST)	1067 (20.6)	822 (14.1)
Reduced intensity (RIC)	2637 (51.0)	2966 (51.0)
Not reported	10 (0.2)	12 (0.2)
GVHD prophylaxis - no. (%)		
Ex-vivo T-cell depletion	0 (0.0)	36 (0.6)
CD34 selection	0 (0.0)	194 (3.3)
Post-CY + other(s)	5139 (99.3)	0 (0.0)
Post-CY alone	36 (0.7)	0 (0.0)
CNI (TAC/CSA) + MMF +/- Other(except post-CY)	0 (0.0)	1341 (23.1)
CNI (TAC/CSA) + MTX +/- Other(except MMF, post-CY)	0 (0.0)	3433 (59.0)
CNI (TAC/CSA) +/- Other (except MMF, MTX, post-CY)	0 (0.0)	433 (7.4)
TAC alone	0 (0.0)	223 (3.8)
CSA alone	0 (0.0)	11 (0.2)
Others	0 (0.0)	146 (2.5)
Year of current transplant - no. (%)		
2018	767 (14.8)	1393 (23.9)
2019	832 (16.1)	1211 (20.8)
2020	540 (10.4)	811 (13.9)
2021	501 (9.7)	846 (14.5)
2022	555 (10.7)	644 (11.1)
2023	831 (16.1)	446 (7.7)
2024	999 (19.3)	435 (7.5)
2025	150 (2.9)	31 (0.5)
Infection by 100 day		
Community Respiratory Virus (excluding COVID-19) within 100 days post-transplant - no. (%)		
No	4748 (91.7)	5409 (93.0)
Yes	427 (8.3)	408 (7.0)
COVID-19 (SARS-CoV-2) within 100 days post-transplant - no. (%)		
No	5063 (97.8)	5713 (98.2)
Yes	112 (2.2)	104 (1.8)
Community Respiratory Virus (excluding COVID-19) within 100 days, by year of transplant - no. (%)		
2018		
No	685 (13.2)	1251 (21.5)
Yes	82 (1.6)	142 (2.4)
2019		

Characteristic	PTCY (alone or with others)	Other GVHD prophylaxis
No	727 (14.0)	1080 (18.6)
Yes	105 (2.0)	131 (2.3)
2020		
No	508 (9.8)	789 (13.6)
Yes	32 (0.6)	22 (0.4)
2021		
No	470 (9.1)	822 (14.1)
Yes	31 (0.6)	24 (0.4)
2022		
No	508 (9.8)	604 (10.4)
Yes	47 (0.9)	40 (0.7)
2023		
No	780 (15.1)	421 (7.2)
Yes	51 (1.0)	25 (0.4)
2024		
No	933 (18.0)	413 (7.1)
Yes	66 (1.3)	22 (0.4)
2025		
No	137 (2.6)	29 (0.5)
Yes	13 (0.3)	2 (0.0)
COVID-19 (SARS-CoV-2) within 100 days, by year of transplant - no. (%)		
2018		
No	767 (14.8)	1393 (23.9)
2019		
No	832 (16.1)	1211 (20.8)
2020		
No	535 (10.3)	802 (13.8)
Yes	5 (0.1)	9 (0.2)
2021		
No	494 (9.5)	815 (14.0)
Yes	7 (0.1)	31 (0.5)
2022		
No	528 (10.2)	608 (10.5)
Yes	27 (0.5)	36 (0.6)
2023		
No	800 (15.5)	429 (7.4)
Yes	31 (0.6)	17 (0.3)
2024		
No	961 (18.6)	424 (7.3)

Characteristic	PTCY (alone or with others)	Other GVHD prophylaxis
Yes	38 (0.7)	11 (0.2)
2025		
No	146 (2.8)	31 (0.5)
Yes	4 (0.1)	0 (0.0)
Follow-up of survivors, months - median (range)	25.6 (0.8-86.3)	48.3 (0.3-85.2)

Field	Response
Proposal Number	2509-102-LITTLE
Proposal Title	The Impact of HLA-B*35 Expression on CMV Viremia and Clinically Significant CMV Infection following PTCy-based Hematopoietic Cell Transplantation
Key Words	HLA-B*35, cytomegalovirus, Post-transplant cyclophophamide, infection risk
Principal Investigator #1: - First and last name, degree(s)	Jessica S. Little, MD
Principal Investigator #1: - Email address	jlittle@bwh.harvard.edu
Principal Investigator #1: - Institution name	Brigham and Women's Hospital
Principal Investigator #1: - Academic rank	Instructor
Junior investigator status (defined as 㑊、5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Susan Prockop, MD
Principal Investigator #2 (If applicable): - Email address:)	Susan.Prockop@childrens.harvard.edu
Principal Investigator #2 (If applicable): - Institution name:	Boston Children's Hospital
Principal Investigator #2 (If applicable): - Academic rank:	Associate Professor
Junior investigator status (defined as 㑊、5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	Jessica S. Little
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	None
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Infection and Immune Reconstitution
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	Yes
If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:	Dr. Joshua Hill

Field	Response
RESEARCH QUESTION:	Does HLA-B*35 expression in recipients and/or donors increase the risk of CMV DNAemia and clinically significant CMV infection (CS-CMVi) after allogeneic hematopoietic cell transplantation (HCT), particularly in the setting of post-transplant cyclophosphamide (PTCy)-based GVHD prophylaxis?
RESEARCH HYPOTHESIS:	Expression of HLA-B*35 in either recipient or donor is associated with increased risk of CMV DNAemia and of CS-CMVi in HCT recipients, including those receiving PTCy-based GVHD prophylaxis.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary Objective: 1. Evaluate the association of HLA-B*35 expression in recipients and donors with CMV DNAemia and CS-CMVi following hematopoietic cell transplantation (HCT) Secondary Objectives: 1. Compare the impact of HLA-B*35 on CMV DNAemia and CS-CMVi based on HCT donor type (Matched, Mismatched, Haploidentical, Sibling) as well as PTCy use. 2. Assess the independent contribution of donor vs. recipient HLA-B*35 expression on CMV outcomes in mismatched transplant recipients. 3. Evaluate associations of HLA-B*35 with transplant-related outcomes, including acute GVHD, chronic GVHD, relapse, non-relapse mortality (NRM), disease-free survival, and overall survival. 4. Explore the association of HLA-B*35 with CMV infections in the pre- and post-letermovir periods (2012 2018 vs. 2019 2024). Exploratory Objective: 1. Investigate whether other HLA alleles previously implicated in viral control influence CMV risk. 2. Explore whether other HLA alleles responsible for immunodominant CMV responses (eg HLA-A*0201 and HLA-B*0702) can mediate the negative impact of HLA-B*35 alleles.
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	Despite advances in prophylaxis, CMV remains a leading cause of morbidity and mortality after allogeneic HCT. Identification of novel immunogenetic risk factors in the era of PTCy and letermovir could enable personalized prevention strategies, such as risk-adapted monitoring, extended prophylaxis, or modified thresholds for preemptive therapy. Because HLA typing is universally available prior to HCT, findings could be readily integrated into clinical decision-making for both donor and recipient selection and post-transplant CMV management.

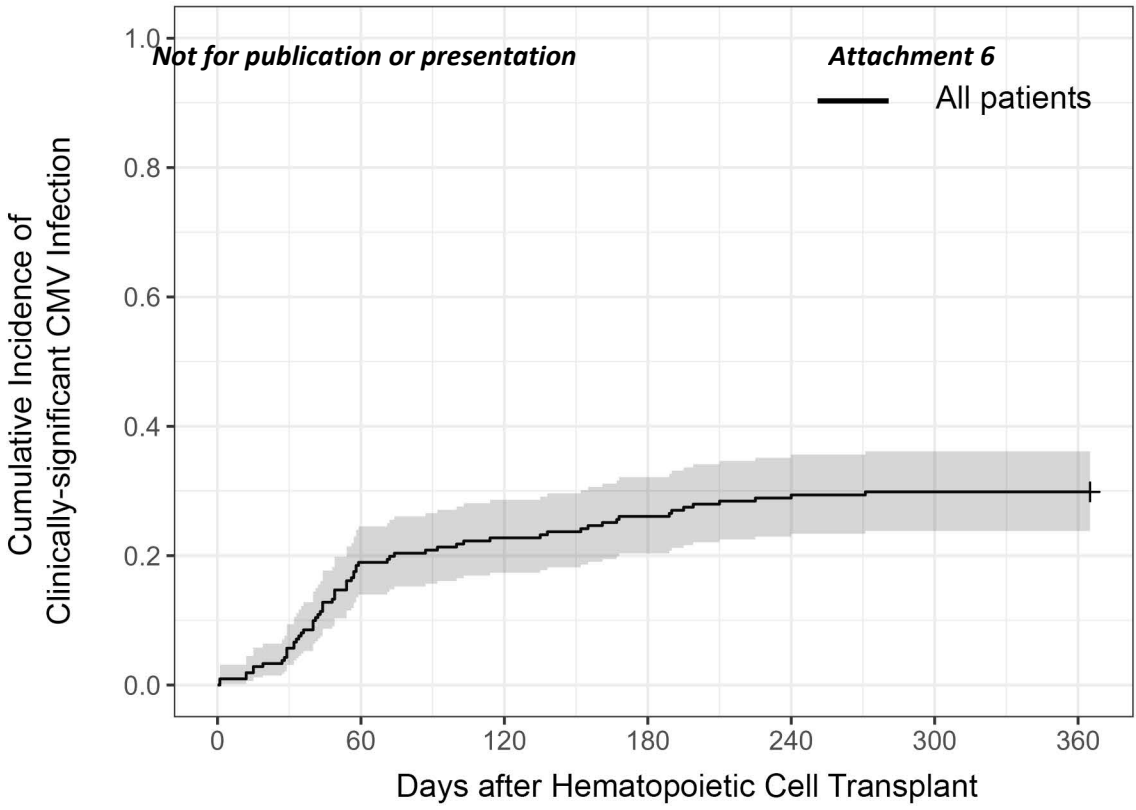
Field	Response
SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.	CMV seropositivity is the strongest known risk factor for post-HCT CMV infection, but immunogenetic contributors are less well understood. HLA-B*35 expression has previously been associated with impaired immunologic control and rapid progression of viral infections such as human immunodeficiency virus (HIV). In addition, one recent study by Hasan and colleagues demonstrated impaired CMVpp65 cytotoxic T-cells (CTLs) restricted by HLA-B*35 alleles, raising the question of whether expression of this HLA locus may increase the risk of clinical CMV infections after transplantation. We hypothesized that HLA-B*35 may be a risk factor for CMV infections after HCT based on this prior literature and in an institutional cohort of 211 PTCy-based HCT recipients (2015 2022), we found: Recipient HLA-B*35 positivity was associated with an increased risk of CS-CMVi (HR 2.81; 95% CI 1.1 7.2; p=0.03) and CMV viremia (HR 2.28; 95% CI 1.15 4.55; p=0.02). These data strongly suggest a role for HLA-B*35 in CMV risk after PTCy-based HCT and will soon be published in JTCT. However, validation in a large, diverse cohort is needed to: 1. Establish generalizability beyond single-center data. 2. Clarify donor vs. recipient contributions. 3. Inform the potential clinical use of HLA-B*35 in risk stratification. 4. Establish whether co-expression of other HLA alleles mediates the HLA-B*35 risk. We propose evaluating this question in a large cohort of allogeneic HCT recipients spanning the pre- and post-letermovir periods.
SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Id	F_2uKyfjENuyHOo0F
SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Name	Figure 1 TCT CMV HLA.png
SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Size	226646
SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Type	image/png

Field	Response
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion Criteria: 1. All patients reported to the CIBMTR receiving their first allogeneic HCT for AML, ALL, or MDS between 2012 2024 with complete data for donor and recipient high resolution HLA typing, and CMV serostatus. Exclusion Criteria: 1. Umbilical cord blood transplant recipients. 2. Recipients of ex vivo T-cell manipulation (CD34 selection, T-cell depletion, ATG, alemtuzumab). 3. Patients lacking post-transplant infection reporting or with documented CMV infection before day 0.
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	Given our preliminary data is suggestive of an association between HLA-B*35 and CMV outcomes in adults, we hope to first validate these findings in another adult cohort.
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Outline any supplementary data required.	Data Requirements: Patient Variables Age at transplant Sex Race/ethnicity Recipient CMV serostatus Recipient HLA type (including B*35) Karnofsky/Lansky performance status HCT-CI Disease/Transplant Variables Primary diagnosis (AML, ALL, MDS) Donor type Graft Type Conditioning intensity GVHD prophylaxis regimen TBI use Year of transplant Donor CMV serostatus Donor age Donor sex Donor HLA type (including B*35) Infection Outcomes (from CIBMTR infection forms) CMV DNAemia Clinically significant CMV infection (CS-CMVi) Dates of onset relative to transplant Letermovir use (if available) Other Outcomes Acute GVHD (grade II IV) Chronic GVHD Relapse, non-relapse mortality, disease-free survival, overall survival Supplementary Data Required None anticipated; all required variables are available through CIBMTR standard forms.
Types of cellular therapy data this proposal includes:	Hematopoietic Cell Transplantation (HCT)

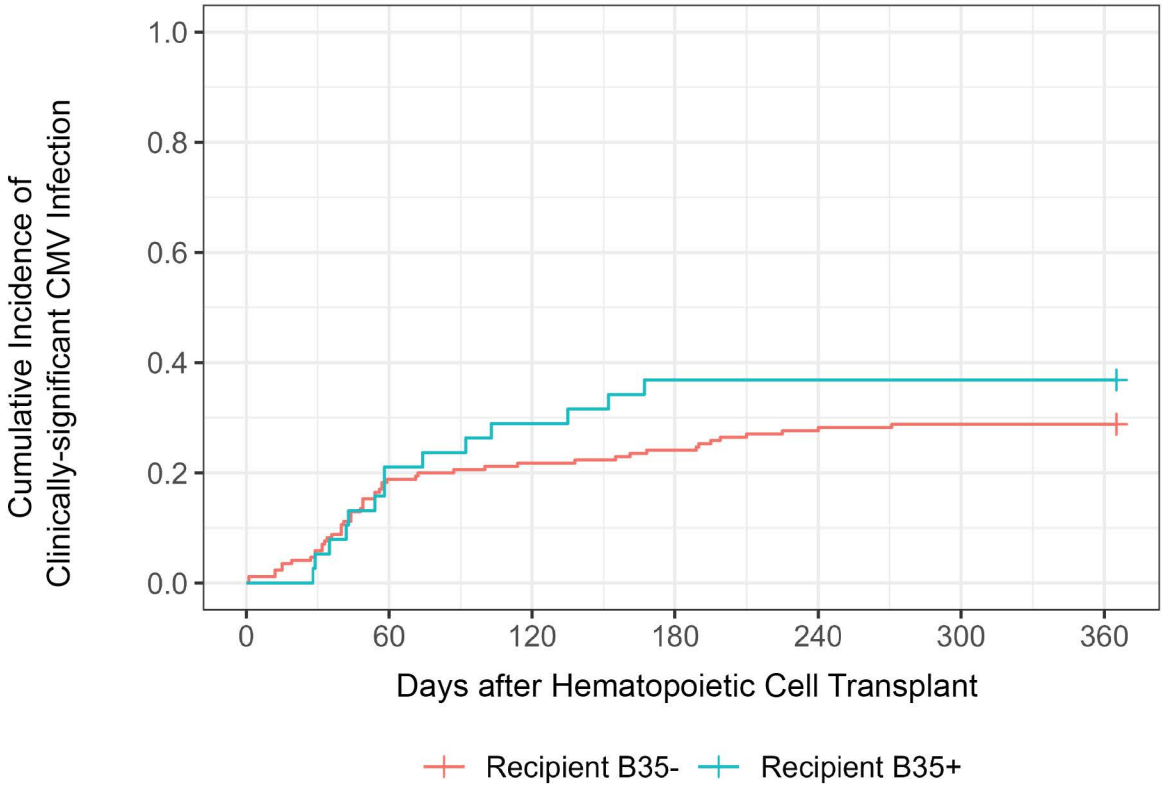
Field	Response
PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis speci	N/A
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	N/A
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	N/A
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	N/A

REFERENCES:	Bola os-Meade J, Hamadani M, Wu J, et al. Post-Transplantation Cyclophosphamide-Based Graft-versus-Host Disease Prophylaxis. New England Journal of Medicine 2023;388(25):2338 2348. Carrington M, Nelson GW, Martin MP, et al. HLA and HIV-1: heterozygote advantage and B*35-Cw*04 disadvantage. Science 1999;283(5408):1748 52. Goldsmith SR, Abid MB, Auletta JJ, et al. Posttransplant cyclophosphamide is associated with increased cytomegalovirus infection: a CIBMTR analysis. Blood 2021;137(23):3291 3305. Hasan AN, Doubrovina E, Sottile R, et al. Dominant epitopes presented by prevalent HLA alleles permit wide use of banked CMVpp65 T cells in adoptive therapy. Blood Adv 2022;6(16):4859 4872. Jin X, Gao X, Ramanathan M, et al. Human immunodeficiency virus type 1 (HIV-1)-specific CD8+-T-cell responses for groups of HIV-1-infected individuals with different HLA-B*35 genotypes. J Virol 2002;76(24):12603 10. Little JS, Dul ry R, Shapiro RM, et al. Opportunistic Infections in Patients Receiving Post-Transplantation Cyclophosphamide: Impact of Haploidentical versus Unrelated Donor Allograft. Transplant Cell Ther 2024;30(2):233.e1-233.e14. Ljungman P, Boeckh M, Hirsch HH, et al. Definitions of cytomegalovirus infection and disease in transplant patients for use in clinical trials. Clinical Infectious Diseases 2017;64(1):87 91. Luznik L, Bola os-Meade J, Zahurak M, et al. High-dose cyclophosphamide as single-agent, short-course prophylaxis of graft-versus-host disease. Blood 2010;115(16):3224 3230. Marty FM, Ljungman P, Chemaly RF, et al. Letermovir Prophylaxis for Cytomegalovirus in Hematopoietic-Cell Transplantation. New England Journal of Medicine 2017;377(25):2433 2444. Chemaly RF, El Haddad L, Winston DJ, et al. Cytomegalovirus (CMV) Cell-Mediated Immunity and CMV Infection after Allogeneic Hematopoietic Cell Transplantation: The REACT Study. Clinical Infectious Diseases 2020;71(9):2365 2374. Rambaldi B, Kim HT, Reynolds C, et al. Impaired T- And NK-cell reconstitution after haploidentical HCT with posttransplant cyclophosphamide. Blood Adv 2021;5(2):352 364. Russo D, Schmitt M, Pilorge S, et al. Efficacy and safety of extended duration letermovir prophylaxis in recipients of haematopoietic stem-cell transplantation at risk of cytomegalovirus

Field	Response
	infection: a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Haematol 2024;11(2):e127 e135. Sadowska-Klasa A, zk k S, Xie H, et al. Late cytomegalovirus disease after hematopoietic cell transplantation: significance of novel transplantation techniques. Blood Adv 2024;8(14):3639.
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	No, I do not have any conflicts of interest pertinent to this proposal



At Risk	211	160	137	119	107	100	98



	At Risk						
Recipient B35-	170	130	111	100	89	82	80
Recipient B35+	38	29	25	18	17	17	17

PROP2509-102 The Impact of HLA-B*35 Expression on CMV Viremia and Clinically Significant CMV Infection following PTCy-based Hematopoietic Cell Transplantation

Characteristics of U.S. adult patients underwent first allo transplant for AML/ALL/MDS between 2012 to 2024

Characteristic	
Number of patients	9739
No. of centers	144
Patient related	
Age by deciles - no. (%)	
Median (min-max)	61.7 (18.0-82.3)
18-29	736 (7.6)
30-39	683 (7.0)
40-49	990 (10.2)
50-59	1935 (19.9)
60-69	3961 (40.7)
70+	1434 (14.7)
Sex - no. (%)	
Male	5725 (58.8)
Female	4014 (41.2)
Karnofsky score prior to HCT - no. (%)	
90-100	4993 (51.3)
80	2981 (30.6)
< 80	1679 (17.2)
Not reported	86 (0.9)
Race - no. (%)	
White	7996 (82.1)
Black or African American	729 (7.5)
Asian	527 (5.4)
Native Hawaiian or other Pacific Islander	30 (0.3)
American Indian or Alaska Native	52 (0.5)
More than one race	60 (0.6)
Not reported	345 (3.5)
Ethnicity - no. (%)	
Hispanic or Latino	923 (9.5)
Non-Hispanic or non-Latino	8569 (88.0)
Non-resident of the U.S.	44 (0.5)
Not reported	203 (2.1)
Disease related	
Primary disease - no. (%)	
Acute myelogenous leukemia or ANLL	4540 (46.6)

Characteristic	
Acute lymphoblastic leukemia	1472 (15.1)
Myelodysplastic/myeloproliferative disorders (please classify all preleukemia)	3727 (38.3)
Transplant related	
Stem cell source - no. (%)	
Bone Marrow	1475 (15.1)
Peripheral Blood	8264 (84.9)
Donor type - no. (%)	
HLA-identical sibling	2119 (21.8)
Twin	34 (0.3)
1 Ag/allele	88 (0.9)
Haploidentical transplant	*88 (0.9)*
>=2 Ag/allele	1825 (18.7)
Haploidentical transplant	*1825 (18.7)*
Other related(matching TBD)	84 (0.9)
Non-Haploidentical transplant	*81 (0.8)*
Not reported	*3 (0.0)*
Well-matched unrelated (8/8)	4317 (44.3)
Partially matched unrelated (7/8)	1095 (11.2)
Mis-matched unrelated (<=6/8)	117 (1.2)
Multi-donor	60 (0.6)
Non-Haploidentical transplant	*1 (0.0)*
Haploidentical transplant	*12 (0.1)*
Not reported	*47 (0.5)*
Classify the recipient's prescribed preparative regimen - no. (%)	
Myeloablative	4141 (42.5)
Non-myeloablative (NST)	1359 (14.0)
Reduced intensity (RIC)	3773 (38.7)
Not myeloablative, either NST or RIC (02Core)	452 (4.6)
Not reported	14 (0.1)
GVHD prophylaxis - no. (%)	
None	140 (1.4)
PtCy + other(s)	3566 (36.6)
PtCy alone	76 (0.8)
TAC + MMF +- other(s) (except PtCy)	898 (9.2)
TAC + MTX +- other(s) (except MMF, PtCy)	3761 (38.6)
TAC + other(s) (except MMF, MTX, PtCy)	615 (6.3)
TAC alone	88 (0.9)
CSA + MMF +- other(s) (except PtCy,TAC)	314 (3.2)
CSA + MTX +- other(s) (except PtCy,TAC,MMF)	190 (2.0)
CSA + other(s) (except PtCy,TAC,MMF,MTX)	2 (0.0)

Characteristic	
CSA alone	5 (0.1)
Other(s)	84 (0.9)
TBI use - no. (%)	
Yes	3437 (35.3)
No	6302 (64.7)
Donor / Recipient CMV-antibodies - no. (%)	
D+/R+	3334 (34.2)
D+/R-	1092 (11.2)
D-/R+	2866 (29.4)
D-/R-	2447 (25.1)
Donor CMV-antibodies (IgG or Total) - no. (%)	
Negative	5313 (54.6)
Positive	4426 (45.4)
Recipient CMV-antibodies (IgG or Total) - no. (%)	
Negative	3539 (36.3)
Positive	6200 (63.7)
Year of current transplant - no. (%)	
2012	390 (4.0)
2013	788 (8.1)
2014	1050 (10.8)
2015	1055 (10.8)
2016	977 (10.0)
2017	915 (9.4)
2018	949 (9.7)
2019	857 (8.8)
2020	595 (6.1)
2021	608 (6.2)
2022	470 (4.8)
2023	495 (5.1)
2024	590 (6.1)
Follow-up of survivors, months - median (range)	71.7 (1.5-149.7)
Infection related	
CMV within 100 days post-transplant - no. (%)	
Yes	1190 (12.2)
No	8549 (87.8)
CMV within 1-year post-transplant - no. (%)	
Yes	2395 (25)
No	7344 (75)

Field	Response
Proposal Number	2509-117-BEALE
Proposal Title	Retrospective study of the impact of mammalian target of rapamycin inhibitors (mTORi) in the incidence of virus-associated complications after allogeneic hematopoietic cell transplantation (HCT)
Key Words	mTOR inhibitors, Human herpesviruses, CMV infection/disease, EBV, PTLD, HHV6, BK virus-associated hemorrhagic cystitis
Principal Investigator #1: - First and last name, degree(s)	Peter Beale, MD
Principal Investigator #1: - Email address	peter.a.beale.mil@health.mil
Principal Investigator #1: - Institution name	Walter Reed National Military Medical Center
Principal Investigator #1: - Academic rank	Fellow
Junior investigator status (defined as 㑊、5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Kamil Rechache
Principal Investigator #2 (If applicable): - Email address:)	Kamil.Rechache@medstar.net
Principal Investigator #2 (If applicable): - Institution name:	MedStar Georgetown University Hospital
Principal Investigator #2 (If applicable): - Academic rank:	Assistant Professor
Junior investigator status (defined as 㑊、5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	Yes
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	Peter Beale
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	Dr. Rechache has an ongoing CIBMTR study with Dr. Hamadani: A retrospective review at transplant outcomes for T cell lymphoma subtypes
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Infection and Immune Reconstitution
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	Yes

Field	Response
If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:	Anna Huppler
RESEARCH QUESTION:	Do mTORi reduce risk for viral infections compared with CNI-based regimens following allo-SCT w/ PTCy based therapy?
RESEARCH HYPOTHESIS:	Graft-versus-host disease (GVHD) prophylaxis regimens containing mTORi may be associated with lower incidence of viral infection, reactivation, and disease in the first year post-HCT. While PTCy may be associated with increased risk of viral events, such as CMV infection, choice of adjunct agents in PTCy-based regimens (mTORi vs CNI) may modulate this risk.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Estimate the cumulative incidences of herpesvirus complications (human cytomegalovirus (CMV) infection, CMV disease, EBV-posttransplantation lymphoproliferative disorder (PTLD), and human herpesvirus 6 (HHV6) encephalitis), and BK virus-associated hemorrhagic cystitis at 100 days and through 1 year post-HCT, comparing outcomes between mTORi-containing vs non-mTORi-containing GVHD regimens If numbers allow, perform additional sub-group analyses: Evaluate these outcomes for mTORi-containing regimens vs non-mTORi-containing regimens among those HCTs that are post-transplantation cyclophosphamide (PTCy)-based Evaluate these outcomes for mTORi-containing regimens vs non-mTORi-containing regimens among those HCTs that are proximal serotherapy-based Compare NRM, OS, and GVHD rates at 1 year between mTORi-containing approaches and non-mTORi-containing approaches Evaluate cofactors related to differences in the incidence of viral complications, including conditioning intensity (NMA/RIC vs MAC), donor and recipient serostatus (for CMV and EBV), graft source (PBSC vs BM)

SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	The results from this study could help identify the relative impact of mTORi, increasingly included in GVHD prophylaxis strategies, in virus-associated complications post-HCT. This could provide registry-based clinical data to further evaluate the findings of smaller studies that indicate that mTORi may be associated with fewer CMV-related post-HCT complications and to then provide the impetus to better understand this finding on a pre-clinical, mechanistic level. In addition, there is an active question in the field of if PTCy may negate or modulate the protection seemingly afforded by mTORi. Given CIBMTR working committee project that demonstrated that PTCy-based approaches are associated with higher rates of CMV infection, higher rates of non-CMV herpesvirus infection (namely HHV6 reactivation), and CRVIs,1-3 a better understanding of the roles that the adjunct immunosuppressants have in viral control will help the field further understand how to optimize PTCy-based platforms and ameliorate the potential for control and prevention of virus-associated HCT complications. While these 3 recent CIBMTR studies showing higher viral infectious complications with PTCy might suggest that PTCy is an inferior approach to HCT, the benefits and superior HCT outcomes that PTCy affords cannot be disregarded. Thus, these recent CIBMTR data motivate further evaluation of these virus-associated complications as they relate to HCT platform approaches to continue to improve upon HCT platforms and associated outcomes. Regarding CMV, approval of letermovir in 2017 will allow for post-approval data collection to determine incidence of infection or disease while controlling for prophylactic use when comparing mTORi- vs. CNI-containing regimens. This proposal was first presented as a herpesvirus-specific proposal 2019 (1810-10) and there was significant interest. On assessment of patient numbers, this was feasible with regard to the number of patients receiving GVHD prophylaxis with sirolimus and those receiving pharmacologic GVHD prophylaxis without sirolimus. There were data on CMV infection, EBV infection, HHV6 infection. However, while the proposal scored well, only one proposal could move forward and this was not selected. We were encouraged at that time to re-submit the proposal in 1-2 years, which we did in 2020 (PROP 2010-71), but the prioritization at that time was COVID19, with limited resources in the

Field	Response
	Working Committee for non-COVID19 related questions so the proposal was not accepted for consideration due to relative scientific impact compared to other proposals. In the last year, there have been 3 major publications related to viral infectious complications by CIBMTR, all showing increased infections with PTCy-based approaches (IN17-01a-c).1-3

SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.	In the solid organ transplant setting, mTORi-based regimens have been associated with lower rates of CMV infection and disease, although this effect does not seem to be related to inhibition of viral replication.4-9 In renal transplant recipients, the addition of an mTORi to a reduced-dose of calcineurin inhibitor (CNI) was associated with lower rates of CMV infection compared to regular dose CNI-based approaches.10-12 However, this has been less studied in HCT patients where CMV, as well as other herpesvirus complications, are of concern in the early period post-HCT. Thus, the effect, if real, is likely indirect and related to modulation of the cellular immune system. If due to this indirect effect, even viruses that cause diseases post-HCT through mechanisms unrelated to viral replication, such as EBV and the latent viral proliferation that gives rise to EBV-PTLD, may be lower in the setting of mTORi-containing approaches to GVHD prophylaxis. Indeed, there are pre-clinical data to suggest that mTORi may have anti-tumor activity against gammaherpesviruses, EBV and HHV8.13,14 However, there is a paucity of clinical data with regard to mTORi and EBV control and some reviews suggest that mTORi may not protect against EBV.15 In prior CIBMTR analyses of CMV-associated complications post-HCT, the role of mTORi was not evaluated.3,16,17 We recently published the CMV-related infection and disease outcomes across a broad range of transplant approaches at the National Institutes of Health (NIH).18 In that study, we found that the cumulative incidence of CMV infection was significantly higher for HCT recipients whose GVHD prophylaxis was CNI-based, as compared to those with CNI+mTORi-based approaches. We acknowledge that there have been randomized trials that have shown no difference in CMV infection rates between CNI/methotrexate-based regimens and CNI/mTORi-based regimens.19,20 Additionally, submitted as an abstract to the TCT 2019 conference, we have evaluated the rates of EBV-related issues post-HCT across the range of HCT approaches at the NIH.21 We have found that in the NIH cohort of 356 HCT recipients, mTORi-containing regimens were associated with lower incidence of EBV elevations in the blood and less EBV-directed pre-emptive therapy. Among PTCy-based approaches, EBV detection was higher for those receiving CNIs as adjunctive GVHD prophylaxis, as compared to mTORi adjunctive

	therapy. However, the numbers were overall small in these single-institution analyses, fueling interest in evaluating these same questions in a larger cohort. Since this proposal has been submitted previously, we have benefited from review, feedback, and recommendations. Herein, we submit our justification for the proposed study objectives and inclusion criteria. One recommendation was to focus on CMV only, as the data are most robust there. While this is certainly a reasonable suggestion, we would like to still propose that CMV, EBV, BKV, and HHV6 are examined here, as details of all of these infections are available since July 2017 and, before that time, there are data on organism and site of infection. Thus, the specific disease entities that we aim to evaluate (CMV infection, CMV disease, EBV disease, EBV-PTLD, BK virus-associated hemorrhagic cystitis, HHV6 encephalitis) are entities that should be captured and are different/distinct from data related to virus detection in blood of no clinical significance. Given the rarity of events and the limitation in data, as well as the potential for both primary and reactivation events post-HCT, we do propose to not look at adenovirus-related disease events. For the proposed viruses, the data should be present both in form 2150 after July 2017 and before. While BK virus-associated hemorrhagic cystitis was not captured as an entity until July 2017 on 2150, in our pre-submission discussion with Dr. Riches and the WC, it is felt that the incidence of BK virus-associated hemorrhagic cystitis could be extracted to cover the entire proposed study period, using data on form 2100 for events prior to July 2017. Another recommendation was to limit the transplant indications to AML/ALL/MDS. However, in delving further into this recommendation, this is primarily (understandably) recommended if outcomes of interest are relapse and TRM. We do not propose to focus on outcomes such as relapse that would be tied more specifically to underlying disease. Rather, virus-associated events and outcomes should largely not be tied to HCT indication. While our initial proposal did aim to include patients transplanted for any indication, to study a more homogeneous population, we have revised this submission to include only patients transplanted for a hematologic malignancy, as patients transplanted for non-malignant diseases may truly have a different baseline risk of viral complications of HCT inherent to their underlying disease process and

Field	Response
	pre-HCT state (such as in primary immunodeficiency diseases). It was recommended that the study timeframe be moved to more recent times, so we have shifted the proposed dates of study to evaluate patients in the post-letermovir era, from 2017 to 2024.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion criteria: Patients undergoing first allo HCT for any hematologic malignancy between January 2017 to December 2024. Exclusion criteria: UCB graft recipients, ex vivo T-cell depleted grafts, approaches that included planned post-HCT donor lymphocyte infusions. VIII. Data Requirements Supplemental data collection will not be required CIBMTR data will not need to be combined with data from another group Collection forms: 2000 Recipient Baseline Data; 2006 HCT Infusion; 2004 Infectious Disease Markers; 2400 Pre-TED; 2402 Pre-TED Disease Classification; 2450 Post-TED; 2100 Post-HSCT Data; 2900 Recipient Death Data; 2150 CMV/EBV/ADV/HHV6/BK
Does this study include pediatric patients?	Yes

Field	Response
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Outline any supplementary data required.	Supplemental data collection will not be required CIBMTR data will not need to be combined with data from another group Collection forms: 2000 Recipient Baseline Data; 2006 HCT Infusion; 2004 Infectious Disease Markers; 2400 Pre-TED; 2402 Pre-TED Disease Classification; 2450 Post-TED; 2100 Post-HSCT Data; 2900 Recipient Death Data; 2150 CMV/EBV/ADV/HHV6/BK Patient/disease characteristic variables: sex (male/female); age at HCT; Karnofsky performance status (>90% vs <90%); HCT-CI; disease; malignancy Graft characteristic variables: donor age; donor-recipient sex (female into male vs other); degree of HLA match and relatedness (MUD vs MRD vs haplo); CMV IgG serostatus (donor, recipient); EBV IgG serostatus (donor, recipient); source of stem cells (bone marrow vs. peripheral blood) Center effect: use of PTCy-based regimens, use of prophylactic letermovir for CMV + recipients may vary from center to center. Transplantation regimen variables: year of transplant; conditioning: myeloablative vs. reduced intensity/nonmyeloablative; PTCy with mTOR inhibitor vs. PTCy with CNI; pre-HCT rituximab administration; GVHD prophylaxis (mTORi-containing vs non-mTORi-containing); post-HCT rituximab administration Viral Infection variables: time from transplant to infection, organ involved, type of infection Post-HCT event variables: time to graft failure, onset of grade 2-4 acute GVHD, onset of chronic GVHD, mortality, cause of death Desired outcome variables: Cumulative incidence of CMV infection, CMV disease, EBV-PTLD, BK virus-associated hemorrhagic cystitis, and HHV6-encephalitis with death as a competing risk, evaluated at 100-days post-HCT for CMV infection, BK virus-associated HC, and HHV6 encephalitis and at 1 year post-HCT for CMV disease, and EBV-PTLD OS at 100-days and 1 year: defined as the time to death; surviving patients censored at last follow-up NRM at 100-days and 1 year: defined as the time to death without evidence of disease presence; with relapse/progressive disease as a competing risk Cause of death Grades II-IV aGVHD incidence, grades III-IV aGVHD incidence, with graft failure, relapse, donor lymphocyte infusion, chronic GVHD, and death as competing risks cGVHD incidence (any, as well as limited vs. extensive and mild vs. moderate vs. severe), with graft failure, relapse, donor lymphocyte infusion, and death as competing risks

Field	Response
Types of cellular therapy data this proposal includes:	Hematopoietic Cell Transplantation (HCT)
PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis speci	N/A
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	N/A
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	N/A
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	N/A

REFERENCES:	1. Singh A, Dandoy CE, Chen M, et al. Post-Transplant cyclophosphamide is associated with increase in Non-CMV Herpesvirus infections in Acute leukemia and MDS patients. Transplant Cell Ther 2021. DOI: 10.1016/j.jtct.2021.09.015. 2. Taplitz R, Maziarz RT, Mulroney C, et al. Incidence and Impact of Community Respiratory Viral Infection (CRV) in Haploidentical and Matched Sibling Donors Receiving Post-Transplant Cyclophosphamide (PTCy): A CIBMTR Analysis. Biol Blood Marrow Tr 2020;26(3):S71-S72. (In English) (<Go to ISI>://WOS:000516887900095). 3. Goldsmith SR, Abid MB, Auletta JJ, et al. Posttransplant cyclophosphamide is associated with increased cytomegalovirus infection: a CIBMTR analysis. Blood 2021;137(23):3291-3305. (In English). DOI: 10.1182/blood.2020009362. 4. Ritta M, Costa C, Solidoro P, et al. Everolimus-based immunosuppressive regimens in lung transplant recipients: impact on CMV infection. Antiviral Res 2015;113:19-26. DOI: 10.1016/j.antiviral.2014.10.016. 5. Radtke J, Dietze N, Spetzler VN, et al. Fewer cytomegalovirus complications after kidney transplantation by de novo use of mTOR inhibitors in comparison to mycophenolic acid. Transpl Infect Dis 2016;18(1):79-88. DOI: 10.1111/tid.12494. 6. Havenith SH, Yong SL, van Donselaar-van der Pant KA, van Lier RA, ten Berge IJ, Bemelman FJ. Everolimus-treated renal transplant recipients have a more robust CMV-specific CD8+ T-cell response compared with cyclosporine- or mycophenolate-treated patients. Transplantation 2013;95(1):184-91. DOI: 10.1097/TP.0b013e318276a1ef. 7. Nashan B, Gaston R, Emery V, et al. Review of cytomegalovirus infection findings with mammalian target of rapamycin inhibitor-based immunosuppressive therapy in de novo renal transplant recipients. Transplantation 2012;93(11):1075-85. DOI: 10.1097/TP.0b013e31824810e6. 8. Jennings DL, Lange N, Shullo M, et al. Outcomes associated with mammalian target of rapamycin (mTOR) inhibitors in heart transplant recipients: A meta-analysis. Int J Cardiol 2018;265:71-76. DOI: 10.1016/j.ijcard.2018.03.111. 9. Devresse A, Leruez-Ville M, Scemla A, et al. Reduction in late onset cytomegalovirus primary disease after discontinuation of antiviral prophylaxis in kidney transplant recipients

treated with de novo everolimus. Transpl Infect Dis 2018;20(2):e12846. DOI: 10.1111/tid.12846.

10. Mallat SG, Tanios BY, Itani HS, et al. CMV and BKPyV Infections in Renal Transplant Recipients Receiving an mTOR Inhibitor-Based Regimen Versus a CNI-Based Regimen: A Systematic Review and Meta-Analysis of Randomized, Controlled Trials. Clin J Am Soc Nephrol 2017;12(8):1321-1336. DOI: 10.2215/CJN.13221216. 11. Hiramitsu T, Okada M,
Futamura K, et al. 5-year follow-up of a randomized clinical study comparing everolimus plus reduced-dose cyclosporine with mycophenolate mofetil plus standard-dose cyclosporine in de novo kidney transplantation: Retrospective single center assessment. Int Immunopharmacol 2016;39:192-198. DOI: 10.1016/j.intimp.2016.07.019. 12. Hocker B, Zencke S, Pape L, et al. Impact of Everolimus and Low-Dose Cyclosporin on Cytomegalovirus Replication and Disease in Pediatric Renal Transplantation. Am J Transplant 2016;16(3):921-9. DOI: 10.1111/ajt.13649.

13. Cen O, Longnecker R. Rapamycin reverses splenomegaly and inhibits tumor development in a transgenic model of Epstein-Barr virus-related Burkitt's lymphoma. Mol Cancer Ther 2011;10(4):679-86. DOI: 10.1158/1535-7163.MCT-10-0833. 14. Holtan SG, Porrata LF, Colgan JP, Zent CS, Habermann TM, Markovic SN. mTOR inhibitor monotherapy is insufficient to suppress viremia and disease progression in Epstein-Barr virus-driven lymphoproliferative disorders (EBV-LPD). Am J Hematol 2008;83(8):688-9. DOI: 10.1002/ajh.21216.

15. Pascual J, Royuela A, Fernandez AM, et al. Role of mTOR inhibitors for the control of viral infection in solid organ transplant recipients. Transpl Infect Dis 2016;18(6):819-831. DOI: 10.1111/tid.12601.

16. Teira P, Battiwalla M, Ramanathan M, et al. Early cytomegalovirus reactivation remains associated with increased transplant-related mortality in the current era: a CIBMTR analysis. Blood 2016;127(20):2427-38. DOI: 10.1182/blood-2015-11-679639. 17. Ramanathan
M, Teira P, Battiwalla M, et al. Impact of early CMV reactivation in cord blood stem cell recipients in the current era. Bone Marrow Transplant 2016;51(8):1113-20. DOI: 10.1038/bmt.2016.89.

18. Melendez-Munoz R, Marchalik R, Jerussi T, et al.
Cytomegalovirus Infection Incidence and Risk Factors

Field	Response
	Across Diverse Hematopoietic Cell Transplantation Platforms Using a Standardized Monitoring and Treatment Approach: A Comprehensive Evaluation from a Single Institution. Biol Blood Marrow Transplant 2019;25(3):577-586. DOI: 10.1016/j.bbmt.2018.10.011. 19. Torlen J, Ringden O, Garming-Legert K, et al. A prospective randomized trial comparing cyclosporine/methotrexate and tacrolimus/sirolimus as graft-versus-host disease prophylaxis after allogeneic hematopoietic stem cell transplantation. Haematologica 2016;101(11):1417-1425. DOI: 10.3324/haematol.2016.149294. 20. Cutler C, Logan B, Nakamura R, et al. Tacrolimus/sirolimus vs tacrolimus/methotrexate as GVHD prophylaxis after matched, related donor allogeneic HCT. Blood 2014;124(8):1372-7. DOI: 10.1182/blood-2014-04-567164. 21. Hellewell EM, Skeffington LR, Kenyon MI, et al. Incidence of Epstein-Barr Virus (EBV) Detection in the Blood, Pre-Emptive Therapy, and EBV-Posttransplantation Lymphoproliferative Disorder (EBV-PTLD) after Allogeneic Hematopoietic Cell Transplantation (HCT) across a Broad Range of HCT Approaches and All Graft Sources. Biol Blood Marrow Tr 2019;25(3) (In English) (<Go to ISI>://WOS:000540655500537).
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	No, I do not have any conflicts of interest pertinent to this proposal

PROP2509-117 Retrospective study of the impact of mammalian target of rapamycin inhibitors (mTORi) in the incidence of virus-associated complications after allogeneic hematopoietic cell transplantation (HCT)

Characteristics of U.S. patients who underwent their first allogeneic transplant between 2017 and 2024 for a hematologic malignancy.

Characteristic	Sirolimus	CNI	Other drug	No or missing drug
Number of patients	413	9757	172	295
No. of centers	48	164	52	62
Patient related				
Age by deciles - no. (%)				
Median (min-max)	64.0 (3.2-82.2)	60.9 (0.6-82.7)	57.8 (19.9-76.0)	63.8 (10.6-78.9)
0-<18	3 (0.7)	422 (4.3)	0 (0.0)	4 (1.4)
18-29	29 (7.0)	666 (6.8)	7 (4.1)	14 (4.7)
30-39	27 (6.5)	628 (6.4)	18 (10.5)	17 (5.8)
40-49	37 (9.0)	976 (10.0)	29 (16.9)	31 (10.5)
50-59	69 (16.7)	1922 (19.7)	41 (23.8)	39 (13.2)
60-69	154 (37.3)	3819 (39.1)	59 (34.3)	134 (45.4)
70+	94 (22.8)	1324 (13.6)	18 (10.5)	56 (19.0)
Sex - no. (%)				
male	237 (57.4)	5766 (59.1)	107 (62.2)	164 (55.6)
female	176 (42.6)	3991 (40.9)	65 (37.8)	131 (44.4)
Karnofsky score prior to HCT - no. (%)				
90-100	212 (51.3)	4868 (49.9)	79 (45.9)	171 (58.0)
80	109 (26.4)	2989 (30.6)	59 (34.3)	88 (29.8)
< 80	90 (21.8)	1772 (18.2)	34 (19.8)	35 (11.9)
Not reported	2 (0.5)	128 (1.3)	0 (0.0)	1 (0.3)
Race - no. (%)				
White	312 (75.5)	7740 (79.3)	144 (83.7)	249 (84.4)
Black or African American	55 (13.3)	929 (9.5)	7 (4.1)	15 (5.1)
Asian	16 (3.9)	485 (5.0)	8 (4.7)	16 (5.4)
Native Hawaiian or other Pacific Islander	1 (0.2)	33 (0.3)	0 (0.0)	0 (0.0)
American Indian or Alaska Native	3 (0.7)	62 (0.6)	2 (1.2)	1 (0.3)
More than one race	3 (0.7)	104 (1.1)	0 (0.0)	0 (0.0)
Not reported	23 (5.6)	404 (4.1)	11 (6.4)	14 (4.7)
Ethnicity - no. (%)				
Hispanic or Latino	51 (12.3)	1027 (10.5)	13 (7.6)	20 (6.8)
Not Hispanic or Latino	345 (83.5)	8440 (86.5)	154 (89.5)	260 (88.1)
NA, not a US resident	5 (1.2)	47 (0.5)	1 (0.6)	1 (0.3)

Characteristic	Sirolimus	CNI	Other drug	No or missing drug
Not reported	12 (2.9)	243 (2.5)	4 (2.3)	14 (4.7)
Disease related				
Primary disease - no. (%)				
AML or ANLL	137 (33.2)	2703 (27.7)	57 (33.1)	65 (22.0)
ALL	37 (9.0)	1108 (11.4)	25 (14.5)	26 (8.8)
Other Leukemia	5 (1.2)	141 (1.4)	1 (0.6)	2 (0.7)
CML	4 (1.0)	165 (1.7)	3 (1.7)	3 (1.0)
MDS	88 (21.3)	2138 (21.9)	37 (21.5)	51 (17.3)
Acute Leukemia	5 (1.2)	82 (0.8)	0 (0.0)	5 (1.7)
NHL	34 (8.2)	598 (6.1)	4 (2.3)	27 (9.2)
HD	24 (5.8)	438 (4.5)	8 (4.7)	15 (5.1)
Plasma cell disorder	5 (1.2)	138 (1.4)	2 (1.2)	11 (3.7)
Myeloproliferative neoplasms	74 (17.9)	2246 (23.0)	35 (20.3)	90 (30.5)
Transplant related				
Stem cell source - no. (%)				
Bone Marrow	97 (23.5)	1316 (13.5)	64 (37.2)	10 (3.4)
Peripheral Blood	316 (76.5)	8427 (86.4)	108 (62.8)	284 (96.3)
Cord Blood	0 (0.0)	14 (0.1)	0 (0.0)	0 (0.0)
Missing or Other	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Donor type - no. (%)				
HLA-identical sibling	20 (4.8)	1643 (16.8)	33 (19.2)	23 (7.8)
Twin	0 (0.0)	3 (0.0)	1 (0.6)	39 (13.2)
1 Ag/allele	6 (1.5)	85 (0.9)	0 (0.0)	3 (1.0)
>=2 Ag/allele	102 (24.7)	2123 (21.8)	14 (8.1)	40 (13.6)
Other related(matching TBD)	7 (1.7)	152 (1.6)	5 (2.9)	0 (0.0)
Well-matched unrelated (8/8)	121 (29.3)	4227 (43.3)	98 (57.0)	130 (44.1)
Partially-matched unrelated (7/8)	102 (24.7)	1115 (11.4)	14 (8.1)	42 (14.2)
Mis-matched unrelated (<=6/8)	39 (9.4)	116 (1.2)	3 (1.7)	4 (1.4)
Multi-donor	5 (1.2)	53 (0.5)	1 (0.6)	3 (1.0)
Unrelated (matching TBD)	11 (2.7)	226 (2.3)	3 (1.7)	11 (3.7)
Cord blood	0 (0.0)	14 (0.1)	0 (0.0)	0 (0.0)
Classify the recipient's prescribed preparative regimen - no. (%)				
Myeloablative	86 (20.8)	3728 (38.2)	90 (52.3)	90 (30.5)
Non-myeloablative (NST)	70 (16.9)	1375 (14.1)	14 (8.1)	35 (11.9)
Reduced intensity (RIC)	255 (61.7)	4642 (47.6)	68 (39.5)	169 (57.3)
Not reported	2 (0.5)	12 (0.1)	0 (0.0)	1 (0.3)
Rituximab (Rituxan, anti CD20) - no. (%)				

Characteristic	Sirolimus	CNI	Other drug	No or missing drug
No	1 (0.2)	86 (0.9)	0 (0.0)	0 (0.0)
Yes	0 (0.0)	44 (0.5)	0 (0.0)	4 (1.4)
Not reported	190 (46.0)	4673 (47.9)	104 (60.5)	54 (18.3)
Not selected	222 (53.8)	4954 (50.8)	68 (39.5)	237 (80.3)
GVHD prophylaxis - no. (%)				
Post-CY + other(s)	383 (92.7)	4562 (46.8)	25 (14.5)	0 (0.0)
Post-CY alone	0 (0.0)	0 (0.0)	76 (44.2)	0 (0.0)
CNI (TAC/CSA) + MMF +/- Other(except post-CY)	0 (0.0)	1067 (10.9)	0 (0.0)	0 (0.0)
CNI (TAC/CSA) + MTX +/- Other(except MMF, post-CY)	0 (0.0)	3863 (39.6)	0 (0.0)	0 (0.0)
CNI (TAC/CSA) +/- Other (except MMF, MTX, post-CY)	0 (0.0)	35 (0.4)	0 (0.0)	0 (0.0)
TAC alone	0 (0.0)	225 (2.3)	0 (0.0)	0 (0.0)
CSA alone	0 (0.0)	4 (0.0)	0 (0.0)	0 (0.0)
Others	30 (7.3)	1 (0.0)	71 (41.3)	0 (0.0)
Missing	0 (0.0)	0 (0.0)	0 (0.0)	295 (100)
Cyclophosphamide (Cytoxan) used post-prep for acute GVHD prevention - no. (%)				
Yes	383 (92.7)	4562 (46.8)	101 (58.7)	0 (0.0)
Not reported	0 (0.0)	0 (0.0)	0 (0.0)	5 (1.7)
Not selected	30 (7.3)	5195 (53.2)	71 (41.3)	290 (98.3)
Sirolimus / Tacrolimus / Cyclosporine - no. (%)				
Cyclosporine (CSA, Neoral, Sandimmune)	0 (0.0)	415 (4.3)	0 (0.0)	0 (0.0)
Sirolimus (Rapamycin, Rapamune)	413 (100)	0 (0.0)	0 (0.0)	0 (0.0)
Tacrolimus (Prograf)	0 (0.0)	9282 (95.1)	0 (0.0)	0 (0.0)
Tacrolimus (Prograf) + Cyclosporine (CSA, Neoral, Sandimmune)	0 (0.0)	60 (0.6)	0 (0.0)	0 (0.0)
None specified	0 (0.0)	0 (0.0)	172 (100)	295 (100)
Donor / Recipient CMV-antibodies - no. (%)				
D+/R+	133 (32.2)	3296 (33.8)	58 (33.7)	83 (28.1)
D+/R-	56 (13.6)	1144 (11.7)	21 (12.2)	41 (13.9)
D-/R+	86 (20.8)	2701 (27.7)	45 (26.2)	69 (23.4)
D-/R-	135 (32.7)	2581 (26.5)	48 (27.9)	101 (34.2)
Not reported	3 (0.7)	35 (0.4)	0 (0.0)	1 (0.3)
Donor CMV-antibodies (IgG or Total) - no. (%)				
Negative(Non-reactive)	221 (53.5)	5295 (54.3)	93 (54.1)	170 (57.6)
Positive(Reactive)	191 (46.2)	4452 (45.6)	79 (45.9)	124 (42.0)
Not reported	1 (0.2)	10 (0.1)	0 (0.0)	1 (0.3)

Characteristic	Sirolimus	CNI	Other drug	No or missing drug
Recipient CMV-antibodies (IgG or Total) - no. (%)				
Negative(Non-reactive)	191 (46.2)	3729 (38.2)	69 (40.1)	142 (48.1)
Positive(Reactive)	220 (53.3)	6003 (61.5)	103 (59.9)	153 (51.9)
Not done or Not tested or NA to release HIV(5/95)	0 (0.0)	13 (0.1)	0 (0.0)	0 (0.0)
Indeterminant	1 (0.2)	9 (0.1)	0 (0.0)	0 (0.0)
Not reported	1 (0.2)	3 (0.0)	0 (0.0)	0 (0.0)
Year of current transplant - no. (%)				
2017	57 (13.8)	1572 (16.1)	58 (33.7)	21 (7.1)
2018	62 (15.0)	1622 (16.6)	32 (18.6)	23 (7.8)
2019	63 (15.3)	1582 (16.2)	16 (9.3)	10 (3.4)
2020	35 (8.5)	1010 (10.4)	15 (8.7)	57 (19.3)
2021	36 (8.7)	1010 (10.4)	12 (7.0)	51 (17.3)
2022	58 (14.0)	858 (8.8)	20 (11.6)	38 (12.9)
2023	50 (12.1)	966 (9.9)	11 (6.4)	44 (14.9)
2024	52 (12.6)	1137 (11.7)	8 (4.7)	51 (17.3)
Infection related				
Was letermovir (Prevymis) given as prophylaxis? - no. (%)				
No	119 (28.8)	2057 (21.1)	30 (17.4)	134 (45.4)
Yes	73 (17.7)	1960 (20.1)	24 (14.0)	38 (12.9)
Not reported	2 (0.5)	225 (2.3)	0 (0.0)	8 (2.7)
Other antiviral prophylaxis	219 (53.0)	5515 (56.5)	118 (68.6)	115 (39.0)
CMV infection by 100 days post-transplant - no. (%)				
No	358 (86.7)	8213 (84.2)	153 (89.0)	276 (93.6)
Yes	55 (13.3)	1544 (15.8)	19 (11.0)	19 (6.4)
CMV infection by 1-year post-transplant - no. (%)				
No	341 (82.6)	7734 (79.3)	147 (85.5)	271 (91.9)
Yes	72 (17.4)	2023 (20.7)	25 (14.5)	24 (8.1)
Follow-up of survivors, months - median (range)	39.6 (3.2-96.3)	48.6 (0.8-101.1)	61.6 (3.0-97.1)	36.2 (2.8-99.8)

Field	Response
Proposal Number	2509-148-CLARA
Proposal Title	Impact of Early Natural Killer Cell Reconstitution on Relapse and Survival after Allogeneic HCT in the PTCy Era
Key Words	Natural killer cells (NK), CD56, Immune reconstitution, Post-transplant cyclophosphamide (PTCy), Absolute lymphocyte count (ALC), High-risk AML, Relapse, Overall survival (OS), Day +100
Principal Investigator #1: - First and last name, degree(s)	Joseph Clara, MD
Principal Investigator #1: - Email address	rtt8dw@uvahealth.org
Principal Investigator #1: - Institution name	University of Virginia
Principal Investigator #1: - Academic rank	Assistant Professor
Junior investigator status (defined as 㑊、5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	No current ongoing work with CIBMTR
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Infection and Immune Reconstitution
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	No
RESEARCH QUESTION:	Does early natural killer (NK) cell recovery (CD56+ NK absolute count at day +100 and kinetics where available) independently predict relapse, non-relapse mortality (NRM), and overall survival (OS) after allogeneic hematopoietic cell transplantation (HCT) in patients receiving post-transplant cyclophosphamide (PTCy)? Secondary questions examine whether NK recovery modifies the effect of high-risk AML features on relapse, and how peri-transplant exposures (e.g., ATG, conditioning intensity, donor type, graft source, G-CSF) influence NK kinetics.

Field	Response
RESEARCH HYPOTHESIS:	1. Early NK cell recovery, measured as CD56+ NK absolute counts at day +100, is independently associated with reduced relapse incidence and improved OS in patients receiving PTCy. 2. Patients with inadequate NK recovery (and/or impaired NK kinetics between day +30 and day +100) will have higher relapse and worse post-relapse survival, especially among patients with high-risk AML. 3. Peri-transplant exposures including ATG, conditioning intensity, donor type, graft source, and peri-transplant G-CSF meaningfully modify NK recovery, and thereby indirectly influence relapse, NRM, and OS.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary Objective (NK-focused): Assess the association between CD56+ NK absolute count at day +100 and cumulative incidence of relapse (primary) and OS (co-primary) in adult allogeneic HCT recipients who received PTCy. Co-primary Objective (ALC-focused): Evaluate absolute lymphocyte count (ALC) at day +30 and day +100 as an additional immune metric and complementary analysis. This will ensure broad feasibility across the registry cohort and provide validation for NK-specific findings. Secondary Objectives: 1. Evaluate the change in NK cell counts from day +30 to day +100 and determine how these kinetics relate to infections, GVHD, NRM, and post-relapse survival. 2. Test whether the effect of NK recovery differs by high-risk AML status, defined by molecular, cytogenetic, or clinical features. 3. Determine the effect of peri-transplant exposures (e.g., ATG use, conditioning intensity, donor type, graft source, peri-transplant G-CSF) on NK and lymphocyte recovery and downstream outcomes. 4. Assess the association between NK recovery at day +30 and day +100 and viral reactivation, particularly CMV, within the first 100 days post-transplant. Exploratory Aims: Describe center-level heterogeneity in NK and lymphocyte reporting, and evaluate whether predictive value is consistent across centers and transplant eras. Examine NK subset phenotypes, including CD56^bright versus CD56^dim, and their potential associations with relapse, survival, GVHD, and viral reactivation where data are available.

Field	Response
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	Novelty: Although ALC and general immune reconstitution have been studied at scale, systematic registry-level analyses of NK-specific recovery in the contemporary PTCy era remain limited. Clinical relevance: NK cells are early mediators of graft-versus-leukemia (GVL), but their numbers and functional maturation may be delayed or altered in the PTCy era, and their independent association with relapse and survival remains undefined. Demonstrating an independent link between NK recovery and relapse or OS would inform risk-adapted post-transplant monitoring, prioritization for post-transplant maintenance or cellular therapies, and donor/prophylaxis choice for high-risk AML. Registry-level feasibility is supported by prior CIBMTR Working Committee reports documenting CD56+/NK subset data at day +100 for over 5,000 allogeneic HCT recipients, enabling adequately powered analyses. Translational value: Findings will provide a registry-scale rationale for prospective NK-directed interventions (e.g., NK adoptive transfer, immune-modulating approaches) and a foundation for mechanistic and translational investigations, including the role of NK recovery in viral control and NK subset function. These results will help guide the design of future NK-directed or immune-based interventions in early-phase clinical trials, supporting hypothesis-driven studies to improve outcomes post-HCT.

Field	Response
SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.	Background evidence: Prior multicenter and single-center studies have established that delayed overall immune reconstitution after allogeneic HCT is associated with increased infection risk and higher mortality (Bejanyan et al., 2018). Single-center studies have also suggested that early NK cell recovery may reduce relapse and viral reactivation, providing mechanistic support for the importance of NK reconstitution (Minculescu et al., 2016). PTCy can alter NK cell recovery kinetics, potentially delaying both numerical and functional reconstitution (Meyer et al., 2025). While prior studies demonstrate these effects at the institutional level, large-scale, multicenter analyses linking CD56+ NK cell recovery at day +100 to relapse and OS across diverse transplant settings remain limited (Rambaldi et al., 2021; Zhao et al., 2022). Furthermore, the broader immunologic and clinical implications of NK recovery including viral control and GVL effects have been highlighted in recent reviews (Hadjis & McCurdy, 2024), reinforcing the need for a registry-level analysis. Registry feasibility: Previous Working Committee reports document CD56+/NK subset data at day +100 for ~5,600 allogeneic HCT patients, demonstrating NK data exist at scale for registry analysis. This supports an NK-centric analysis with ALC as a robust complementary measure. Gap & justification: Given the mechanistic role of NK cells in early GVL and the contemporary widespread use of PTCy, a registry-level study testing NK recovery as an independent predictor of relapse and survival in PTCy recipients and its interaction with high-risk AML features fills a clear knowledge gap and has direct clinical implications.

Field	Response
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion Criteria: Adult patients (18 years) undergoing first allogeneic HCT for hematologic malignancy (primary focus: AML) reported to CIBMTR during the PTCy era (2015 2024). Received PTCy-based GVHD prophylaxis for the index transplant. Recorded CD56+/NK absolute count at day +100 (primary NK cohort). Availability of core outcome data (relapse date, survival, GVHD, infection by day +100). Exclusion Criteria: Prior allogeneic HCT. Missing core outcome data (relapse or survival) or missing key covariates. Umbilical cord blood recipients only if NK data capture is inconsistent; otherwise include as exploratory.
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	Pediatric patients are excluded due to differences in NK cell reconstitution kinetics, conditioning regimens, graft sources, and post-transplant outcomes, which would introduce heterogeneity and confound analyses focused on adult PTCy recipients.

Field	Response
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Outline any supplementary data required.	Patient/Disease Variables: Age, sex, diagnosis (AML primary focus; ALL/MDS allowed for exploratory analysis). Disease status at HCT: o CR1 (morphologic complete remission, MRD-negative) o CR1 MRD-positive o CR2 (MRD-negative or MRD-positive where available) o Active disease (morphologic evidence of leukemia) High-risk AML status (composite variable): o Molecular: TP53 mutation, FLT3-ITD (other mutations if captured) o Cytogenetic: complex or monosomal karyotype o Clinical: treatment-related AML, advanced disease status beyond CR2 Performance status, HCT-CI, CMV serostatus Donor/Transplant Variables: Donor type (matched sibling, MUD, 7/8 MMUD, haplo), graft source (PBSC vs BM), conditioning intensity (MAC vs RIC/NMA). In vivo T-cell depletion (ATG/alemtuzumab; dose if available), PTCy dosing schedule, peri-transplant G-CSF. Immune Variables: Primary: Absolute CD56+ NK cell count (cells/µL) in peripheral blood at day +100. Secondary: ALC at day +30 and day +100. Day +30 CD56+ NK cell count if available. NK subset phenotypes (if reported). Exploratory: NK subset phenotypes (CD56^bright vs CD56^dim) where reported. Functional assays (e.g., CD16 expression, cytotoxicity) if captured, acknowledging these are likely rare. Outcome Variables: Relapse (date), OS (date of death), NRM. Acute GVHD (grade), chronic GVHD (presence/severity). Infection events by day +100 (bacterial, viral, fungal). Optional secondary endpoint: CMV reactivation by day +100, if available, to capture NK-mediated antiviral effects. Post-relapse survival.
Types of cellular therapy data this proposal includes:	Hematopoietic Cell Transplantation (HCT)
PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis speci	No PROs required.

Field	Response
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	No machine-learning methods required.
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	No biologic specimens requested from the CIBMTR Repository.
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	No external data linkage planned.
REFERENCES:	1. Bejanyan N, Brunstein CG, Cao Q, et al. Delayed immune reconstitution after allogeneic transplantation increases the risks of mortality and chronic GVHD. Blood Adv. 2018;2(8):909 922. 2. Minculescu L, et al. Early natural killer cell reconstitution predicts overall survival in T cell replete allogeneic hematopoietic stem cell transplantation. Biol Blood Marrow Transplant. 2016;22(9):1682-1690. doi:10.1016/j.bbmt.2016.05.016. 3. Meyer, T., et al. (2025). Immune reconstitution dynamics after unrelated allogeneic hematopoietic stem cell transplantation with post-transplantation cyclophosphamide. Nature Communications, 10(1), 2478 4. Rambaldi A, et al. Impaired T- and NK-cell reconstitution after haploidentical HCT with PTCy. Blood Adv. 2021;5(2):352 365. 5. Zhao L, et al. Post-transplant cyclophosphamide alters immune signatures and leads to impaired T cell reconstitution. Front Immunol. 2022;13:879012. 6. Hadjis, A. D., & McCurdy, S. R. (2024). The role and novel use of natural killer cells in graft-versus-leukemia. Frontiers in Immunology, 15, 1358668.
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	No, I do not have any conflicts of interest pertinent to this proposal

PROP2509-148 Impact of Early Natural Killer Cell Reconstitution on Relapse and Survival after Allogeneic HCT in the PTCy Era

Characteristics of U.S. adult patients underwent first allo transplant for AML/ALL/MDS between 2015 to 2024

Characteristic	NK cell data available	NK cell data not available
Number of patients	614	3208
No. of centers	48	121
Patient related		
Age by deciles - no. (%)		
Median (min-max)	60.2 (19.2-87.8)	61.8 (18.0-82.2)
18-29	73 (11.9)	261 (8.1)
30-39	43 (7.0)	243 (7.6)
40-49	76 (12.4)	328 (10.2)
50-59	114 (18.6)	591 (18.4)
60-69	208 (33.9)	1296 (40.4)
70+	100 (16.3)	489 (15.2)
Karnofsky score prior to HCT - no. (%)		
90-100	327 (53.3)	1522 (47.4)
80	176 (28.7)	1021 (31.8)
< 80	107 (17.4)	623 (19.4)
Not reported	4 (0.7)	42 (1.3)
Sex - no. (%)		
Male	341 (55.5)	1873 (58.4)
Female	273 (44.5)	1335 (41.6)
Race - no. (%)		
White	480 (78.2)	2410 (75.1)
Black or African American	81 (13.2)	372 (11.6)
Asian	21 (3.4)	207 (6.5)
Native Hawaiian or other Pacific Islander	1 (0.2)	14 (0.4)
American Indian or Alaska Native	1 (0.2)	25 (0.8)
More than one race	4 (0.7)	24 (0.7)
Not reported	26 (4.2)	156 (4.9)
Ethnicity - no. (%)		
Hispanic or Latino	87 (14.2)	405 (12.6)
Non-Hispanic or non-Latino	513 (83.6)	2714 (84.6)
Non-resident of the U.S.	2 (0.3)	20 (0.6)
Not reported	12 (2.0)	69 (2.2)
Disease related		

Characteristic	NK cell data available	NK cell data not available
Primary disease - no. (%)		
Acute myelogenous leukemia or ANLL	313 (51.0)	1660 (51.7)
Acute lymphoblastic leukemia	121 (19.7)	551 (17.2)
Myelodysplastic/myeloproliferative disorders (please classify all preleukemia)	180 (29.3)	997 (31.1)
Transplant related		
Stem cell source - no. (%)		
Bone Marrow	105 (17.1)	588 (18.3)
Peripheral Blood	509 (82.9)	2618 (81.6)
Cord Blood	0 (0.0)	2 (0.1)
Classify the recipient's prescribed preparative regimen - no. (%)		
Myeloablative	223 (36.3)	1154 (36.0)
Non-myeloablative (NST)	89 (14.5)	607 (18.9)
Reduced intensity (RIC)	298 (48.5)	1439 (44.9)
Not myeloablative, either NST or RIC (02Core)	1 (0.2)	2 (0.1)
Not reported	3 (0.5)	6 (0.2)
GVHD prophylaxis - no. (%)		
PtCy alone	17 (2.8)	61 (1.9)
PtCy + other(s)	597 (97.2)	3147 (98.1)
Year of current transplant - no. (%)		
2015	54 (8.8)	231 (7.2)
2016	46 (7.5)	304 (9.5)
2017	79 (12.9)	340 (10.6)
2018	65 (10.6)	457 (14.2)
2019	59 (9.6)	455 (14.2)
2020	38 (6.2)	278 (8.7)
2021	45 (7.3)	217 (6.8)
2022	43 (7.0)	240 (7.5)
2023	82 (13.4)	308 (9.6)
2024	103 (16.8)	378 (11.8)
Death within 1 year after transplant - no. (%)		
No	483 (78.7)	2243 (69.9)
Yes	131 (21.3)	965 (30.1)
Follow-up of survivors, months - median (range)	49.0 (3.2-120.4)	49.2 (2.3-123.2)