Not for publication or presentation

A G E N D A
CIBMTR WORKING COMMITTEE FOR INFECTION AND IMMUNE RECONSTITUTION
San Antonio, TX
Wednesday, February 21, 2024, 1:00 – 3:00 PM CST

Co-Chair:	**Roy Chemaly, MD, MPH, UT MD Anderson Cancer Center, Houston, TX; Telephone: 713-792-0007; E-mail: rfchemaly@mdanderson.org;**
Co-Chair:	**Christopher Dandoy, MD, MS, Cincinnati Children's Hospital Medical Center, Cincinnati, OH; Telephone: 513-803-7495; E-mail: christopher.dandoy@cchmc.org;**
Co-Chair:	**Joshua Hill, MD; Fred Hutchinson Cancer Center, Seattle, WA; E-mail: jahill3@fredhutch.org**
Scientific Director:	**Marcie Riches, MD, MS; CIBMTR Statistical Center, Milwaukee, WI; Telephone: 813-943-2800; E-mail: mlrichesmd@outlook.com**
Statistical Director:	**Michael Martens, PhD, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-955-8371; E-mail: mmartens@mcw.edu;**
Statistician:	**Qiran(Lexie) Ye, MPH, CIBMTR Statistical Center, Milwaukee, WI; E-mail: qye@mcw.edu**
WCTL Program Participant	**Zeinab El Boghdadly, Ohio State University, Columbus, OH; Email: Zeinab.ElBoghdadly@osumc.edu**

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1. **Introduction**

   a. Welcome and Introduction
   b. Minutes from February 2023 meeting (Attachment 1)

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

3. **Presentations, Published or Submitted papers**

   a. **1801a** Celalettin Ustun, Min Chen, Soyoung Kim, Jeffery J Auletta, Marjorie V Batist, Minoo Battiwalla, Jan Cerny, Lohith Gowda, Joshua A Hill, Hongtao Liu, Pashna N Munshi, Sunita Nathan, Matthew D Seftel, John R Wingard, Roy F Chemaly, Christopher E Dandoy, Miguel-Angel Perales, Marcie Riches, Genovefa A Papnicolaou, Post-transplantation cyclophosphamide is associated with increased bacterial infections. ***Bone Marrow Transplant, 2023, PMID: 37903992, doi.org:10.1038/s41409-023-02131-z.***
   b. **1801b** Genovefa A. Papanicolaou, Min Chen, Naya He, Michael J. Martens, Soyoung Kim, Marjorie V. Batista, Neel S. Bhatt, Peiman Hematti, Joshua A. Hill, Hongtao Liu, Sunita Nathan, Matthew D. Seftel, Akshay Sharma, Edmund K. Waller, John R. Wingard, Jo-Anne H. Young, Christopher E. Dandoy, Miguel-Angel Perales, Roy F. Chemaly, Marcie Riches, Celalettin Ustun, Incidence and Impact of Fungal Infections in Post-Transplantation Cyclophosphamide-Based Graft-versus-Host Disease Prophylaxis and Haploidentical Hematopoietic Cell Transplantation: A Center for International Blood and Marrow Transplant Research Analysis, ***Transplantation and Cellular Therapy, 2023, ISSN 2666-6367, doi.org:10.1016/j.jtct.2023.09.017.***

4. Studies in progress (Attachment 3)

a. **IN19-01** Immune recovery predicts post-transplant outcomes (MA Perales/ P Szabolcs): Tandem 2023 Abstract. **Manuscript preparation**.
b. **IN19-02** Impact of Antibiotic Prophylaxis in Patients Undergoing Allogeneic Hematopoietic Cell Transplantation in the Current Era (Z El Boghdadly/ C Dandoy/ P Badia Alonso). **Protocol development**.
c. **IN20-01** Infectious complications in patients with B-Lymphoid hematologic malignancy treated with CD19 chimeric antigen receptor T cell therapy (K Wudhikarn/ M McGhee/ J Hill/ M Herr). **Analysis**.
d. **CV20-04d** COVID-19 in Hematopoietic Cell Transplant Recipients- Outcomes early v late (R Chemaly/ MS Infante). **Protocol development**.
e. **IN22-01** Viral Hepatitis after allogeneic hematopoietic cell transplant using post-transplant cyclophosphamide for graft versus host disease prophylaxis (K Wudhikarn/ MA Perales). **Protocol development.**
f. **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). **Protocol development.**

5. Future/proposed studies

a. **PROP 2310-49** Infection and Immune Reconstitution Factors Associated with Poor Outcomes for Acute Invasive Fungal Sinusitis (L Roland/I Pusic) (Attachment 4)
b. **PROP 2310-52** Impact of Donor Stem Cell Graft Composition on Immune Reconstitution in Allogeneic Hematopoietic Cell Transplantation (H Murthy/N Farhadfar) (Attachment 5)
c. **PROP 2310-57** Impact Of Mycophenolate Mofetil And Cytomegalovirus Serostatus In Patients Undergoing HLA Matched Donor HCT (R Mehta/R Saliba) (Attachment 6)
d. **PROP 2310-75** Evaluating Infection Rates in Autologous Hematopoietic Stem Cell Transplants for Primary Solid Tumors and Lymphoma (J Koo/C Dandoy) (Attachment 7)
e. **PROP 2310-185** PBSC versus BM Grafts in AlloHSCT for Hematological Malignancies with PTCY-Based GVHD Prophylaxis: A Comparative Analysis (A Mina/S Pavletic) (Attachment 8)

Proposed studies; not accepted for consideration at this time

f. **PROP 2310-29** Infection and Immune Reconstitution Respiratory Syncytial Virus (RSV), Severe Acute Respiratory Syndrome Coronavirus 2 (Sars-CoV-2, Also Referred to as Covid-19), and Influenza (Flu) Virus Infections Occurring Among Patients as Eras in Vaccination Practice are Evolving. *Supplemental data needed.*
g. **PROP 2310-30** Viral Infections After CD19 and BCMA CAR T Cell Therapy. *Overlap with current study/publication.*
h. **PROP 2310-56** Incidence of Late Cytomegalovirus (CMV) reactivation in the Era of Post-transplant Cyclophosphamide (PtCY) in patients receiving Letermovir Prophylaxis. *Small sample size.*
i. **PROP 2310-207** Incidence, Risk factors, and Outcomes of Infections Following Anti-CD19 Directed CAR T-Cell Therapy in B-Cell Non-Hodgkin Lymphoma. *Overlap with current study/publication.*
j. **PROP 2310-241** A Comprehensive Analysis of Cytomegalovirus (CMV) Reactivation and its Impact on Outcomes After CAR-T Cell Therapy. *Overlap with current study/publication.*

k. **PROP 2310-248** Potential for Granulocyte-Colony Stimulating Factor in Preventing Infections in CAR-T Recipients without Worsening Immune-Related Toxicities. *Supplemental data needed.*
l. **PROP 2310-251** Impact of Corticosteroid Usage on the Risk of Infections in Patients Receiving CAR-T Therapy. *Overlap with current study/publication.*
m. **PROP 2310-254** Impact of Antibiotics on the Efficacy and Toxicity of Anti-CD19 CAR T Cell Therapy. *Supplemental data needed.*

6. Other business

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR INFECTION AND IMMUNE RECONSTITUTION
Orlando, FL
Wednesday, February 15, 2023, 1:00 PM – 3:00 PM (EST)

Co-Chair:	**Christopher Dandoy, MD, MS, Cincinnati Children's Hospital Medical Center, Cincinnati, OH; Telephone: 513-803-7495; E-mail: christopher.dandoy@cchmc.org;**
Co-Chair:	**Miguel-Angel Perales, MD, Memorial Sloan Kettering Cancer Center, New York, NY; Telephone: 212-639-8682; E-mail: peralesm@mskcc.org;**
Co-Chair:	**Roy Chemaly, MD, MPH, UT MD Anderson Cancer Center, Houston, TX; Telephone: 713-792-0007; E-mail: rfchemaly@mdanderson.org;**
Scientific Director:	**Marcie Riches, MD, MS; CIBMTR Statistical Center, Milwaukee, WI; Telephone: 813-943-2800; E-mail: mlrichesmd@outlook.com**
Statistical Directors:	**Michael Martens, PhD, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-955-8371; E-mail: mmartens@mcw.edu;**
Statistician:	**Naya He, MS, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-805-0685; E-mail: nhe@mcw.edu**

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1. **Introduction**
   a. **Welcome and introduction**
   b. **Minutes from February 2022 meeting** (Attachment 1)

   The meeting was called to order at 1pm by Dr. Marcie Riches. She introduced the current working committee leadership and reviewed the CIBMTR COI policy, described Working Committee Membership, goals, expectations, guidelines for voting, and rules of authorship. The two sources of HCT data (TED vs. CRF level) were introduced as well as cellular therapy data.

2. **Accrual Summary** (Attachment 2)
   Due to the full agenda, the accrual summary of registration and research cases between 2008 and 2019 were not presented to the committee but were available as part of the Working Committee attachments.

3. **Presentations, Published or Submitted Papers**
   Dr. Marcie Riches gave an update on study presentations, and manuscripts that were published or submitted within the last year.

a. **CV20-04b** Bhatt NS, Sharma A, St Martin A, Abid MB, Brown VI, Diaz Perez MA, Frangoul H, Gadalla SM, Herr MM, Krem MM, Lazarus HM, Martens MJ, Mehta PA, Nishihori T, Prestidge T, Pulsipher MA, Rangarajan HG, Williams KM, Winestone LE, Yin DE, Riches ML, Dandoy CE, Auletta JJ. Clinical Characteristics and Outcomes of COVID-19 in Pediatric and Early Adolescent and Young Adult Hematopoietic Stem Cell Transplant Recipients: A Cohort Study. ***Transplant Cell Ther. 2022 Oct; 28(10):696.e1-696.e7. doi: 10.1016/j.jtct.2022.06.026. Epub 2022 Jul 4. PMID: 35798233; PMCID: PMC9251957.***

b. **IN18-02** Muthalagu Ramanathan, Soyoung Kim, Naya He, Min Chen, Peiman Hematti, Muhammad Bilal Abid, Seth J. Rotz, Kirsten M. Williams, Hillard M. Lazarus, Baldeep Wirk, Dwight E. Yin, Christopher G. Kanakry, Miguel-Angel Perales, Roy F. Chemaly, Christopher E. Dandoy, Marcie Riches, Celalettin Ustun; The Incidence and Impact of Clostridioides Difficile Infection on Transplant Outcomes in Acute Leukemia and MDS after Allogeneic Hematopoietic Cell Transplant– A CIBMTR Study. ***Bone Marrow Transplant. 2022 Dec 21. doi: 10.1038/s41409-022-01896-z. Online ahead of print. PMID: 36543999.***

c. **IN19-01** Miguel-Angel Perales, Paul Szabolcs, Michael Martens, Naya He, Christopher Dandoy, Roy Chemaly, Marcie Riches. Delayed immune recovery after allogeneic hematopoietic cell transplantation is associated with decreased overall survival in adult but not pediatric recipients. ***Poster Presentation, 2023 Tandem Meetings.***

4. Studies in Progress (Attachment 3)

Dr. Marcie Riches briefly listed all studies in progress.

a. **IN18-01a** Comparison of early (by day 180) bacterial infections after haploidentical HSCT between patients receiving cyclophosphamide-based or other GVHD prophylaxis (Celalettin Ustun/Genovefa Papanicolaou): **Manuscript Preparation.**

b. **IN18-01b** Comparison of early (by day 180) fungal infections after haploidentical HSCT between patients receiving cyclophosphamide-based or other GVHD prophylaxis (Celalettin Ustun/Genovefa Papanicolaou): **Manuscript Preparation.**

c. **IN19-01** Immune recovery predicts post-transplant outcomes (Miguel-Angel Perales/ Paul Szabolcs): **Tandem 2023 Abstract, Manuscript Preparation.**

d. **IN19-02** Impact of Antibiotic Prophylaxis in Patients Undergoing Allogeneic Hematopoietic Cell Transplantation in the Current Era (Zeinab El Boghdadly/ Christopher Eugene Dandoy/ Priscila Badia Alonso): **Protocol Development.**

e. **IN20-01** Infectious complications in patients with B-Lymphoid hematologic malignancy treated with CD19 chimeric antigen receptor T cell therapy (Kitsada Wudhikarn/ Miranda McGhee/ Joshua A. Hill/ Megan Herr, etc): **Datafile Preparation.**

f. **CV20-04c** COVID-19 in Hematopoietic Cell Transplant Recipients-Race/Ethnicity (Abid, Gowda, Chemaly): **Protocol Development.**

h. **CV20-04d** COVID-19 in Hematopoietic Cell Transplant Recipients- Outcomes early v late (Chemaly,Infante): **Protocol Development.**

i. **CV20-04e** COVID-19 in CAR-T Recipients (G Shah, Politikos, Murthy, Hamandani, N Shah, Hossain, Stiff): **Protocol Development.**

5. Future/Proposed Studies

a. **PROP 2210-175** Influence of non-enterobacterales gram-negative bacilli bloodstream infections (BSIs) on hematopoietic cell transplantation (HCT) and cellular therapy outcomes (N Tran/ Z El Boghdadly) (Attachment 4)

Dr Boghdadly presented the proposal. The specific aims of this study are four-fold: 1) Determine the cumulative incidence and timing of non-Enterobacterales Gram negative bacilli BSIs within the first 100 days post-HCT and cellular therapy. 2) Identify risk factors within the first 100 days post HCT & cellular therapy. 3) Determine impact on transplant related outcomes (time to engraftment, overall survival, GVHD, etc.) 4) Compare clinical characteristics, risk factors, and post-HCT & cellular therapy outcomes between patients with no BSIs vs. Enterobacterales BSIs vs. non-Enterobacterales Gram negative bacilli BSIs cohort (if sample size allows).

Discussion:

1. Recommendations from the committee were to include the following:
    a. CAR-T population.
    b. Time to engraftment as one variable
2. Questioned about the management of patients with a BSI that is neither Enterobacterales BSIs nor non-Enterobacterales Gram negative bacilli. The recommendation was to include this group of patients as "Other BSI" so there will be four groups compared.
3. Concerns about timing of infection and whether the study would limit to only the transplant hospitalization or any infection through 100 days. The study will analyze BSI through day 100, particularly since not all patients are hospitalized for transplant.
4. Concerns about data:
    a. CIBMTR doesn't collect treatment data for bacterial infection.
    b. How much data that CIBMTR has for one year point. Will look at completeness of follow up to make sure have complete data through one year.

b. **PROP 2210-36; 2210-57; 2210-163; 2210-241** Infectious complications in patients with relapsed/refractory multiple myeloma receiving B-cell maturation antigen (BCMA) targeted chimeric antigen receptor (CAR) T cells (M B Abid/ Kitsada Wudhikarn/ M-A Perales/ S Mirza/ L Gowda/ S Devarakonda/ Y Efebera) (Attachment 5)

Dr Perales presented the proposal. The specific aims of this study are three-fold: 1. To describe the incidence, infection density, patterns and outcomes of infections in patients treated with BCMA CAR T-cell therapy. 2. To identify risk factors for infection in patients treated with BCMA CAR T-cell therapy. 3. To explore the impact of infectious complications on both short-term and long-term clinical outcomes following CAR T-cell therapy.

It was also pointed out that this proposal would essentially be an additional population to examine as the INWC is already looking at infectious complications in the lymphoma and ALL population (IN 20-01)

Discussion:

The WC has several suggestions including:

1. Incorporate IVIG use. The data have limitations as we only know if the patient received IVIG without information on IgG levels or the frequency of IVIG infusions.
2. Include number of hospitalizations. These data are not captured.

3. Consider a formal comparison between the lymphoma and the myeloma populations
4. Compare early infection vs later infection if there are sufficient patients.

Potential concerns raised during the disucssion:

1. No prophylaxis data collected on CAR-T forms.
2. Not all the centers reporting the clinical trial patients and only 50% of CAR-T patients being reported to the CIBMTR. Therefore, will need to examine center effect.
3. Will need to account for the effects of proteasome inhibitors and immunomodulatory agents on outcomes.

c. **PROP 2210-64** Epidemiology and risk factors associated with polyoma virus (BKV) viremia/viruria and/or BKV associated hemorrhagic cystitis (HC) in allogeneic Hematopoietic Cell Transplant (HCT) recipients (Z Shahid/ R Chemaly) (Attachment 6)

Dr Shahid presented the proposal. The specific aims of this study are six-fold: 1. To understand incidence of BKv associated HC, BK viremia and/or BK viuria in allogeneic HCT recipients including cord blood transplants. 2.To study the differences in epidemiology of BKV associated disease based on underlying malignancy, conditioning regimens and intensity, graft source, GvHD prophylaxis including post-transplant cyclophosphamide and presence of GvHD. 3.Identify risk factors associated with the development of BKv associated HC, BK viremia and BK viuria. 4.To study the impact of BK viremia and BK viuria on kidney function in the absence or presence of BKv associated HC. 5. To study the association of BKv disease with other viral reactivations in early and late post-transplant period for 1 year. 6.To study the impact of BKv associated disease on clinical outcomes including overall survival and non-relapse mortality at 1 year.

It was pointed out that there are more than 900 patients reported with BK who have a supplemental 2150 form providing more granular detail on the infection including viral loads and treatment.

Discussion:
Suggested additions to the proposal:

1. Examine TMA association with BK infection and renal dysfunction
2. Incorporate treatment in the analysis

Concerns raised by the committee:

1. IGG level and CD4 are captured on Day 100 and Day 180, but not at the other times of interest proposed in the study.
2. For kidney function, CIBMTR collects renal toxicity but won't have decline in creatinine.
3. Discordant surveillance at centers will limit the ability to detect a true incidence.

d. **PROP 2210-124** Impact of anti-fungal prophylaxis agent on the incidence of invasive fungal infections (IFI) among allogeneic transplant recipients (H Imlay/ S Patel) (Attachment 7)

Dr Imlay presented the proposal. The specific aims of this study are three-fold: 1. Compare the efficacy of specific antifungal prophylaxis agents (fluconazole, posaconazole, isavuconazole, voriconazole, echinocandin) on diagnosis of IFI, invasive Aspergillosis, and invasive non-

Aspergillosis mold infections among allogeneic HCT recipients. 2. Determine other risk factors associated with diagnosis of IFI, invasive mold infection (IMI), and invasive non-Aspergillus mold infection. 3. Determine the impact of IFI diagnosis and use of anti-mold prophylaxis on relapse, non-relapse mortality (NRM), acute and chronic graft-versus-host disease (GVHD), disease-free survival (DFS).

Discussion:
The committee suggested the following:

1. Adjusting for center effect due to the ascertainment bias with differential monitoring and the choice of prophylaxis may be driven by uncaptured data (i.e. marijuana use).
2. Consider excluding patients with pre HCT IFI

There are certain limitations on this analysis including

1. CIBMTR data only capture the first prophylaxis drug used and can't capture the drug switch.
2. Will not be able to include CAR-T patients as prophylaxis is not captured on the Cell Therapy forms.
3. CIBMTR prophylaxis data before 2017 are not analyzable due to how the data were collected.

There were some suggestions on how to improve reporting of prophylaxis.

e. **PROP 2210-188** The impact of donor source and graft-vs-host disease prophylaxis on the incidence of late viral infections after allogeneic hematopoietic cell transplantation (M B Abid/ Emily Baumrin/ Alison Loren) (Attachment 8)

Dr Loren presented the proposal. The specific aims of this study are three-fold: 1. To describe the types and incidence of late CMV and non-CMV viral infections in alloHCT pts. 2. Compare types and incidence of late CMV and non-CMV infections between donor types (MRD/MUD vs haploHCT) and GVHD prophylaxis (PTCy vs non-PTCy). 3. Compare the impact of late viral infections on transplant outcomes between donor types (MRD/MUD vs haploHCT) and GVHD prophylaxis (PTCy vs non-PTCy).

Discussion:

1. There are concerns with ensuring a comparison of pre-letermovir and post-letermovir by time frames as letermovir prophylaxis was not well captured and the forms have recently been revised to allow for this.
2. Recommendation to examine as a landmark analysis for patients alive at day 180.

f. **PROP 2210-244** Early Infectious Complications Associated with CART Cell Therapy Compared to Autologous Stem Cell Transplant in Lymphoma (F Khwaja/ S Ahmed) (Attachment 9)

Dr Khawaja presented the proposal. The specific aims of this study are four-fold: 1. To compare the rates of infections between non Hodgkin lymphoma (NHL) patients post

CAR T cell or autologous HCT within 100 days after cellular therapy. 2. Rates of specific infectious etiologies (viral, bacterial and fungal) and severity of infection. 3. Identify unique host or therapy related characteristics that increase the risk of viral, bacterial or fungal infections. 4. Comparison of clinical outcomes between patients with infections after CAR T cell therapy and after autologous HCT.

Discussion:
The committee had several recommendations:

1. The study should focus only on infections and not compare outcomes such as relapse.
2. The comparison should be auto no CAR-T vs CAR-T with no prior auto vs CAR-T with prior auto.

Potential limitations identified include:

1. CIBMTR doesn't collect the hospitalization of ICU level of care, only mortality information.
2. There are limited numbers of auto patients as the algorithm for CRF track has these patients at a lower priority.

Dropped Proposed Studies

a. **PROP 2208-01** Outcomes and Management of SARS-CoV2 Omicron Variant in Recipients of Hematopoietic Cell Transplantation (HCT) and CAR-T therapy. *Dropped due to overlap with current study/publication.*
b. **PROP 2209-11** Impact of Gastrointestinal Graft versus Host Disease on Infections occurring among patients with Steroid Sensitive, Steroid Dependent, and Steroid Resistant acute Graft versus Host Disease. *Dropped due to supplemental data needed.*
c. **PROP 2210-34** Impact of corticosteroid usage on the risk of infections in patients receiving CAR-T therapy. *Dropped due to supplemental data needed.*
d. **PROP 2210-37** Incidence of hypogammaglobulinemia following CD19-directed CAR-T therapy and its impact on CAR-T persistence and outcomes. *Dropped due to supplemental data needed.*
e. **PROP 2210-101** Reactivation of Chagas disease (CD) following autologous and allogeneic hematopoietic cell transplantation (HCT). A CIBMTR Analysis. *Dropped-small sample size.*
f. **PROP 2210-118** Characteristics of hypogammaglobulinemia after CAR T-cell therapy and effect of immunoglobulin replacement on infectious complications. *Dropped due to supplemental data needed.*
g. **PROP 2210-125** Incidence of CMV infection and disease in low-risk CMV serostatus (D+R-) allogeneic transplant recipients. *Dropped due to overlap with recent publications [IN1201, IN1701]*
h. **PROP 2210-154** Early platelet count recovery before white cell count recovery after allogeneic hematopoietic cell transplantation and effect on clinical outcome. *Dropped due to lower scientific priority.*
i. **PROP 2210-226** Impact of seasons and climates on outcomes of allogenic hematopoietic cell transplantation (HCT) in North America. *Dropped due to lower scientific priority.*
j. **PROP 2210-249** Incidence and Impact of Invasive Fungal Infection in Allogeneic Hematopoietic Stem Cell Transplant Recipients with FLT3-ITD-mutated Acute Myeloid Leukemia. *Dropped due to lower scientific priority.*

Working Committee Overview Plan for 2023-24		
Study number and title	**Current status**	**Chairs priority**
IN18-01a: Comparison of early (by day+100) viral infections between post transplantation cyclophosphamide and other graft-vs-host disease prophylaxis	Submitted	1
IN18-01b: Comparison of early (by day+100) bacterial infections between post transplantation cyclophosphamide and other graft-vs-host disease prophylaxis	Manuscript Preparation	1
IN19-01: Immune recovery predicts post-transplant outcomes	Manuscript Preparation	2
IN19-02: Impact of antibacterial prophylaxis on outcomes after allogeneic hematopoietic stem cell transplant	Protocol Development	4
IN20-01: Infectious complications after CAR.T Cell therapy	Data File Preparation	3
IN22-01 Viral Hepatitis after allogeneic hematopoietic cell transplant using post-transplant cyclophosphamide for graft versus host disease prophylaxis	Protocol Development	4
IN23-01 Infectious complications in patients with relapsed/refractory multiple myeloma receiving B-cell maturation antigen targeted chimeric antigen receptor T cells	Protocol Pending	3

Not for publication or presentation

Work Assignments for Working Committee Leadership (April 2023)	
Miguel-Angel Perales	**IN18-01a:** Comparison of early (by day+100) viral infections between post transplantation cyclophosphamide and other graft-vs-host disease prophylaxis **IN18-01b:** Comparison of early (by day+100) bacterial infections between post transplantation cyclophosphamide and other graft-vs-host disease prophylaxis
Chris Dandoy	**IN18-02:** Study the Incidence, and impact of C diff infection within 100 days on Transplant outcomes after allogeneic stem cell transplant (Muthalagu Ramanathan/ Bipin Savani) **IN20-01:** Infectious complications after CAR.T Cell therapy
Roy Chemaly	**IN19-01:** Immune recovery predicts post-transplant outcomes (Miguel-Angel Perales) **IN19-02:** Impact of antibacterial prophylaxis on outcomes after allogeneic hematopoietic stem cell transplant (C Dandoy/ P Alonso/ Z El Boghdadly)
Joshua Hill	**IN23-01:** Infectious complications in patients with relapsed/refractory multiple myeloma receiving B-cell maturation antigen targeted chimeric antigen receptor T cells

Accrual Summary for Infection and Immune Reconstitution Working Committee
Donor-recipient and Infection information reported to the CIBMTR after 2008

Variable	Allogeneic N(%)	Autologous N(%)
Number of Patients	32905	14843
Infection		
Donor/recipient CMV status		N/A
-/-	8332 (25)	
+/-	3217 (10)	
-/+	9879 (30)	
+/+	10793 (33)	
Missing/not tested	684 (2)	
Donor/recipient hepatitis B status		N/A
-/-	11169 (34)	
+/-	332 (1)	
-/+	3049 (9)	
+/+	281 (<1)	
-/?	221 (<1)	
+/?	7 (<1)	
?/-	13964 (42)	
?/+	3291 (10)	
Missing/not tested	591 (2)	
Donor/recipient hepatitis C status		N/A
-/-	18990 (58)	
+/-	95 (<1)	
-/+	200 (<1)	
+/+	9 (<1)	
-/?	120 (<1)	
+/?	1 (<1)	
?/-	11378 (35)	
?/+	135 (<1)	
Missing/not tested	1977 (6)	
Fungal Infection history		
No	30458 (93)	14699 (99)
Yes	2426 (7)	142 (<1)
Missing	21 (<1)	2 (<1)
Fungal Infection after starting of conditioning		
No	27472 (83)	14137 (95)
Yes	5429 (16)	706 (5)
Missing	4 (<1)	0
Infection prophylaxis after starting of conditioning		
No	397 (1)	248 (2)
Yes	32481 (99)	14584 (98)

Variable	Allogeneic N(%)	Autologous N(%)
Missing	27 (<1)	11 (<1)
Immune Reconstitution		
IgG at 100 day		
Data not available	11587 (35)	5501 (37)
Data available	21318 (65)	9342 (63)
IgM at 100 day		
Data not available	21831 (66)	6484 (44)
Data available	11074 (34)	8359 (56)
IgA at 100 day		
Data not available	21832 (66)	6417 (43)
Data available	11073 (34)	8426 (57)
CD3 at 100 day		
Lymphocyte analyses were not performed	18363 (56)	13370 (90)
Data not available	6100 (19)	706 (5)
Data available	8442 (26)	767 (5)
CD4 at 100 day		
Lymphocyte analyses were not performed	18363 (56)	13370 (90)
Data not available	6099 (19)	669 (5)
Data available	8443 (26)	804 (5)
CD8 at 100 day		
Lymphocyte analyses were not performed	18363 (56)	13370 (90)
Data not available	6329 (19)	730 (5)
Data available	8213 (25)	743 (5)
CD20 at 100 day		
Lymphocyte analyses were not performed	18363 (56)	13370 (90)
Data not available	12526 (38)	1343 (9)
Data available	2016 (6)	130 (<1)
CD56 at 100 day		
Lymphocyte analyses were not performed	18363 (56)	13370 (90)
Data not available	8898 (27)	1165 (8)
Data available	5644 (17)	308 (2)
Infection Prophylaxis		
Antibiotics		
No	8922 (27)	3609 (24)
Yes	23956 (73)	11223 (76)
Missing	27 (<1)	11 (<1)
Amoxicillin clavulanate oral (Augmentin)(after 2017)		
No	8605 (96)	4518 (96)
Yes	152 (2)	49 (1)
Missing	178 (2)	137 (3)
Cefdinir oral (Omnicef)(after 2017)		

Variable	Allogeneic N(%)	Autologous N(%)
No	8719 (98)	4515 (96)
Yes	38 (<1)	52 (1)
Missing	178 (2)	137 (3)
Cefpodoxime oral (Vantin)(after 2017)		
No	8719 (98)	4549 (97)
Yes	38 (<1)	18 (<1)
Missing	178 (2)	137 (3)
Ciprofloxacin IV or oral (Cipro)(after 2017)		
No	7236 (81)	3738 (79)
Yes	1521 (17)	829 (18)
Missing	178 (2)	137 (3)
Ertapenem IV(after 2017)		
No	8745 (98)	4560 (97)
Yes	12 (<1)	7 (<1)
Missing	178 (2)	137 (3)
Levofloxacin IV or oral (Levaquin)(after 2017)		
No	5419 (61)	1931 (41)
Yes	3338 (37)	2636 (56)
Missing	178 (2)	137 (3)
Moxifloxacin IV or oral (Avelox)(after 2017)		
No	8631 (97)	4508 (96)
Yes	126 (1)	59 (1)
Missing	178 (2)	137 (3)
Vancomycin IV(after 2017)		
No	8263 (92)	4386 (93)
Yes	494 (6)	181 (4)
Missing	178 (2)	137 (3)
Other antibacterial drug (after 2017)		
No	7120 (80)	3855 (82)
Yes	1637 (18)	712 (15)
Missing	178 (2)	137 (3)
Antifungal agent		
No	9525 (29)	6692 (45)
Yes	23353 (71)	8140 (55)
Missing	27 (<1)	11 (<1)
Amphotericin		
No	30780 (94)	14504 (98)
Yes	1785 (5)	89 (<1)
Missing	340 (1)	250 (2)
Caspofungin		
No	31041 (94)	14519 (98)

Variable	Allogeneic N(%)	Autologous N(%)
Yes	1524 (5)	74 (<1)
Missing	340 (1)	250 (2)
Fluconazole		
No	20070 (61)	6880 (46)
Yes	12495 (38)	7713 (52)
Missing	340 (1)	250 (2)
Itraconazole		
No	32102 (98)	14537 (98)
Yes	463 (1)	56 (<1)
Missing	340 (1)	250 (2)
Micafungin		
No	27739 (84)	14381 (97)
Yes	4826 (15)	212 (1)
Missing	340 (1)	250 (2)
Posaconazole		
No	28780 (87)	14543 (98)
Yes	3784 (11)	50 (<1)
Missing	341 (1)	250 (2)
Ravuconazole		
No	32542 (99)	14588 (98)
Yes	23 (<1)	5 (<1)
Missing	340 (1)	250 (2)
Voriconazole		
No	25629 (78)	14396 (97)
Yes	6936 (21)	197 (1)
Missing	340 (1)	250 (2)
Other systemic antifungal agent		
No	31826 (97)	14471 (97)
Yes	761 (2)	122 (<1)
Missing	318 (<1)	250 (2)
Antiviral agent		
No	4740 (14)	1598 (11)
Yes	28138 (86)	13234 (89)
Missing	27 (<1)	11 (<1)
Acyclovir		
No	9759 (30)	3512 (24)
Yes	22829 (69)	11081 (75)
Missing	317 (<1)	250 (2)
Foscarnet		
No	31878 (97)	14567 (98)
Yes	709 (2)	26 (<1)

Variable	Allogeneic N(%)	Autologous N(%)
Missing	318 (<1)	250 (2)
Ganciclovir		
No	30927 (94)	14554 (98)
Yes	1661 (5)	39 (<1)
Missing	317 (<1)	250 (2)
Valganciclovir		
No	30664 (93)	14475 (98)
Yes	1924 (6)	118 (<1)
Missing	317 (<1)	250 (2)
Valacyclovir		
No	25705 (78)	11655 (79)
Yes	6883 (21)	2938 (20)
Missing	317 (<1)	250 (2)
Other antiviral agent		
No	31722 (96)	14423 (97)
Yes	865 (3)	170 (1)
Missing	318 (<1)	250 (2)
Pneumocystis agent		
No	4331 (13)	5971 (40)
Yes	28547 (87)	8861 (60)
Missing	27 (<1)	11 (<1)
Other prophylaxis agent(Before 2017)		
No	19399 (81)	8281 (82)
Yes	2773 (12)	743 (7)
Missing	1798 (8)	1115 (11)
Disease		
Acute Leukemia/MDS	21570 (66)	183 (1)
Chronic Leukemia	924 (3)	0
Non-Hodgkin Lymphoma	1899 (6)	3377 (23)
Hodgkin Lymphoma	202 (<1)	1093 (7)
Solid tumors	24 (<1)	912 (6)
Myeloma/Plasma Cell Disorder	167 (<1)	9178 (62)
Non-malignant disorders	8119 (25)	100 (<1)
Year of transplant		
2008	3262 (10)	2195 (15)
2009	2998 (9)	931 (6)
2010	1860 (6)	414 (3)
2011	1345 (4)	497 (3)
2012	1436 (4)	537 (4)
2013	2669 (8)	1209 (8)
2014	3535 (11)	1296 (9)

Variable	Allogeneic N(%)	Autologous N(%)
2015	3536 (11)	1489 (10)
2016	3329 (10)	1571 (11)
2017	3121 (9)	1461 (10)
2018	3023 (9)	2069 (14)
2019	2791 (8)	1174 (8)

Footnote: Data reported later than April 2020 is not included in this table since data is not complete in the current retrieval.

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TO: Infection and Immune Reconstitution Working Committee Members

FROM: Marcie Riches, MD, MS, Scientific Director for the Infection and Immune Reconstitution Working Committee

RE: Studies in Progress Summary

Studies with Preliminary Results

IN19-01 [MA Perales/ P Szabolcs]

Delayed CD4+ T cell recovery after allogeneic hematopoietic cell transplantation is associated with decreased overall survival in adult but not pediatric recipients

Background: AlloHCT can provide curative treatment for hematologic malignancies but is associated with prolonged lymphopenia that may contribute to increased risk of infection and relapse, resulting in decreased survival. We hypothesized that patients (pts) with rapid and robust immune recovery would have improved survival and decreased non-relapse mortality.

Methods: 2089 pts who underwent 1st alloHCT for AML/ALL/MDS from 2008 to 2019 reported to CIBMTR with available CD4 counts at days 100 and 180 were included. Optimal cut points for CD4 were obtained using likelihood test based upon a drop in OS. Cox proportional hazards regression was used for each outcome from d100 and d180 landmark separately. Logistic regression was used to identify risk factors associated with high CD4 at d100 by using stepwise variable selection method with significance level 0.01.

Results: Pts (median age 51, range 2-75) were categorized into 4 groups based on GVHD prophylaxis: TCD/CD34 = 207, PTCY = 304, CNI = 1203, CNI+ATG = 375. Pts with TCD/CD34 had more MA conditioning (80%) vs PTCY (44%), CNI (70%), and CNI+ATG (60%)($p<0.01$), whereas PTCY pts were more likely to receive bone marrow graft (31%) vs TCD/CD34 (1%), CNI (15%) and CNI+ATG (16%)($p<0.01$). More pts in the CNI group received systemic steroids in the 1st 100 days (48%) vs 27% in TCD/CD34, 34% in PTCY, and 39% in CNI+ATG ($p<0.01$). Median CD4 count ($x10^6$/L) at d100 and d180 were lowest in TCD/CD34 group (82, 140, respectively) vs PTCY (135, 184), CNI (201, 246) and CNI+ATG (106, 143)(Fig. 1, $p<0.01$). IgA levels (mg/dL) at d100 were highest in the CNI+ATG (74) vs TCD/CD34 (49), PTCY (59) and CNI (59) groups ($p<0.01$). There were no significant differences in IgA level or infections between the 4 groups at d180. We identified different cut points based on OS in adult ($\geq$ 20y) and pediatric (< 20y) pts: d100 CD4 (10^6/L): 104 and 248, respectively; d180 CD4 115 and 420, respectively; d180 IgA (mg/dL) 114 and 29, respectively. In a d100 landmark model, factors that impacted achieving the CD4 cut point in adults were graft source (PB vs BM OR 1.66 $p=0.003$), GVHD prophylaxis (vs CNI: CNI+ATG OR 0.19, TCD/CD34 OR 0.16, PTCY OR 0.33; all $p<0.001$) and steroid use (OR 0.60; $p<0.001$). The results of the COX regression model for OS are in Fig. 2. Several factors, including CD4 recovery, impacted OS in adult but not pediatric pts. In adults, d100 CD4 was associated with PFS, TRM but not relapse, infections, or cGVHD. Similarly, CD4 above the cut point at

day 180 was associated with improved OS, PFS, and TRM but no other outcomes in adults. No associations were identified in pediatric pts for d100 or 180 CD4.

Conclusions: Delayed immune recovery post alloHCT in adult pts is influenced by graft source and GVHD prophylaxis and is associated with decreased OS, PFS, TRM but not relapse. A non-involuted thymus and higher graft T cell dose/kg in children likely explain improved immune recovery and lesser impact on outcomes.

Figure 1: CD4 recovery at days 100 and 180.

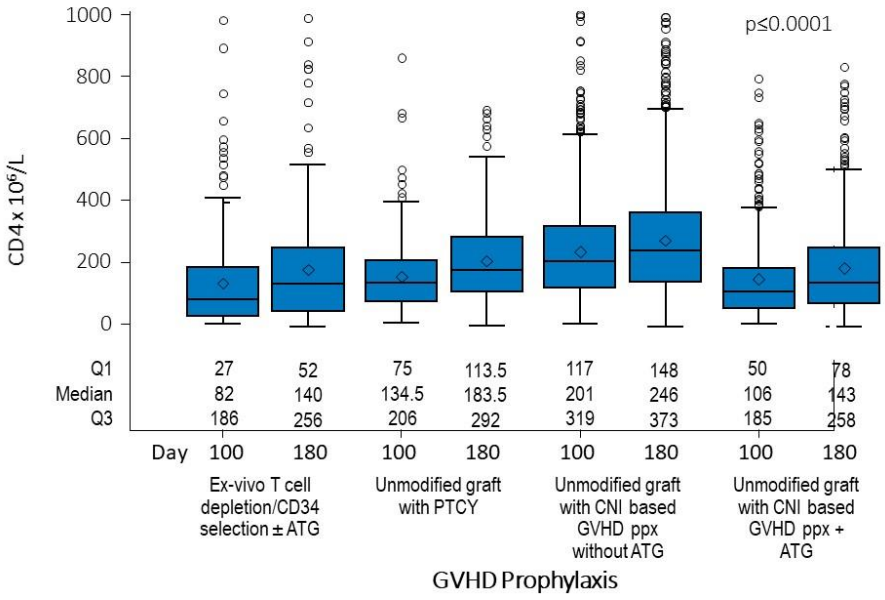

Figure 2. Cox Regression model for OS

Variable	Category	N	Events	Hazard Ratio	99% CI	p-value
Adult Patients						
CD4 Count at Day 100	< 104 x 10^6/L	529	205	1.000	-	0.001 (2 df)
	>= 104 x 10^6/L, within 12 months Post-TX	1101	386	0.595	(0.416, 0.853)	< 0.001
	>= 104 x 10^6/L, after 12 months Post-TX			1.031	(0.772, 1.376)	0.788
Patient Age (years)		1630		1.016	(1.008, 1.025)	< 0.001
Primary Disease	Acute Leukemia Early or Intermediate Stage	820	269	1.000	-	< 0.001 (3 df)
	Acute Leukemia Advanced Stage	170	79	1.697	(1.220, 2.362)	< 0.001
	Acute Leukemia Unknown Stage	26	14	1.552	(0.765, 3.151)	0.110
	MDS Any Stage	614	229	1.105	(0.865, 1.411)	0.295
Steroid Use	No	943	302	1.000	-	
	Yes	687	289	1.379	(1.114, 1.708)	< 0.001
Pediatric Patients						
CD4 Count at Day 100	< 248 x 10^6/L	316	61	1.000	-	
	>= 248 x 10^6/L	143	37	1.375	(0.802, 2.358)	0.128
Graft Source	Bone Marrow	131	25	1.000	-	< 0.001 (2 df)
	Peripheral Blood	70	27	2.400	(1.171, 4.919)	0.002
	Cord Blood	258	46	0.879	(0.462, 1.675)	0.608

Studies in Progress

IN18-01a Comparison of early (by day 180) bacterial infections after haploidentical HSCT between patients receiving cyclophosphamide-based or other GVHD prophylaxis (C Ustun/ G Papanicolaou) This study is under manuscript preparation. The goal of this study is to have the manuscript submitted by June 2023.

IN18-01b Comparison of early (by day 180) fungal infections after haploidentical HSCT between patients receiving cyclophosphamide-based or other GVHD prophylaxis (C Ustun/ G Papanicolaou) This study is under manuscript preparation. The goal of this study is to have the manuscript submitted by June 2023.

IN19-01 Immune recovery predicts post-transplant outcomes (MA Perales/ P Szabolcs)
The study is under analysis. The goal of this study is to have the manuscript submitted by June 2023.

IN19-02 Impact of Antibiotic Prophylaxis in Patients Undergoing Allogeneic Hematopoietic Cell Transplantation in the Current Era (Z El Boghdadly/ C Dandoy/ P Badia Alonso). The study protocol is under development.

IN20-01 Infectious complications in patients with B-Lymphoid hematologic malignancy treated with CD19 chimeric antigen receptor T cell therapy (K Wudhikarn/ M McGhee/ J Hill/ M Herr). The study is in datafile preparation phase.

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 protocol is under development.

COV20-04(c) COVID-19 in Hematopoietic Cell Transplant Recipients-Race/Ethnicity (MB Abid/ L Gowda/ R Chemaly). The study protocol is under development.

COV20-04(d) COVID-19 in Hematopoietic Cell Transplant Recipients- Outcomes early v late (R Chemaly/ MS Infante). The study protocol is under development.

COV20-04 (e) COVID-19 in CAR-T Recipients (G Shah/ L Politikos/ H Murthy/ M Hamandani/ N Shah/ N Hossain/ P Stiff): The study protocol is under development.

Field	Response
Proposal Number	2310-49-ROLAND
Proposal Title	Factors Associated with Poor Outcomes for Acute Invasive Fungal Sinusitis
Key Words	acute invasive fungal sinusitis, outcomes
Principal Investigator #1: - First and last name, degree(s)	Lauren Roland, MD, MSCI
Principal Investigator #1: - Email address	rolandl@wustl.edu
Principal Investigator #1: - Institution name	Washington University School of Medicine in St. Louis
Principal Investigator #1: - Academic rank	Assistant Professor
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Iskra Pusic, MD, MSCI
Principal Investigator #2 (If applicable): - Email address:)	iskrapusic@wustl.edu
Principal Investigator #2 (If applicable): - Institution name:	Washington University School of Medicine in St. Louis
Principal Investigator #2 (If applicable): - Academic rank:	Associate Professor
Junior investigator status (defined as ≤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:	Dr. Lauren Roland
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	None
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. Marcie Riches and Dr. Bronwen Shaw
RESEARCH QUESTION:	Our primary question is what factors are associated with the development of acute invasive fungal sinusitis (AIFS) and poor outcomes from AIFS after allogeneic hematopoietic cell transplantation (alloHCT).
RESEARCH HYPOTHESIS:	We expect patients who are older, have a longer ANC nadir, and more comorbidities to be more likely to develop AIFS and have worse outcomes.

Field	Response
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Our primary objective is to identify factors that are associated with poor outcomes for adults who develop AIFS after alloHCT. Our secondary objectives are to investigate factors associated with development of AIFS and changes in the incidence and geographical distribution of AIFS over time based on transplant recipient area of residence.
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	We know that factors like prolonged neutropenia and immunosuppression are risk factors for developing AIFS, so patients with these risk factors generally receive antifungal prophylaxis. However, we don't know much about the degree to which different risk factors affect prognosis or which antifungal prophylactic regimens are the most effective for preventing AIFS. Having a better understanding of risk factors for development of AIFS and their impact on prognosis will allow physicians to better counsel patients and their families. Additionally, learning more about which prophylactic regimens are most effective at preventing AIFS will help physicians choose the optimal treatment for patients who are at high risk for developing AIFS.

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.	A study conducted on over 3,000 bone marrow transplant (BMT) patients at our institution showed that around 1% of those who received alloHCT developed AIFS.1 Among those who received allografts, incidence of AIFS in patients with a history of multiple transplants and an intermediate HCT-CI score or higher was 4.2%, indicating that a combination of these factors increased risk of developing AIFS. Within the allograft bone marrow transplant population, patients diagnosed with AML who have longer ANC nadirs are also more likely to develop invasive fungal sinusitis.2 Other risk factors for development of IFS include graft-vs-host disease, delayed WBC engraftment, and lymphopenia.1 Most (66%) patients in Munyemana et al's study developed IFS within 30 days of transplant or between 100-230 days after transplant.1 Those who were in the latter group mostly had graft-versus-host disease. While these results are all from single-institution studies,1,2 we expect similar risk factors for development of AIFS in this multi-institutional database. AIFS is an aggressive infection characterized by fungal invasion of the nasal and sinus mucosa. It progresses rapidly and is often fatal, with one of the largest metanalyses showing mortality rates of around 50%.3 While it's agreed that early diagnosis is the most significant predictor of mortality,4 making the diagnosis can be challenging due to its rarity and nonspecific clinical presentation5 and often requires a combination of clinical suspicion through signs and symptoms, endoscopy and biopsy, imaging, culture, laboratory tests, and pathology.6 Although this disease almost exclusively affects immunocompromised patients such as those with hematologic malignancies or uncontrolled diabetes and is rare with incidence rates of around 2%,7 invasive fungal infections, including AIFS, are a growing problem.8 This is thought to be driven by widespread adoption of aggressive immunosuppressive therapy (e.g., chemotherapy, transplants), increasing use of invasive devices such as central venous catheters, and increase in diabetes.8 There have also been increased rates of AIFS in post-COVID patients, especially in those who already had other risk factors for developing rhinosinusitis.9 There have been some smaller single-institution studies exploring factors that impact prognoses for AIFS patients, but there haven't been any recent large-scale studies examining patient and disease characteristics that could lead to the development of the disease and worsened outcomes. Additionally, while there have been some studies looking at epidemiology and overall mortality in AIFS patients, little is known about how geographical distribution of the disease and fungal species involved have changed over time.

Field	Response
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	o Inclusion criteria: At least 18 years old Diagnosis of AML, ALL, Non-Hodgkin lymphoma, or MDS since these are strongly associated with development of AIFS based on the AIFS population at our institution Allogeneic HCT between 2018-2023 since antifungal prophylaxis data was not collected prior to 2018 Donors: HLA matched or mismatched related or unrelated, haploidentical related, single or double cord blood Any GvHD prophylaxis Pathology-proven fungal sinusitis in the first year after transplant o Exclusion criteria Alemtuzumab as a part of conditioning regimen
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	We conducted a similar study on adult bone marrow transplant patients at our institution and want to expand on our prior work in a larger database.

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.	o 2400 (Pre-Transplant Essential Data) Recipient info • Demographics (DOB, sex, ethnicity, race, country of primary residence, State/providence/territory of residence, zip) Comorbid conditions o 2402 (Disease classification) Primary disease for HCT and date of diagnosis Disease status at the time of transplant o 2000 (Baseline data) Smoking history Conditioning regimen • Myeloablative vs RIC/NMA • Y/N radiation, total dose (<800 vs >800) Fungal infection prior to HCT o 2006 (Hematopoietic Stem Cell Transplant Infusion) Date and type of transplant o 2100 (Post-HSCT Data) or 2450 (Post-transplant Essential Data) Granulopoiesis/neutrophil recovery Anti-thymocyte globulin Y/N GvHD prophylaxis Acute and chronic GvHD extent/severity and treatment Antifungal prophylaxis in peri-transplant period Fungal organism Infection site of fungal infection (sinus) o 2146 (Fungal Infection Post-Infusion Data) CIBMTR center Organism Date of diagnosis Radiographic finding: sinus imaging supports diagnosis of fungal infection? Pathology: sample from sinus supports diagnosis of fungal infection? Culture: sample from sinus supports diagnosis of fungal infection? KOH/calcofluor/giemsa stain: sample from sinus supports diagnosis of fungal infection? Galactomannan assay: sample from sinus supports diagnosis of fungal infection? 1,3-beta-D-glucan assay: sample from sinus supports diagnosis of fungal infection? PCR assay: sample from sinus supports diagnosis of fungal infection CBC closest to day of infection • Date • WBC • Neutrophils • Monocytes • Lymphocytes • Platelets • Cr • ALT

Field	Response
	All antifungals received by patient from 7 days prior to infection diagnosis until end of reporting period for the form Status of infection at end of reporting period (ongoing, improved, resolved, unknown) o 2900 Recipient Death Date, primary cause of death, contributing cause of death
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 desc	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 o	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

Field	Response
REFERENCES:	1. Munyemana MA, Pande A, Kallogjeri D, et al. Invasive fungal sinusitis risk factors among immunosuppressed hematopoietic stem cell transplant recipients. International Forum of Allergy & Rhinology. n/a(n/a). doi:10.1002/alr.23200 2. Chen CY, Sheng WH, Cheng A, et al. Invasive fungal sinusitis in patients with hematological malignancy: 15 years experience in a single university hospital in Taiwan. BMC Infect Dis. 2011;11(1):250. doi:10.1186/1471-2334-11-250 3. Turner JH, Soudry E, Nayak JV, Hwang PH. Survival outcomes in acute invasive fungal sinusitis: A systematic review and quantitative synthesis of published evidence. The Laryngoscope. 2013;123(5):1112-1118. doi:10.1002/LARY.23912 4. Piromchai P, Thanaviratananich S. Impact of Treatment Time on the Survival of Patients Suffering From Invasive Fungal Rhinosinusitis. Clinical Medicine Insights Ear, Nose and Throat. 2014;7:31-31. doi:10.4137/CMENT.S18875 5. Craig JR. Updates in management of acute invasive fungal rhinosinusitis. Current opinion in otolaryngology & head and neck surgery. 2019;27(1):29-36. doi:10.1097/MOO.0000000000000507 6. Roland LT, Humphreys IM, Le CH, et al. Diagnosis, Prognosticators, and Management of Acute Invasive Fungal Rhinosinusitis: Multidisciplinary Consensus Statement and Evidence-Based Review with Recommendations. International Forum of Allergy & Rhinology. 2023;13(9):1615-1714. doi:10.1002/alr.23132 7. Kennedy CA, Adams GL, Neglia JP, Giebink GS. Impact of surgical treatment on paranasal fungal infections in bone marrow transplant patients. Otolaryngology - Head and Neck Surgery. 1997;116(6):610-616. doi:10.1016/S0194-5998(97)70236-5 8. Enoch DA, Yang H, Aliyu SH, Micallef C. The changing epidemiology of invasive fungal infections. Methods in Molecular Biology. 2017;1508:17-65. doi:10.1007/978-1-4939-6515-1_2/TABLES/6 9. Ismaiel WF, Abdelazim MH, Eldsoky I, et al. The impact of COVID-19 outbreak on the incidence of acute invasive fungal rhinosinusitis. American Journal of Otolaryngology. 2021;42(6):103080-103080. doi:10.1016/J.AMJOTO.2021.103080
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

2310-49 Factors Associated with Poor Outcomes for Acute Invasive Fungal Sinusitis

Characteristics of Allo-HCT patients in 2018-2022 with AML/ALL/MDS/NHL, with Mold spp and infection sites in Sinus/Upper respiratory tract.

Characteristic	
Number of patients	38
No. of centers	28
Patient Characteristics	
Age at HCT - no. (%)	
0-9	2 (5.3)
10-19	3 (7.9)
20-29	2 (5.3)
30-39	2 (5.3)
40-49	5 (13.2)
50-59	6 (15.8)
60-69	12 (31.6)
70+	6 (15.8)
Region - no. (%)	
US	37 (97.4)
Europe	1 (2.6)
Disease characteristics	
Disease - no. (%)	
AML or ANLL	15 (39.5)
ALL	8 (21.1)
MDS	11 (28.9)
NHL	4 (10.5)
HCT related	
Donor type - no. (%)	
HLA-identical sibling	6 (15.8)
Other related	12 (31.6)
Well-matched unrelated (8/8)	11 (28.9)
Partially-matched unrelated (7/8)	2 (5.3)
Multi-donor	3 (7.9)
Cord blood	4 (10.5)
Product type - no. (%)	
Bone Marrow	7 (18.4)
Peripheral Blood	27 (71.1)
Umbilical Cord Blood	4 (10.5)
Year of HCT - no. (%)	
2018	17 (44.7)

Characteristic	
2019	11 (28.9)
2020	6 (15.8)
2021	3 (7.9)
2022	1 (2.6)
Organism - no. (%)	
Aspergillus spp	32 (84.2)
Zygomycetes	5 (13.2)
Scedosporium	1 (2.6)

** Antifungal prophylaxis is not completed in current retrival*

Field	Response
Proposal Number	2310-52-MURTHY
Proposal Title	Impact of Donor Stem Cell Graft Composition on Immune Reconstitution in Allogeneic Hematopoietic Cell Transplantation
Key Words	donor graft subsets of CD4+, CD8+ and cd56+ Immune Reconstitution in Allogeneic Hematopoietic Cell Transplantation
Principal Investigator #1: - First and last name, degree(s)	Hemant Murthy MD
Principal Investigator #1: - Email address	murthy.hemant@mayo.edu
Principal Investigator #1: - Institution name	Mayo Clinic Florida
Principal Investigator #1: - Academic rank	Associate Professor
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Nosha Farhadfar MD
Principal Investigator #2 (If applicable): - Email address:)	noshafarhadfar@yahoo.com
Principal Investigator #2 (If applicable): - Institution name:	SCRI-Methodist Hospical
Principal Investigator #2 (If applicable): - Academic rank:	Associate Professor
Junior investigator status (defined as ≤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:	Hemant Murthy
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	LK 20-03- Outcomes of HCT in T-ALL
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 donor graft composition influence allo-HCT outcomes
RESEARCH HYPOTHESIS:	Donor graft composition, defined as donor stem cell cd4+, cd8+ and cd56+ dose are predictive for immune recovery, rate of post-transplant infection and outcomes in allogeneic HCT recipients

Field	Response
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	- To determine the effect of donor graft subsets of CD4+, CD8+ and cd56+ on incidence of day 100 infection rate (viral, bacterial, fungal) - To determine the effect of donor graft subsets of CD4+, CD8+ and cd56+ on day 100 immune recovery of o Cd4+ o Cd8+ o Cd56+ - To determine the effect of donor graft subsets of CD4+, CD8+ and cd56+ on o Infection free survival o Non-relapse mortality o acute GVHD (II-IV and II-IV) o chronic GVHD o relapse/progression o Progression Free Survival o Overall Survival Primary outcomes: • Day 100 Immune recovery (cd4+, cd8+, cd56+) •Day 100 cumulative rate of infection Secondary Outcomes: •Day 100 cd56+ • Day 100 Absolute lymphocyte count o Median time to infection (any, bacterial, viral, fungal) o Incidence of bacterial infections by day 100 post -allo-HCT o Incidence of invasive fungal infections by day 100 post -allo-HCT o Incidence of viral reactivation/infection by day 100 post allo-HCT • Cumulative incidence of infections prior to engraftment (any, bacterial, viral, fungal) and following engraftment (any, bacterial, viral, fungal) • Infection free survival • Incidence of grade II-IV and grade III-IV acute and chronic GVHD •Cumulative incidence of Non-relapse mortality (NRM) • Disease relapse and/or progression • Progression-free survival (PFS) • Time to engraftment: Defined as time between day of transplantation and recovery of neutrophils (ANC>500/mm3 x3 days) and platelets (platelets > 20,000/mm3 unsupported by platelet transfusions). • GVHD free/relapse free survival (GFRS) •Primary graft failure (failure to achieve ANC>500/mm3 for three days or donor chimerism < 5%
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	very few studies have not investigated immune reconstitution as a primary endpoint nor have investigated graft composition influence on immune reconstitution.

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.	Allogeneic hematopoietic cell transplantation (Allo-hct) represents a curative therapy for many malignant and nonmalignant hematological disorders. Complications from allo-hct include relapse, graft versus host disease, and infection. Post-transplant immune recovery has been linked with allo-HCT outcomes(1) . Notably, delayed post allo-hct recovery of CD4+(1,2) can result in increased infection risk and transplant related mortality. T cell depletion of the stem cell graft has been utilized in an effort to decrease rates of graft-versus-host disease (GVHD). While effective in preventing acute GVHD, T cell depletion can adversely affect engraftment, immune reconstitution, and incidence of infections. Adequate donor cell dose and T cell composition of stem cell graft are recognized as important donor factors influencing the outcome of hematopoietic stem cell transplantation (HSCT. Reshef and colleagues showed that higher graft CD8+ T-cell dose was associated with improved survival due to a reduction in the risk for cancer relapse without a significant increase in graft-versus-host disease (3). This seems to be contradicted by Mothy and colleagues who in multivariable analysis showed CD8+ cell dose as significantly influencing risk of developing acute GVHD(4). A Large CIBMTR study investigated CD3+ T cell dose effect in allogeneic HLA-matched T-cell replete peripheral blood stem cell transplantation in patients between 2008 and 2014. CD3+ cell dose did not influence the risk of aGVHD or cGVHD or other transplantation outcomes when using an MSD or an 8/8-matched MUD. CD4+ and CD8+ did not influence transplant outcomes but sample size was reported as suboptimal. (5) What is less understood is the effect of the donor T cell subsets on immune reconstitution. Few studies have broached this subject. Higher CD4+ cell dose led to early recovery of absolute lymphocyte count (ALC) after allo-hct which was predictive of better OS, DFS, and lower rates of relapse, fungal infections and GVHD(6). Patel and colleagues reported observed trends suggesting an association of high CD8+ cell doses with faster recipient lymphocyte recovery and higher CD4+/ CD8+ ratio associated increased infection within the first 100 days after HCT (P = 0.014).(7) Another study revealed that higher CD8+ and cd56+ cell dose resulted in improved immune reconstitution and decreased NRM(8) Overall, studies have provided some conflicting results regarding impact of non-cd34+ content in allografts on allogeneic HCT outcomes. All have some limitation due to small samples sizes, and very few studies have not investigated immune reconstitution as a primary endpoint nor have

Field	Response
	investigated graft composition influence on immune reconstitution.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion Criteria: Patients who received their first allogeneic transplant from 2000-2020. Exclusion Criteria: Umbilical cord blood, graft recipients. T-cell depleted grafts GCSF stimulated bone marrow grafts Ex-vivo T-cell depletion, CD34+ selection Patients who required cryopreserved grafts due to ongoing infection will also need to be excluded. Exclude cases with missing data (conditioning intensity, cytogenetic, disease status) Haploidentical transplants without post-transplant cyclophosphamide will be excluded
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	would add too much heterogeneity to proposed question

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-related: • Age at transplant: continuous & by age group: decades • Patient sex: male vs. female • Karnofsky performance status at transplant: ≥ 90 vs. < 90 vs. missing • HCT comorbidity index at transplant: 0 vs 1-2 vs ≥ 3 vs. missing • Race: Caucasian vs. others vs. missing Disease-related: • Disease: AML, MDS, ALL, Lymphoma, Myeloma, non hematological malignancy, other • Disease state at time of transplant: CR1 vs CR2 vs PR vs SD vs PD • Time from diagnosis to HCT • Number of pre-transplant lines of therapy • BM involvement: (yes/no) • Cytogenetic abnormalities at diagnosis • Disease risk index: low vs. intermediate vs. high Transplant-related: • Cell source: bone marrow vs. peripheral blood • Transplant donor type: Match related donor vs. match unrelated donor vs. mismatch unrelated donor vs haploidentical donor • Conditioning intensity: myeloablative vs. reduced intensity conditioning/non-myeloablative • T-cell depletion: ATG/alemtuzumab (yes/no) • Total Body Irradiation: TBI vs non-TBI based conditioning regimen • Myeloablative: TBI vs non-TBI based conditioning regimen • RIC/NMA: TBI vs non-TBI based conditioning regimen • GVHD prophylaxis: CNI + MTX ± others except MMF, post Cy vs. CNI + MMF ±others except post Cy vs. CNI + others except MMF, MTX vs. missing vs. other • Donor-recipient sex match: male-male vs. male-female vs. female-male vs. female-female vs. missing • CMV serostatus matching (+/-, +/+, -/-, -/+) between donor and recipient • ABO compatibility: Minor vs Major

Field	Response
REFERENCES:	1. Bejanyan N, Brunstein CG, Cao Q, Lazaryan A, Luo X, Curtsinger J, et al. Delayed immune reconstitution after allogeneic transplantation increases the risks of mortality and chronic GVHD. Blood Adv. 2018 Apr 24;2(8):909–922. 2. Servais S, Lengline E, Porcher R, Carmagnat M, Peffault de Latour R, Robin M, et al. Long term Immune Reconstitution and infection burden after Mismatched Hematopoietic Stem Cell Transplantation. Biol Blood Marrow Transplant. 2014 Jan 6; 3. Reshef R, Huffman AP, Gao A, Luskin MR, Frey NV, Gill SI, et al. High Graft CD8 Cell Dose Predicts Improved Survival and Enables Better Donor Selection in Allogeneic Stem-Cell Transplantation With Reduced-Intensity Conditioning. J Clin Oncol. 2015 Jun 8;33(21):2392–2398. 4. Mohty M, Bagattini S, Chabannon C, Faucher C, Bardou V-J, Bilger K, et al. CD8+ T cell dose affects development of acute graft-vs-host disease following reduced-intensity conditioning allogeneic peripheral blood stem cell transplantation. Exp Hematol. 2004 Nov;32(11):1097–1102. 5. Saad A, Lamb L, Wang T, Hemmer MT, Spellman S, Couriel D, et al. Impact of T-cell dose on the outcome of T-cell replete HLA matched allogeneic peripheral blood stem cell transplantation. Biol Blood Marrow Transplant. 2019 May 11; 6. Kim DH, Kim JG, Sohn SK, Sung WJ, Suh JS, Lee KS, et al. Clinical impact of early absolute lymphocyte count after allogeneic stem cell transplantation. Br J Haematol. 2004 Apr 1;125(2):217–224. 7. Patel SS, Rybicki LA, Corrigan D, Dumont C, Bolwell B, Dean R, et al. Effect of bone marrow CD34+cells and T-cell subsets on clinical outcomes after myeloablative allogeneic hematopoietic cell transplantation. Bone Marrow Transplant. 2019 May;54(5):775–781. 8. Kim DH, Won DI, Lee NY, Sohn SK, Suh JS, Lee KB. Non-CD34+ cells, especially CD8+ cytotoxic T cells and CD56+ natural killer cells, rather than CD34 cells, predict early engraftment and better transplantation outcomes in patients with hematologic malignancies after allogeneic peripheral stem cell transplantation. Biol Blood Marrow Transplant. 2006 Jul 1;12(7):719–728.
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

2310-52 Impact of Donor Stem Cell Graft Composition on Immune Reconstitution in Allogeneic Hematopoietic Cell Transplantation

Table 1. Characteristic of First Allo Patients with CD4/CD8 between 2008 and 2020 reported to the CIBMTR

Characteristic	
Number of patients	748
No. of centers	43
Patient Characteristics	
Age at HCT - no. (%)	
0-9	43 (5.7)
10-19	49 (6.6)
20-29	70 (9.4)
30-39	46 (6.1)
40-49	65 (8.7)
50-59	160 (21.4)
60-69	235 (31.4)
70+	80 (10.7)
Region - no. (%)	
US	717 (95.9)
Europe	9 (1.2)
Asia	6 (0.8)
Australia/New Zealand	14 (1.9)
Central/South America	2 (0.3)
Disease characteristics	
Disease - no. (%)	
AML or ANLL	204 (27.3)
ALL	78 (10.4)
Other Leukemia	31 (4.1)
CML	14 (1.9)
MDS	186 (24.9)
Acute Leukemia	8 (1.1)
NHL	44 (5.9)
HD	1 (0.1)
Plasma cell disorder	9 (1.2)
Severe aplastic anemia	28 (3.7)
Inherited abnormal of erythrocyte differ.	50 (6.7)
Immune Deficiencies (ID)	9 (1.2)
Inherited platelet abn	1 (0.1)
Inherited disorders of metabolism	1 (0.1)

Characteristic	
Histiocytic disorder	5 (0.7)
Other Disease	1 (0.1)
Myeloproliferative neoplasms	78 (10.4)
HCT related	
Donor type - no. (%)	
HLA-identical sibling	187 (25.0)
Twin	5 (0.7)
Other related	163 (21.8)
Well-matched unrelated (8/8)	335 (44.8)
Partially matched unrelated (7/8)	35 (4.7)
Mis-matched unrelated (<= 6/8)	3 (0.4)
Multi-donor	2 (0.3)
Unrelated (matching TBD)	18 (2.4)
Product type - no. (%)	
BM	110 (14.7)
PB	638 (85.3)
Conditioning regimen intensity - no. (%)	
MAC	356 (47.6)
RIC	290 (38.8)
NMA	77 (10.3)
TBD	16 (2.1)
Not reported	9 (1.2)
Year of HCT - no. (%)	
2012	3 (0.4)
2013	59 (7.9)
2014	159 (21.3)
2015	109 (14.6)
2016	110 (14.7)
2017	100 (13.4)
2018	125 (16.7)
2019	78 (10.4)
2020	5 (0.7)
Immune Recovery data at day 100 - no. (%)	
CD4 @ day100 - no. (%)	
Yes	132 (17.6)
No	616 (82.4)
CD8 @ day100 - no. (%)	
Yes	108 (14.4)
No	640 (85.6)
CD56 @ day100 - no. (%)	

Characteristic	
Yes	72 (9.6)
No	676 (90.4)

**The data of 2020 is not completed in current CRF retrieval*

Field	Response
Proposal Number	2310-57-MEHTA
Proposal Title	Impact Of Mycophenolate Mofetil And Cytomegalovirus Serostatus In Patients Undergoing HLA Matched Donor HCT
Key Words	CMV, MMF, Relapse, mortality, CMV reactivation, allogeneic stem cell transplant
Principal Investigator #1: - First and last name, degree(s)	Rohtesh S. Mehta
Principal Investigator #1: - Email address	rmehta@fredhutch.org
Principal Investigator #1: - Institution name	Fred Hutchinson Cancer Center, Seattle, WA
Principal Investigator #1: - Academic rank	Associate Professor
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Rima M. Saliba
Principal Investigator #2 (If applicable): - Email address:)	rsaliba@mdanderson.org
Principal Investigator #2 (If applicable): - Institution name:	The University of Texas MD Anderson Cancer Center
Principal Investigator #2 (If applicable): - Academic rank:	Professor
Junior investigator status (defined as ≤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:	Rohtesh S. Mehta
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	PI of IB23-02 co-PI of GV23-01
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:	Briefly discussed with Marcie Riches about statistical analysis plan

Field	Response
RESEARCH QUESTION:	1. Does the use of mycophenolate mofetil (MMF) for graft-versus-host disease (GVHD) prophylaxis [with either conventional or post-transplant cyclophosphamide (PTCy)-based regimens] with HLA-matched donor hematopoietic cell transplantation (HCT) lead to worse outcomes, and does this effect depend on recipient's cytomegalovirus (CMV) serostatus? 2. Is the effect of CMV seropositivity on outcomes different in patients with acute myeloid leukemia (AML) vs acute lymphoblastic leukemia (ALL) vs myelodysplastic neoplasia (MDS)? 3. Is there any independent impact of donor CMV serostatus on these outcomes?
RESEARCH HYPOTHESIS:	We hypothesize that the inclusion of MMF in the GVHD prophylaxis with HLA-matched donor HCT will lead to worse overall survival (OS) but only in CMV seropositive patients with AML.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	To determine the impact of MMF GVHD prophylaxis by patient's CMV serostatus, and to determine whether that affect varies by the underlying disease (AML vs ALL vs MDS).
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	If our hypothesis stands, the results of this study could call for a change in the GVHD prophylaxis in select patients, i.e. exclusion of MMF in CMV seropositive AML patients.

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 a recent secondary analysis of an existing Center for International Blood and Marrow Transplant Research (CIBMTR) dataset [abstract submitted to ASH 2023], we evaluated 3105 patients with AML (n=1572), ALL (n=453) or MDS (n=1080) who underwent HLA-matched unrelated donor (MUD) peripheral blood (PB) HCT from 2008-2017. Four groups were compared: Methotrexate (MTX)/ CMV+ recipient (n=1527), MTX/ CMV-(n=916), MMF/ CMV+ (n=395), and MMF/ CMV- (n=267). All patients also received tacrolimus; none received PTCy. In multivariate models stratified by disease, we noted significantly worse overall survival (OS) in CMV+ patients who received MMF, but this effect was restricted to AML. Among AML patients, OS was only 31% (95% confidence interval [CI] 25-37) among the MMF/CMV+ group, but was higher and not significantly different for the MMF/CMV- (54%, 95% CI 45-63) and MTX/CMV+ (51%, 95% CI 48-55) groups compared to the MTX/CMV- group (58%, 95% CI 53-63) [Figure 1, Table 1] In ALL, GVHD prophylaxis type/CMV serostatus had no significant association with OS. In MDS, CMV+ patients had worse OS (HR 1.2, 95% CI 1.01-1.4, p=0.03) than CMV- patients irrespective of GVHD prophylaxis (MMF/CMV+ vs MTX/CMV+: HR=1.1, 95% CI 0.8-1.4, p=0.5). Donor CMV serostatus had no impact on these associations. [Saliba et al. Abstract submitted to ASH 2023] Data on CMV reactivation/infection and causes of death were not available because of which several questions remained unanswered. Moreover, we propose to study the same question in the letermovir era (post 2017) to see how the use of CMV prophylaxis alters those conclusions. Also, with an increasing use of PTCy prophylaxis in HLA matched donors, we wish to examine this effect in patients receiving PTCy (with MMF vs without MMF) as the use of PTCy itself has been associated with an increased risk of CMV reactivation/infection.1 The underlying mechanism of why MMF may lead to worse outcomes in CMV seropositive individuals may be explained as following. CMV reactivation is postulated to be protective against relapse as certain T cells show peptide-specific activity against cytomegalovirus as well as and leukemia cells.2 Also, an exaggerated proliferation of NK cells, γ/δ T cells and cytotoxic T cells by CMV may counteract AML blasts by virtue of cross-reactivity, thus intensifying the graft-versus-leukemia effect.3 This effect is seen mostly in AML patients, 4-6 but not in those with lymphoid malignancies 4,6,7 or MDS5,6. As MMF inhibits both B and T lymphocytes,8 it is associated with a broad immunosuppressive effects as compared to methotrexate. The CMV-induced expansion of T- and NK cells9,10 is suppressed by MMF more than

	methotrexate.11 Moreover, MMF is administered for an extended period of time after HCT, while methotrexate is given for a short course (days +1, +3, +6 and/or +11 post HCT). Therefore, it is conceivable that MMF can inhibit CMV-induced expansion of both innate and adaptive immune cells, which not only negates any protective effects of CMV on relapse, but also increases the risk of other infections and hence non-relapse mortality. Study Design: We are proposing that Rima Saliba (co-PI on the proposal) perform the analysis. She has prior experience with working with the CIBMTR datasets [Saliba et al. Transplant Cell Ther . 2022 Oct;28(10):681-693]. If acceptable to the CIBMTR working committee, we will simply need the dataset and no statistical support from the CIBMTR team. Patients will be grouped based on the type of prophylaxis regimen (MMF vs no MMF) and recipient CMV serostatus (positive vs negative). Outcomes will be compared across the 4 subgroups in univariate and multivariate analyses. Analyses will be initially stratified (ran separately) for PTCy and conventional GVHD prophylaxis. Within each of these subsets, outcomes by CMV status and MMF will be compared separately for patients with AML vs ALL vs MDS. Methods of analysis: Overall survival: defined from time of HCT to death from any cause. Actuarial OS will be estimated using the Kaplan-Meier method. Predictors of OS will be evaluated in univariate and multivariate analyses using the Cox's proportional hazards regression analysis. GVHD, relapse, non-relapse mortality, and CMV reactivation: defined from the time of HCT to the event of interest. The cumulative incidence of these outcomes will be estimated accounting for competing risks. Competing risks include: death or relapse for GVHD, death of any cause for relapse, relapse or relapse-death for NRM, death of any cause for CMV infection/reactivation. Precitors of these outcomes will be evaluated using Fine and Gray subdistribution hazard regression models. All factors clinically or statistically significant in univariate analysis will be considered in multivariate analysis. The variables representing the type of prophylaxis (MMF vs no MMF) and recipient CMV status will be included in all regression models regardless of statistical significance. Backward elimination method will be used to select the subset of variables that will be retained in multivariate regression models. Statistical significance will be defined at the 5% (≤0.05) level. The proportionality of the hazards assumption will be tested graphically and statistically and adjusted for as indicated. First degree interaction effects will be tested for clinically and/or statistically significant predictors and will be accounted for as

Field	Response
	indicated. Classification and Regression Tree (CART) analysis, a predictive algorithm used in machine learning, will be used to determine the prognostic hierarchy of the factors found to be predictive in univariate or multivariate analysis. Results of the CART analysis will be presented in case they complement or enhance the interpretation of the results of conventional regression analysis. Statistical analyses will be performed using primarily STATA 16.1 (StataCorp LLC, College Station)
SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Id	F_3DcjvhvBZgUL2gA
SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Name	ASH Figure.jpg
SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Size	320842
SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Type	image/jpeg
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	All patients who received HLA-matched allogeneic HCT, matched sibling (MSD) or 8/8 unrelated (MUD), and had data reported in CIBMTR between *2008-2022. Conditioning: MAC or RIC/NMA. Disease type: AML, ALL, or MDS Graft: PB or BM GVHD prophylaxis: PTCy-based (with and without MMF) and conventional (CNI-based with or without MMF). Exclude patients with ex-vivo T cell depletion/CD34+selected grafts
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.	i) Patient-related: • Age at HCT, years-continuous • Sex: male vs female • Karnofsky performance score: ≥90% vs. <90% • HCT comorbidity index at transplant 0, 1, 2, 3, 4, 5+ • Race/ethnicity: Non-Hispanic White vs. NH-Black vs. Hispanic vs. Asian/pacific islander vs. others • CMV status: seropositive vs. seronegative • ABO type ii) Disease-related: • Disease diagnosis • Disease stage • Disease status at transplant • Disease-Risk Index • MRD status pre-HCT for leukemia patients • Time from diagnosis to HCT iii) Donor/Transplant-related: • BM vs. PB graft • Conditioning: MAC vs RIC vs. NMA (using standard CIBMTR definitions) • Conditioning: high vs low-dose total body irradiation (TBI) • GVHD prophylaxis: PTCy-based (with and without MMF) and conventional (CNI-based with or without MMF) • Year of HCT • Donor age, in years – continuous • Donor gender • Donor CMV: seropositive vs. seronegative • Donor relationship (for MRD: sibling vs other related) • Donor ABO type • Donor type (HLA matched related vs 8/8- HLA matched unrelated (MUD) • DQB1 match status (for MUD): matched vs mismatched • DPB1 match status (for MUD): matched, vs permissive mismatch, vs non-permissive mismatch • In vivo T cell depletion (ATG/Campath-vs not) • Viable CD34+ cells/kg of recipient infused (if available) • TNC/kg of recipient (if available) • CD3+/kg of recipient before thawing (if available) • Letermovir use post HCT: yes/no • Date letermovir started iv) Outcome related • Primary endpoint: Overall Survival • Secondary endpoints: o Incidence of grade I, II and grade III-IV acute GVHD o Incidence of overall chronic GVHD o cGVHD NIH severity grading: mild, moderate and severe chronic GVHD o Incidence of Relapse o Non-relapse mortality o Relapse-related mortality o CMV reactivation/infection: Yes/No and date of first episode • Descriptive outcomes o Engraftment: Primary graft failure vs early death (without engraftment) vs engrafted o Time to neutrophil engraftment o Time to Platelets engraftment o Causes of Death

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 desc	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 o	No requirement for patient samples.
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:	We are proposing that Rima Saliba (co-PI on the proposal) perform the analysis. She has prior experience with working with the CIBMTR datasets [Saliba et al. Transplant Cell Ther . 2022 Oct;28(10):681-693]. If acceptable to the CIBMTR working committee, we will simply need the dataset and no statistical support from the CIBMTR team. Patients will be grouped based on the type of prophylaxis regimen (MMF vs no MMF) and recipient CMV serostatus (positive vs negative). Outcomes will be compared across the 4 subgroups in univariate and multivariate analyses. Analyses will be initially stratified (ran separately) for PTCy and conventional GVHD prophylaxis. Within each of these subsets, outcomes by CMV status and MMF will be compared separately for patients with AML vs ALL vs MDS. Methods of analysis: Overall survival: defined from time of HCT to death from any cause. Actuarial OS will be estimated using the Kaplan-Meier method. Predictors of OS will be evaluated in univariate and multivariate analyses using the Cox's proportional hazards regression analysis. GVHD, relapse, non-relapse mortality, and CMV reactivation: defined from the time of HCT to the event of interest. The cumulative incidence of these outcomes will be estimated accounting for competing risks. Competing risks include: death or relapse for GVHD, death of any cause for relapse, relapse or relapse-death for NRM, death of any cause for CMV infection/reactivation. Precitors of these outcomes will be evaluated using Fine and Gray subdistribution hazard regression models. All factors clinically or statistically significant in univariate analysis will be considered in multivariate analysis. The variables representing the type of prophylaxis (MMF vs no MMF) and recipient CMV status will be included in all regression models regardless of statistical significance. Backward elimination method will be used to select the subset of variables that will be retained in multivariate regression models. Statistical significance will be defined at the 5% (≤0.05) level. The proportionality of the hazards assumption will be tested graphically and statistically and adjusted for as indicated. First degree interaction effects will be tested for clinically and/or statistically significant predictors and will be accounted for as indicated. Classification and Regression Tree (CART) analysis, a predictive algorithm used in machine learning, will be used to determine the prognostic hierarchy of the factors found to be predictive in univariate or multivariate analysis. Results of the CART analysis will be presented in case they complement or enhance the interpretation of the results of conventional regression analysis. Statistical analyses will be performed using primarily STATA 16.1 (StataCorp

	LLC, College Station) References: 1. Goldsmith SR, Abid MB, Auletta JJ, et al: Posttransplant cyclophosphamide is associated with increased cytomegalovirus infection: a CIBMTR analysis. Blood 137:3291-3305, 2021 2. Nachbaur D, Bonatti H, Oberaigner W, et al: Survival after bone marrow transplantation from cytomegalovirus seropositive sibling donors. Lancet 358:1157-9, 2001 3. Elmaagacli AH, Koldehoff M: Cytomegalovirus replication reduces the relapse incidence in patients with acute myeloid leukemia. Blood 128:456-9, 2016 4. Ruggeri L, Capanni M, Casucci M, et al: Role of natural killer cell alloreactivity in HLA-mismatched hematopoietic stem cell transplantation. Blood 94:333-9, 1999 5. Green ML, Leisenring WM, Xie H, et al: CMV reactivation after allogeneic HCT and relapse risk: evidence for early protection in acute myeloid leukemia. Blood 122:1316-24, 2013 6. Manjappa S, Bhamidipati PK, Stokerl-Goldstein KE, et al: Protective effect of cytomegalovirus reactivation on relapse after allogeneic hematopoietic cell transplantation in acute myeloid leukemia patients is influenced by conditioning regimen. Biol Blood Marrow Transplant 20:46-52, 2014 7. Mariotti J, Maura F, Spina F, et al: Impact of cytomegalovirus replication and cytomegalovirus serostatus on the outcome of patients with B cell lymphoma after allogeneic stem cell transplantation. Biol Blood Marrow Transplant 20:885-90, 2014 8. Ueda Oshima M, Xie H, Zamora D, et al: Impact of GVHD prophylaxis on CMV reactivation and disease after HLA-matched peripheral blood stem cell transplantation. Blood Adv 7:1394-1403, 2023 9. Beziat V, Liu LL, Malmberg JA, et al: NK cell responses to cytomegalovirus infection lead to stable imprints in the human KIR repertoire and involve activating KIRs. Blood 121:2678-88, 2013 10. Foley B, Cooley S, Verneris MR, et al: Cytomegalovirus reactivation after allogeneic transplantation promotes a lasting increase in educated NKG2C+ natural killer cells with potent function. Blood 119:2665-74, 2012 11. Ohata K, Espinoza JL, Lu X, et al: Mycophenolic acid inhibits natural killer cell proliferation and cytotoxic function: a possible disadvantage of including mycophenolate mofetil in the

Field	Response
	graft-versus-host disease prophylaxis regimen. Biol Blood Marrow Transplant 17:205-13, 2011
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.	N.A

Table 1. Characteristic of first allo-HCT patients in 2008-2022 with AML/ALL/MDS, matched sibling/unrelated with GVHD Prophylaxis in either Tac/CSA and/or PTCy, reported to the CIBMTR

Characteristic	MMF in GVHD prophylaxis	No MMF in GVHD prophylaxis
Number of patients	3441	10701
No. of centers	182	251
Patient Characteristics		
Age at HCT - no. (%)		
0-9	56 (1.6)	392 (3.7)
10-19	88 (2.6)	491 (4.6)
20-29	152 (4.4)	768 (7.2)
30-39	139 (4.0)	854 (8.0)
40-49	294 (8.5)	1392 (13.0)
50-59	680 (19.8)	2515 (23.5)
60-69	1490 (43.3)	3444 (32.2)
70+	542 (15.8)	845 (7.9)
Region - no. (%)		
US	3226 (93.8)	9657 (90.2)
Canada	13 (0.4)	76 (0.7)
Europe	110 (3.2)	193 (1.8)
Asia	32 (0.9)	217 (2.0)
Australia/New Zealand	16 (0.5)	278 (2.6)
Mideast/Africa	19 (0.6)	90 (0.8)
Central/South America	25 (0.7)	190 (1.8)
Disease characteristics		
Disease - no. (%)		
AML	1436 (41.7)	4811 (45.0)
ALL	356 (10.3)	1673 (15.6)
Myelodysplastic/myeloprolifterative disorders	1649 (47.9)	4217 (39.4)
HCT related		
Donor type - no. (%)		
HLA-identical sibling	1140 (33.1)	4128 (38.6)
Well-matched unrelated (8/8)	2301 (66.9)	6573 (61.4)
Product type - no. (%)		
Bone Marrow	317 (9.2)	1898 (17.7)
Peripheral Blood	3124 (90.8)	8803 (82.3)
Conditioning Intensity - no. (%)		
Conditioning Intensity - no. (%)	1127 (32.8)	6392 (59.7)
Myeloablative	635 (18.5)	611 (5.7)

Characteristic	MMF in GVHD prophylaxis	No MMF in GVHD prophylaxis
Non-myeloablative (NST)	1091 (31.7)	2676 (25.0)
Reduced intensity (RIC)	574 (16.7)	963 (9.0)
Not myeloablative, either NST or RIC (02Core)	14 (0.4)	59 (0.6)
Donor/recipient CMV serostatus - no. (%)		
+/+	1127 (32.8)	3599 (33.6)
+/-	369 (10.7)	1213 (11.3)
-/+	1019 (29.6)	3038 (28.4)
-/-	899 (26.1)	2732 (25.5)
Not reported	27 (0.8)	119 (1.1)
Year of HCT - no. (%)		
2008	305 (8.9)	912 (8.5)
2009	268 (7.8)	828 (7.7)
2010	124 (3.6)	698 (6.5)
2011	132 (3.8)	402 (3.8)
2012	135 (3.9)	437 (4.1)
2013	273 (7.9)	860 (8.0)
2014	361 (10.5)	1138 (10.6)
2015	333 (9.7)	1065 (10.0)
2016	301 (8.7)	957 (8.9)
2017	230 (6.7)	866 (8.1)
2018	249 (7.2)	824 (7.7)
2019	223 (6.5)	710 (6.6)
2020	208 (6.0)	381 (3.6)
2021	199 (5.8)	383 (3.6)
2022	100 (2.9)	240 (2.2)
GVHD Prophylaxis - no. (%)		
PTCy based	591 (17.2)	345 (3.2)
CNI based	2850 (82.8)	10356 (96.8)

Field	Response
Proposal Number	2310-75-KOO
Proposal Title	Evaluating Infection Rates in Autologous Hematopoietic Stem Cell Transplants for Primary Solid Tumors and Lymphoma
Key Words	bacterial, viral, fungal, infection, autologous hematopoietic stem cell transplant, solid tumor, lymphoma
Principal Investigator #1: - First and last name, degree(s)	Jane Koo, MD, MA
Principal Investigator #1: - Email address	jane.koo@cchmc.org
Principal Investigator #1: - Institution name	Cincinnati Children's Hospital Medical Center
Principal Investigator #1: - Academic rank	Assistant Professor of Pediatrics
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Christopher E. Dandoy, MD, MS
Principal Investigator #2 (If applicable): - Email address:)	christopher.dandoy@cchmc.org
Principal Investigator #2 (If applicable): - Institution name:	Cincinnati Children's Hospital Medical Center
Principal Investigator #2 (If applicable): - Academic rank:	Associate Professor of Pediatrics
Junior investigator status (defined as ≤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.	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:	Christopher Dandoy
RESEARCH QUESTION:	What is the incidence of clinically significant bacterial, viral and fungal infections is low among autologous hematopoietic stem cell transplant (auto-HSCT) recipients for the treatment of primary solid tumors and lymphoma
RESEARCH HYPOTHESIS:	The incidence of clinically significant bacterial, viral and fungal infections is low among autologous hematopoietic stem cell transplant (auto-HSCT) recipients for the treatment of primary solid tumors and lymphoma.

Field	Response
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	2.1. Report the incidence of clinically significant bacterial infection during the first 100 days following auto-HSCT for solid tumor and lymphoma recipients. 2.1.1. Sub-Aim: Compare the use of systemic antibacterial agents for primary prophylaxis strategies in solid tumor and lymphoma auto-HSCT recipients. 2.2. Report the incidence of clinically significant viral infection during the first 100 days following auto-HSCT for solid tumor and lymphoma recipients. 2.2.1. Sub-Aim: Compare the use of systemic antiviral agents for primary prophylaxis in auto-HSCT for solid tumor and lymphoma recipients. 2.3. Report the incidence of proven invasive fungal infection (IFD) during the first 100 days following auto-HSCT for solid tumor and lymphoma recipients. 2.3.1. Sub-Aim: Compare primary prophylaxis strategies of proven IFDs prior to engraftment in solid tumor and lymphoma auto-HSCT recipients. 2.4. Evaluate the overall survival (OS), non-relapse mortality (NRM), transplant-related mortality (TRM) between solid tumor and lymphoma auto-HSCT recipients who developed clinically significant infections and who did not develop 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.	3.1. Results from this study would highlight important factors to consider in the incidence, morbidity and mortality of clinically significant bacterial, viral and fungal infections in the pediatric and adult patients receiving auto-HSCT for solid tumors or lymphoma. Additionally, this study would provide information on primary prophylaxis practices for the prevention of these major infections among these patients. These results may emphasize the utility of universal primary infection prophylaxis within this specific patient population and provide some guidance toward the creation of standardized guidelines for the duration and type of primary infection prophylaxis to be used following auto-HSCT for solid tumors and lymphomas. Furthermore, results from this study would inform us about additional disease and treatment-related risk factors that may need to be considered to determine the use and duration of primary infection prophylaxis in this patient population.

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.	High-dose chemotherapy followed by autologous hematopoietic stem cell transplantation (auto-HSCT) is a well-recognized therapy option for patients with primary solid tumors and relapsed lymphoma1-7, but can have increased risk for infectious complications. In the past several decades, new developments in the diagnostic/therapeutic strategies and supportive care mechanisms have markedly improved the burden of infections in this particular setting8. Optimal management of infection is a primary goal in every HSCT strategy in order to limit infection-related morbidity and mortality. This has led to the use of newer antimicrobial agents which have led to the better control and prevention of bacterial, viral and fungal infections, but also to the increased use of antimicrobial agents and microorganism resistance. Transplant centers and healthcare professionals employ a range of preventive and monitoring techniques to reduce the occurrence of complications. Nonetheless, there remains limited understanding of the diversity in these approaches. This information will prove invaluable in assisting both transplant centers and physicians in assessing the infection risk associated with autologous stem cell transplantation. Infection risk in the transplant setting depends on multiple factors including, mucosal barrier injury from chemotherapy or radiation, presence of central venous catheters and the recipient's overall pace of immune system reconstitution and recovery9. Guidelines for monitoring and preventing infectious complications among HSCT recipients exist, however practice varies tremendously across centers10. The incidence of bacterial, viral and fungal infections is known to be high in allo-HSCT recipients, but the incidence of such infections in auto-HSCT recipients are presumed to be lower11-19. Much of the existing data evaluating infection risk in the transplant setting focuses on patients who have completed allo-HSCT7,20-24. Furthermore, studies focusing on infection risk and incidence of clinically significant infections for auto-HSCT recipients are limited to single center cohort studies9,25. Limited studies have investigated the actual incidence of clinically significant infections in solid tumor and lymphoma both pediatric and adult patients undergoing auto-HSCT. To our knowledge, there are currently no recent large, multi-institutional studies analyzing the incidence of clinically significant infections in either solid tumor or lymphoma auto-HSCT recipients. The CIBMTR currently captures patients who were diagnosed with bacterial, viral and fungal infections in the first 100 days after auto-HSCT. The CIBMTR also captures objective diagnostic data for patients who were diagnosed with infection including: radiographic imaging, pathology, culture, polymerase chain reaction

Field	Response
	(PCR) assays and the specific sites that were queried for these diagnostic methods. Additionally, the CIBMR also documents information on patients who receive or do not receive antibacterial, antiviral and antifungal drugs for primary infection prophylaxis. Additionally, the CIBMTR allows centers to input the type of prophylactic medications used. The CIBMTR also asks for the date when these prophylactic antifungal therapies were started. In this study we will analyze the incidence of bacterial, viral and fungal infections, OS, NRM, and TRM of solid tumor and lymphoma auto-HSCT recipients.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	5. Patient Eligibility Population: 5.1. The study population will consist of all pediatric and adult patients who underwent first autologous hematopoietic stem cell transplant reported to the CIBMTR between 2010 and 2022. Inclusion Criteria: • Any pediatric and adult patient receiving a first-time autologous stem cell transplantation for a primary diagnosis of solid tumor, lymphoma, or multiple myeloma. Patients undergoing tandem transplants will be included in the analysis. Exclusion Criteria: • Previous allogeneic or autologous stem cell transplant • Underlying known immune deficiency • Prior diagnosis of clinically significant bacterial, viral or possible, probable or proven IFD prior to first stem cell transplant
Does this study include pediatric patients?	Yes

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.	6. Data Requirements: 6.1. Outcomes • Incidence of clinically significant bacterial infection: Bacterial infection in the first 100 days post-HSCT. Clinically significant bacterial infection as coded and reported to the CIBMTR. This will include date of diagnosis, organism and site of infection. • Incidence of clinically significant viral infection: Viral infection in the first 100 days post-HSCT. Clinically significant viral infection as coded and reported to the CIBMTR. This will include date of diagnosis, organism and site of infection. • Proven Invasive Fungal Disease (IFD): Proven fungal disease in the first 100 days post-HSCT. Proven IFD as coded and reported to the CIBMTR. This will include both localized fungal infections as well as fungemia. IFDs were defined as proven, probable and possible according to the 2008 revision of the criteria set forth by the European Organization for Research and Treatment of Cancer-Invasive Fungal Infections Cooperative Mycoses Study Group (EORTC/MSG)26. • Non-relapse mortality (NRM): Defined as time to death without evidence of recurrence of malignancy. Patients are censored at the date of last follow-up. The event will be summarized by the cumulative incidence estimate with relapse as a competing risk. We will compare NRM between patients with and without invasive fungal infection in the first 100 days post-HSCT. • Overall survival (OS): Time to death, patients will be censored at last follow-up. We will compare OS between patients with and without invasive fungal infection in the first 100 days post-HSCT. • Transplant-related mortality (TRM): Death due to any transplantation-related cause other than disease relapse • Cause of death: Infection as primary or secondary cause of death up through the first 100 days post-HSCT. 6.2. Patient-related variables • Recipient age at first transplant (continuous, patients ⍰ 0 years) • Sex: male vs. female • Underlying primary disease • Disease status at time of HSCT o Complete response, partial response, stable disease, progressive disease, etc • Specific co-existing diseases or organ impairment present that would increase infection risk o Diabetes mellitus requiring insulin or oral hypoglycemic drugs o Moderate/severe renal disease requiring renal replacement therapy o Prior history of infection o Obesity (patients >18 years old with body mass index (BMI) >35kg/m2 prior to start of conditioning or BMI of the 95th percentile or higher for patients <18 years old) 6.3. Transplant related variables

	• Year of HSCT: o 2010-2013 vs 2014-2017 vs 2018-2022 • Baseline Karnofsky/Lansky performance status at time of first HSCT • Conditioning: conditioning regimen • Bacterial infections in first 100 days: o Date of infection diagnosis o Site of infection o Organism o Number of infections o Co-infections o Septic shock from bacterial infection: yes or no o Primary prophylaxis for bacterial infection prevention: yes or no Antibacterial agent used for prophylaxis. • Viral infections in first 100 days: o Organism o Site of infection o Number of infections o Co-infections o Date of infection diagnosis o Polymerase chain reaction assay Sample source: nasal wash, blood, bronchial fluid, cerebrospinal fluid, pericardial fluid, stool, tissue, urine o Radiographic findings of infection: yes or no Radiographic imaging findings to support infection diagnosis o Histopathologic findings: yes or no Sample source to support infection diagnosis o Culture: yes or no Sample source to support infection diagnosis o Clinical signs present on diagnosis of infection: oxygen supplementation, hepatosplenomegaly, diarrhea, neurologic symptoms, lymphadenopathy o Antiviral prophylaxis: yes or no Antiviral agent used for prophylaxis • Fungal infections in first 100 days: o Date of infection diagnosis o Site of infection oOrganism: Aspergillus species, Blastomyces, Candida species, Cryptococcus species, Fusarium, Histoplasma, Mucorales, Rhizopus, Scadeosporium, Zygomycetes NOS o Radiographic findings if infection: yes or no Radiographic imaging findings to support infection diagnosis o Histopathologic findings: yes or no Sample source to support infection diagnosis o Culture: yes or no Sample source to support infection diagnosis. o Galactomannan assay: yes or no Sample source to support fungal infection diagnosis. o 1,3-Beta-D-glucan (Fungitell) assay: yes or no Sample source to support fungal infection diagnosis. o PCR Assay: yes or no Sample source to support fungal infection diagnosis. o Antifungal

Field	Response
	used for infection prophylaxis: yes or no. Agent used for antifungal prophylaxis. • Survival status at the end of the reporting period • Cause of death: primary and secondary
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 desc	None
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	None
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 o	None
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.	None

REFERENCES:	10. References: 1. Majhail NS, Farnia SH, Carpenter PA, et al. Indications for Autologous and Allogeneic Hematopoietic Cell Transplantation: Guidelines from the American Society for Blood and Marrow Transplantation. Biol Blood Marrow Transplant. 2015;21(11):1863-1869. 2. Ladenstein R, Potschger U, Le Deley MC, et al. Primary disseminated multifocal Ewing sarcoma: results of the Euro-EWING 99 trial. J Clin Oncol. 2010;28(20):3284-3291. 3. Ladenstein R, Potschger U, Pearson ADJ, et al. Busulfan and melphalan versus carboplatin, etoposide, and melphalan as high-dose chemotherapy for high-risk neuroblastoma (HR-NBL1/SIOPEN): an international, randomised, multi-arm, open-label, phase 3 trial. Lancet Oncol. 2017;18(4):500-514. 4. Baker KS, Gordon BG, Gross TG, et al. Autologous hematopoietic stem-cell transplantation for relapsed or refractory Hodgkin's disease in children and adolescents. J Clin Oncol. 1999;17(3):825-831. 5. Harris RE, Termuhlen AM, Smith LM, et al. Autologous peripheral blood stem cell transplantation in children with refractory or relapsed lymphoma: results of Children's Oncology Group study A5962. Biol Blood Marrow Transplant. 2011;17(2):249-258. 6. Cohen BH, Geyer JR, Miller DC, et al. Pilot Study of Intensive Chemotherapy With Peripheral Hematopoietic Cell Support for Children Less Than 3 Years of Age With Malignant Brain Tumors, the CCG-99703 Phase I/II Study. A Report From the Children's Oncology Group. Pediatr Neurol. 2015;53(1):31-46. 7. Styczynski J, Czyzewski K, Wysocki M, et al. Increased risk of infections and infection-related mortality in children undergoing haematopoietic stem cell transplantation compared to conventional anticancer therapy: a multicentre nationwide study. Clin Microbiol Infect. 2016;22(2):179 e171-179 e110. 8. Castagnola E, Bagnasco F, Amoroso L, et al. Role of management strategies in reducing mortality from invasive fungal disease in children with cancer or receiving hemopoietic stem cell transplant: a single center 30-year experience. Pediatr Infect Dis J. 2014;33(3):233-237. 9. Cesaro S, Tridello G, Castagnola E, et al. Retrospective study on the incidence and outcome of proven and probable invasive fungal infections in high-risk pediatric onco-hematological patients. Eur J Haematol. 2017;99(3):240-248. 10. Tomblyn M, Chiller T, Einsele H, et al. Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. Biol Blood Marrow

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Volin L, Parkkali T, Koukila-Kahkola P, Ruutu T. Incidence and risk factors for invasive fungal infections in allogeneic BMT recipients. Bone Marrow Transplant.
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Field	Response
	2003;101(9):3365-3372. 22. Martino R, Subira M, Rovira M, et al. Invasive fungal infections after allogeneic peripheral blood stem cell transplantation: incidence and risk factors in 395 patients. Br J Haematol. 2002;116(2):475-482. 23. Annaloro C, Serpenti F, Saporiti G, et al. Viral Infections in HSCT: Detection, Monitoring, Clinical Management, and Immunologic Implications. Front Immunol. 2020;11:569381. 24. Duver F, Weissbrich B, Eyrich M, Wolfl M, Schlegel PG, Wiegering V. Viral reactivations following hematopoietic stem cell transplantation in pediatric patients - A single center 11-year analysis. PLoS One. 2020;15(2):e0228451. 25. Gassas RS, Absi AN, Alghamdi AA, et al. Early infection in post-autologous hematopoietic stem cell transplant patients: Princess Noorah Oncology Center experience. Saudi Med J. 2021;42(8):847-852. 26. De Pauw B, Walsh TJ, Donnelly JP, et al. Revised definitions of invasive fungal disease from the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group. Clin Infect Dis. 2008;46(12):1813-1821.
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

Table 1. Characteristic of first Auto-HCT patients with HL/NHL/MM/Solid tumors without prior fungal infection between 2010 and 2022 reported to the CIBMTR

Characteristic	
Number of patients	12077
No. of centers	223
Patient Characteristics	
Age at HCT - no. (%)	
0-9	377 (3.1)
10-19	208 (1.7)
20-29	412 (3.4)
30-39	621 (5.1)
40-49	1502 (12.4)
50-59	3440 (28.5)
60-69	4430 (36.7)
70+	1087 (9.0)
Gender - no. (%)	
Male	6943 (57.5)
Female	5134 (42.5)
Region - no. (%)	
US	11315 (93.7)
Canada	125 (1.0)
Europe	52 (0.4)
Asia	206 (1.7)
Australia/New Zealand	18 (0.1)
Mideast/Africa	32 (0.3)
Central/South America	329 (2.7)
Disease characteristics	
Disease - no. (%)	
Non-Hodgkin lymphoma	2690 (22.3)
Hodgkin lymphoma	851 (7.0)
Plasma cell disorder/Multiple Myeloma	7969 (66.0)
Solid Tumors	567 (4.7)
Infection related	
Infection in first 100 days	
Bacterial	
Yes	2238 (18.5)
No	9839 (81.5)
Fungal	
Yes	203 (1.7)
No	11874 (98.3)

Characteristic	
Viral	
Yes	850 (7.0)
No	11227 (93.0)

Field	Response
Proposal Number	2310-185-MINA
Proposal Title	PBSC versus BM Grafts in AlloHSCT for Hematological Malignancies with PTCY-based GVHD Prophylaxis: A Comparative Analysis
Key Words	allogeneic stem cell transplantation; GVHD; post-transplant cyclophosphamide;graft source
Principal Investigator #1: - First and last name, degree(s)	Alain Mina, MD
Principal Investigator #1: - Email address	alain.mina@nih.gov
Principal Investigator #1: - Institution name	NIH
Principal Investigator #1: - Academic rank	Assistant Research Physician
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	Yes
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Steven Pavletic, MD, PHD
Principal Investigator #2 (If applicable): - Email address:)	pavletis@mail.nih.gov
Principal Investigator #2 (If applicable): - Institution name:	NIH
Principal Investigator #2 (If applicable): - Academic rank:	Senior Investigator
Junior investigator status (defined as ≤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:	Alain Mina
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	I currently serve as a member of several CIBMTR working committees including "Infection and Immune Reconstitution", "Acute Leukemia" and "Graft-versus-Host-Disease" and currently working on the CIBMTR abstract team ("Acute Regimen-Related Toxicity and Supportive Care") as an abstract reviewer.
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:	Are peripheral blood stem cells (PBSC) superior to bone marrow (BM) grafts in adult patients undergoing allogeneic hematopoietic stem cell transplantation (alloHSCT) for hematological malignancies with post-transplant cyclophosphamide (PTCY)-based graft-versus-host-disease (GVHD) prophylaxis?

Field	Response
RESEARCH HYPOTHESIS:	Among adult patients receiving PTCY-based GVHD prophylaxis, using PBSC compared to a BM graft will yield different key outcomes, such as rates of engraftment, engraftment failure, infectious complications, and causes of death.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	The primary aim of this study is to compare rates of engraftment (neutrophils, erythroid, platelets), immune reconstitution (lymphocytes), engraftment failure, and peri-transplant infections in adult patients with hematological malignancies undergoing allogeneic hematopoietic stem cell transplantation (alloHSCT) with either a bone marrow (BM) graft or peripheral blood stem cell graft and post-transplant cyclophosphamide (PTCY). Primary Objectives: a- Rates of hematopoietic recovery (absolute neutrophil count, absolute lymphocyte count, platelets) b- Incidence of primary engraftment failure and secondary engraftment failure c- 100-day post-transplant infectious complications Secondary Objectives: a- Overall survival b- Non-relapse mortality c- Malignancy progression d- Acute GVHD rates and severity e- Chronic GVHD rates and severity f- GVHD-free survival g- GVHD-free, relapse-free survival (GRFS) h- 100-day post-transplant bleeding complications i- Primary and proximal causes of death j- Duration of hospitalization k- RBC and platelet transfusion independence l- Neutropenic fevers
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 use of PTCY in alloHSCT has been associated with low rates of GVHD, but linked to delayed engraftment and slower immune reconstitution (1). The use of BM grafts in alloHSCT remains a common practice (~25% of all alloHSCT grafts (2)) that has also been associated with lower rates of GVHD. The purpose of our analysis would be to compare BM to PBSC grafts in the setting of PTCY to help inform providers choice of graft source when using PTCY for GVHD prophylaxis.

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 early days of alloHSCT, graft source was solely from BM harvested from the pelvis of a donor under anesthesia (3). Practice evolved to then use filgrastim-stimulated peripheral blood, which was associated with more robust engraftment and lower rates of infectious complications, but the higher number of T-cells in the product led to increased rates of GVHD (4). These data have been corroborated by several large, randomized trials using PBSCs specifically from matched donors, which showed PBSCs were associated with faster engraftment, fewer infections, and decreased rates of relapse, but increased rates of acute and chronic GVHD, although there were no differences in overall survival (4–8). To mitigate GVHD, PTCy has evolved as a prophylaxis strategy. The success of PTCy in preventing acute and chronic GVHD, without affecting rates of relapse, led to its expanded use across all donor types and graft sources (9–11). PTCy functions by impairing allo-reactive T-cells while preferentially sparing regulatory T cells (12). However, this T-cell modulation may influence cellular immunity, resulting in increased rates of CMV infections (13) slower immune reconstitution of T-cell subtypes, and delayed neutrophil engraftment, compared to use of anti-T cell lymphocyte globulin for GVHD prophylaxis (14). When Massoud et al. compared these two GVHD prophylaxis modalities, PTCy resulted in a slower reconstitution of CD8+, T, NK, NKT and γδ T cellsT cells, but similar reconstitution of regulatory T- and B-cells was observed in both groups. These findings could explain the increased incidence of CMV infections in patients receiving PTCy and could affect a higher occurrence of other peri-transplant infectious complications (14). The most common PTCy protocol uses BM grafts (15). Although findings were consistent with reduced rates of GVHD, the incidence of higher graft failure remains a concern (16). Since then, different approaches that included myeloablative conditioning and PBSC grafts were used to improve outcomes. Several retrospective studies have compared graft sources in T-cell replete alloHSCT with PTCy, but these studies were either too small and focused solely on haploidentical transplantation (17–19), or limited to few (20) or a single disease entity (21). Aside from one recent CIBMTR analysis evaluating clinical CMV infections in patients treated with PTCy, most studies did not look specifically at peri-transplant infectious complications (13) (Table). The purpose of our analysis would be a broad comparison, across donor types, conditioning regimens, and hematological malignancies, between BM and PBSC grafts in the setting of PTCy. We hypothesize that our findings might influence clinical

Field	Response
	practice when making decisions about preferential use of PBSCT versus BM grafts when PTCy is used.
SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Id	F_1gcsnzKWha1Owdq
SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Name	CIBMTR Table.docx
SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Size	18149
SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Type	application/vnd.openxmlformats-officedocument .wordprocessingml.document
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Patient data will be extracted from the CIBMTR patient registry. Inclusion criteria: • Patients are 18 years of age or older. • Have a diagnosis of a hematological malignancy (acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), chronic myelogenous leukemia (CML), myelodysplastic syndromes (MDS), myeloproliferative neoplasms (MPN) and myelodysplastic/myeloproliferative overlap neoplasms, NK cell neoplasms, B-chronic lymphocytic leukemia (CLL), prolymphocytic leukemia (PLL), Hodgkin lymphoma, follicular lymphoma, marginal zone lymphoma, Burkitt's or lymphoblastic lymphoma, diffuse large B-cell lymphoma (DLBCL), follicular large cell lymphoma, mantle cell lymphoma, anaplastic large cell lymphoma, cutaneous T-cell lymphoma (Mycosis fungoides, Sezary syndrome), mature T-cell Non-Hodgkin lymphoma, multiple myeloma (MM). • Received their first peripheral blood or bone marrow allo-HCT between 2013 and 2021 using post-transplant cyclophosphamide (PTCY)-based GVHD prophylaxis, from a haploidentical, HLA-MSD, 8/8 HLA-MUD, or 7/8 HLA-MUD. Exclusion criteria: • Patients younger than 18 years of age. • Non-malignant disease. • Cord blood donor source. • Recipients of ex vivo T-cell depleted or CD34 selected grafts. • Recipients of alemtuzumab or antithymocyte globulin (ATG). • Patients with malignancy progression through conditioning therapy. • Alive with less than 3 months of follow up.
Does this study include pediatric patients?	No

Field	Response
If this study does not include pediatric patients, please provide justification:	As adult hematologists and transplant specialists, it's worth noting that the utilization of Post-Transplant Cyclophosphamide (PTCy) as a graft-versus-host disease (GVHD) prophylaxis is a common practice within the adult population.

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-related: - Age at transplant - Recipient gender -Recipient ethnicity - HCT-specific comorbidity index (HCT-CI) - Karnofsky performance score (KPS) HCT - Recipient cytomegalovirus (CMV) status - ABO typing - Race/ethnicity -History of clinically significant fungal infections in the 6 months prior to start of preparative regimen and organism -History of clinically significant viral infections in the 6 months prior to start of preparative regimen -History of clinically significant bacterial infections in the 6 months prior to start of preparative regimen Disease-related: - Disease - Disease status at HCT -Measurable Residual Disease (MRD) status if AML or ALL - Revised disease risk index (DRI) Donor/graft-related: - Donor type - Donor age - Donor gender - Donor parity (if female) - Donor relationship (if related) - Donor cytomegalovirus (CMV) status - Donor ABO typing - Donor race/ethnicity - Graft source (PB, BM) - Donor type (Matched sibling, matched unrelated, haploidentical, mismatched unrelated MMUD) Transplant-related: - Conditioning regimen intensity - Specific conditioning regimen - Radiation used and dose - Graft characteristics: a) Total number of nucleated cells (TNC) given (cells per kilogram) b) Total number of CD34+ cells c) Total number of CD3+ cells d) Total number of CD3+CD4+ cells e) Total number of CD3+CD8+ cells - GVHD prophylaxis drugs used with PTCy - Dose of PTCy - Year of transplant - Follow up duration Outcome related data: -Growth factors routinely administered after transplant (G-CSF, filgrastim, neupogen, pegfilgrastim, Neulasta) - Acute GVHD II-IV - Acute GVHD III-IV - Chronic GVHD: any, and requiring immunosuppressive therapy - Days to platelet engraftment - Days to neutrophil engraftment - Days to lymphocyte engraftment - Primary Engraftment failure - Secondary Engraftment failure - Day 100 peripheral blood chimerism (total, myeloid, lymphoid) - Cell therapy boost given and the first date - Viral infections within 100 days of transplant - Bacterial infections within 100 days of transplant and organism - Fungal infections within 100 days of transplant and organism - Neutropenic fever without identified infection - Relapse - Time to relapse - Survival - Death - Causes of death - Duration of hospitalization - RBC transfusion independence date (if available)

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 desc	not applicable
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	Study will not require methodology related machine-learning and clinical predictions
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 o	No biologic samples from the CIBMTR will be required

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Field	Response
	Using Post-Transplant Cyclophosphamide. Journal of Clinical Oncology. 2017 Sep 10;35(26):3002–9. 20. Ruggeri A, Labopin M, Bacigalupo A, Gülbas Z, Koc Y, Blaise D, et al. Bone marrow versus mobilized peripheral blood stem cells in haploidentical transplants using posttransplantation cyclophosphamide. Cancer. 2018 Apr 23;124(7):1428–37. 21. Nagler A, Dholaria B, Labopin M, Savani BN, Angelucci E, Koc Y, et al. Bone marrow versus mobilized peripheral blood stem cell graft in T-cell-replete haploidentical transplantation in acute lymphoblastic leukemia. Leukemia. 2020 Oct 11;34(10):2766–75.
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

Table:

Study (year)	Comparison Groups	Donor Source	Clinical Outcomes	Limitations
Castagna et al. 2014	PB (n = 23) vs BM (n = 46)	Haploidentical	Similar engraftment rates between groups No significant difference in NRM, GVHD or OS	Small sample size Limited to haploidentical donors Retrospective
Bradstock et al. 2015	PB (n = 23) vs BM (n = 13)	Haploidentical	Similar relapse, acute and chronic GVHD rates Significantly improved OS with PBSC 3 patients, all in PBSC, failed to engraft	Small sample size Limited to haploidentical donors Retrospective
Bashey et al. 2017	PB (n = 190) vs BM (n = 481)	Haploidentical	Rates of grade 2-4 acute GVHD higher in PBSC Rate of chronic GVHD higher in PBSC Higher relapse rates in BM Leukemia patients Similar OS	Limited to haploidentical Retrospective
Ruggeri et al. 2018	PB (n = 191) vs BM (n = 260)	Haploidentical	Rates of grade 2-4 acute GVHD higher in PBSC No difference in chronic GVHD Similar OS, relapse, NRM and DFS	Limited to haploidentical Retrospective Limited to ALL and AML populations
Yu et al. 2019	Meta-analysis PB (n = 462) vs BM (n = 1297)	Haploidentical	Similar OS, relapse, NRM and DFS	Limited to haploidentical Retrospective Did not look into infectious complications
Nagler et al. 2020	PB (n = 157) vs BM (n = 157)	Haploidentical	Cumulative incidence of engraftment PBSC>BM No difference in acute or chronic GVHD No difference in relapse PBSC significantly better in DFS, OS and GRFS	Limited to haploidentical Retrospective Limited to ALL population

2310-185 PBSC versus BM Grafts in AlloHSCT for Hematological Malignancies with PTCY-based GVHD Prophylaxis: A Comparative Analysis

Characteristics of adult patients underwent first allo-HCT with Hematological Malignancy in 2013-2021, with sibling or matched/partially matched donor and PTCy-based GVHD.

Characteristic	Bone Marrow	Peripheral blood graft
Number of patients	177	895
No. of centers	40	92
Patient Characteristics		
Age at HCT - no. (%)		
10-19	3 (1.7)	1 (0.1)
20-29	12 (6.8)	33 (3.7)
30-39	19 (10.7)	37 (4.1)
40-49	38 (21.5)	76 (8.5)
50-59	44 (24.9)	139 (15.5)
60-69	53 (29.9)	454 (50.7)
70+	8 (4.5)	155 (17.3)
Region - no. (%)		
US	175 (98.9)	868 (97.0)
Europe	0 (0.0)	12 (1.3)
Asia	0 (0.0)	10 (1.1)
Australia/New Zealand	1 (0.6)	5 (0.6)
Mideast/Africa	1 (0.6)	0 (0.0)
Disease characteristics		
Disease - no. (%)		
Acute myelogenous leukemia or ANLL	89 (50.3)	346 (38.7)
Acute lymphoblastic leukemia	39 (22.0)	91 (10.2)
Myelodysplastic/myeloprolifterative disorders (please classify all preleukemias)	47 (26.6)	381 (42.6)
Myeloproliferative Neoplasms	2 (1.1)	77 (8.6)
HCT related		
Donor type - no. (%)		
HLA-identical sibling	44 (24.9)	190 (21.2)
Well-matched unrelated (8/8)	73 (41.2)	532 (59.4)
Partially-matched unrelated (7/8)	60 (33.9)	173 (19.3)
Conditioning Intensity - no. (%)		
Myeloablative	123 (69.5)	251 (28.0)
Non-myeloablative (NST)	20 (11.3)	164 (18.3)
Reduced intensity (RIC)	30 (16.9)	473 (52.8)

Characteristic	Bone Marrow	Peripheral blood graft
Not myeloablative, either NST or RIC (02Core)	4 (2.3)	6 (0.7)
Not reported	0 (0.0)	1 (0.1)
GVHD prophylaxis - no. (%)		
PtCy + other(s)	111 (62.7)	888 (99.2)
PtCy alone	66 (37.3)	7 (0.8)
Year of HCT - no. (%)		
2013	5 (2.8)	11 (1.2)
2014	7 (4.0)	28 (3.1)
2015	8 (4.5)	68 (7.6)
2016	34 (19.2)	59 (6.6)
2017	70 (39.5)	68 (7.6)
2018	30 (16.9)	121 (13.5)
2019	14 (7.9)	145 (16.2)
2020	7 (4.0)	183 (20.4)
2021	2 (1.1)	212 (23.7)
Infection in first 100 days		
Bacterial - no. (%)		
No	85 (48.0)	500 (55.9)
Yes	92 (52.0)	395 (44.1)
Fungal - no. (%)		
No	168 (94.9)	841 (94.0)
Yes	9 (5.1)	54 (6.0)
Virus* - no. (%)		
No	89 (50.3)	572 (63.9)
Yes	88 (49.7)	323 (36.1)

*168 patients with viral infection have a 2150 form (details for CMV/EBV/ADV/HHV6/BK)